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The Therapeutic Potential of Phloretin: Implications for Diabetic Nephropathy and Oxidative Stress Management By Griffin Rick

Abstract

Diabetes mellitus is a chronic metabolic disorder affecting a significant proportion of the global population. According to recent statistics, an estimated 463 million individuals worldwide are living with diabetes. Among the various complications associated with diabetes, diabetic nephropathy, a progressive kidney disease, poses a substantial burden on affected individuals. Approximately 40% of people with diabetes develop diabetic nephropathy, making it a prevalent complication of diabetes.1

Diabetic kidney disease, also known as diabetic nephropathy, is a complication associated with diabetes where the overall ability of the kidneys to filter blood is impaired. Patients may experience mild symptoms such as proteinuria (excessive protein in urine) and hypertension (high blood pressure) in the early stages.2 However, as the condition progresses, more severe complications can arise, including chronic kidney disease (CKD), end-stage renal disease (ESRD), and the need for dialysis or kidney transplantation. These complications can significantly impact a person's quality of life, leading to fatigue, fluid retention, electrolyte imbalances, anemia, and an increased risk of cardiovascular problems. 3, 4

Oxidative stress plays a significant role in diabetic kidney disease (DKD). One notable contributing factor to DKD is oxidative stress, which refers to an imbalance between the production of reactive oxygen species (ROS) and the body's ability to neutralize them.5 Hyperglycemia, a hallmark of diabetes, mediates oxidative stress in the kidney by triggering the overproduction of ROS during cellular metabolism, leading to cellular damage and inflammation within the renal tissue.6, 7

Phloretin, a dihydrochalcone, has been shown to act as a glucose transporter 2 (GLUT2) inhibitor in early cancer studies that prevent glucose absorption and metabolism in cancerous tissues. Beyond the scope of cancer cells, phloretin may serve other physiological roles, which, in the kidneys, could act in response to severe oxidative stress both proactively via mitigating glucose-induced ROS production and retroactively via acting as an antioxidant and promoting the expression of antioxidant enzymes.8 Moreover, phloretin possesses certain chelation properties that may further prevent and treat complications related to heavy metal toxicity-induced diabetes mellitus, a relevant contributor to the development of diabetic nephropathy via oxidative stress. 9

This paper focuses on the positive potential of phloretin therapy on overall kidney function while speculating on the negative implications for phloretin that involve short-term damage to the liver and pancreas. To this extent, this paper concludes by introducing the concepts of 1) a metformin-based phloretin treatment plan and 2) maximizing the localization of phloretin to the kidneys to minimize off-target effects.

Introduction

Diabetic kidney disease, more commonly known as diabetic nephropathy, is a serious and relatively common complication associated with diabetes that significantly impairs kidney function and the kidney's ability to remove harmful waste products from the bloodstream sufficiently.2, 3

One of the key factors contributing to the progression of diabetes and its complications is oxidative stress, which refers to an imbalance between the formation of reactive oxygen species (ROS) and the body's antioxidant defense system.10 In diabetic nephropathy, prolonged exposure to high blood glucose concentrations can lead to increased ROS production, which is generally attributed to accelerations in cellular metabolism, namely glycolysis, whereby glucose is broken down to produce energy.6

In the context of chronic hyperglycemia relating to the kidneys, overstimulation of glycolysis and the citric acid cycle (TCA cycle) can lead to overproduction of NADH, a major electron carrier that is generated via the two aforementioned pathways.11, 12 The respective increased flux of NADH flooding into the electron transport chain (ETC) within the mitochondria can overwhelm the system and lead to electron leakage, prompting the formation of reactive oxygen species. 11, 13

Furthermore, heavy metal toxicity-induced diabetes mellitus is another relevant factor in developing diabetic nephropathy.14, 15 Exposure to heavy metals like lead, cadmium, or arsenic can induce oxidative stress by promoting certain oxidative pathways, which can alter glucose metabolism and induce oxidative stress, leading to diabetes. 16

Understanding the relationships between oxidative stress, diabetic nephropathy, diabetes, and central carbon metabolism is critical in discovering therapeutic opportunities for some of the underlying conditions surrounding the development of diabetic nephropathy. Targeting these processes through therapeutic interventions, like the use of phloretin, are worth exploring to mitigate oxidative stress and improve kidney function in diabetic patients.

1. ROS Formation-1.1 Glycolysis and NADH Formation

Glycolysis is a ten-step process that results in the formation of two pyruvate molecules. Glucose + NAD+ + 2 ATP + 2 Pi \rightarrow 2 Pyruvate + 2 NADH + 2 ATP Pyruvate undergoes decarboxylation, forming Acetyl-CoA, which can enter the citric acid cycle. NADH, the electron-carrying molecule which can enter. Complex 1 of the ETC, plays a crucial role in cellular processes. Specifically, the sixth step of glycolysis involves two glyceraldehyde 3-phosphate molecules, which react with NAD+ and Mg++ and are catalyzed by glyceraldehyde

1.2 Electron Transport Chain and ROS Formation

phosphate dehydrogenase to form 1,3-phosphoglycerate and NADH.

The electron transport chain (ETC) is an important set of reactions that occur along the mitochondrial membrane. It is instrumental in forming two components, electrons and hydrogen ions, to fuel its main goal: ATP production. The ETC is, however, an extremely complex and

fickle process that requires delicate transfer of electrons between many different enzymes, all of which are susceptible to changes in function due to external factors. One major outcome of inefficient electron transfer is the formation of reactive oxygen species (ROS).

The first step of ETC is commenced by Complex 1, which comprises FMN, Fe-S, N-2, and Ubiquinone-Q, each of which directly supports the electron transport chain by aiding in the transfer of electrons (See Figure 2). To initiate the process, FMN oxidizes NADH to NAD+, and the two electrons removed during this process are then moved from FMN to Fe-S, N-2, then eventually transferred to the ubiquinone-q substrata, which can accept the electrons alongside two free hydrogen ions to form Ubiquinol.

Complex 2 involves the movement of electrons into the intermembrane space by FADH2. In Complex 2, the enzyme succinate dehydrogenase is a membrane-bound enzyme that catalyzes the transport of two electrons from the FADH2 molecule2, which is oxidized to FAD+, and the electrons removed during this process move to Ubiquinone-Q to form Ubiquinol by taking hydrogen ions from the mitochondrial matrix.

Complex 3, the Q-cytochrome C oxidoreductase or the cytochrome bc1 complex, comprises two main subunits, cytochrome b and cytochrome c1. In the reaction, electrons from QH2, as the result of complex 2, are transferred to cytochrome c. When two cytochrome c molecules are reduced, one molecule of QH2 is oxidized, meaning two hydrogen ions are removed from the matrix.

Ultimately, the pumping of hydrogen ions into the intermembrane space creates a concentration gradient that favours the flow of protons back into the mitochondrial matrix.

Complex 4, also known as the cytochrome oxidase complex, oxidizes cytochrome c.Electrons travel through the enzyme and eventually reduce O2 to H2O. During the electron transfer and reduction step, complex 4 pumps protons across the inner mitochondrial membrane from within the matrix to the intermembrane space. This also contributes to the generation of the aforementioned proton gradient that ultimately powers ATP synthase, also known as complex 5. As a result of the reaction, four electrons and four protons are used to form two water molecules (H2O), and this ensures the disposal of electrons from the ETC thereby aiding in the prevention of electron leakage and subsequent ROS formation.

Contribution of two electrons from glycolysis-derived NADH to complex 1 is coupled with proton pumping from the mitochondrial matrix to the intermembrane space. In the case of diabetes, kidney-associated cells experience persistently heavy glycolytic flux, leading to a surplus of NADH that saturates electron transport in the mitochondria.19 The overflow is further perpetuated by insufficient proton pumping, and it ultimately results in substantial electron leakage and subsequent formation of superoxide (O2-), the most common type of ROS.20, 21 The ETC is considered the primary physiological event associated with ROS formation in diabetic patients, and elevated glycolytic flux in kidney tissue as a result of chronic hyperglycemia overruns the body's ability to prevent oxidative stress. 22, 23

2. Effects of ROS on Renal Structure and Function–2.1 ROS-Induced Nephron Deterioration

The introduction of excess ROS through the glomerular apparatus can contribute significantly to structural impairments, such as damage to endothelial cells, the glomerular basement membrane, and the podocytes.24

The podocytes are incredibly delicate structures that, when functionally operative, allow the nephrons to screen waste for proteins that would otherwise be released through urination. The mechanism that affects the function of the podocytes is the balance of intracellular redox signaling. Excessive ROS can perturb this balance, leading to altered cellular metabolism that significantly impairs the podocyte's ability to repair its damaged tissues.24, 25

In addition, ROS is also known to affect the cytoskeletal organization of podocytes. 26 Specifically, the actin cytoskeleton is essential for maintaining the kidneys' structural integrity and proper function of the kidneys. Disruption of the actin cytoskeleton can result in podocyte foot process effacement, leading to the flattening or loss of finger-like protrusions on the podocyte membrane.27 This disruption can impact the efficacy of the filtration barrier, causing selective permeability and allowing proteins to leak into the urine, a condition known as proteinuria. Additionally, prolonged exposure to ROS has also been shown to promote pro-fibrotic changes within the podocytes, leading to the accumulation of extracellular matrix proteins that can result in the development of glomerulosclerosis, which is characterized by intense stiffening of the glomerular filtration apparatus and the hardening of the glomerular basement membrane (GBM), which further impairs kidney function (see figure 3).27, 29

One of the critical features of the GBM is its selective permeability, whereby the renin-angiotensin system (RAAS) may alter the permeability of the GBM and endothelial cells to increase or decrease the rate by which the glomerular apparatus can filter waste.30 In the context of oxidative stress, modifications to the GBM components such as collagen IV and heparan sulfate proteoglycans (HSPGs), both of which affect tissue organization and interact with growth factors, cytokines, enzymes, and extracellular matrix components, can lead to increased permeability and subsequent leakage of proteins into the urine. 31, 32

ROS can also damage the structure and function of the endothelium. Increased ROS causes poly (ADP-ribose) polymerase to become active within endothelial cells, which is associated with decreased activity of glyceraldehyde-3-phosphate dehydrogenase (GAPDH).33 Reduced GAPDH activity is associated with NF-kB activation and increased expression of certain isoforms of protein kinase c (PKC), both of which decrease eNOS expression by impairing or uncoupling NOS enzymes.34 These enzymes typically serve to dilate vascular smooth muscle cells through the production of nitric oxide (NO). In the absence of NO, vasoconstriction is likely to occur as there is a substantial lack of counteraction against potent vasoconstrictors like angiotensin II (Ang II) and endothelin-1 (ET-1).34, 35, 36, Ultimately, cardiovascular deterioration can occur as a result of the increased pressure exerted on these constricted capillaries.

The enhancement of alternative metabolic pathways by hyperglycemia can lead to increased diacylglycerol and a subsequent increase in the expression of particular isoforms of PKC that are typically associated with the dilation of vascular smooth muscle cells.35, 36 In the context of the kidneys, elevated PKC may be associated with the dilation of the afferent arterioles that flow into the glomerular apparatus, ultimately leading to an increase in intraglomerular pressure.37 As eNOS expression decreases and vasoconstrictors are released following ROS induction in the bowman's capsule, Ang II and ET-1 constrict the efferent arterioles and limit the rate at which fluid can commute from the glomerulus after initial filtration. 36

The combination of these renal-vascular modifications forces an increased amount of blood plasma through the glomerulus and through the remainder of the nephron. Oftentimes the hyperflow of blood plasma causes increased urination by elevating the volume of fluid that is filtered through the kidneys. This hyperfiltration can contribute to certain issues related to dehydration, electrolyte imbalance, and the loss of blood and proteins.

Overall, the damage caused by ROS in the kidneys can be severe in high enough concentrations and can significantly damage the structure and function of the kidneys. The removal of ROS or prevention of ROS formation in renal tissues is a potential way of preventing or treating diabetic nephropathy. 39

3. Introduction to Glucose Transporter 2 (GLUT2)

Glucose transporter 2 (GLUT2) is a specialized transporter protein responsible for moving extracellular glucose to the cytoplasm, where it is the starting substrate for glycolysis. GLUT2 is most commonly found in the liver, kidneys, and pancreas, all of which do not require large amounts of glucose to maintain metabolic homeostasis. For these reasons, GLUT2 has a relatively low affinity for glucose. It requires a high venous glucose concentration to initiate glucose transport into GLUT2 cells/tissues, which can be useful in the signaling of certain sensitive pathways like insulin secretion and glycogen storage.

In the pancreas, GLUT2 is the primary glucose transporter in pancreatic β -cells, which are responsible for triggering insulin release in response to elevated blood glucose levels. Insulin secretion initiates glucose transport in GLUT4 tissues such as adipose tissue and skeletal muscle, which require insulin to facilitate glucose transport into the cytoplasm.

In the liver, the role of GLUT2 is to harvest blood glucose when in higher concentrations and store the glucose in the form of glycogen, which can then be reconverted to glucose when blood levels of this metabolite are low. The byproduct of glucose utilization by muscle is lactate, which can be re-harvested from the blood by the liver. The captured lactate can be recycled into glucose via gluconeogenesis to be used for glycogen storage or stabilization of blood glucose levels. It is also worth noting that the reason GLUT2 is found in the liver is likely because of its relatively low affinity for blood glucose uptake, making it a prime candidate for limiting the amount of glucose taken from the blood to be used in glycogen conversion/storage, making it a retroactive energy supplier to the body that serves as a critical aid in maintaining a consistent blood glucose level.

3.1 The Role of GLUT 2 in the Kidneys:

In the kidneys, GLUT 2 is utilized primarily in the proximal tubules, which are responsible for filtering blood and turning its waste into urine. The main function of GLUT2 in the kidneys is to facilitate the movement of glucose across the luminal membrane of the proximal tubule cells, allowing glucose to be transported from the tubular fluid into the cells.40Once inside these cells, glucose can either be utilized in glucose metabolism or be transported across the basolateral membrane into the interstitial fluid and then back into the bloodstream in a process known as reabsorption or reuptake. This process of glucose reabsorption is crucial in maintaining glucose homeostasis in the body.38

Normally, the kidneys filter a large amount of glucose from the blood into the glomerular filtrate in the initial phase of filtration, which occurs in the glomerulus/bowman's capsule.41, 42 Still, under normal physiological conditions, almost all of this filtered glucose is reabsorbed by the proximal tubules via GLUT2, preventing excess loss of glucose in the urine. 40, Due to GLUT2 having a low affinity for glucose, the kidneys are able to reabsorb glucose in response to varying glucose concentrations in the blood, ensuring efficient glucose reabsorption.40 The primary physiological issue with GLUT2 reabsorption in the kidneys is that in diabetes, proximal reabsorption of glucose is extremely high because of glucosuria, or increased glucose concentration in the filtrate, which indicates to the GLUT2 cells that glucose should be reabsorbed into the blood, thus preventing excess glucose from being filtered out. 40, 43,

Furthermore, sodium-glucose cotransporter (SGLT2) is responsible for maintaining venous electrolyte balance via reabsorption of both glucose and salts in the proximal tubules.45 Therefore, a change in urine glucose concentrations common in glycosuria may perpetuate blood electrolyte imbalance, leading to a variety of negative health effects like certain neurological abnormalities such as cardiac arrhythmia.46, 47 Hence, the regulation of this interface is crucial in maintaining overall homeostasis.

4. Phloretin Therapy – GLUT 2 Inhibitors:

One potential therapeutic option for mitigating chronic hyperglycemia is inhibiting proximal reabsorption of glucose in the kidneys, which would facilitate the passage of glucose through the nephron body towards the bladder for eventual secretion.

Similarly, phloretin possesses certain chelation properties that may further prevent and treat complications related to heavy metal toxicity-induced diabetes mellitus. This characteristic of phloretin may be significant in defending against heavy metal-ROS formation pathways like the Fenton and Haber-Weiss0 pathways.

4.1 GLUT2 in Competitive Inhibition

Phloretin works to inhibit GLUT2 through a process known as competitive inhibition.48

Phloretin competes with glucose to bind the active site of the GLUT2 transport protein, which prevents glucose from being transported across the cell, and has been shown to inhibit GLUT2 in cancer-based clinical trials.8, 49, 50, 51 Because phloretin only remains in the active site for a brief

period of time, it can bind and unbind from the active site in predictable intervals and as necessary.52, 53, Additionally, the predictability of this interaction is beneficial because varying concentrations and quantities of phloretin can be used for different strengths of interference, allowing for diversification of treatment plans for different patients at varying stages of diabetic nephropathy.

The specific molecular mechanism surrounding the interaction of phloretin with GLUT2 is largely unknown. However, we can draw likely conclusions based on the molecular composition of the phloretin molecule, namely a combination of hydrophobic and hydrogen bond interactions.

Phloretin is composed of aromatic rings and hydrophobic regions (See Figure 4). The hydrophobic regions of the phloretin molecule can interact with the hydrophobic amino acid residues present in the transmembrane region of the GLUT2 protein that includes the active site. This interaction largely involves Van der Waals forces. It enables the formation of non-polar contacts between phloretin and the protein, which are not particularly strong in terms of bond strength.

In addition to the hydrophobic interactions, phloretin also contains hydroxyl groups (-OH) that can act as hydrogen bond donors or acceptors: so these hydroxyl groups may form hydrogen bonds with specific amino acid residues in the active site of GLUT2, leading to stronger bonds between the active site and the phloretin molecule than the previously mentioned contacts involving Van der Waals forces

It is also important to note that the actual bond affinity of phloretin to GLUT2 is unknown, so it is unknown whether glucose or phloretin is more likely to bind to GLUT2. Nevertheless, phloretin, if proven to hold a stronger affinity towards GLUT2, may have implications for fast-acting effects in cases of acute renal failure.

4.2 GLUT2 in the Antioxidant Defense System

Phloretin exhibits antioxidant activity primarily through its ability to scavenge free radicals and inhibit oxidative stress.54 Phloretin possesses phenolic groups that can donate hydrogen atoms or electrons to free radicals, neutralizing their reactivity.

Phloretin is also a highly capable chelation molecule, which can bind to metal ions like iron or copper. Metal ions, in high concentrations, can catalyze the generation of free radicals through Fenton and Haber-Weiss reactions, and by chelating these ions, phloretin may help prevent heavy metals' participation in these reactions by essentially wrapping the metal ion in the phloretin molecules, reducing the harmful free radical production.

The Fenton reaction involves the catalytic role of iron II in generating hydroxyl radicals. Fe+2 + H2O2 \rightarrow Fe+3 + OH- + OH

Hydroxyl radicals are highly reactive and can cause oxidative damage to cellular components such as lipids, proteins, and nucleic acids.55

The significance of the chelation properties of phloretin lies in the correlation between heavy metal toxicity and diabetes. Elevated venous heavy metal concentration has been shown to contribute to the severity of diabetes and some of its complications.56, 57 Specifically, exposure to lead, cadmium, arsenic, and mercury has been associated with an increased risk of developing diabetes or exacerbating its symptoms, specifically in developing insulin resistance and inducing pancreatic β -cell death.

Heavy metals are also fairly common in the environment. They can enter the body through various sources such as contaminated water, food, air pollution, occupational exposure, and many consumer products. Prolonged exposure to any heavy metal source significantly increases the risk of developing diabetes or worsening its complications.56, 58 It is also worth noting that by removing harmful heavy metals from the bloodstream via chelation, phloretin may prevent the formation of advanced glycation end-products by sequestering metal ions.

For instance, chronically elevated blood glucose levels can lead to the glycation of hemoglobin, known as HbA1c.59 Importantly, iron can promote the glycation of hemoglobin specifically by utilizing the Fenton reaction within the bloodstream. The process of glycation is facilitated by the attachment of glucose to nitrogen in the formation of a Schiff base. It is formed largely as a result of hyperglycemia. The Schiff base turns into a ketone via the Amadori Adduct, which results in the crosslinking of arginine and lysine residues, subsequently forming an Amadori product that can easily bind to hemoglobin. The glycation of HbA1c renders it incapable of transporting oxygen in the bloodstream. The introduction of phloretin could both minimize hyperglycemia and limit reactive iron concentrations in the blood thereby mitigating the effects of glycation.

Phloretin has also been shown to induce the expression of certain antioxidant enzymes, including superoxide dismutase (SOD) and catalase, both of which play crucial roles in neutralizing free radicals and detoxifying reactive oxygen species.60

4.3 Improvements in Kidney Function

Phloretin treatment will likely lead to improvements in kidney function by decreasing ROS formation and increasing proactive mechanisms to help eliminate radicals. Additionally, the decrease in the formation of advanced glycation end products (AGEs), specifically advanced glycated enzymes, will likely lead to decreased intraglomerular hypertension. The corresponding decrease in blood pressure may result in lessening the damaging effects of ROS-induced glomerulosclerosis, heightened glomerular filtration rate, glomerular basement membrane deterioration, podocyte dysfunction, and in severe cases, endothelial dysfunction.

5. Negative Externalities--5.1 Renal Function

Although the potential local effects of inhibiting GLUT2 in the kidneys are fairly optimistic, it is also important to understand the possible negative impacts phloretin could have

on the kidneys and other organ systems.

Although overall function may improve, the kidneys may see negative effects due to phloretin-induced glucosuria. As mentioned above, sodium-glucose cotransporter (SGLT2) is responsible for maintaining venous electrolyte balance through reabsorption in the proximal tubules, and a change in urine glucose concentration in glucosuria may perpetuate venous electrolyte imbalance.45 In addition, chronic glucosuria may result in progressive deterioration of the kidneys in events similar to glycation. It could limit reuptake potentials for other proteins/cells and lead to osmotic diuresis as the body attempts to level the glucose gradient by attempting to dilute the urine by increasing water secretion.

5.2 Hepatic Function

In the liver, GLUT2 is crucial in maintaining glucose homeostasis all over the body, and inhibiting GLUT2 may disrupt the normal uptake and utilization of glucose by the hepatocytes, which may lead to altered glucose metabolism, abnormal blood glucose levels, and further contribute to altered hepatic insulin resistance.

The liver's primary function in terms of blood glucose management is the storage of glucose in the form of glycogen, which can be broken down and released back into the bloodstream in the form of glucose when concentrations decrease such that metabolic homeostasis is jeopardized. The role of GLUT2 in the liver is to regulate this exchange, and by inhibiting GLUT2, glucose uptake by the liver may change such that glycogen synthesis, storage, and signaling are jeopardized, leading to a decreased capacity to store glycogen and regulate blood glucose concentrations.

GLUT2 inhibition may also impact liver metabolism beyond glycolysis, as the liver plays a crucial role in various metabolic processes, including lipid metabolism, protein synthesis, and blood detoxification. One such metabolic change could alter the process of gluconeogenesis, such that lactate, a major input for gluconeogenesis, shifts to a point where lactate concentrations increase in the bloodstream and can cause serious adverse health effects like metabolic acidosis, increased myocardial oxygen consumption, tissue hypoxia, or even organ failure.

5.3 Pancreatic Function

In the pancreas, GLUT2 is primarily expressed in pancreatic β -cells responsible for producing and secreting insulin into the bloodstream. GLUT2 allows for the entry of glucose into beta cells, which can trigger insulin release in response to elevated blood glucose levels to attempt to increase cellular glucose uptake by GLUT4 (insulin-dependent) tissues to decrease blood glucose levels. Inhibiting GLUT2 can disrupt normal glucose sensing and impair glucose-stimulated insulin secretion, leading to reduced β -cell insulin production and further compromising blood glucose regulation. In addition, GLUT2 is also involved in glucose metabolism within pancreatic β -cells, and limiting normal glucose utilization and metabolism within beta cells could potentially affect energy production and other cellular processes. GLUT2 inhibition may also lead to changes in gene expression within the pancreas, including genes

related to insulin synthesis, glucose metabolism, and pancreatic cell differentiation. By disrupting the normal expression of these genes, developmental abnormalities may present as reduced cellular proliferation, differentiation, apoptosis, and impaired immune response.

6. Phloretin v. Other Antioxidants

Concerning their antioxidant properties, phloretin and other antioxidants share a few characteristics in terms of their ability to regulate oxidative stress and limit free radical damage. Compared to some of its antioxidant counterparts like vitamin C, vitamin E, resveratrol, and curcumin, phloretin does not perform as well, mainly because of the wide range of tissues that the alternate antioxidants can target. Due to its insolubility in water, phloretin cannot readily transverse the bloodstream, making it difficult to promote as an all-around solution to inhibiting oxidative damage across the entirety of the kidneys.

For example, Vitamin C (ascorbic acid) is a potent antioxidant that, like phloretin, scavenges free radicals and protects against oxidative damage. Unlike phloretin, Vitamin C's water-soluble characteristics allow it to maneuver across many different tissue types. Vitamin E (tocopherol) is a fat-soluble antioxidant that primarily protects cell membranes, specifically, from oxidative damage by neutralizing lipid peroxyl radicals, and also carries specific anti-inflammatory properties, which could be an option for limiting oxidative damages within the glomerular basement membrane and podocyte foot processes as well as being able to navigate fatty tissues easily.

However, as stated before, the beneficial aspects of phloretin extend beyond its ability to prevent oxidative damage. Examples of its beneficial effect include retroactively inducing antioxidant enzymes to help prevent oxidative stress in the long term, anti-diabetic chelation potential, the ability to inhibit glycolysis and subsequent electron leakage in GLUT2 renal tissues, and anti-AGE formation.54, 55, 59

It is also worth noting that the possibility of using phloretin as a broad-spectrum antioxidant is relatively slim, as the damage to the pancreas and liver would likely be too severe for the benefits in antioxidant prevention to outweigh the negative externalities. However, there are some modern solutions that could address the challenge of localization.

Modern Implications for Therapeutic Phloretin Interventions

Modern innovation in localized drug administration could have significant implications for the delivery method of phloretin to renal tissues without the invasive injection method that phloretin would require for localization. Phloretin, because of its water-insoluble nature, is not likely to transfer to other organ systems in large quantities if administered directly to the kidneys themselves, so the administration of phloretin in an organ-specific manner would likely be an effective work-around to the administration of phloretin intravenously.

Modern nanotechnology and advancements in delivery systems could mean a simple oral administration of phloretin encapsulated in nanoparticles designed to target the kidney could provide the level of localization required to aid the body in treating the oxidative damages of diabetic nephropathy.61, 62

Specifically, through targeting renal tubular cells directly involved in diabetic nephropathy, surface modifications on nanoparticles can be designed to bind to receptors or transporters expressed in renal tubular cells, allowing for the delivery of phloretin directly to the desired site of action within the kidneys, maximizing therapeutic efficacy and minimizing the effects on other organ systems.62

Metformin is commonly known and used as an oral medication for type 2 diabetes. Recent research has explored the potential protective effects of metformin to be used on the kidneys specifically. Still, the combination of metformin and phloretin might be a serious therapeutic option for diabetic nephropathy.

Metformin has demonstrated renoprotective properties in preclinical studies, and metformin reduces inflammation and fibrosis in the kidneys, which have implications for diabetic nephropathy.63, 64 Metformin is also commonly used for its ability to lower blood glucose levels in individuals with diabetes, and by improving insulin sensitivity and reducing glucose production by the liver, metformin can help control blood sugar levels. The ability of metformin to remove glucose from the bloodstream by reactivating insulin-dependent cells/tissues in type 2 diabetes alongside the beneficial properties of phloretin on the kidneys may lead to significant improvements in overall kidney function by allowing for urination to occur without perpetuating glucosuria, electrolyte imbalances, and dehydration, making this combination an appealing treatment for cases of acute renal failure.

Conclusion

The use of phloretin as a therapeutic option for mitigating chronic hyperglycemia and heavy metal toxicity-induced diabetes mellitus holds promise. Its ability to inhibit GLUT2 and compete with glucose for binding sites shows potential for fast-acting effects in cases of acute renal failure. Additionally, phloretin's antioxidant properties, including scavenging free radicals and chelating metal ions, offer a means to prevent oxidative stress and limit the formation of advanced glycation end-products. While negative externalities such as potential impacts on renal, hepatic, and pancreatic function should be considered, modern innovations in localized drug administration, such as nanotechnology-based delivery systems, may help address these concerns. Combining phloretin with other therapeutic agents like metformin could provide a comprehensive approach to treating diabetic nephropathy and improving overall kidney function. Overall, the potential benefits of phloretin-based antioxidant therapy in preventing and treating diabetic nephropathy are significant and warrant further investigation and development.

Works Cited

- 1.Zhu T, Li K, Herrero P, Georgiou P. Deep Learning for Diabetes: A Systematic Review. *IEEE Journal of Biomedical and Health Informatics*. 2021;25(7):2744-2757. doi:https://doi.org/10.1109/jbhi.2020.3040225
- 2.Sheira G, Noreldin N, Tamer A, Saad M. Urinary biomarker N-acetyl-β-D-glucosaminidase can predict severity of renal damage in diabetic nephropathy. *Journal of Diabetes & Metabolic Disorders*. 2015;14(1). doi:https://doi.org/10.1186/s40200-015-0133-6
- 3.Fu H, Liu S, Bastacky SI, Wang X, Tian XJ, Zhou D. Diabetic kidney diseases revisited: A new perspective for a new era. *Molecular Metabolism*. 2019;30:250-263. doi:https://doi.org/10.1016/j.molmet.2019.10.005
- 4.Doria A. Genetics of Diabetes Complications. *Current Diabetes Reports*. 2010;10(6):467-475. doi:https://doi.org/10.1007/s11892-010-0147-x
- 5.Turkmen K. Inflammation, oxidative stress, apoptosis, and autophagy in diabetes mellitus and diabetic kidney disease: the Four Horsemen of the Apocalypse. *International Urology and Nephrology*. 2016;49(5):837-844. doi:https://doi.org/10.1007/s11255-016-1488-4
- 6.Bhatti JS, Sehrawat A, Mishra J, et al. Oxidative stress in the pathophysiology of type 2 diabetes and related complications: Current therapeutics strategies and future perspectives. *Free Radical Biology and Medicine*. 2022;184:114-134. doi:https://doi.org/10.1016/j.freeradbiomed.2022.03.019
- 7.Rochette L, Zeller M, Cottin Y, Vergely C. Diabetes, oxidative stress and therapeutic strategies. Biochimica et Biophysica Acta (BBA) - General Subjects. 2014;1840(9):2709-2729. doi:https://doi.org/10.1016/j.bbagen.2014.05.017
- 8.Wu C, Yuan Soon Ho, Chia Ti Tsai, et al. *In vitro and in vivo study* of phloretin-induced apoptosis in human liver cancer cells involving inhibition of type II glucose transporter. *Cancer*. 2009;124(9):2210-2219. doi:https://doi.org/10.1002/ijc.24189
- 9.Hu H, Bai X, Xu K, Zhang C, Chen L. Effect of phloretin on growth performance, serum biochemical parameters and antioxidant profile in heat-stressed broilers. 2021;100(8):101217-101217. doi:https://doi.org/10.1016/j.psj.2021.101217
- 10.Uttara B, Singh AV, Zamboni P, Mahajan RT. Oxidative stress and neurodegenerative diseases: a review of upstream and downstream antioxidant therapeutic options. *Current neuropharmacology*. 2009;7(1):65-74. doi:https://doi.org/10.2174/157015909787602823
- 11.Naudi A, Jove M, Ayala V, et al. Cellular Dysfunction in Diabetes as Maladaptive Response to Mitochondrial Oxidative Stress. *Experimental Diabetes Research*. 2012;2012:e696215. doi:https://doi.org/10.1155/2012/696215
- 12.Mokini Z, Marcovecchio ML, Chiarelli F. Molecular pathology of oxidative stress in diabetic angiopathy: Role of mitochondrial and cellular pathways. *Diabetes Research and Clinical Practice*. 2010;87(3):313-321. doi:https://doi.org/10.1016/j.diabres.2009.11.018
- 13.Galvan DL, Green NH, Danesh FR. The hallmarks of mitochondrial dysfunction in chronic kidney disease. *Kidney International*. 2017;92(5):1051-1057. doi:https://doi.org/10.1016/j.kint.2017.05.034

- 14.Mitra S, Chakraborty AJ, Tareq AM, et al. Impact of heavy metals on the environment and human health: Novel therapeutic insights to counter the toxicity. *Journal of King Saud University - Science*. 2022;34(3):101865. doi:https://doi.org/10.1016/j.jksus.2022.101865
- 15.Cooper RG. Effect of tobacco smoking on renal function. 2006;124(3):261-268. 16.Jomova K, Valko M. Advances in metal-induced oxidative stress and human disease.
- Toxicology. 2011;283(2-3):65-87. doi:https://doi.org/10.1016/j.tox.2011.03.001
- 17.Dasika S. Glycolysis and TCA Cycle. ResearchGate. Published January 2007. https://www.researchgate.net/figure/Glycolysis-and-TCA-cycle-13 fig5 241825789
- 18.Turton N. Coenzyme Q 10 and the exclusive club of diseases that show a limited response to treatment. ResearchGate. Published May 2021. https://www.researchgate.net/figure/Diagram-of-electron-transport-chain-ETC-and-ATP-s ynthas e-illustrating-the-pumping-of-H fig2 351722900
- 19.Kanasaki K, Maeshima A, Taduri G, Revuelta I. Combating Kidney Fibrosis. *BioMed Research International*. 2014;2014:1-2. doi:https://doi.org/10.1155/2014/679154
- 20.Jankovic A, Korac A, Buzadzic B, et al. Redox implications in adipose tissue (dys)function—A new look at old acquaintances. *Redox Biology*. 2015;6:19-32. doi:https://doi.org/10.1016/j.redox.2015.06.018
- 21.Oliveira HCF, Vercesi AE. Mitochondrial bioenergetics and redox dysfunctions in hypercholesterolemia and atherosclerosis. *Molecular Aspects of Medicine*. 2020;71:100840. doi:https://doi.org/10.1016/j.mam.2019.100840
- 22.He L, He T, Farrar S, Ji L, Liu T, Ma X. Antioxidants Maintain Cellular Redox Homeostasis by Elimination of Reactive Oxygen Species. *Cellular Physiology and Biochemistry*. 2017;44(2):532-553. doi:https://doi.org/10.1159/000485089
- 23.Sies H, Jones DP. Reactive oxygen species (ROS) as pleiotropic physiological signalling agents. *Nature Reviews Molecular Cell Biology*. Published online March 30, 2020. doi:https://doi.org/10.1038/s41580-020-0230-3
- 24.Rask-Madsen C, King George L. Vascular Complications of Diabetes: Mechanisms of Injury and Protective Factors. *Cell Metabolism*. 2013;17(1):20-33. doi:https://doi.org/10.1016/j.cmet.2012.11.012
- 25.Singh A, Kukreti R, Saso L, Kukreti S. Mechanistic Insight into Oxidative Stress-Triggered Signaling Pathways and Type 2 Diabetes. *Molecules*. 2022;27(3):950. doi:https://doi.org/10.3390/molecules27030950
- 26.Hsu HH, Hoffmann S, Endlich N, et al. Mechanisms of angiotensin II signaling on cytoskeleton of podocytes. 2008;86(12):1379-1394. doi:https://doi.org/10.1007/s00109-008-0399-y
- 27.Suleiman HY, Roth R, Jain S, Heuser JE, Shaw AS, Miner JH. Injury-induced actin cytoskeleton reorganization in podocytes revealed by super-resolution microscopy. JCI Insight. 2017;2(16). doi:https://doi.org/10.1172/jci.insight.94137
- 28.Murray I. Normal Histology: Glomeruli Interstitium Tubules Vessels . Kidney Pathology. Published October 12, 2006.

https://kidneypathology.com/English_version/Glomeruli_histology.html

- 29.Hu C, Sun L, Xiao L, et al. Insights into the Mechanisms Involved in the Expression and Regulation of Extracellular Matrix Proteins in Diabetic Nephropathy. *Current Medicinal Chemistry*. 2015;22(24):2858-2870. doi:https://doi.org/10.2174/0929867322666150625095407
- 30.Jourde-Chiche N, Fakhouri F, Dou L, et al. Endothelium structure and function in kidney health and disease. *Nature Reviews Nephrology*. 2019;15(2):87-108. doi:https://doi.org/10.1038/s41581-018-0098-z
- 31.Marchand M, Monnot C, Muller L, Germain S. Extracellular matrix scaffolding in angiogenesis and capillary homeostasis. *Seminars in Cell & Developmental Biology*. 2019;89:147-156. doi:https://doi.org/10.1016/j.semcdb.2018.08.007
- 32.Karamanos NK, Theocharis AD. Matrix modeling and remodeling: A biological interplay regulating tissue homeostasis and diseases. *Matrix Biology*. 2019;75-76:1-11. doi:https://doi.org/10.1016/j.matbio.2018.08.007
- 33.Fiorentino T, Prioletta A, Zuo P, Folli F. Hyperglycemia-induced Oxidative Stress and its Role in Diabetes Mellitus Related Cardiovascular Diseases. *Current Pharmaceutical Design*. 2013;19(32):5695-5703. doi:https://doi.org/10.2174/1381612811319320005
- 34.Pandolfi A, De EA. Chronic hyperglycemia and nitric oxide bioavailability play a pivotal role in pro-atherogenic vascular modifications. *Genes & Nutrition*. 2007;2(2):195-208. doi:https://doi.org/10.1007/s12263-007-0050-5
- 35.C. Adam Kirton, Loutzenhiser R. Alterations in basal protein kinase C activity modulate renal afferent arteriolar myogenic reactivity. *American Journal of Physiology*. 1998;275(2):H467-H475. doi:https://doi.org/10.1152/ajpheart.1998.275.2.h467
- 36.Gschwend SK. Small Artery Tone under Control of the Endothelium: On the Importance of EDHF and Myogenic Tone in Organ (Dys)Function. University of Gronigen; 2003. https://pure.rug.nl/ws/portalfiles/portal/3024541/thesis.pdf
- 37.Sasson AN. Renal hyperfiltration related to diabetes mellitus and obesity in human disease. *World Journal of Diabetes*. 2012;3(1):1. doi:https://doi.org/10.4239/wjd.v3.i1.1
- 38.Liamis G. Diabetes mellitus and electrolyte disorders. *World Journal of Clinical Cases*. 2014;2(10):488. doi:https://doi.org/10.12998/wjcc.v2.i10.488
- 39.Jha JC, Gray SP, Barit D, et al. Genetic Targeting or Pharmacologic Inhibition of NADPH Oxidase Nox4 Provides Renoprotection in Long-Term Diabetic Nephropathy. *Journal of the American Society of Nephrology*. 2014;25(6):1237-1254. doi:https://doi.org/10.1681/asn.2013070810
- 40.Vallon V. Glucose transporters in the kidney in health and disease. *Pflügers Archiv European Journal of Physiology*. 2020;472(9):1345-1370. doi:https://doi.org/10.1007/s00424-020-02361-w
- 41. Eaton DC. Vander's Renal Physiology. Mcgraw-Hill Medical; 2018.
- 42.Sasaki T, Tsuboi N, Haruhara K, et al. Bowman Capsule Volume and Related Factors in Adults With Normal Renal Function. *Kidney International Reports*. 2018;3(2):314-320.

doi:https://doi.org/10.1016/j.ekir.2017.10.007

- 43.Gerich JE. Role of the kidney in normal glucose homeostasis and in the hyperglycaemia of diabetes mellitus: therapeutic implications. *Diabetic Medicine*. 2010;27(2):136-142. doi:https://doi.org/10.1111/j.1464-5491.2009.02894.x
- 44.Vallon V, Thomson SC. The tubular hypothesis of nephron filtration and diabetic kidney disease. *Nature Reviews Nephrology*. 2020;16(6):317-336. doi:https://doi.org/10.1038/s41581-020-0256-y
- 45.Bjornstad P, Greasley PJ, Wheeler DC, et al. The Potential Roles of Osmotic and Nonosmotic Sodium Handling in Mediating the Effects of Sodium-Glucose Cotransporter 2 Inhibitors on Heart Failure. *Journal of Cardiac Failure*. 2021;27(12):1447-1455.
- doi:https://doi.org/10.1016/j.cardfail.2021.07.003
- 46.Arnold R, Issar T, Krishnan AV, Pussell BA. Neurological complications in chronic kidney disease. JRSM Cardiovascular Disease. 2016;5(5):204800401667768. doi:https://doi.org/10.1177/2048004016677687
- 47.R. Brouns. Neurological complications in renal failure: a review. *Clinical Neurology and Neurosurgery*. 2004;107(1):1-16. doi:https://doi.org/10.1016/j.clineuro.2004.07.012
- 48.Hytti M, Ruuth J, Kanerva Ii, et al. Phloretin inhibits glucose transport and reduces inflammation in human retinal pigment epithelial cells. *Molecular and Cellular Biochemistry*. 2022;478(1):215-227. doi:https://doi.org/10.1007/s11010-022-04504-2
- 49.Choi B. Biochemical Basis of Anti-Cancer-Effects of Phloretin—A Natural Dihydrochalcone. *Molecules*. 2019;24(2):278. doi:https://doi.org/10.3390/molecules24020278
- 50.Ho YS. The apple polyphenol phloretin inhibits breast cancer cell migration and proliferation via inhibition of signals by type 2 glucose transporter. *Journal of Nutrition & Food Sciences*. 2018;08. doi:https://doi.org/10.4172/2155-9600-c1-054
- 51.Shriwas P, Roberts D, Li Y, et al. A small-molecule pan-class I glucose transporter inhibitor reduces cancer cell proliferation in vitro and tumor growth in vivo by targeting glucose-based metabolism. *Cancer & Metabolism*. 2021;9(1). doi:https://doi.org/10.1186/s40170-021-00248-7
- 52.Cheon D, Kim J, Shin HC, Kim Y. Target Proteins of Phloretin for Its Anti-Inflammatory and Antibacterial Activities Against Propionibacterium acnes-Induced Skin Infection. *Molecules*. 2019;24(7):1319. doi:https://doi.org/10.3390/molecules24071319
- 53.Behzad S, Sureda A, Barreca D, Nabavi SF, Rastrelli L, Nabavi SM. Health effects of phloretin: from chemistry to medicine. *Phytochemistry Reviews*. 2017;16(3):527-533. doi:https://doi.org/10.1007/s11101-017-9500-x
- 54.Anand V, Ramachandran Vinyagam, Vinothkumar Rajamanickam, Sankaran V, Venkatesan S, David E. Pharmacological Aspects and Potential Use of Phloretin: A Systemic Review. 2019;19(13):1060-1067. doi:https://doi.org/10.2174/1389557519666190311154425
- 55.Valko M, Leibfritz D, Moncol J, Cronin MTD, Mazur M, Telser J. Free radicals and antioxidants in normal physiological functions and human disease. *The International Journal of Biochemistry & Cell Biology*. 2007;39(1):44-84.

doi:https://doi.org/10.1016/j.biocel.2006.07.001

- 56.Peng S, Liu L, Zhang X, et al. A nested case-control study indicating heavy metal residues in meconium associate with maternal gestational diabetes mellitus risk. *Environmental Health*. 2015;14(1). doi:https://doi.org/10.1186/s12940-015-0004-0
- 57.Flores CR, Puga MP, Wrobel K, Garay Sevilla ME, Wrobel K. Trace elements status in diabetes mellitus type 2: possible role of the interaction between molybdenum and copper in the progress of typical complications. *Diabetes Research and Clinical Practice*. 2011;91(3):333-341. doi:https://doi.org/10.1016/j.diabres.2010.12.014
- 58.Chen YW, Yang CY, Huang CF, Hung DZ, Leung YM, Liu SH. Heavy metals, islet function and diabetes development. *Islets*. 2009;1(3):169-176. doi:https://doi.org/10.4161/isl.1.3.9262
- 59.Lippi G, Targher G. Glycated hemoglobin (HbA1c): old dogmas, a new perspective? *Clinical Chemistry and Laboratory Medicine*. 2010;48(5). doi:https://doi.org/10.1515/cclm.2010.144
- 60.Yang YC, Lii CK, Lin AH, et al. Induction of glutathione synthesis and heme oxygenase 1 by the flavonoids butein and phloretin is mediated through the ERK/Nrf2 pathway and protects against oxidative stress. 2011;51(11):2073-2081. doi:https://doi.org/10.1016/j.freeradbiomed.2011.09.007
- 61.Khalil I, Yehye WA, Etxeberria AE, et al. Nanoantioxidants: Recent Trends in Antioxidant Delivery Applications. *Antioxidants*. 2019;9(1):24. doi:https://doi.org/10.3390/antiox9010024
- 62.Li CW, Li LL, Chen S, Zhang JX, Lu WL. Antioxidant Nanotherapies for the Treatment of Inflammatory Diseases. *Frontiers in Bioengineering and Biotechnology*. 2020;8. doi:https://doi.org/10.3389/fbioe.2020.00200
- 63.Nasri H, Azar Baradaran, Ardalan M, Saeed Mardani, Momeni A, Mahmoud Rafieian-Kopaei. Bright renoprotective properties of metformin: beyond blood glucose regulatory effects. 2013;7(6):423-428.
- 64.De Broe Marc E, Kajbaf F, Lalau JD. Renoprotective Effects of Metformin. *Nephron*. 2017;138(4):261-274. doi:https://doi.org/10.1159/000481951

Gender Difference in Proportion of Licensed Drivers Among Teenagers in California By Brian Chang

Abstract

There are numerous studies about gender differences in teenager's driving behavior and safety, but little attention has been given to gender disparity in license acquisition rate among teenagers. This study examined 2010-2019 California data and discovered that at age 16 and 17, females were slightly more likely (1-2 % higher) than males to obtain their first driver's license. However, at age 18, the proportion of licensure in males was much higher than the proportion in females, ranging from 2.2% to 5.0% higher in the study period. This indicated teenage males were more likely to delay one to two years in obtaining driver's license than teenage females.

Introduction

Gender differences in teenage drivers have been a subject of interest in the field of traffic safety and psychology. Many studies show that teenage male drivers are more likely to be involved in severe car accidents compared to teenage females. Swedler's study reported that compared with female teenagers, crashes of male teenagers were significantly more likely to involve having higher than illegal alcohol level (21% vs. 12%), speeding (38% vs. 25%), reckless driving (17% vs. 14%), night driving (41% vs. 36%) and felony crashes (8% vs. 6%) (1). This may be attributed to their higher likelihood of engaging in risky behaviors and overestimating their driving skills (2, 3). Both male and female teenage drivers can be prone to distractions, such as using mobile phones while driving. However, studies have suggested that teenage males might be slightly more prone to using phones or engaging in other distractions while driving (4). Moreover, teenage male drivers perceive themselves to be safe drivers, but report engaging in more distracted driving and risky behaviors compared to females (5). Despite abundant research on gender differences in driver behavior, little attention has been given to gender differences in driver's licensure rate among teenagers. Popular belief is that teenage males are likely to obtain their driver's licenses earlier than their female counterparts. This study aimed to discover if this perception is true.

Methods

I extracted the number of teenagers (16-18 years old) who obtained driver's licenses in 2010-2019 in California from The Highway Statistics Series published by the Federal Highway Administration, U.S. Department of Transportation (6). Year 2013 was omitted from the analysis due to inconsistency in data reporting that year. Total population of teenagers was obtained from the U.S. Census Bureau, Population Division. Based on the 2010 census, annual estimates of population count by year, age and sex for California were downloaded from Census website (7). Proportion of licensed 16-year-old male drivers was calculated using the number of 16-year-old male drivers divided by the total number of 16-year-old male in each year. Proportion was calculated in the same fashion for other ages and sex for each year. Table 1A, 1B and 1C showed

the proportions and the difference between gender. Standard error for each proportion was calculated using $\sqrt{[\hat{p}(1-\hat{p})/n]}$ (\hat{p} is the estimated proportion, n is the sample size). 95% confidence interval for each proportion was calculated. Figure 1A,1B and 1C illustrated the proportions with their 95% confidence interval. For each age group and each year, two-proportion Z-tests were performed for male vs. female comparison. The Z score test was performed using the Social Science Statistics Calculator.

https://www.socscistatistics.com/tests/ztest/ All other analyses were conducted in Microsoft Office Excel 2013.

Results

In California, during the study period, the licensure rate for male was 12.7%, 29.2% and 51.5% at age 16, 17 and 18 respectively; rate for females was 14.0%, 29.8% and 47.9% at age 16, 17 and 18 respectively.

Year	Age 16		Difference	
	Male	Female	Female-Male	
2010	11.6%	12.8%	1.1%	
2011	12.0%	13.3%	1.3%	
2012	12.8%	14.0%	1.2%	
2014	12.6%	14.0%	1.3%	
2015	12.5%	13.8%	1.3%	
2016	12.9%	14.9%	2.0%	
2017	13.1%	14.3%	1.1%	
2018	12.7%	14.3%	1.7%	
2019	12.7%	13.9%	1.2%	

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lable IA.	Proportion	of licensed	l driver -	Age	10

Table 1B. Proportion of ficensed driver - Age 17	Table 1B.	Proportion	of licensed	driver -	Age 17
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Year	Age17		Difference
	Male	Female	Female-Male
2010	27.6%	28.8%	1.2%
2011	27.6%	29.2%	1.6%
2012	28.1%	29.6%	1.6%
2014	29.6%	29.6%	-0.1%
2015	29.0%	29.8%	0.7 %
2016	30.0%	31.2%	1.3%
2017	29.7%	30.9%	1.2%
2018	29.3%	30.6%	1.3%
2019	29.2%	31.0%	1.8%

Year	Age18		Difference
	Male	Female	Female-Male
2010	50.6%	47.9%	-2.7%
2011	50.8%	47.9%	-2.9%
2012	50.6%	48.4%	-2.2%
2014	52.3%	49.4%	-2.9%
2015	52.9%	47.9%	-5.0%
2016	53.7%	49.7%	-4.0%
2017	53.9%	49.4%	-4.5%
2018	51.5%	47.6%	-3.9%
2019	50.4%	47.8%	-2.5%

Table 1C. Proportion of licensed driver - Age 18







At age 16 and 17, females were slightly more likely than males to obtain their first driver's license. Proportion of licensure in females was 1-2 % higher than the proportion in males. However, at age 18, the proportion in male was much higher than in females. In 2015, 52.9% of 18-year-old male had obtained their first driver's license, compared to 47.9% for females. As shown in Figures, this phenomenon was observed throughout the entire study period (except for 2014).

Two-proportion Z-tests for male vs. female comparison at each age group at each year were all statistically significant (p-value<0.05, except for age 17, year 2014). Also shown in Figure 1A, 1B and IC, all 95% confidence intervals of male and female at the same year and the

same age did not overlap (except for age 17, year 2014). But this significance may be due to the large sample size, which makes the standard error of each proportion very small.

Discussion

Contrary to popular belief, my study showed that in California, age 16 and 17 females were slightly more likely than males to obtain their first driver's license. However, at age 18, the proportion of licensure in males was much higher than the proportion in females, ranging from 2.2% to 5.0% higher in the study period. This indicated male teenagers tend to delay obtaining driver's license until age 18.

Using a nationally representative survey sample for ages 15 to 20 years old, Vaca et al. reported that the odds of having 1-2 years of delayed licensure for male is 12% higher than the odds for females (OR=1.12 95% confidence interval 0.88, 1.42. p-value=0.33). Furthermore, the odds of having more than two years of delay for male is 25% lower than females (OR=0.75, 95% confidence interval 0.49, 1.14. p-value=0.16) (8) Although not statistically significant, Vaca et al.'s study showed similar findings as my study.

Studies about the factors associated with delay or lower licensure rate identified minority race/ethnicity, lower socioeconomic status, urbanicity and parenting factors (8,9). However, most of these factors apply to both boys and girls. It was speculated that the gender disparity may be influenced by parental support as well as differing cognitive development.

Previous studies have investigated the role of parents in teaching and supervising teen drivers, and whether parental involvement differs based on the gender of the teen driver. Simons-Morton et al. reported parental attitudes and expectations can play an important role in when teenagers obtain their driver's licenses. They concluded that the two most important decisions parents can make to reduce teenagers' driving risk is to delay licensure and impose limits on high-risk driving conditions (such as driving at night and with teenage passengers) during the first year of licensure (10). Parental attitudes, support, and willingness to provide driving opportunities significantly impact teenagers' licensing decisions. Parental concerns about safety might lead to differences in the encouragement and timing of licensing for male and female teenagers. In addition, a study in Sweden indicated that female driver licenses test-takers performed statistically significantly better than male test-takers on the theory test (11). Failing the written test could delay the process of obtaining a driver's license. To my knowledge, no similar study has been conducted in the U.S.

The factors contributing to the gender difference on timing of obtaining driver's license are not very clear. Future research could be conducted on how parents, peer groups and social influences impact licensure of male and female teenagers differently. More research could be done for the effectiveness of driver education programs, and whether certain approaches are more beneficial for one gender over the other. These results would help develop gender-specific educational and injury prevention programs for teenage drivers.

Efforts to improve teenage driving safety often involve parent involvement and supervision, educational programs, and promoting safe driving behaviors. Regardless of gender,

promoting responsible and safe driving habits among teenagers is crucial for reducing accidents and saving lives on the road.

Conclusion

This study examined 2010 to 2019 data and discovered gender differences in driver's license acquisition among teenagers. At age 16 and 17, females were slightly more likely than males to obtain their first driver's license. However, at age 18, the acquisition rate among males was much higher than the rate in females, indicating male teenagers delay obtaining driver's license until age 18. Identifying and understanding the underlying reasons for the gender disparity can help tailor interventions to promote safer driving behaviors among both male and female teenagers.

Works Cited

- Swedler DI, Bowman SM, Baker SP. Gender and Age Differences among Teen Drivers in Fatal Crashes. Ann Adv Automot Med. 2012;56:97-106. PMID: 23169121; PMCID: PMC3503410.
- (2). Cordellieri P, Baralla F, Ferlazzo F, Sgalla R, Piccardi L, Giannini AM. Gender Effects in Young Road Users on Road Safety Attitudes, Behaviors and Risk Perception. Front Psychol. 2016 Sep 27;7:1412. doi: 10.3389/fpsyg.2016.01412. PMID: 27729877; PMCID: PMC5037216.
- (3). Croisant SA, Haque Laz T, Rahman M, Berenson AB. Gender differences in risk behaviors among high school youth. Glob Adv Health Med. 2013 Sep;2(5):16-22. doi: 10.7453/gahmj.2013.045. PMID: 24416689; PMCID: PMC3833558.
- (4). Tim Jannusch, Darren Shannon, Michaele Völler, Finbarr Murphy, Martin Mullins. Smartphone Use While Driving: An Investigation of Young Novice Driver (YND) Behaviour. Transportation Research Part F: Traffic Psychology and Behaviour, Volume 77, 2021, Pages 209-220,ISSN 1369-8478,https://doi.org/10.1016/j.trf.2020.12.013.
- (5). Gavin C. Barr, Kathleen E. Kane, Robert D. Barraco, Timarie Rayburg, Lauren Demers, Chadd K. Kraus, Marna Rayl Greenberg, Valerie A. Rupp, Kimberly M. Hamilton, Bryan G. Kane, Gender Differences in Perceptions and Self-reported Driving Behaviors Among Teenagers, The Journal of Emergency Medicine,
- Volume 48, Issue 3, 2015, Pages 366-370.e3, ISSN 0736-4679, https://doi.org/10.1016/j.jemermed.2014.09.055.
- [6] Highway Statistics Series published by the Federal Highway Administration, U.S. Department of Transportation <u>https://www.fhwa.dot.gov/policyinformation/statistics.cfm</u>
- [7] Annual Estimates of the Resident Population by Single Year of Age and Sex for California: April 1, 2010 to July 1, 2019 (SC-EST2019-SYASEX-06)
- (8) Vaca FE, Li K, Tewahade S, Fell JC, Haynie DL, Simons-Morton BG, Romano E. Factors Contributing to Delay in Driving Licensure Among U.S. High School Students and Young Adults. J Adolesc Health. 2021 Jan;68(1):191-198. doi: 10.1016/j.jadohealth.2020.05.003. Epub 2020 Jul 6. PMID: 32646830; PMCID: PMC8136290.
- (9) Brown, Rod and Susan L. Handy (2015) Factors Associated with High School Students' Delayed Acquisition of a Driver's License: Insights from Three Northern California Schools. Transportation Research Record 2495, 1 – 13)
- (10) Simons-Morton BG, Ouimet MC, Catalano RF. Parenting and the young driver problem. Am J Prev Med. 2008 Sep;35(3 Suppl):S294-303. doi: 10.1016/j.amepre.2008.06.018. PMID: 18702985; PMCID: PMC2562681.
- (11) Wiberg M. Gender differences in the Swedish driving-license test. Journal of Safety Research. 2006 ;37(3):285-291. DOI: 10.1016/j.jsr.2006.02.005. PMID: 16815446.

How Can Effective Policies Close Loopholes in Carbon Markets? By Tulesi Suresh

Abstract

Surprisingly, 90% of offsetting credits approved by the world's leading standard for the carbon offset market, Verra, do not genuinely represent carbon reductions (SourceMaterial et al., 2023). By buying carbon credits, companies can invest money into projects geared towards improving the future climate that would not have otherwise been funded. These carbon credits allow them to offset emissions. However, due to the unregulated nature of carbon markets worldwide, there are many loopholes and limitations. In addition, large corporations can exploit carbon markets for their personal interests or capital gain and not necessarily to reduce greenhouse gas emissions. By compiling information from various sources on carbon markets and their limitations, this paper analyzes how effective policies can be written to close existing loopholes. A summary will be presented to recommend how the carbon market could become a more reliable tool for curbing carbon emissions. In the conclusion of this paper, it is deduced that carbon market loopholes could be closed with better government regulation, increased development of clean technologies, and a more free market for carbon credit pricing.

Introduction

Forest fires blazing across North America, ocean levels rising worldwide, and record heat waves have one driving force in common: carbon. In 2021, carbon dioxide was responsible for two-thirds of the total heating influence of all greenhouse gases combined, drastically affecting global climate change events (Lindsay, 2023). Since carbon is not returned to the earth as fast as humans emit it, its atmospheric levels have skyrocketed to above 400 ppm (NOAA Global Monitoring Lab, 2023). Atmospheric carbon levels should not exceed 350 ppm, according to climate scientists (Hansen et al, 2008). When carbon levels are too high, heat gets trapped in the atmosphere and creates a chain reaction of global warming effects. This chain reaction disrupts the physical and biological systems of Earth on which humans depend.

This concentration of carbon in the air is not sustainable for future generations. This problem is recognized by The United Nations in their 17 Sustainable Development Goals, which are a blueprint for achieving a "more sustainable future for all" (United Nations, 2015). For the future prosperity of people and the planet, each of these goals must be worked on simultaneously to be successful by 2030 (United Nations, 2015). From climate change to economic development, each goal's successes cannot come at the cost of another goal. Thus, new strategies that combat multiple goals at the same time are necessary for a more sustainable future.

The United Nations' concern over carbon has set a precedent for consumers' concerns. In recent years, there has been an increase in carbon-conscious customers who care about the environmental practices of their favorite companies. They are willing to spend more money on companies that have made environmental, social, and governance (ESG) related claims (NielsenIQ & McKinsey, 2022). In the United States, products with ESG-related claims have achieved disproportionate growth compared to products that do not have these claims (NielsenIQ

& McKinsey, 2022). Driven by these consumer demands, companies have begun to embrace ESG, which is a quantifiable measure of a company's effects on the environment.

To market their environmental social governance, companies publish ESG reports. Companies often greenwash their brand, falsely marketing themselves as environmentally friendly. Quantifiable greenhouse gas emission reports can prevent greenwashing and empty environmental claims. In summary, ESG will grow in importance as companies use it to appeal to informed, eco-conscious customers and investors (Corporate Governance Institute, n.d.).

Societal pressures such as consumer demand impact decisions that companies make about their operations. However, the bottom line for all companies is to make a profit. Thus, strategies that stimulate economic growth while tackling climate change are crucial for a sustainable future. To do this, carbon reductions must fit within the current economic system.

As one attempt to reduce carbon emissions in a capitalistic society, carbon markets have raced to the forefront. Carbon markets are trading systems where "carbon credits" are bought and sold. Carbon credits help companies that are unable to eliminate emissions along their supply chains. Instead, carbon credits allow them to offset emissions. These credits are especially helpful for companies aiming for net-zero emissions, meaning that they remove the same amount of greenhouse gases (GHG) from the air as they produce (Blaufelder et al., 2021). Each carbon credit purchased by a company represents the equivalent of one ton of carbon. Then, the money spent on this credit is invested in a project that reduces carbon emissions. In theory, this process aligns with the sustainable development goals; it allows companies to grow while investing in sustainable solutions and meeting their climate goals. However, in practice, there is a multitude of issues with carbon markets including the validity and accountability of the emissions reductions. This article will define the loopholes present in current carbon markets and propose how effective policy can stop companies from exploiting those loopholes.

How Carbon Markets Operate

The carbon market system aims to reduce the amount of greenhouse gas emissions that industries release into the atmosphere. It works as a trading platform for "carbon credits." Each credit represents a certain amount of reduced emissions. Companies that produce fewer emissions can earn these credits, while those that emit more than their limit can buy credits from others to offset their excess emissions. Thus, the carbon market encourages businesses to be more environmentally friendly.

Carbon Market Basics

Carbon markets are places where carbon credits are bought and sold. It is a method used by businesses to reduce their carbon footprints. Each carbon credit is equal to one ton of carbon. This credit becomes a commodity that gets assigned a price. This price differs based on the market; overall, many argue that the price of emissions is too cheap to effectively reduce emissions (Black, Perry, & Zhunussova, 2022). Since carbon is relatively inexpensive, companies often choose to offset emissions rather than reduce their emissions. Carbon markets are similar to the stock market because their success or failure is reliant on the supply and demand of emissions. To explain, if the price of carbon credits is low, demand increases while supply decreases.

Furthermore, carbon markets were created to help companies meet emissions reduction goals. Companies that were unable to reduce their emissions can invest in projects that reduce carbon emissions. Thus, the carbon that is still being used by one company is "canceled out" by the reduction projects of the other entity.

Types of Markets

Compliance markets and voluntary markets are the two main types of carbon markets. In compliance markets, companies are forced to comply with regulatory acts by purchasing carbon credits. These compliance markets house "cap-and-trade" programs, which give carbon allowances to companies that can then purchase credits if they go over their budgeted amount of carbon (Carbon Offset Guide, n.d.). Then, companies with lower emissions can sell their extra allocation of carbon to the companies that need it. An example of a compliance market will be dissected in a later section of this paper.

On the other hand, businesses use voluntary markets by choice. By purchasing carbon offsets in voluntary markets, the business is investing in projects that can avoid or reduce GHG emissions (Carbon Offset Guide, n.d.). This system is different from compliance markets because voluntary markets can finance new projects. Carbon credits and offsets are slightly different due to their use in the two different markets but will be used interchangeably for this article (CarbonCredits.com, n.d.).

Moving on, international carbon markets became more commonplace after The Kyoto Protocol (1997) described international emissions trading to the United Nations Framework Convention on Climate Change (UNFCCC). However, regional and national markets have grown in popularity in recent years. For example, China started the world's largest emissions trading system in 2021 which is estimated to cover 1/7 of global emissions from burning fossil fuels (International Energy Agency, 2021). The carbon market has also been a tool to fund environmental projects in underdeveloped communities in the global south. In Tanzania, more than 20 companies have committed to an investment of over \$20 billion in carbon offset credits to fund carbon trading around the country (DGB Group, 2023). Investments in carbon trading can fund projects that protect biodiversity, prevent pollution, improve public health, and create jobs (Blaufelder et al., 2021). However, it should be immediately mentioned that these international projects provide an outlet for companies to send their emissions overseas, rather than dealing with it domestically.

In summary, carbon credits are permits to emit carbon that can be used by a company. They exist in carbon markets, which are either voluntary or compliance markets. Most carbon markets exist to help companies reach their environmental goals, reduce carbon emissions, and fund upcoming projects that will create a more sustainable future. However, carbon markets differ greatly based on the type of market and scope–an international voluntary market does not operate the same as a regional compliance market. Thus, regulating carbon markets is complicated (Kollmuss et al., 2008). Complex systems require policies to effectively manage them. Otherwise, exploitation of the system slips through the cracks and undermines the purpose of the carbon markets. In the next section of this article, various policies governing carbon markets around the world will be examined and compared.

Existing Policies that Regulate Carbon Markets-The Kyoto Protocol

The first carbon market was entered into full force in 2005 as a part of the Kyoto Protocol. This international climate treaty set the stage for future carbon market policy. It established the Clean Development Mechanism (CDM) and the Emissions Trading Scheme (ETS) as a market-based approach for reducing emissions (Kyoto Protocol to the UNFCCC, 1997). These mechanisms marked the beginning of carbon trading.

The central feature of this protocol required countries to limit or reduce their emissions to specified levels. In global politics, this is the first example of carbon reductions having value. It introduced the concept of additionality, which shows that the emissions reductions produced by the projects would not have happened without the investment into them (Kyoto Protocol to the UNFCCC, 1997). As an example, if a carbon credit is traded, the project it funds is reliant on that credit. This means the carbon-reducing project would not have happened without this carbon credit system, ensuring that the credit is valid. However, there was no internationally agreed definition for *additionality*, and assessments were left to justifications case-by-case (Gillenwater, 2012). This does not mean that there were no tools in place. For instance, Legal Tests, Technology Tests, and Common Practice Tests were circulated after the Kyoto Protocol as methods to assess additionality (Trexler, Broefhoff, Kosloff, 2006). Further, the United Nations Framework Convention on Climate Change developed a toolkit recommending scenario-based approaches (UNFCCC Clean Development Mechanism, 2006). However, the analysis is largely subjective. The major problem at hand is the lack of consistency in the assessments. There were no standards set to assess if emission reduction projects happened directly because of investment in carbon marets. Please see *Figure 1* to better understand the term *additionality*.



Figure 1: *Additionality* (American Forest Foundation, 2023). The baseline shows examples of plots that are not matched with the carbon project, and the aggregate shows the carbon reductions of the plots involved with carbon projects. "Carbon Benefit" shows the additionality of a carbon project by comparing the two. The graph shows that the carbon project showed carbon reductions in the long term that did not happen when no carbon project was introduced.

The Paris Agreement

Although the Kyoto Protocol technically remains in force, the Paris Agreement has effectively replaced the Kyoto Protocol after its adoption (Bodansky, 2021). It differs from the Kyoto Protocol because it calls on all countries to set emissions targets rather than just developed countries (Maizland, 2022). In terms of policy, the Paris Agreement is legally binding but calls on each country to make its own policies to meet its goals. It introduces new markets to replace the outdated ones from the Kyoto Protocol and encompasses a wider spectrum of countries to participate in carbon trading.

It is interesting to note that the Paris Agreement also suffers from problems with additionality, but has several tools in place to help mitigate its negative possibilities. The Paris Agreement introduces "Nationally Determined Contributions" which are a requirement for countries to describe their specific climate goals to join the Paris Agreement treaty (Article 4 of the Paris Agreement to the UNFCCC, 2015). Each country must update its post-2020 climate actions every five years to remain as part of the treaty (Article 4 of the Paris Agreement to the UNFCCC, 2015).

Also, the Paris Agreement specifies rules against double-counting of emissions when countries transfer carbon credits to one another (Article 6 of the Paris Agreement to the UNFCCC, 2015). As a review, double counting of emissions is when carbon credits are claimed by more than one entity even though only one carbon benefit is produced.

In conclusion, assessing additionality is becoming more quantifiable under the Paris Agreement, but there is still improvement that can be made to clarify the term in the future.

European Union

The European Union is a leader in the carbon market system. Their Emissions Trading System, a compliance market, has been in effect since 2005 (European Union Climate Action, 2005). It is in its fourth phase (2021-2030) and is constantly revised under its legislative framework (EU Legislative Train Schedule, 2023).

The European Union has many laws in place to ensure the integrity of its carbon markets. One major step they have taken is in applying regulations of financial markets to carbon markets. This puts clear, extensive regulations in place. For example, carbon emissions allowances are classified as financial instruments (Directive on Markets in Financial Instruments, 2014). Additionally, market abuse and misconduct are regulated (Market Abuse Regulation, 2014). Due to these classifications, high integrity standards are applied to all participants in the market. Manipulation, trading of insider information, money laundering, and other problems in financial systems are now prevented in the European Union's carbon markets.

However, there is some debate about whether considering carbon credits as a financial instrument is ideal. This means that climate action and environmentalism are regulated by capitalism. Some argue that capitalism exacerbates, rather than reduces, environmental inequities due to the heart of the system (Bell, 2015). Additionally, aims to keep the price of carbon high will be discussed later on in the paper. Thus, some do not agree that the laws of supply and demand that dictate financial markets should also dictate the carbon market.

China

China holds the global lead in greenhouse gas emissions, and correspondingly, it also occupies a leading position in the scale of its carbon market. Since China emits a high amount of carbon in its industries, its Emissions Trading Scheme (ETS) aims to reduce the impact they have made on the planet in a cost-effective manner. They have the largest operational ETS in the world, which is potentially estimated to cover 1/7 of global fossil fuel emissions (Tiseo, 2023).

Contrary to the European Union, China's policies have not focused on classifying carbon markets as financial systems. Although their most recent Five Year Plan (2021-2025) sets impressive goals for carbon emissions reductions, their policy pathway to deal with carbon finance is ambiguous and complicated (Chen & Wu, 2022). Without carbon markets being considered as financial systems, the mechanisms applied to their economy are not passed over. Thus, the carbon market regulations are not sound and there is not sufficient legal support for carbon transactions (Zhou & Li, 2019). There was a project called "Procedures for the Operation and Management of Clean Development Mechanism Projects" (2005), but it failed to meet the requirements of the current market. Thus, the EU's carbon markets have more thorough policies regulating their carbon markets than China does.

Still, the EU and China cooperate bilaterally on the carbon market (EU and China Partnership on Climate Change, 2005). Some objectives of this partnership are the development

of new technologies for carbon capture and the promotion of clean energy sources. Therefore, due to their cooperation, there are similarities in the technical rules of their carbon markets.

America

Unlike China and the EU, there is no national compliance carbon market system in the United States. However, there is the Regional Greenhouse Gas Initiative (2005), which is a compliance market for participating states in the northeast. Only one state, California, has a formal "cap-and-trade" program (California Board of Regulations, 2012). These compliance markets are heavily regulated. Due to the lack of a national compliance market, policies regulating U.S. markets are mostly based on voluntary markets.

In contrast to the compliance markets in the U.S., voluntary markets do not involve any direct oversight by the government (International Swaps and Derivatives Association [ISDA], 2022). Instead, these carbon credits are issued by "carbon standards" which each have different rules that projects must follow to be certified; some examples of these "standards" are issuing bodies such as Verra, the Gold Standard, and the American Carbon Registry.

Although the government is not directly regulating voluntary markets, U.S. financial regulation considers carbon credits as a "commodity" (ISDA, 2022). Similar to the EU's Emission Trading System, this means that financial rules are imposed on the carbon market in hopes of avoiding abuses of the system.

Inconsistencies

International frameworks exist to keep countries accountable for their carbon reduction claims. They have created international carbon markets–such as the Clean Development Mechanism–where countries can trade carbon credits (2005). However, individual nations are responsible for creating policies to regulate carbon trading. The inconsistency of the policies creates loopholes for exploitation and questions about the future of carbon markets.

How to fix existing loopholes

Due to the lack of consistent policy, various loopholes are exploited in carbon markets. Complex rules based on different countries and different types of markets make accountability and standard practices difficult to judge. This can result in greenwashing, financial exploitation, and false sustainability claims. To prevent these corrupt practices, new policies must be introduced to regulate carbon markets. In this section, each loophole will be followed by a possible solution.

Quality of Carbon Credits

The concept of additionality has been explored in the previous sections of this paper. This concept is one of many that take part in assessing the quality of a carbon credit. Leakage is also considered when looking at the quality of a carbon credit. Leakage occurs when an emission reduction occurs in one place, but causes an increase of emissions in another (Filewod &

McCarney, 2023). This is usually when a country with stricter regulations passes carbon production to a country with weaker regulations, resulting in increased emissions in the producing country. Another term used to assess the quality of carbon credits is permanence. This term states that emissions are prevented forever (Marland et al., 2001). Since carbon dioxide stays in the atmosphere for around 100 years, some have defined permanence as the carbon reduction staying intact for that long, such as in the California compliance market (Song & Moura, 2019). Still, accurately judging a carbon credit's ability to prevent emissions for 100 years is not possible. In reality, permanence is nearly impossible to guarantee. For example, in forest-based offset projects, factors such as land ownership, political turmoil, and fires can unexpectedly damage forests (Song & Moura, 2019). These factors ruin the permanence of carbon credits, but cannot be controlled or avoided.

Leakage and permanence are sufficiently defined, but their regulation is where the biggest loopholes lie. The protocols are not rigorous. The main standard setters have their own procedures and protocols to verify offsets and are not subject to government oversight or regulation (Fredman & Phillips, 2022). Thus, the quality of carbon credits is susceptible to change; credits initially judged to be sound may later be labeled as lower quality, and the system used to judge the credit can warrant different results. In fact, the CEO of Verra, a leading carbon market standard, acknowledges that a large number of once legitimate offsets are now known to be non-additional (Kouchakji, 2022).

Many proposed standards and policy recommendations have been made to remedy the insufficient regulation of carbon credits (Blaufelder et al., 2021). One loophole that needs regulation is leakage–or the distribution of carbon emissions to a country with weaker regulations. One proposed solution to limit leakage is extending carbon constraints to imported goods. This is important because carbon production shifts to the place with the lowest cost to produce. Emissions reductions from more progressive nations are worthless if emissions rise in the country that is producing the good. To account for this problem, imposing the emissions standards of the country importing the goods rather than the country that produced them will reduce leakage. This solution has already been adopted by the European Union in their Carbon Border Adjustment Mechanism (2023). This policy encourages cleaner industrial production in countries that trade with the European Union. If similar policies are implemented in other countries, it would benefit the goals of the importing country while encouraging other countries to reduce their emissions.

However, this only closes the loophole in the domestic market. Since this system depends on the policies of one country being transferred to the country they are importing from, it does not account for the bigger picture of global markets. As more progressive countries decrease their demand for fossil fuels, the price falls in the global market, stimulating the consumption of fossil fuels elsewhere (Mehling, 2021). This is still a form of leakage, since a reduction results in emissions elsewhere.

One way to effectively close this loophole is by decreasing the cost of clean technologies like solar, wind, and geothermal energy (Mehling, 2021). Instead of choosing fossil fuels,
countries will choose clean technologies if the price is competitive. When these technologies can compete on their own, they will become more popular. This has already begun to happen (Nemet, 2019). In fact, solar power is the cheapest electricity in history (International Energy Agency, 2020). Therefore, transitioning to clean energy would reduce leakage in the carbon market.

Altogether, many solutions are in the works to ensure the quality of credits in the carbon market. However, solutions must result in broad systematic changes if the carbon market is to be scaled for major carbon reductions.

The Price of Carbon

For each carbon credit purchased, the buyer is investing in one ton of carbon dioxide being avoided. Interestingly, this does not equate to the same price of one carbon credit. There is a wide range of pricing based on what project and where the carbon credit is bought from, even ranging from \$5 to \$500 or more (Whiting, 2022).

Why is there so much variety? This comes back to the quality of the carbon credit. Since the voluntary market is not effectively regulated, some projects aim to sell as many credits as possible. These low-quality projects lack permanence, additionality, and all factors that make the credit legitimate. These projects can afford to lower the price of their credits because they have lower running costs. The projects save money if they don't properly research and examine how a carbon reduction will be made with their credit (Whiting, 2022). Although these low-cost credits may be desirable for companies looking to offset, it has negative implications for the carbon project and the trustworthiness of the carbon market. High-quality projects cost more and are vital to an effective carbon market.

Along with low-cost credits usually being low-quality, they will also prevent the world from reaching climate goals. According to the Report of the High-Level Commission on Carbon Prices (2017), carbon credits must cost \$40-\$80 each to meet the Paris Agreement target of 2°C warming. To increase the price of carbon, the law of supply and demand can be part of the solution. If the average cost of carbon increases, companies will value carbon more, and may even choose to reduce emissions instead of offsetting. Right now, the demand for credits is increasing rapidly. McKinsey estimates that demand for credits could increase by a factor of 15 or more by 2030 (Blaufelder et al., 2021). If demand increases for carbon credits at this rate, the price of carbon credits will increase on its own.

Fraud

Exploitation of the market begins right from the purchase of credits. Fraud is a significant risk in carbon markets. One example of this is in New Hampshire; a timber company was paid millions of dollars to not cut down trees, even though they were not planning on cutting them down in the first place (Elgin, 2022). This is a case of a misleading claim in the benefit of an investment.

Other problems include manipulating measurements to claim more credits than were truly purchased, as well as selling credits that do not exist, and exploiting weak regulations to commit various financial crimes (Interpol, 2013).

It is relatively simple for companies to purchase carbon credits. After the purchase, however, it is not simple to keep track of the carbon projects that were funded. Throughout the course of the actual carbon project, there is also a lack of accountability. Buyers of carbon credits often "retire" their certificates shortly after purchasing them to remove them from the marketplace (Kaplan et al., 2023). Then, they claim the removal of carbon from the atmosphere for their own calculations even if the carbon project has not been completed. This is not a sufficient accounting system because the buyers are not incentivized to see if the project they have funded follows through (Kaplan et al., 2023). Even though there are systems to file claims if carbon projects are not truthful about their reductions, the buyers of carbon credits may not have the desire or bandwidth to go through this process.

There are multiple solutions to hold buyers and project developers accountable for fraud in the carbon market. One of these is government oversight and higher standards. In the U.S., the Commodity Futures Trading Commission (CFTC) could play a significant role in overseeing the offsetting market (Fredman & Phillips, 2022). As was mentioned in previous sections, the U.S. carbon market considers carbon credits as "commodities" that follow the regulations of the financial market. Therefore, the CFTC could ensure the stability and efficiency of the carbon market. According to CFTC Commissioner Romero, the commission has antifraud authority over spot markets (2023). For these registries that are currently unregulated, CFTC oversight would be vital to keeping the integrity of the U.S. carbon market.

Expanding these standards beyond the U.S. would be much more difficult. Still, solutions to increase accountability are in the works. The Climate Action Data Trust (2023) was developed to connect and aggregate data about the carbon market. This system would enable the transparent accounting of carbon and put an end to various acts of carbon market fraud. It is important to note that the Climate Action Data Trust is not the only system being used to tabulate carbon purchased but is an example of a system that can be part of the solution.

The Real Goal: Carbon Reduction

The low cost of carbon credits raises questions about how much people value emissions reductions. If carbon credits are cheaper than reducing emissions for a company, they will likely opt for offsetting. The GHG Protocol, the dominant global standard for carbon accounting, does not differentiate between removal offsets and avoidance offsets (Kaplan et al., 2023). This means that in the world of carbon credits, avoiding carbon emissions is valued the same as removing carbon emissions. The bottom line is that emissions must be reduced, not just distributed elsewhere. This is widely recognized as the major problem with carbon markets. Thus, the major loophole in carbon markets is choosing to offset rather than reduce emissions.

Discussion of the Future

If carbon emissions reduction goals are not met, mass species extinction, extreme heat, and agriculture crises will make regions of the world uninhabitable (The Nature Conservancy, 2018). Thus, the race to expand carbon markets begins. By 2050, voluntary carbon markets alone are poised to surge to \$250 billion (Morgan Stanley, 2023). As demand for more carbon credits increases, scaling the size of carbon markets to meet demand is the next challenge. There are many discussions about how to scale carbon markets, such as McKinsey's blueprint that prioritizes clear signs of demand (Blaufelder et al., 2021). Critical improvements to markets must be made if it is to be a prominent tool to fight the climate crisis.

Contrary to future catastrophes, positive motivators can also guide the growth of carbon markets. One of these motivators is happiness. There is a direct, significant correlation between a climate-friendly life and a happy life, and the happiest countries are the ones closest to meeting the United Nations' 17 Sustainable Development Goals (Sameer et al., 2021). This means that the growth and improvements of more sustainable systems will not limit people's happiness; having enjoyment and living sustainably are not mutually exclusive. In fact, it has been found that happiness levels plateau in wealthy countries such as the United States unless they become more sustainable (De Neve & Sachs, 2020). This counters the assumption that countries that are attempting to be more sustainable have to give up on a fulfilling quality of life. Improving carbon markets both domestically and internationally can help countries be happier and avoid climate grief.

Even if carbon markets may help improve mental health in different countries, some have questioned if carbon markets are truly beneficial. Skeptics of scaling up carbon markets argue that it is not what the climate needs due to the loopholes mentioned earlier in this paper. The Green Finance Observatory expressed serious concerns about scaling up voluntary carbon markets, including human rights abuses (2020). Additionally, concerns over environmental injustice have been noticed, meaning that disadvantaged communities systematically experience higher pollution levels (Hernandez-Cortes & Meng, 2023). To explain, some believe that the issues within current carbon markets are too much to overcome while trying to remedy them.

With critics and supporters alike, carbon markets have received more attention in recent years. As they are scaled, their role in the future of sustainability will be uncovered.

Conclusion

The current state of carbon markets reveals critical flaws that must be urgently rectified. By implementing standardized evaluation processes, robust regulatory frameworks, and transparent oversight, the credibility of carbon credits can be enhanced. However, carbon markets alone are insufficient to combat climate change; a comprehensive approach involving innovation of clean technologies, supportive policies, and responsible consumption is essential. Governments, industries, and individuals must collectively drive systemic changes by prioritizing emissions reduction. By taking action now, the potential of carbon markets can be harvested to help mold a sustainable future.

Works Cited

- About Climate Action Data Trust. (n.d.). Climate Action Data Trust. Retrieved August 27, 2023, from https://climateactiondata.org/about/
- [Additionality] [Infographic]. (2023). American Forest Foundation.
- Bell, K. (2015). Can the capitalist economic system deliver environmental justice? Environmental Research Letters, 10(12). https://doi.org/10.1088/1748-9326/10/12/125017
- Black, S., Parry, I., & Zhunussova, K. (2022, July 21). More Countries Are Pricing Carbon, but Emissions Are Still Too Cheap. https://www.imf.org/en/Blogs/Articles/2022/07/21/blog-more-countries-are-pricing-carbo n-but-emissions-are-still-too-cheap
- Blaufelder, C., Levy, C., Mannion, P., & Pinner, D. (2021, January 29). A blueprint for scaling voluntary carbon markets to meet the climate challenge. McKinsey & Company. https://www.mckinsey.com/capabilities/sustainability/our-insights/a-blueprint-for-scalingvoluntary-carbon-markets-to-meet-the-climate-challenge
- Bodansky, D. (2015). *Introductory Note of Paris Agreement* [Audiovisual Library of International Law]. https://legal.un.org/avl/ha/pa/pa.html
- *A brief history of RGGI.* (n.d.). The Regional Greenhouse Gas Initiative. Retrieved August 27, 2023, from https://www.rggi.org/program-overview-and-design/design-archive
- *Cap-and-Trade Program.* (n.d.). California Air Resources Board. Retrieved August 27, 2023, from https://ww2.arb.ca.gov/our-work/programs/cap-and-trade-program/about
- Cassisa, C., & Fischer, D. (2021, June). *China's Emissions Trading Scheme*. International Energy Agency.
- Chen, B., & Wu, R. (2022). Legal and policy pathways of carbon finance: Comparative analysis of the carbon market in the EU and China. *European Business Organization Law Review*, 24(1), 41-68. https://doi.org/10.1007/s40804-022-00259-x
- *The Clean Development Mechanism*. (n.d.). UNFCCC. Retrieved August 27, 2023, from https://unfccc.int/process-and-meetings/the-kyoto-protocol/mechanisms-under-the-kyotoprotocol/the-clean-development-mechanism
- Clean Development Mechanism. (2006). *Combined tool to identify the baseline scenario and demonstrate additionality* (Methodological Tool No. 02). UNFCCC.
- De Neve, J.-E., & Sachs, J. D. (2020). The SDGs and human well-being: A global analysis of synergies, trade-offs, and regional differences. *Scientific Reports*, 10(1). https://doi.org/10.1038/s41598-020-71916-9
- Department of Climate Change, National Development and Reform Commission. (2005). Measures for Operation and Management of Clean Development Mechanism Projects in China.
- Elgin, B. (2022, March). This Timber Company Sold Millions of Dollars of Useless Carbon Offsets.

https://www.bloomberg.com/news/articles/2022-03-17/timber-ceo-wants-to-reform-flawe d-carbon-offset-market?in_source=embedded-checkout-banner

- *EU and China Partnership on Climate Change* [Press release]. (2005, September 2). https://ec.europa.eu/commission/presscorner/detail/en/MEMO_05_298
- European Commission on Climate Action. (n.d.). *Development of EU ETS (2005-2020)*. Retrieved August 27, 2023, from https://climate.ec.europa.eu/eu-action/eu-emissions-trading-system-eu-ets/development-e u-ets-2005-2020 en
- European Parliament, & Council of the European Union. (2014). DIRECTIVE 2014/65/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 15 May 2014 on markets in financial instruments and amending Directive 2002/92/EC and Directive 2011/61/EU. *Official Journal of the European Union*. http://data.europa.eu/eli/dir/2014/65/oj
- The European Parliament, & Council of the European Union. (2014). REGULATION (EU) No 596/2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 April 2014 on market abuse (market abuse regulation) and repealing Directive 2003/6/EC of the European Parliament and of the Council and Commission Directives. *Official Journal of the European Union*. http://data.europa.eu/eli/reg/2014/596/oj
- European Parliament, & Liese, P. (2023, June 20). *Revision of the EU emission trading system* (*ETS*). Legislative Train Schedule. Retrieved August 27, 2023, from https://www.europarl.europa.eu/legislative-train/package-fit-for-55/file-revision-of-the-eu -emission-trading-system-(ETS)?sid=7101
- Filewod, B., & McCarney, G. (2023). Avoiding carbon leakage from nature-based offsets by design. *One Earth*, *6*(7), 790-802. https://doi.org/10.1016/j.oneear.2023.05.024
- Fredman, A., & Phillips, T. (n.d.). *The CFTC Should Raise Standards and Mitigate Fraud in the Carbon Offsets Market*. Center for American Progress.
- Gillenwater, M. (2012, January). *What is Additionality?* (Part 1: A long-standing problem; Publication No. 001). Greenhouse Gas Management Institute.
- Hansen, J., Sato, M., Kharecha, P., Beerling, D., Berner, R., Masson-Delmotte, V., Pagani, M., Raymo, M., Royer, D. L., & Zachos, J. C. (2008). Target atmospheric co: Where should humanity aim? *The Open Atmospheric Science Journal*, 2(1), 217-231. https://doi.org/10.2174/1874282300802010217
- Hernandez-Cortes, D., & Meng, K. C. (2023). Do environmental markets cause environmental injustice? Evidence from California's carbon market. *Journal of Public Economics*, 217. https://doi.org/10.1016/j.jpubeco.2022.104786
- Interpol. (2013, June). *Guide to Carbon Trading Crime*. Global Initiative Against Transnational Organized Crime.

https://globalinitiative.net/analysis/interpol-guide-to-carbon-trading-crime/

Is scaling up voluntary carbon offset markets really what the climate needs? (2020). Green Finance Observatory.

- Kaplan, R. S., Ramanna, K., & Roston, M. (2023, July/August). Accounting for Carbon Offsets. *Harvard Business Review*.
- Kollmuss, A., Zink, H., & Polycarp, C. (2008, March). *Making Sense of the Voluntary Carbon Market: A Comparison of Carbon Offset Standards*. World Wildlife Fund.
- Kouchakji, K. (2022, April 5). Do renewables need carbon markets? Energy Monitor.
- Kyoto Protocol to the UNFCCC. (2007). In *United Nations Treaties*. https://treaties.un.org/Pages/ViewDetails.aspx?src=IND&mtdsg_no=XXVII-7-a&chapter =27&clang=_en
- Lindsey, R. (2023, May 12). *Climate Change: Atmospheric Carbon Dioxide* (E. Dlugonkencky, Ed.). Climate.gov.

https://www.climate.gov/news-features/understanding-climate/climate-change-atmospher ic-carbon-dioxide

Maizland, L. (2022, November 4). *Global Climate Agreements: Successes and Failures*. Council on Foreign Relations.

https://www.cfr.org/backgrounder/paris-global-climate-change-agreements#:~:text=The% 20Kyoto%20Protocol%20required%20only,countries%20to%20set%20emissions%20tar gets

Mandatory & Voluntary Offset Markets. (n.d.). Carbon Offset Guide. Retrieved August 27, 2023, from

https://www.offsetguide.org/understanding-carbon-offsets/carbon-offset-programs/manda tory-voluntary-offset-markets/

- Marland, G., Fruit, K., & Sedjo, R. (2001). Accounting for sequestered carbon: The question of permanence. *Environmental Science & Policy*, 4(6), 259-268. https://doi.org/10.1016/s1462-9011(01)00038-7
- Mehling, M. (2021). Close the carbon loophole. Elsevier Inc.
- National Oceanic and Atmospheric Administration. (n.d.). *Trends in Atmospheric Carbon Dioxide*. Global Monitoring Laboratory. Retrieved August 26, 2023, from https://gml.noaa.gov/ccgg/trends/
- The Nature Conservancy. (2021, October). Climate Change FAQs. Climate Change Stories.
- Nemet, G. F. (2019). How solar energy became cheap. *A Model for Low-Carbon Innovation*. https://doi.org/10.4324/9780367136604
- NielsenIQ, & McKinsey & Co. (2023, February 6). *Consumers care about sustainability—and back it up with their wallets*. https://www.mckinsey.com/industries/consumer-packaged-goods/our-insights/consumerscare-about-sustainability-and-back-it-up-with-their-wallets#/
- O'Neill, S. (n.d.). *What is the difference between CSR and ESG?* https://www.thecorporategovernanceinstitute.com/insights/lexicon/what-is-the-difference -between-csr-and-esg/
- People's Republic of China. (2021). *Outline of the 14th Five-Year Plan (2021-2025)*. The People's Government of Fujian Province.

https://www.fujian.gov.cn/english/news/202108/t20210809_5665713.htm#:~:text=China %20will%20focus%20on%20the,innovation%20and%20application%20of%20core

- *Report of the High-Level Commission on Carbon Prices*. (2017). Carbon Pricing Leadership Coalition.
- Romero, C. G. (2023, July). *Opening Statement of Commissioner Christy Goldsmith Romero: The CFTC's Role with Voluntary Carbon Credit Markets* [Press release]. https://www.cftc.gov/PressRoom/SpeechesTestimony/romerostatement071923b
- Sameer, Y. M., Elmassah, S., Mertzanis, C., & El-Maghraby, L. (2021). Correction to: Are happier nations more responsible? Examining the link between happiness and sustainability. *Social Indicators Research*, 158(1), 373. https://doi.org/10.1007/s11205-021-02725-4

Song, L. (2019, May 22). An Even More Inconvenient Truth. ProPublica.

SourceMaterial, The Guardian, & Die Zeit. (2023, January 18). The Carbon Con. SourceMaterial.

https://www.source-material.org/vercompanies-carbon-offsetting-claims-inflated-method ologies-flawed/

- Tanzania attracts \$20 billion investment in carbon offset credits. (2023, July 21). DGB Group. https://www.green.earth/news/tanzania-attracts-20-billion-investment-in-carbon-offset-cr edits?utm_medium=email&_hsmi=267248585&_hsenc=p2ANqtz-8blt038UMOvwrW6 MeAsHr9RVAVJzbQmHVg-B0MWKAgy35Zu7B8ptE8BkqquHIcZDwKNhUQcilMU31 qEPd3Ul0hsa3L-P3Meyrd_VJ9DbgZRu21jZ0&utm_content=267248585&utm_source= hs email
- Taxation and Customs Union. (n.d.). *Carbon Border Adjustment Mechanism*. European Commission.

https://taxation-customs.ec.europa.eu/carbon-border-adjustment-mechanism_en

Tiseo, I. (2022, February 6). Coverage of largest emissions trading systems (ETS) worldwide as of 2022 [Chart]. Statista.

https://www.statista.com/statistics/1315109/largest-ets-markets-by-coverage/

- Trexler, M. C., Broekhoff, D. J., & Kosloff, L. H. (2006). A Statistically-driven Approach to Offset-based GHG Additionality Determinations: What Can We Learn? *Sustainable Development Law & Policy*, 6(2).
- *The Ultimate Guide to Understanding Carbon Credits.* (n.d.). CarbonCredits.com. Retrieved August 27, 2023, from

https://carboncredits.com/the-ultimate-guide-to-understanding-carbon-credits/#1 UNFCCC. (2016). *The Paris Agreement* (COP21). UNFCCC.

- United Nations General Assembly. (2015). *Transforming our world: the 2030 Agenda for Sustainable Development*. https://digitallibrary.un.org/record/3923923?ln=en
- *Voluntary Carbon Markets: Analysis of Regulatory Oversight in the US.* (2022, June). International Swaps and Derivatives Association.
- Where the Carbon Offset Market Is Poised to Surge. (2023, April 11). Morgan Stanley.

- Whiting, T. (2022, September). \$500 vs \$5 carbon credits why does cost vary so much in carbon offsetting? https://lune.co/blog/500-vs-5-carbon-credits-why-does-cost-vary-so-much-in-carbon-offs etting/#:~:text=So%20why%20is%20there%20such,of%20costs%20in%20carbon%20cre dits%3F&text=Varying%20carbon%20credit%20costs%20typically,a%20direct%20air% 20capture%20project
- *World Energy Outlook 2020.* (2020, October). International Energy Agency. https://www.iea.org/reports/world-energy-outlook-2020
- Zhou, K., & Li, Y. (2019). Carbon finance and carbon market in China: Progress and challenges. *Journal of Cleaner Production*, *214*, 536-549. https://doi.org/10.1016/j.jclepro.2018.12.298

Effects Of Trash Talk On High School Athletes By Hiram Lannes

Abstract

Trash talk is a captivating, complex part of sports that is often overlooked. The purpose of this paper was to explore how trash talk affects high school athletes. 63 male and female high school athletes completed a survey containing both quantitative and qualitative questions examining how often they trash talked, how often they were the target of trash talk, how large of a role their peers played in teaching them how to trash talk, how often trash talk affected them in a negative way, how early they started using trash talk, and their purpose for using trash talk. Results revealed that high school athletes trash talk often, and they use it with a specific purpose (hinder their opponent's performance/improve their own performance). They start using it from an early age (pre-adolescence), and they learn it primarily thanks to their teammates, parents, coaches, and professionals. Furthermore, trash talk experiences differ between gender, age, and sport played. Males, older athletes, and contact sport athletes have more experience trash talking than females, younger athletes, and non-contact sport athletes, respectively. Trash talk affects high school athletes in a negative way both on and off the field. Thus, trash talk has reached a level of normative acceptance and has both immediate and long-lasting negative effects on high school athletes, and it may harm their mental health. Competition in sport is now more than merely physical; trash talk enhances the mental component of sports beyond what it is thus far.

Introduction

Trash talk has many different definitions. Jeremy Yip defined it as "boastful remarks about the self or insulting remarks about an opponent delivered by a competitor typically before or during a competition," (Yip, 126) whilst Ben Commy defined it as "a deliberate form of verbal communication utilized by individuals for both affirmative personal reasons (i.e., motivation, fun), and disruptive motives toward opponents (i.e., distraction, intimidation)" (Commy, 1002). During this research, anything that falls into either of those definitions will be considered as trash talk. Regardless, trash talk is an especially important but often overlooked aspect in sports. A simple insult or taunt can completely throw off an opponent, causing them to lose their concentration or their cool, resulting in a negative impact on performance. This was perfectly illustrated by the 2006 World Cup Final, where Zidane, a player for the French national team, headbutted an Italian opponent after they made a remark on his sister, causing him to earn a red card and sit out the rest of the match. That match ended up being the last of his career. This is one of many examples of trash talk being used to offset an opponent, and trash talk is highly controversial and often talked about. However, although psychologists and social scientists have previously researched trash talk, they have never focused on trash talk in high school athletes; they have only focused on college athletes and professionals. It is important to conduct research on trash talk because trash talk is widely used in sports, and it not only has a major influence on the playing experience of athletes, but also on the viewing experience of spectators. Furthermore, trash talk may be considered as an unfair advantage, and especially since so many high school

athletes constantly use trash talk whilst playing sports, it is important to consider its effects on society and on their development, as well as the influence trash talk has outside the field on matters such as mental health and self-confidence. High school athletes are still growing and developing, and their experiences with trash talk can impact future generations and how trash talk evolves.

Literature Review – Acceptance in Sports

Trash talk is both widely used and accepted in sports. It is common in esports, face-to-face sports, among fans, and it is considered as an inherent part of sports. According to Jeremy Yip, "trash-talking is a common form of competitive incivility in the workplace" (Yip, 140), and Kevin Kniffin states that, "across domains, trash-talking is a part of communications between rivals" (Kniffin, 366). Furthermore, the average college athlete has been targeted with trash talk by opposing players and fans in one out of every three games (Rainey, 16), which demonstrates how trash talk is a major part of sports. However, not only is trash talk prominent in sports, but it is also accepted as a part of it and has reached normative acceptance (Rainey, 25). According to Jesse Fox, "trash talk where players insult other's ability is generally accepted or excused, even by targeted players who reported negative emotions" (Fox, 4068). Even though the intentions of using trash talk may be different between people, trash talk is an inevitable form of communication that comes up within competitive settings. This is not only limited to traditional sports, trickling down to other forms of competition such as esports. An example of this is within the esports community of CS:GO, where trash talk is predominantly accepted and even considered as a distinct part of the sport (Irwin, 17). Trash talk is thus not only widely used but also accepted in esports, just as much as it is in real sports. The level of acceptance and normality of trash talk in high school athletes will be researched in this paper.

Factors Influencing Trash Talk

Trash talk experiences depend on many factors, such as one's age, gender, background, and past behaviors, but the reasons for trash talking are always similar. First, gender is one of the biggest factors influencing trash talk. Males begin to use trash talk at a younger age than females, and they report higher frequencies of both using and being targeted by trash talk (Granito, 26). This is confirmed in a paper by Dylan Palacio, where it was found that "men trash-talk significantly more than women" (Palacio, 364). Furthermore, the sport being played also has an impact on trash talk: "basketball players reported targeting their opponents with trash talk significantly more often than did swimmers and golfers" (Granito, 28). This is because swimming and golf are seen as more eloquent and educated sports, and because the opponents are closer to each other in basketball. Indeed, "there is more trash-talking in contact sports than noncontact sports" (Kniffin, 364). Basketball is a contact sport, whilst swimming and golf are not, which increases the amount of opportunity to trash talk. Moreover, the level of competition also matters, with trash talk being more prominent among higher competition (Rainey, 26). This is because the higher the level, the more important the result will be, and thus players will be

incentivized to trash talk more to gain any advantage they can. In fact, trash talk is generally always used to gain a competitive advantage, with athletes reporting that they "trash talk to motivate themselves, to psych out and intimidate opponents, and to impair their opponents' performance, suggesting that the ultimate motivation for trash talk is to gain a competitive advantage" (Rainey, 24). Moreover, if an athlete has previously used trash talk, they are more likely to use it again (Kitchings, 33). The factors influencing trash talk in high school athletes will also be researched in this paper.

Impact on Performance

Trash talk also has a negative impact on performance. Trash can throw players off their game, causing them to lose concentration, primarily by being a source of auditory distraction, which in turn increases cognitive distraction (McDermott, 50). This is because, unlike other auditory distractions, trash talk has a negative connotation to it, and thus holds emotional value: "humans are generally able to filter out sound that has no cognitive or emotional value to them, but as noted earlier, the purpose of trash talk is to engage a competitor's mind in psychological stress by manipulating the threat of failure" (McDermott, 50). Competitors cannot filter trash talk out unlike other forms of distraction because of its emotional value, which makes it such an effective source of distraction. Trash talk induces anger (Ring, 13), and this anger influences performance by "indirectly distracting attention away from the task" (Ring, 17). Thus, trash talk harms performance and focus well because it is a source of distraction that induces anger, which consequently "directs attention away from the task and on to the provoker" (Ring, 16-17). The impact of trash talk on performance in high school athletes will equally be researched in this paper.

Ethics

However, it is important to consider the ethics of trash talking. On one hand, trash talk is legitimate when it helps to achieve goals or overcome difficulties, which consequently elevates physical or strategic performance (Johnson, 46). If trash talk helps an individual in their performance, it should be considered as a legitimate part of play. However, trash talk should not distract from the fun of play, be used as a tool to distract an opponent to gain a competitive advantage, or harm the opponent (Duncan, 195). Duncan states that "for [trash talk] to be a genuine part of play it should be spontaneous, creative, light-hearted and fun." However, Nicolas Dixon disagrees with both papers previously mentioned, arguing that trash talking deliberately insults and disrespects opponents (Dixon, 95), and elaborates in a different paper in which he claims that trash talk degrades and humiliates its victims, treating them in a worthless and dismissive manner (Dixon, 211). Moreover, he argues that trash talk is unconnected to skill or strategy, and that instead, trash talk takes away from the skills that sports are designed to test (Dixon, 95). Thus, trash talk is not connected to skill and simply disrespects opponents and takes away from the competition. He concludes by saying that "we cannot immunize trash talking from the moral condemnation that we direct at verbal insults in other contexts" (Dixon, 95). Trash talk

should be considered just as illegitimate in sports as other verbal insults, and it should be condemned and not a part of play. Thus, the ethics of trash talking in sports are unclear.

Gap in the Literature

Although general research has been done on trash talk, no research about trash talk has been done on high school athletes. Thus, my gap is high school athletes, and the question guiding this research is "How does trash talk affect high school athletes?" All research papers have been done on college athletes or other populations, all above high school age. Thus, a research paper on high school athletes is necessary to examine, explore, and assess trash talk in those populations. According to Vincent Granito, "surveys of high school and younger athletes will be necessary to assess trash talk in those populations" (Granito, 31). Furthermore, research that "examines whether trash-talking about distantly related topics such as physical appearance also exists at different levels of sport such as high school would be helpful" (Kniffin, 363). Therefore, this research paper will attempt to explore how trash talk affects high school athletes.

Hypotheses and Rationale

First Hypothesis: Overall trash talk usage in high school athletes will be on the lower side, and trash talk will only affect them on the field, not off the field.

Second hypothesis: Boys will report trash talking more, being the recipient of more trash talk, trash talking and being the target of trash talk from a younger age, and that trash talk affects them less both on and off the field compared to girls.

Third and fourth hypotheses: Same hypotheses as the second hypothesis, except replacing males with older athletes and contact sport athletes, and females with younger athletes and non-contact sport athletes for the third and fourth hypotheses, respectively.

Rationale for Hypotheses: The rationale for these hypotheses is that these are the findings of previous papers examining trash talk in college athletes, such as Vincent Granito's paper, Dylan Palacio's paper, and Jesse Fox's paper. Therefore, it makes sense that the findings in this paper, which examines high school athletes, should be like those found in previous papers examining college athletes.

Methodology

A mix of quantitative and qualitative research will be used for this paper. This is called "mixed research," which according to Shorten and Smith, is a research method where "researchers collect and analyze both quantitative and qualitative data within the same study" (Shorten, 2). This type of research will be beneficial because it will help us "gain a better understanding of connections or contradictions between qualitative and quantitative data" (Shorten, 2-3). However, quantitative research will be the research method guiding this paper, with only one single question in the survey being qualitative, all other questions being quantitative data will be useful because according to Kim Astroth,"quantitative research is a method used to answer questions about or explain a phenomenon of interest by

collecting and analyzing objective numerical data, as opposed to subjective narrative data contained in a qualitative study" (Astroth, 283). Therefore, quantitative research will allow us to better understand trash talk by using numerical data. Furthermore, quantitative data was proven to be effective in papers by Kevin M. Kniffin, Dylan Palacio, William Kitchings, and Vincent Granito and David Rainey, where they sent a survey to college athletes about their trash talk experiences to learn how trash talk affects them. However, through qualitative data, we will also be able to qualify the point of view of people who have experienced trash talk happening live themselves rather than solely relying on numbers, and qualitative data was equally proven to be effective in papers by William Kitchings and Vincent Granito. As stated by Shagufta Bhangu, "qualitative research techniques provide a lens for learning about non quantifiable phenomena such as people's experiences" (Banghu, 39). To collect the data, a survey was sent out to high school athletes in Los Angeles using a Google Forms link. All survey questions were based on the paper by Vincent Granito and David Rainey, with minor adjustments to focus the survey on high school athletes. These participants were asked to send the survey to any other high school athletes they knew, and the survey was also sent out to high school coaches so they could give the survey to their players. This survey had a sample size of 63 participants, and these participants played a variety of sports (soccer, basketball, volleyball, tennis, fencing, dance, martial arts), and ranged from younger athletes (freshmen and sophomores, n = 26) to older athletes (juniors and seniors, n = 37), with about half boys (n = 31) and half girls (n = 32). No incentives were given for completing this survey, and participants could simply exit the survey at any moment if they wished to do so. All data collected was completely anonymous.

Survey Questions

The survey had fifteen questions, all based on a paper by Vincent Granito and David Rainey (with minor modifications for high school athletes), and it began by asking participants to identify their grade, gender, and primary sport. Next, participants were asked, to the best of their memory, the age in which they had first been the target of trash talk and the age in which they first directed trash talk at others whilst playing sports. Participants then rated on a Likert type scale ranging from 1-7 (1 = never to 7 = always) how often they have: 1) been the target of trash talk by opposing players, coaches, and fans, 2) targeted opposing players, coaches, and fans with trash talk, 3) heard their teammates or coaches engage in trash talk, 4) had trash talk have a negative effect on their performance, 5) used trash talk to psych themselves up, intimidate their opponent, or hinder the performance of their opponent 6) engaged in trash talk by "getting ugly" (swearing/calling names/belittling the opponent), 7) how large a role parents, siblings, coaches, teammates, opponents, professional athletes, and fans played in teaching them how to use trash talk. As for the qualitative part of the survey, participants would be presented with a box in which they could freely type, where they were asked to identify their primary purpose of using trash talk. Afterwards, back into a quantitative method, participants answered either "yes" or "no" to if trash talk has ever affected them outside of sports, and they then selected any specific

game circumstances that influenced their likelihood of engaging in trash talk (such as if they were playing an important rival).

Collection and Analysis of Data

This research method is easily replicable, since it is no more than a simple survey, and these questions were all asked with the purpose of identifying how often high school athletes use trash talk, how it affects them both on and off the field, and if there are any differences in the use of trash talk in between diverse groups (such as different sports, genders, or grades). For the quantitative data, the mean was calculated for all the data collected, and this data was then tabulated, comparing the different results to each other through gender, sports, and grade, as well as overall results. The mean of the data was collected because it was the simplest and most efficient way of comparing the data to each other, to effectively examine the role of different circumstances influencing the use and perception of trash talk. Means and averages were also not only used in a paper by Vincent Granito and David Rainey, but also in a paper by Kevin M. Kniffin and Dylan Palacio, which are the two papers on which the survey is based on, further justifying the effectiveness of using means to analyze the data. Furthermore, procedures such as MANOVAs, ANOVAs, and analyses conducted using SPSS, were too difficult to execute due to the limited resources, time, and knowledge available. As for the qualitative data, a thematic analysis of the data obtained through the qualitative question was performed. A thematic analysis is "a method for identifying, analyzing and reporting patterns (themes) within data" (Braun and Clarke, 79). In this case, a thematic analysis was useful to elaborate on the intentions behind the use of trash talk, allowing a deeper understanding of the use of trash talk beyond only numbers. The answers to the question were analyzed and codified and were then sorted into six categories (excluding those who had never used trash talk) (Punch, 169).

Results – **Overall Results**

Before examining trash talk differences between gender, age, and type of sport played, the data was analyzed for the entire sample, all of which are listed in Table 1.

Trash Talk Usage and Effects of Trash Talk

Item	High school athletes
Age first targeted by trash talk	9.57
	(2.79)
Age first using trash talk	10.26
	(2.91)

 Table 1

 Overall Results in High School Athletes: Means. (Standard Deviations)

Frequency of being the target of trash talk (1-7)	4.76
	(1.84)
Frequency of opposing other players with trash talk (1-7)	3.97
	(2.21)
Frequency of teammates engaging in trash talk (1-7)	5.16
	(1.79)
Frequency of negative impacts of trash talk (1-7)	4.03
	(2.02)
Frequency of trash talk with a competitive purpose (1-7)	4.35
	(2.14)
Frequency of "ugly" trash talk engagement (1-7)	1.95
	(1.4)
Role of surrounding people (1-5)	3.57
	(1.2)
Trash talk has affected me outside of sports	61.9%
	(n = 39)
Trash talk has never affected me outside of sports	38.1%
	(n = 24)

Reasons for Using Trash Talk

Table 2

Reasons for Using Trash Talk: Definition of Themes and their Frequency Mentioned

Theme	Definition	Frequency of Appearance
Hinder the opponent's performance	Participants used trash talk with the intention of hindering their opponent's performance by pestering hem, getting in their head, distracting them, or messing with them.	39 times 54%
Psych themselves up	Participants used trash talk to increase their own confidence and improve their own performance. They used trash talk to psych themselves up into believing in their own capabilities.	10 times 14%

Release anger	Participants used trash talk to express and release anger over the score of the game, a referee call, being substituted, or getting fouled.	6 times 8.3%
Revenge	Participants used trash talk in retaliation for getting trash talked themselves.	6 times 8.3%
No reason/ never used trash talk	Participants either had no specific reason to use trash talk or had never used trash talk before.	6 times 8.3%
Friendly competition and fun	Participants used trash talk to make the game more fun and interesting, and to include drama in the game.	5 times 7%

Exploring the Role of Gender, Age, and Sport Played

To ascertain if trash talk experiences varied between different genders, ages, and sports played, the mean result of each survey question was calculated and compared to one another, as explained in the methodology.

Examining the role of gender

These results were based on 63 participants (31 boys and 32 girls). Eleven key dissimilarities were uncovered, and these are tabulated in Table 3. Throughout, a pattern arises from these findings, with trash talk having a greater presence among boys, and boys clearly having more experience in trash talk than girls.

	Gender	
Item	Boys	Girls
Age first targeted by trash talk	8.68 (1.21)	10.44 (2.85)
Age first using trash talk	9.3 (2.87)	11.23 (2.67)
Frequency of being the target of trash talk (1-7)	5.26 (1.81)	4.28 (1.76)

 Table 3

 Gender Differences: Means, (Standard Deviations)

Frequency of opposing other players with	4.71	3.25
trash talk	(2.07)	(2.14)
(1-7)		
requency of teammates engaging in trash talk	5.77	4.56
(1-7)	(1.26)	(2.03)
Frequency of negative impacts of trash talk	3.9	4.16
(1-7)	(2.02)	(2.03)
Frequency of trash talk with a competitive	5.16	3.56
purpose	(1.85)	(2.14)
(1-7)		
Frequency of "ugly" trash talk engagement	2.58	1.34
(1-7)	(2.85)	(0.6)
Role of surrounding people (1-5)	3.9	3.25
	(1.19)	(1.14)
Trash talk has affected me outside of sports	38.1%	84.4%
(1-7)	(n = 12)	(n = 27)
Trash talk has never affected me outside of	61.9%	15.6%
sports	(n = 19)	(n = 5)
(1-7)		

Examining the role of age

These results were based on 37 upper-class athletes (juniors and seniors) and 26 underclass athletes (first-year students and sophomores). Eleven distinctions were uncovered, all of which are tabulated in Table 4. Once more, a pattern emerges from these findings, suggesting upper-class athletes also have more experience in trash talk than under-class athletes.

Age Dijjerences. Means, (Standard Deviations)		
	Grade	
Item	9 th and 10 th	11 th and 12 th
Age first targeted by trash talk	9.46 (2.5)	9.65 (3.01)

 Table 4

 Age Differences: Means, (Standard Deviations)

Age first using trash talk	10.42	10.14
	(2.66)	(3.12)
Frequency of being the target of trash talk	4.69	4.81
(1-7)	(1.95)	(1.78)
Frequency of opposing other players with	3.58	4.24
trash talk	(5.05)	(2.18)
(1-7)		
Frequency of teammates engaging in trash	5	5.27
talk	(1.85)	(1.76)
(1-7)		
Frequency of negative impacts of trash talk	4.42	3.76
(1-7)	(1.86)	(2.1)
Frequency of trash talk with a competitive	3.96	4.62
purpose	(2.11)	(2.15)
(1-7)		
Frequency of "ugly" trash talk engagement	1.54	2.24
(1-7)	(0.9)	(1.61)
Role of surrounding people (1-5)	3.5	3.62
	(1.21)	(1.21)
Frash talk has affected me outside of sports	69.2%	56.8%
(1-7)	(n = 18)	(n = 21)
Trash talk has never affected me outside of	30.8%	43.2%
sports	(n = 8)	(n = 16)
(1-7)		

Examining the role of sports

These results were based on 45 athletes that played a contact sport (soccer, basketball, fencing, and martial arts) and 18 athletes that played a non-contact sport (volleyball, tennis, dance, and swimming). Eleven notable dissimilarities were discovered, all of which are tabulated in Table 5. One last time, a pattern emanates from these results, suggesting trash talk has a greater presence in contact sports.

	Sport	
Item	Contact Sport	Non-Contact Sport
Age first targeted by trash talk	9.2 (2.5)	10.5 (3.31)
Age first using trash talk	9.75 (2.72)	11.5 (3.07)
Frequency of being the target of trash talk (1 = never, 7 = always)	5.22 (1.76)	3.61 (1.54)
Frequency of opposing other players with trash talk (Likert type scale, 1-7)	4.58 (2.03)	2.44 (1.95)
requency of teammates engaging in trash talk (1-7)	5.6 (1.5)	4.06 (2.01)
Frequency of negative impacts of trash talk (1-7)	4.1 (2.03)	3.89 (2.03)
Frequency of trash talk with a competitive purpose (1-7)	4.8 (1.98)	3.22 (2.16)
Frequency of "ugly" trash talk engagement (1-7)	2.18 (1.54)	1.39 (0.7)
Role of surrounding people (1-5)	3.67 (1.17)	3.33 (1.28)
Trash talk has affected me outside of sports (1-7)	55.6% (n = 25)	77.8% (n = 14)
Trash talk has never affected me outside of sports (1-7)	44.4% (n = 20)	22.2% (n = 4)

Table 5Sport Differences: Means, (Standard Deviations)

Discussion

The survey results suggest several things. First off, a considerable amount of trash talk is happening, with participants reporting being the target of trash talk often (4.76 on a scale of 1-7), and reporting trash talking sometimes (3.97 on a scale from 1-7). It starts from an early age as well, with the average participant having started trash talking before they were eleven years old, and first being trash talked from an even earlier age, before ten years old. The mean age of initially using trash talk was older than the mean age of first being the target of trash talk, and the reported frequency of trash talk usage was lower than the reported frequency of being targeted with trash talk. Therefore, high school athletes believe others trash talk more than they do. Thus, an explanation for the trash talk present may be that these high schoolers see themselves as victims of trash talk, and therefore justify their trash talking because they feel that they were the ones originally confronted with trash talk. Another explanation may be that peers, colleagues, and contemporaries play a huge part in teaching athletes how to trash talk in the first place (3.57 on a scale from 1-7), perhaps subconsciously, thereby increasing the likelihood of these athletes engaging in trash talk. This demonstrates that trash talk does not come from within the athlete, but instead, that they learned how to trash talk from elsewhere. Therefore, it is a process that is learned and internalized. This may also explain why it is present at such an early age, especially in a world where technology is readily available to all kids and teenagers. Young athletes can easily see professional athletes trash talking to each other and may decide to copy that behavior.

However, a trend that was immensely clear among all groups was that high school athletes almost never got "ugly" (using swear words, harsh insults) when trash talking (1.97 on a scale from 1-7 with a standard deviation of only 1.4). This may be because the level of competition of high school sports is not high enough to a degree that would incentivize more extreme trash talk, or simply because the athletes are still young, and are therefore not comfortable with degrading their opponent through harsher methods. Despite this, high school athletes do use trash talk with a purpose. The main reason for using trash talk, with a frequency of appearance of 54%, was to hinder their opponent's performance, followed by to psych themselves up, with a frequency of appearance of 14%. They use trash talk as a strategy to gain a competitive advantage, whether that be by messing with or distracting the opponent, thereby hindering their performance, or by enhancing their own performance by increasing their confidence and belief in their own capabilities. Furthermore, an explanation for the high number of athletes using trash talk to hinder their opponent's performance may be that they know its effects firsthand. Trash talk often had a negative effect on the performance of athletes (4.07 on a scale from 1-7), and 61.9% of participants reported that trash talk had affected them outside of sports. Therefore, since they know how powerful trash talk can be, they try to use it to their advantage. Furthermore, these statistics show the immense influence and power that trash talk holds over athletes. Not only can trash talk throw them off their game, but it also affects them outside of sports. This brings up the question of the effects of trash talk on the mental health of athletes; it may have lasting effects on them, and it can be dangerous for these high school athletes, considering they are still mentally developing.

The game circumstance that increased the likelihood of engaging in trash talk the most was "the opponent is an important rival" (76.2%). This can be explained because of the level of competition and stakes behind the game. Trash talks increases with the level of competition (Granito, 27), and therefore, if the opponent is an important rival, the level of competition is automatically increased, because there are stakes behind the game, such as pride and leaderboard standings, which incentivizes both teams to play as well as possible. Thus, it makes sense that a noteworthy competitor would increase the probability of using trash talk, because athletes would want to use trash talk to gain a competitive advantage to win the game. The next highest circumstance was "your teammates do a lot of trash talking" (66.7%). This is because of the concept of social proof, which states that "people copy the actions of others in an attempt to emulate behavior in certain situations" (Cialdini, 116). If an athlete sees their teammates doing a great deal of trash talking, they are more probable to join in with them, rather than if they were alone; this comes back to the idea of athletes rationalizing their use of trash talk.

Hence, the first hypothesis is not supported. In reality, trash talk usage in high school athletes is on the higher side, and it affects the majority both on and off the field.

Gender, Age, and Sport Differences

The data suggests that certain variables influence the use of trash talk. Regarding gender, boys reported trash talking more, being the recipient of more trash talk, trash talking and being the target of trash talk from a younger age, and that trash talk affected them less both on and off the field than girls did. Accordingly, the second hypothesis is supported. An explanation for this may be that males often feel like they need to trash talk more to seem manlier and scarier to their opponent, and to establish who the better player is because of gender norms and socialization. This also explains why they use it from a younger age, which, consequently, leads them to get used to it quicker. Because of this, it affects them less than it does for girls. Another explanation may be that female athletes are not as disposed to disclose their use in trash talk, or that males, either purposefully or subconsciously, over-report their trash talk to boast. Furthermore, females have simply not had as much competitive experience as males have and may still be catching up in terms of their trash talk. It is possible that both groups will trash talk the same amount in the future.

Older athletes reported trash talking more, being the recipient of more trash talk, trash talking and being the target of trash talk from a younger age, and that trash talk affected them less both on and off the field than younger athletes did. Thus, the third hypothesis is supported. An explanation for this is that older athletes have had more opportunities to trash talk, since they have been in high school for longer. Consequently, they have gotten more used to it and have more experience trash talking compared to younger athletes, who are still learning how to trash talk. Furthermore, because of this experience, older athletes learn to deal with trash talk better than younger athletes do, and so trash talk affects them less. Furthermore, older athletes may also

trash talk more because they feel older and superior, especially because of the height and growth differences.

CSA reported trash talking more, being the victim of more trash talk, trash talking and being the target of trash talk from a younger age, and that trash talk affected them less both on and off the field than NCSA did. Therefore, the fourth hypothesis is supported. An explanation is that since opponents are closer to each other in contact sports, there are naturally more opportunities to trash talk with each other. The proximity of contact sports may encourage trash talk, especially considering that trash talk sports tend to be rougher and more physical than non-contact sports, further creating opportunities for tension in between opponents, which may lead to more trash talk. This leads to these athletes using it at a younger age, getting used to it quicker, and thus it affects them less.

Previous Research

The results of this research are like results from previous research regarding trash talk conducted on college athletes (instead of high school athletes). These previous papers with comparable results were by Vincent Granito, Karen McDermott, Ben Conmy, and Dylan Palacio. The same results were found for gender and sports differences (and no research had been done on age differences). However, one difference between this research and previous research is that previous research, done on college athletes, had findings that indicated that trash talk did not affect college athletes in a negative way outside of sports, it only affected them whilst playing. In contrast, this paper has findings that suggest trash talk does, in fact, affect high school athletes in a negative way, both on and off the field. Thus, this paper suggests that talk has both immediate and long-lasting negative effects on high school athletes. Otherwise, all other results are similar, if not the same.

Limitations

However, it is crucial to identify several limitations in this research. First off, the sample size of this survey was only sixty-three people. A survey with far more participants would certainly represent the effect of trash talk on high school athletes more accurately. Furthermore, there was not an equal representation of people in the survey. Although the number of boys (32) and girls (33) was close, there were far more participants who played a contact sport (45) than participants who played a non-contact sport (18), and only seven sports were represented. Moreover, there were more older athletes (37) than younger athletes (26), with most being 11th graders (20). In addition to this, the sample was demographically narrow; many of the participants came from the same high school and from the same sports teams in Los Angeles, so they might have naturally reported more similar answers than if they had come from many various high schools in Los Angeles. The limitations regarding sample sizes and representation are due to limited resources and time. Furthermore, procedures such as MANOVAs, ANOVAs, and analyses conducted using SPSS, were equally too difficult to execute due to the limited resources, time, and knowledge available. Moreover, various limitations center on surveys

requiring participants to self-report rather than direct observation. For example, participants may have had biases when answering the questions, such as males saying they trash talk more to appear manlier. Similarly, participants may have had an overestimation or an underestimated reality. They may have perceived events to have happened more, or less, than the amount they happened. The perception of the scale may also be different between participants. For example, what one participant believes is a rating of 5, another participant may think is a rating of 4 or 6. Finally, participants may simply not have fully understood a question or may not have fully concentrated on the survey whilst they were taking it, leading to inaccurate answers.

Conclusion

Trash talk is an established practice within high school athletes with normative acceptance; high school athletes trash talk often and it is an accepted custom in high school sports. They do not get as harsh with it as do college athletes, but they do use it with a specific purpose (hinder their opponent's performance/improve their own performance). They start using it from an early age (pre-adolescence), and they learn it primarily thanks to their teammates, parents, coaches, and professionals. Furthermore, trash talk experiences differ between gender, age, and sport played. Trash talk affects high school athletes in a negative way (by harming their performance/making them lose confidence) both on and off the field. Thus, trash talk has both immediate and long-lasting negative effects on high school athletes.

Implications

Trash talk is an established part of sports that will not go away any time soon. This research confirms the presence of trash talk within high school athletes, now in addition to college athletes. This presence has multiple implications; the first of which being that competition in sport is more than merely physical. Trash talk enhances the mental component of sports beyond what it is thus far. Previously, athletes had to deal with mental components such as pressure, anxiety, confidence, and mental toughness, but now, with the establishment of trash talk as an accepted practice, athletes must deal with being pestered by their opponents. Thus, athletes who obtain the ability to become numb to the effects of trash talk gain an immense advantage over those who do not. Furthermore, because trash talk is uncivil (Yip, 140), it may harm the mental health of athletes, specifically high school athletes, who have not finished developing yet. This brings up the question of the ethics of trash talk; how should it be dealt with? Should it be banned in all competitions? This would certainly be hard to regulate. Or perhaps it should only be banned within high school sports, which is the demographic it affects the most anyway.

Future Research

Future research should have larger sample sizes with full representation in terms of demography, age, sports, and gender. Furthermore, observational studies and experiments should be done to see how trash talk functions in real time, because there is only so much to learn with quantitative and qualitative data. Research on how trash talk affects adults and children would

also be beneficial; they are the only groups in which trash talk has not yet been researched. More precisely, regarding adults, research should be done to see the difference in trash talk between professional athletes and recreational athletes. More in-depth research on trash talk within genders would also be useful. Moreover, research on the evolution of trash talk could be useful to understand trash talk better. Finally, research should be conducted on whether trash talk is harmful to mental health eventually, because based on this research, it is clear trash talk does affect high school athletes in a negative way, both on and off the field. More research on the ethics of trash talk would also be beneficial. Trash talk is a captivating, complex part of sports that warrants further research.

Works Cited

- Astroth, Kim Schafer, and Seon Yoon Chung. "Focusing on the Fundamentals: Reading Quantitative Research with a Critical Eye." *Nephrology Nursing Journal: Journal of the American Nephrology Nurses' Association*, U.S. National Library of Medicine, 2018, <u>https://pubmed.ncbi.nlm.nih.gov/30304622/</u>.
- Bhangu, Shagufta, et al. "Introduction to Qualitative Research Methods Part I." Perspectives in Clinical Research, vol. 14, no. 1, Jan. 2023, pp. 39–42. EBSCOhost, <u>https://doi.org/10.4103/picr.picr_253_22</u>.
- Braun, Virginia, and Victoria Clarke. "Using Thematic Analysis in Psychology." Qualitative Research in Psychology, vol. 3, no. 2, Apr. 2006, pp. 77–101. EBSCOhost, <u>https://doi.org/10.1191/1478088706qp0630a</u>.
- Cialdini, Robert B. Influence: The Psychology of Persuasion. Collins, 2007.
- Conmy, Ben, et al. "Trash Talk in a Competitive Setting: Impact on ... Wiley Online Library." *Wiley Online Library*, Journal of Applied Social Psychology, 3 Apr. 2013, <u>https://onlinelibrary.wiley.com/doi/full/10.1111/jasp.12064</u>.
- Dixon, Nicholas. "The Intrinsic Wrongness of Trash Talking and How It Diminishes the Practice of Sport: Reply to Kershnar." *Digital Object Identifier System*, Sport, Ethics and Philosophy, 22 June 2018, <u>https://doi.org/10.1080/17511321.2017.1421699</u>.
- Dixon, Nicholas. "Trash Talking as Irrelevant to Athletic Excellence: Response to Summers." *Taylor & Francis*, Journal of the Philosophy of Sport, 19 Jan. 2012, <u>https://www.tandfonline.com/doi/abs/10.1080/00948705.2008.9714729</u>.
- Duncan, Samuel. "Sledging in Sport—Playful Banter, or Mean-Spirited Insults? A Study of Sledging's Place in Play." *Digital Object Identifier System*, Sport, Ethics and Philosophy, 25 Feb. 2018, <u>https://doi.org/10.1080/17511321.2018.1432677</u>.
- Fox, Jesse, et al. "Player Experiences in a Massively Multiplayer Online Game: A Diary ..." Sage Journals, 11 Apr. 2018, https://journals.sagepub.com/doi/10.1177/1461444818767102.
- Irwin, Sidney V., et al. "The Mind Games Have Already Started: An In-Depth Examination of Trash Talking in Counter-Strike: Global Offensive Esports Using Practice Theory: Sciencegate." *Journal of Gaming & Virtual Worlds*, INTELLECT, 1 June 2021, https://www.sciencegate.app/document/10.1386/jgvw_00035_1.
- Johnson, Christopher, and Jason Taylor. "More than Bullshit: Trash Talk and Other Psychological Tests of Sporting Excellence." *Digital Object Identifier System*, Sport, Ethics and Philosophy, 21 Oct. 2018, <u>https://doi.org/10.1080/17511321.2018.1535521</u>.
- Kitchings, William. "Trash Talk Behavior amongst Collegiate Athletes: An Application of the Theory of Planned Behavior." *Semantic Scholar*, Florida State University, 1 Jan. 1970, <u>https://www.semanticscholar.org/paper/Trash-Talk-Behavior-Amongst-Collegiate-Athlete</u> <u>s%3A-An-Kitchings/dd93147cd5495436365213d14bdf84df73cd6b16</u>.

- Kniffin, Kevin M., and Dylan Palacio. "Trash-Talking and Trolling Human Nature." SpringerLink, Springer US, 26 May 2018, <u>https://link.springer.com/article/10.1007/s12110-018-9317-3</u>.
- McDermott, Karen C. P. "Emotional Manipulation and Cognitive Distraction as Strategy: The Effects of Verbal Insults on Motivation and Performance in a Competitive Setting." *OpenCommons@UConn*, University of Connecticut, 11 June 2019, <u>https://opencommons.uconn.edu/dissertations/2211/</u>.
- Punch, Keith F. Introduction to Social Research Quantitative and Qualitative Approaches. SAGE, 2014.
- Rainey, David W., and Vincent Granito. "[PDF] Running Head: Trash Talk Experiences Trash Talk Experiences of College Athletes: Semantic Scholar." *Running Head: TRASH TALK EXPERIENCES Trash Talk Experiences of College Athletes*, Semantic Scholar, 2013, <u>https://www.semanticscholar.org/paper/Running-head-%3A-TRASH-TALK-EXPERIEN</u> <u>CES-Trash-Talk-of-Carroll/b39dd8697babce114e83615e9889ed547569aec5</u>.
- Ring, Christopher, et al. "Effects of Antisocial Behavior on Opponent's Anger, Attention, and Performance." *Journal of Sports Sciences*, U.S. National Library of Medicine, 29 Oct. 2018, <u>https://pubmed.ncbi.nlm.nih.gov/30371145/</u>.
- Shorten, Allison, and Joanna Smith. "Mixed Methods Research: Expanding the Evidence Base." *BMJ Journals*, University of Leeds, 26 June 2017, <u>https://ebn.bmj.com/content/ebnurs/early/2017/06/13/eb-2017-102699.full.pdf</u>.
- Yip, Jeremy, et al. "Trash-Talking: Competitive Incivility Motivates Rivalry, Performance, and Unethical Behavior." *Organizational Behavior and Human Decision Processes*, Academic Press, 24 July 2017,

https://www.sciencedirect.com/science/article/pii/S0749597816301157?via%3Dihub.

Resilient Communities: Adapting to Climate Change By Lucas Longo de Almeida

Abstract

Climate change, recognized as a paramount global concern, contributes to severe environmental events with substantial implications for communities worldwide. This article aims to examine the proposal of building resilient communities as a solution to climate change's impacts. Using the reputable online database Google scholar, along with newspaper articles from esteemed sources, a thorough analysis of the supposed benefits — risk reduction, variability of strategies, sustainability and economic benefits — and the concerns associated with the approach was performed. Based on current research, this paper argues for the implementation of resilience in order to adapt to the negative consequences of climate change and enhance overall well-being.

Introduction

Due to its severe and far-reaching impacts, the United Nations deems climate change to be "the defining issue" of our century ("Climate change"). Climate change — or persistent changes in global temperature and weather patterns — contributes to the increased prevalence of numerous environmental phenomena, such as droughts, wildfires, floods, and extreme storms, among others (Stallard and Poynting). This rise in frequency of catastrophic environmental events endangers the livelihoods of nearly half of the world's population; according to the IPCC's sixth assessment report, over 3.3 billion people now live in weather-vulnerable situations (Pote). Thus, for global health to be preserved, it is imperative that we adapt to these new changes in a sustainable way, so as to not exacerbate the issue. One such manner, as proposed by Nicola Wheeler — the Programme Lead of Climate Change and Sustainability at Richmond and Wandsworth Councils — is the creation of a framework for building resilience in communities (Wheeler and Watts 171-172). Wheeler argues that executing a resilience implementation plan in societies provides an excellent strategy for adapting to the impacts of climate change, while ensuring the health and safety of its inhabitants.

Although there are multiple divergent definitions and opinions on what resilience is (Rahill et al. 588), in the context of the weather crisis, it is about communities effectively adapting to and managing the repercussions of climate change, whilst preventing these consequences from intensifying. In her TED talk, Julia Watson fully showcases the efficiency of building a resilient community to adapt to the impacts of climate change by discussing the efforts of the Tofinu tribe. In response to the mass flooding of their homes, the Tofinu built the largest lake city in Africa utilizing eco-friendly, resilient technology, which provided better livelihoods for the population of the area (TED 5:03-5:40). Such an example prompts the discussion: Should communities implement resilience to adapt to the negative consequences of climate change? Despite the challenges and high initial investments associated with implementing community resilience, the potential for risk reduction, the flexibility of strategies, job creation, and the prospect of sustainability make this strategy valuable for societies looking to adapt to the consequences of climate change.

Why Communities Should Implement Resilience - Risk Reduction

Building resilience is often touted as a way of adapting to the weather crisis, as communities not only reduce the risks and vulnerabilities associated with climate change, but can ultimately save lives and improve the livelihoods of their populations. A paper published in the *Health Promotion Journal of Australia* supports this claim, arguing that by adopting a climate resilience framework, societies are capable of successfully adapting to the diverse threats of climate change, thereby better protecting their population from natural disasters and creating overall healthier communities (Bajayo 34). The study further emphasizes that resilience building should be done at the community level, since they are "the most effective vehicle for health promotion activity". Moreover, the case of Cyclone Fani exemplifies how resilience may be able to safeguard population health in a community, as the investment in resilient shelters limited the death toll of the natural disaster to 64, while 20 years prior another similar cyclone killed about 10,000 people (Dicker et al.). This example, along with the data provided, suggests that investments in the building of resilient communities are effective at reducing climate change's risks, which results in the saving of lives and improving livelihoods. Therefore, if society must adapt to climate change, building resilience must be considered.

Variability of Strategies

In addition to reducing the risks of climate change's repercussions, building resilience may be beneficial because of the numerous ways in which it can be achieved. This "flexibility" of possible strategies when adapting to climate change makes implementing resilience more practical and effective in suiting the needs and challenges of different communities. In relation to the weather crisis, resilience is measured through three main variables: the amount of disturbance a society can absorb, the degree to which it is capable of adjusting, and how much it can increase its capacity for adaptation (Prasad et al.). Thus, any actions that tackle climate change through the enhancement of these three measures are the ways resilient communities can be built and improved upon, suggesting that there exists a myriad of different methods to do so. For instance, a paper published by the OECD, an intergovernmental organization with 38 member countries. argues for the use of resilient infrastructure to amplify the amount of damage a region can withstand from the harmful effects of the weather crisis (Organization for Economic Cooperation and Development). Alternatively, different research focuses on how those with higher education tend to be more resilient and less susceptible to natural catastrophes instigated by climate change, implying that education may boost communities' potential for adaptation (O'Neill et al. 520). Although both strategies aim to enhance climate resilience in communities, they do so in significantly different manners, validating the claim that there are multiple diverse approaches to improving adaptation to climate change. Furthermore, these diverse strategies can be applied simultaneously along with other initiatives (Prasad et al), providing a more complete method that effectively improves resilience in societies. Depending on the specific need of the community,

the flexible nature of building resilience results in a context-specific approach that is extremely effective at adapting to climate change, further increasing the efficiency of building resilience.

Sustainability

Adaptation to the weather crisis is incredibly valuable; however, its execution is just as important, which is why resilience is closely linked to sustainability. If adaptation were to incorporate unsustainable methods, then it would also contribute to climate change's rapid development. Hence, one of the main goals of building resilience is to slow the weather crisis' growth by reducing the carbon footprint of the community through the use of eco-friendly technologies. In Watson's TED talk, she gives the example of Calcutta, a large city with over 15 million inhabitants, all of whom have to deal with daily floodings and extremely contaminated rivers (Kaushik; TED 3:34-4:17). In an ingenious manner, the people of Calcutta developed the resilient, sustainable practice of using fish ponds in their floodplains to generate both food and purify water for their inhabitants. According to Watson herself, this eco-friendly technology is so effective and clean that countries around the world are replicating the system (TED 4:17-4:50), further propagating resilience in different communities. Research indicates that this increased use of green technology effectively reduces carbon emissions (Cai), implying that societies that utilize this sustainable method of purification will be able to decrease their carbon footprint and therefore contribute to slowing climate change. These findings suggest that eco-friendly technologies successfully implemented in resilient societies can then spread out to other parts of the world, reducing the carbon footprint of numerous regions and contributing to a better overall environment. Thus, resilient communities should be considered not only for their risk reduction and flexibility, but also for their prospect of sustainability.

Concerns

While the benefits of implementing resilience for adapting to climate change's effects are astoundingly positive, the high initial costs and resources demanded in such a strategy lead some specialists into believing it is unviable for many communities, especially impoverished ones. Current research has found that the lower-income groups are disproportionately affected by weather disasters — such as droughts and floods — and therefore are more vulnerable to climate change (Winsemius et al. 328). In order to promote healthy communities, this susceptibility necessitates adaptation; however, in most cases, building resilient infrastructure to adapt to the various consequences of the weather crisis comes with high upfront costs (Minoja et al.), which many lower-income communities cannot afford. While he acknowledges the positive outcomes of building resilience to climate change, Ioan Fazey, a member of The Department of Environmental Geography at the University of York, argues that it "requires a complex array of resources and capacities" (Fazey et al. 1744), suggesting that some groups won't be able to effectively implement this solution due to its substantial costs. In fact, a study published in *climate policy* — an interdisciplinary, peer-reviewed scientific journal — calculated that the probable global cost for developing countries to successfully adapt to climate change by 2050 is

an overwhelming US\$70–100 billion per year (Narain et al. 1003). Hence, the considerable funds required for establishing resilience in climate-vulnerable communities indicate to some that it is unattainable for those who need it the most.

Costs of Inactivity and Creation of Jobs

As previously established, building resilient communities necessitates considerable investment; however, the costs associated with not adapting may be even greater. Due to the increased frequency of natural disasters, societies that do not have the sufficient resilience and infrastructure to overcome these weather events will have to cope with their tremendous costs. For instance, in 2022 alone, the United States spent about US\$165 billion in damages mostly associated with climate change's repercussions (Milman), demonstrating the significant losses of inactivity. Furthermore, research conducted by the International Monetary Fund - an intergovernmental organization composed of 189 member countries — argues that investing in resilient infrastructure protects public and private capital, causes less debt distress, and so dramatically reduces the overall costs of disasters (Marto). Thus, their findings imply that if the United States had implemented resilience into their communities more effectively, these costs could have been drastically reduced. Additionally, the idea of climate resilience reducing disaster spending is further supported by the findings of the United Nations, who discovered that every dollar invested in adaptation saves six dollars in future disaster spending ("For Every Dollar Invested"). The evidence presented suggests that, even though implementing climate resilience requires significant funding, in the long term, it saves more money than just relying on disaster recovery. Therefore, the argument that climate resilience is too expensive is mostly rendered invalid.

Besides being a financially sound investment, building climate resilience may also create new jobs, promoting health and prosperity in their respective communities. According to Sharan Burrow — the Co-Chair of the Global Commission on the Economy & Climate — building resilient infrastructure creates more jobs than the same investment in unsustainable infrastructure (Burrow), indicating that resilience has greater job-creating capacities than other methods. Furthermore, a paper published by the International Labour Organization (2018) claims that investing in adaptation to climate change is essential for creating employment opportunities and preventing job losses, making it a "prerequisite" of economic growth. The study further argues that throughout Europe, approximately 500,000 additional jobs will be generated from these adaptive measures (International Labour Organization); however, nothing in their study suggests that other societies around the world won't achieve the same results. Therefore, by building resilience to adapt to climate change, various different societies will generate more jobs and grow their economies exponentially. In addition to economic growth, a large body of research associates employment with increased community health and prosperity. Their findings link greater employment rates with lower risks of various health problems, such as diabetes, depression, and heart disease, while also associating job creation with solving various societal needs, like maintaining social cohesions (Adams). These discoveries validate the idea that

besides saving lives, resilience building improves the health of a community through the creation of new jobs. Thus, it can be concluded that implementing resilience generates employment opportunities, which improves both the economies and overall health of the communities.

Conclusion

The vast impacts climate change has on humanity warrants a solution that effectively protects the lives and livelihoods of the billions who live in vulnerable situations. Amidst the various proposals, building resilience in communities stood out for its incredible effectiveness. The overwhelming evidence presented throughout this paper supports the implementation of resilience for its multiple benefits. In addition to protecting the health and lives of many, executing such a strategy is even more efficient for its flexibility and prospect of sustainability. While the initial costs are admittedly high, its potential long-term economic benefits, along with the creation of jobs, also point towards building resilience as an excellent approach to adapting to the weather crisis. Therefore, to answer the question: Should communities implement resilience to adapt to the negative consequences of climate change? Absolutely, for the many reasons presented throughout this paper, communities should prioritize building resilient societies in order to successfully adapt to the various detrimental effects of climate change.

Works Cited

Adams, Jerome. "Improving Individual and Community Health Through Better Employment Opportunities." *Health Affairs*, 2018,

www.healthaffairs.org/content/forefront/improving-individual-and-community-health-thr ough-better-employment-opportunities.

- Bajayo, Rachael. "Building Community Resilience to climate change through Public Health Planning." *Health Promotion Journal of Australia*, vol. 23, no. 1, 2012, pp. 30–36, <u>https://doi.org/10.1071/he12030</u>.
- Burrow, Shaaran. "Commentary: Investing in Sustainable Infrastructure with Just Transition Creates Jobs: New Climate Economy: Commission on the Economy and Climate." *CNBC Africa*, 15 Oct. 2021, <u>https://newclimateeconomy.net/content/commentary-investing-sustainable-infrastructure-</u>

just-transition-creates-jobs

- Cai, Aixin, et al. "How does green technology innovation affect carbon emissions? A spatial econometric analysis of China's provincial panel data." *Frontiers in Environmental Science*, vol. 9, 2021, <u>https://doi.org/10.3389/fenvs.2021.813811</u>.
- "Climate Change." *United Nations*, United Nations, <u>www.un.org/en/global-issues/climate-change</u>. Accessed 30 Apr. 2023.
- Dicker, Sophie, et al. "Saving Lives and Livelihoods: The Benefits of Investments in Climate Change Adaptation and Resilience." *The London School of Economics and Political Science*, 30 Mar. 2021,

www.lse.ac.uk/granthaminstitute/publication/saving-lives-and-livelihoods-the-benefits-of -investments-in-climate-change-adaptation-and-resilience/.

- Fazey, I., et al. "Social Dynamics of Community Resilience Building in the face of climate change: The case of three Scottish communities." *Sustainability Science*, vol. 16, no. 5, 2021, pp. 1731–1747, <u>https://doi.org/10.1007/s11625-021-00950-x</u>.
- For Every Dollar Invested in Climate-Resilient Infrastructure Six Dollars Are Saved, Secretary-General Says in Message for Disaster Risk Reduction Day | UN Press, United Nations, 2019, <u>https://press.un.org/en/2019/sgsm19807.doc.htm</u>
- International Labour Organization. "The Employment Impact of Climate Change Adaptation." *International Labour Organization*, 15 Aug. 2018, www.ilo.org/global/topics/green-jobs/WCMS_645572/lang--en/index.htm.
- Kaushik, Tusheeta. "Why Does Kolkata Experience Flooding?" *Real Estate Industry News & Insights*, 2020, https://content.magicbricks.com/property-news/kolkata-real-estate-news/why-does-kolkat

<u>a-experience-flooding/116007.html</u> Marto, Ricardo, et al. "Building Resilience to Natural Disasters: An Application to Small Developing States." *IMF*, 30 Oct. 2017,

www.imf.org/en/Publications/WP/Issues/2017/10/30/Building-Resilience-to-Natural-Disa sters-An-Application-to-Small-Developing-States-45329.

- Mattiuzzi, Elizabeth, and Eileen Hodge. "Climate-related risks faced by low- and moderate-income communities and communities of color: Survey results." *Federal Reserve Bank of San Francisco, Community Development Research Brief Series*, 2021, pp. 01–37, <u>https://doi.org/10.24148/cdrb2021-3</u>.
- Milman, Oliver. "Extreme Weather Caused 18 Disasters in US Last Year, Costing \$165BN." *The Guardian*, Guardian News and Media, 10 Jan. 2023, <u>www.theguardian.com/environment/2023/jan/10/extreme-weather-climate-crisis-us-death</u> <u>s-financial-damage</u>.
- Minoja, Livia. "Building Resilience Comes at a Higher Initial Cost. How Can We Better Finance It?" *IDB*, 24 Mar. 2022, https://blogs.iadb.org/sostenibilidad/en/building-resilience-comes-at-a-higher-initial-cost-

https://blogs.iadb.org/sostenibilidad/en/building-resilience-comes-at-a-higher-initial-costhow-can-we-better-finance-it/

- Narain, Urvashi, et al. "Estimating costs of adaptation to climate change." *Climate Policy*, vol. 11, no. 3, 2011, pp. 1001–1019, <u>https://doi.org/10.1080/14693062.2011.582387</u>.
- Organization for Economic Cooperation and Development. "Climate-resilient infrastructure." *OECD Environment Policy Papers*, 2018, <u>https://doi.org/10.1787/4fdf9eaf-en</u>.
- O'Neill, Brian C., et al. "The effect of education on determinants of climate change risks." *Nature Sustainability*, vol. 3, no. 7, 2020, pp. 520–528, <u>https://doi.org/10.1038/s41893-020-0512-y</u>.
- Pote, Bon. "3,3 Billion People Exposed to Climate Change: The New IPCC Report Is Without Appeal." *Bon Pote*, 21 Jan. 2023, <u>https://bonpote.com/en/33-billion-people-exposed-to-climate-change-the-new-ipcc-report</u> <u>-is-without-appeal</u>
- Prasad, Neeraj, et al. "Climate Resilient Cities : A Primer on Reducing Vulnerabilities to Disasters." *Open Knowledge Repository*, Washington, DC: World Bank, 2009, <u>http://hdl.handle.net/10986/11986</u>..
- Rahill, Guitele J., et al. "In their own words: Resilience among Haitian survivors of the 2010 earthquake." *Journal of Health Care for the Poor and Underserved*, vol. 27, no. 2, 2016, pp. 580–603, <u>https://doi.org/10.1353/hpu.2016.0100</u>.
- Stallard, Esme, and Mark Poynting. "How Climate Change Worsens Heatwaves, Droughts, Wildfires and Floods." *BBC News*, BBC, 25 July 2023, www.bbc.com/news/science-environment-58073295.
- TED. *How to Build a Resilient Future Using Ancient Wisdom | Julia Watson. YouTube*, 21 Aug. 2020, <u>https://www.youtube.com/watch?v=_DOOJx7AZfM</u> . Accessed 29 Mar. 2023.
- Wheeler, Nicola, and Nick Watts. "Climate change: From science to practice." *Current Environmental Health Reports*, vol. 5, no. 1, 2018, pp. 170–178, <u>https://doi.org/10.1007/s40572-018-0187-v</u>.
- Winsemius, Hessel C., et al. "Disaster risk, climate change, and poverty: Assessing the global exposure of poor people to floods and droughts." *Environment and Development*

The Significance of Biomarkers in Alzheimer's Disease Diagnosis By Aditya Krishnan, Lake Nona High school Senior, Orlando 32832, Danish Bhatti MD, Associate Professor of Neurology, University of Central Florida College of Medicine, Orlando 32827

Introduction

Alzheimer's disease (AD) is a debilitating age-related neurodegenerative disease that is progressive and currently has no cure (Watwood). AD was first characterized by a German physician, Dr. Alois Alzheimer, in 1907 when he recorded the symptoms of Auguste Deter, a 51-year old patient whose memory was seriously impaired (Bondi et al.). Specifically, she forgot objects immediately after they were shown to her, she skipped from line to line when reading, and she did not understand certain questions asked to her (Bondi et al.). Fast forward to today where AD is the most prevalent form of dementia, or cognitive decline, in the United States, affecting 6.2 million Americans and costing around \$355 billion for all healthcare expenses according to 2021 estimates (Soria Lopez et al.; Alzheimer's Association). With AD becoming more prevalent and the population becoming older, those costs are expected to increase tenfold between now and 2050 (Tahami Monfared et al.). AD also is the sixth leading cause of death in the United States and with a more at-risk older population, it is bound to cause more deaths than the other top 10 causes (Atri). This alone makes it paramount to find a cure for AD before it affects even more people (Long and Holtzman).

AD is defined by the presence of extracellular amyloid plaques and intracellular neurofibrillary tangles with clinically diagnosed dementia (Dubois et al.). AD is strongly associated with decreased cognition, loss of memory, a reduced ability to recognize faces, and a loss of judgement (Trevisan et al.). Patients with AD usually start off with mild cognitive impairment (MCI), which refers to forgetting details and misplacing items (eBioMedicine). As the disease advances, symptoms tend to include confusion, irritability, aggression, mood swings, language breakdown, and long-term memory loss (Isik). The progressive onset of these symptoms have been well defined and heavily studied in the neurodegeneration field, however an understanding of the molecular mechanisms governing their occurrence is not well understood due to AD's complex pathology (Molinuevo et al.).

There are two types of Alzheimer's disease: Early-onset Alzheimer's disease (EOAD) and Late-onset Alzheimer's disease (LOAD) (Tellechea et al.). EOAD is a form of AD that appears before age 65 and makes up around 5-10% of AD cases while LOAD appears after age 65 (Ayodele et al.; Morris et al.). EOAD differs from LOAD in that most patients develop AD as a result of familial genetic mutations (Mecocci et al.). Additionally, EOAD is associated with an increased impact of dementia risk factors like lower cardiovascular and cognitive fitness, greater psychosocial problems, and greater deficits in attention, executive functions, and visuospatial functions (Mendez). Since EOAD comes from genetics, it is easier to determine whether someone is on track to AD before signs of AD start to appear in a particular person (Nikolac Perkovic et al.). After all, the biggest problem in AD is not being able to accurately diagnose patients who display signs of AD (Nikolac Perkovic et al.). As a result, there has been a push in

the field to find a diagnosis for people with LOAD before their clinical symptoms start to appear (Nikolac Perkovic et al.).

While there have been attempts to find treatments for AD, none have been effective cures (Hampel et al.). Studies have suggested that making modifications to one's lifestyle by getting enough aerobic exercise, eating a Mediterranean diet, staying intellectually and socially engaged as well as getting adequate sleep can help slow the progression of the disease (Gibbs). In addition, it is well understood that certain diseases like diabetes and cardiovascular issues can increase the chance of developing AD (Cheng et al.; Stakos et al.). However, there have not been many drugs developed to treat AD; the success rate of these drugs is less than 7%, which is lower than the already low rate of successful central nervous system (CNS) drugs (Becker and Greig). No new drugs have been approved by the FDA for AD since 2003 (Hampel et al.).

In terms of actual drugs that have been approved, only 4 have been available for AD patients: Donepezil, Rivastigmine, Galantamine and Memantine (Briggs et al.). These medications are typically used for AD-associated symptoms (Weller and Budson). These medications could fail because they are given when widespread neuronal loss has already occurred (Wegiel et al.). The two hallmark pathologies of amyloid beta and tau are present in AD patients well before clinical diagnosis is possible as both accumulate before symptoms start to appear (Zhang et al.; Kazim et al.). Therefore, these medications may not be as effective if administered late in disease progression (Aisen et al.). Thus, it is important to develop an understanding of a tool, or biomarker, that can measure or know when someone is at an early risk for AD (Aisen et al.).

Alzheimer's Disease Neuropathology

There are two major proteins that are implicated in AD: Amyloid-beta (A β) and Tau (Sadleir & Vassar). Specifically, A β is found as extracellular senile plaques (ESP) and Tau is found as intracellular neurofibrillary tangles (INT) (Gallardo & Holtzman; Jeong). The presence of these mutated proteins correlate with the behavioral symptoms of AD (Cahan et al. 2023). In addition, they are directly a consequence of the damage and destruction of synapses that mediate memory and cognition (Cahan et al.). In turn, ESP and INT both lead to neurodegeneration (Jeong). Knowing the harm that A β and Tau can do in their mutated forms, it is important to understand what they both are in their normal states and how they turn into their diseased forms (Serrano-Pozo et al.).

Aβ

 $A\beta$ is a 42 amino-acid peptide that is derived from the amyloid beta precursor protein (APP) on chromosome 21, which, when mutated, can cause AD (Rukmangadachar & Bollu). A β is naturally present in the brain, usually regulating lipid metabolism and reducing cholesterol synthesis (Normando et al.). Cell studies have also shown that $A\beta$ is generated by the endoplasmic reticulum, Golgi apparatus and lysosomal system (Takahashi et al.). In addition, $A\beta$

has also been shown to be a memory enhancer at very minimal concentrations and also helps with forgetting unnecessary memories (Morley & Farr; Lee et al.).

However, in AD patients, $A\beta$ expression increases to toxic levels in synapses (Sharari et al.). There are specifically two types of $A\beta$ whose levels are higher in AD patients: $A\beta40$ and $A\beta42$ (Sharma et al.). Typically, $A\beta42$ is the version of $A\beta$ that will undergo a protein conformation to form senile plaques in the brain (Sharma et al.). This protein confirmation involves APP, which plays a major role in synaptic development and function, being cleaved by α -, β -, and γ -secretases to form the $A\beta$ plaques that are implicated in AD (Cvetkovska et al.). As such, these senile plaques affect the transmission of nerve signals and cause apoptosis of neurons, which leads to cognitive impairment (Cvetkovska et al.). The high levels of senile plaques also cause them to aggregate (Gotla & Matysiak). This aggregation leads to inflammation in the central nervous system, synaptic dysfunction and neuronal damage (Karaahmet et al.). In addition, these plaques are the primary driver of neurotoxicity in the brain of AD patients (Gotla & Matysiak).

The accumulation of A β plaques in the brain can serve as a warning signal that a patient's brain is starting to display signs of AD (Ronning et al.). In addition, the amyloid cascade hypothesis has been the most popular theory that has explained the pathogenesis of AD (Li et al.). Since a biomarker's strength is in its ability to be present before a disease is diagnosed, A β 's presence before AD diagnosis shows why it is a good biomarker (Li et al.).

Tau

Tau is a microtubule-associated protein that is normally soluble and comes from the MAPT gene on chromosome 17 (Young et al.; Rudenko et al.; Antonioni et al.). Tau is also important for the stability of axons and is normally expressed in neurons (Zetterberg). Tau is also secreted into the brain's interstitial fluid and communicates freely with cerebrospinal fluid (CSF) (Zetterberg). Typically, tau levels are kept at a lower level by protein-degradation systems (Lester & Parker). In addition, tau has a tendency to form self-templating fibrillar structures that allow tau to propagate by prion-like mechanisms in the brain (Lester & Parker).

Similar to $A\beta$, normal tau appears to turn into its insoluble disease-causing form by protein mutations and excess aggregation (Mueller et al.). Specifically, in AD patients, INT is composed of insoluble tau and can cause a wide variety of cellular abnormalities including disrupting vesicle trafficking mechanisms, axoplasmic transport, and neuronal polarity (Gendreau & Hall). INT forms from hyperphosphorylated tau, which can occur from the upregulation of kinase or the downregulation of phosphatase (Naskar & Gour). When tau is hyperphosphorylated, tau can no longer bind to microtubules, thus defeating tau's normal purpose (Naskar & Gour). Lots of hyperphosphorylated tau leads to aggregation and INT formation (Chen & Yu). Aggregated tau may contribute to chronic stress and dysfunction of neurons, which in turn increases the severity of memory deficit in AD (Yan et al.).

INT typically are found in the brains of AD patients (Ma et al.). In addition, tau as a CSF and a PET biomarker has already shown a high correlation with AD symptoms (Wang et al.).
However, the toxic form of aggregated tau is also implicated in other neurodegenerative diseases like frontotemporal dementia, therefore tau's presence might not be the best indicator of AD in a patient (Antonioni et al.).

Biomarkers

AD has been notorious for having treatments, specifically drugs, that slow the progression of AD symptoms but they cannot restore various capabilities that have already been lost (Fitzgerald et al.). Not only do these drugs have a low success rate but these drugs also cost lots of money to develop (Greenberg et al.). This explains why the only approved drugs for AD are acetylcholinesterase inhibitors and N-methyl d-aspartate (NMDA) receptor antagonists that address some symptoms but are not life-changing (Reiss et al.). There have been two new treatments that have been approved by the United States Food and Drug Administration that have been shown to lower $A\beta$ levels in the brain: aducanumab and lecanemab (Liu et al.). However, even these treatments have not demonstrated real-world efficacy and both treatments have significant side effects (Reiss et al.).

With there not being any viable treatments for AD that can reverse losses, finding an effective biomarker that is cost-effective, accessible and specific to AD has become paramount (Horie et al.; Halder & Drummond). The accumulation of misfolded and aggregated proteins (specifically A β and Tau) characterizes AD, so a biomarker is needed to detect these proteins early before the characteristic symptoms of AD develop (Kavungal et al.). By doing this, it allows treatments to be given as early as possible so the progression of AD can be slowed and be less impactful in a patient's brain (Jin et al.). A current table of biomarker studies provides insights into the depth of this field of study (**Table 1**).

Aβ Biomarkers

The presence of $A\beta$ as a fluid biomarker in cerebrospinal fluid (CSF) and blood plasma has been previously established (Seubert et al.). In the early 2000s, initial studies on the abundance of $A\beta$ in fluid from AD patients was one of the first indications of a possible correlation between the abundance of $A\beta$ in the brain and in fluid (Blennow & Zetterberg). For instance, a 2003 study done on postmortem patients found that lower $A\beta42$, which is a toxic form of $A\beta$ with a peptide length of 42, levels in the CSF correlate with higher $A\beta42$ levels in the brain (Strozyk et al.). This was supported by a 2006 PET study that used an amyloid-binding agent, PIB (Pittsburgh Compound-B) that found that high brain amyloid deposition results in low $A\beta42$ in the CSF (Fagan et al.). A cross-sectional study done on living patients in 2009 also found that CSF $A\beta42$ levels and brain $A\beta42$ levels had an inverse correlation (Tapiola et al.). The inverse correlation between CSF $A\beta42$ and $A\beta42$ in the brain could be explained by the fact that not having much $A\beta42$ in the CSF means it is not being cleared from the brain and accumulating there (Motter et al.).

Not only were studies finding that CSF A β 42 levels were low in AD patients but this finding was validated when comparing AD patients with non-AD patients (Blennow &

Zetterberg). To start, a 1998 cohort study that looked at AD patients and patients suffering from other neurological disorders found that CSF A β 42 levels decreased in AD patients compared to patients with other neurological disorders and people with normal cognition (Galasko et al.). This finding is important as it shows that very low levels of CSF A β 42 are unique to AD and not other neurological disorders (Galasko et al.). A 2001 prospective study supports this as it looked at 163 patients with possible and probable AD as well as 78 patients with other neurological disorders found decreased CSF A β 42 levels in patients with possible and probable AD (Andreasen et al.). A study that looked for AD biomarkers in blood plasma compared to dementia with lewy bodies (DLB) and control patients in 2023 found that plasma A β 42 levels were lower in AD patients compared to DLB and control patients (Yu et al.). This finding further supports the idea mentioned earlier that decreases in cleared A β 42 in both CSF and plasma have a correlation with the A β pathology in the brain (Yu et al.).

There are also studies that looked at mild cognitive impairment (MCI) patients to see if biomarkers for AD could be found in these patients (Mattsson et al.). This is being done because patients with MCI have more cognitive impairment than age-related non-cognitively impaired people but less cognitive impairment than AD patients (Mattsson et al.). MCI patients typically are on track to develop dementia, and later AD, although that is not the only outcome from an MCI diagnosis (Mattsson et al.). MCI patients are of particular interest because detecting a biomarker, which would represent an early diagnostic tool, in these patients could help diagnose AD before its symptoms become too severe (Mattsson et al.). Specifically, a 2009 longitudinal study that looked at MCI, AD and control patients in 12 centers in Europe and the United States found that the presence of $A\beta42$ in the CSF of MCI patients could identify eventual AD with good accuracy (Mattsson et al.).

A β 42 is not the only version of AD that has been looked at as a potential biomarker for AD (Lewczuk et al.). A β 40 is another version of A β that has a peptide length of 40 instead of 42 (Lewczuk et al.). A study that looked at AD, dementia and control patients in 2003 wanted to see if there was any correlation between levels of CSF A β 40 and CSF A β 42 in terms of whether they could predict AD diagnosis (Lewczuk et al.). The study found that CSF A β 42 levels were decreased in AD patients compared to the dementia and control patients while there was no significant difference in the correlation between CSF Abeta40 levels and AD diagnosis (Lewczuk et al.). This finding is significant as the toxic A β peptide length is 42, which was shown to inversely correlate with AD diagnosis (Lewczuk et al.). This strengthened the idea of A β 42 representing a robust biomarker for the continued accumulation of A β 42 in the brain, demonstrated by its decreased presence in the CSF (Lewczuk et al.).

However, while A β 40 by itself may not have played a role in correlating with AD diagnosis, when combined with A β 42 to form an A β 42/A β 40 ratio, it could predict AD very well (Hansson et al.). This was seen in a 2007 study that looked at the CSF of MCI patients to identify baseline levels of A β 40 and A β 42 and which later followed up with patients to see if they developed AD (Hansson et al.). They actually found that the A β 42/A β 40 ratio was a better

predictor of AD in MCI patients compared to A β 42 alone (Hansson et al.). This finding shows that A β 40 might actually serve a much bigger purpose in identifying AD when it is analyzed with A β 42 (Hansson et al.). Another 2007 study that involved 312 MCI patients at 12 different German universities undergoing lumbar punctures to identify levels of A β 42 and A β 40 in the CSF (Wiltfang et al.). Once again, the A β 42/A β 40 ratio proved to be more reliable at determining which patients developed AD compared to A β 42 by itself (Wiltfang et al.).

The A β 42/A β 40 ratio being effective in determining AD diagnosis can also be seen in plasma Abeta as well (Janelidize et al. 2021). This was proven by a study done in 2021 that used mass spectrometry to effectively identify the A β 42/A β 40 ratio in patients with early AD and found that this ratio can predict AD diagnosis (Janelidze et al.). In addition, a 2019 study found that when measuring the plasma A β 42/A β 40 ratio using an assay and combining it with age and Apolipoprotein E4 (APOE4), which is the main genetic risk factor for AD, it could accurately diagnose brain amyloidosis, which causes AD (Schindler et al.).

Tau Biomarkers

Tau was established as a biomarker when it was discovered that phosphorylated tau (P-tau) is able to create INT, which forms a major pathology of AD (Grundke-Iqbal et al.) As it is well understood that INTs are a neuropathological hallmark in many neurodegenerative diseases, it is important to investigate how P-tau could be an effective biomarker in AD explicitly (Tapiola et al.). To address this question, a research group in 2009 conducted a cross-sectional study with patient groups of AD and other neurological diseases demonstrated that the best predictor of AD pathology was achieved by using a joint metric of CSF Abeta and Tau (Tapiola et al.). They found that lower amounts of Abeta42 in the CSF and higher amounts of P-tau in the CSF are the best predictors for AD pathology (Tapiola et al.).

While correlational studies with CSF and post-mortem analysis give initial insights into how much tau has accumulated in the brain, they do not give us a direct measurement (La Joie et al.). To overcome this issue, groups began to develop tau-PET [18F-AV-1451] probes to determine if the amount of CSF P-tau truly positively correlated with the quantity of P-tau in the brain (La Joie et al.). A 2018 study that used PET scans and CSF in AD and non-AD patients to determine whether Abeta or Tau was a better biomarker at diagnosing AD found that using a combination of a tau PET probe and CSF Tau was better at distinguishing AD from other neurological conditions (La Joie et al.). Adding to this finding, researchers from Sweden found that the tau PET probe was better alone at detecting the early stages of AD symptoms (Mattsson et al.). While CSF P-tau can be used to diagnose AD, it is increased in all stages of AD while the tau PET probe signal is increased only with the disease stages of AD (Mattsson et al.).

However, another group in 2003 found that measurement of P-tau in the CSF was even better at discriminating Creutzfeldt-Jakob disease (CJD) and therefore, it could represent a biomarker that performs better for this less-prevalent disease (Riemenschneider et al.). This idea of total P-tau not being the best biomarker could be seen in the conflicting results between a 2017 study that found that while total tau was associated with cognitive decline, it did not increase the risk for dementia in MCI patients (Mielke et al.), and a 2019 study that used MCI patients from multiple memory clinics in the United States and France that found that total plasma tau levels could be an effective predictor for dementia (Pase et al.). Even though this study also found that higher plasma tau levels were associated with a smaller hippocampus, which is the first brain area to be affected by AD as it deals with learning and memory, and the presence of INTs, which is a major pathology of AD, these conflicting results show that total tau may not be the best biomarker for AD (Pase et al.).

While P-tau has been looked at in terms of its ability to diagnose AD, specific types of P-tau may be more helpful in determining AD early on before it increases in severity (Buerger et al.). Some specific sites for phosphorylated tau that are being looked at as a possible biomarkers are phosphorylated-tau231 (P-tau231) and phosphorylated-tau181 (P-tau181) (Buerger et al.; Simren et al. 2021). A study that measured the concentration of CSF P-tau231 in 26 clinically diagnosed patients in 2006 demonstrated that the more P-tau231 present in the CSF, the more INTs are present in the brain (Buerger et al.). A 2022 study that measured CSF concentrations of various types of P-tau in patients in various stages of AD found that P-tau231 is seen early in AD development, meaning it is able to identify AD before it becomes more severe (Ashton et al.). Additionally, ptau181 was found to discern AD from frontotemporal dementia (FTD) (Thijssen et al.).

However, an even stronger candidate for a potential AD biomarker is phosphorylated-tau217 (P-tau217) (Palmqvist et al.). To start, a 2021 study that looked at a cohort of over 1,400 patients found that P-tau217 was able to discriminate AD from other neurodegenerative diseases (Palmqvist et al.). However, not only is P-tau217 better at determining AD but it does so more accurately than other forms of P-tau (Janelidze et al.). This finding is supported by a study that compared the effectiveness of 10 different types of tau in predicting AD in 2022 (Janelidze et al.). The study found that P-tau217 performed the best when it came to predicting AD from MCI patients (Janelidze et al.). In addition, a mass spectrometry study determined that P-tau217 was superior compared to P-tau181 when it came to determining AD (Barthelemy et al.). This study's result was also supported by a 2020 CSF study that found that P-tau217 correlated with the presence of A β in the brain compared to P-tau181 (Janelidze et al.).

Conclusion

As AD is becoming more prevalent and more of a socioeconomic burden, there is a crucial need for diagnostic tools for early intervention. Previous AD treatments have failed in clinical trials, partly due to being administered late in the clinical progression of the disease. Therefore, confident and robust biomarkers based off of the major pathologies of AD would represent an important advance in the treatment of AD. The 2 major hallmarks of AD, A β and Tau, have shown promise as effective biomarkers in both identifying AD early-on and discriminating AD from other neurodegenerative diseases (**Table 1**). Further research into these avenues of diagnostic tools is important to catch this elusive disease. There is substantial promise

in these diagnostic tools that may be the key to providing AD patients and giving them life-saving treatments.

Date of Study	N	Biomarker	Findings	Citation
February 2003	155 postmortem Japanese-American men	CSF Aβ42	Lower CSF A β 42 = more A β in the brain	Strozyk et al.
February 2006	Clinically characterized research subjects	PIB and CSF Aβ42	More Aβ in brain = low CSF Aβ42	Fagan et al.
March 2009	123 patients (79 with clinical AD, 29 with other dementia and 15 with other neurological disease)	CSF Aβ42, total tau and P-tau	CSF A β 42 correlated inversely with A β in the brain and CSF P-tau correlated directly with A β in the brain	Tapiola et al.
October 1995	AD patients and control subjects	CSF Aβ42, total Aβ peptides and APOE genotype	CSF Aβ42 levels were lower in AD patients compared to controls	Motter et al.
July 1998	82 patients with probable AD (24 with mild dementia and 60 cognitively normal) as well as 74 subjects with neurological disorders	CSF Aβ42 and CSF Tau	CSF Aβ42 levels decrease in AD while CSF Tau levels increase in AD	Galasko et al.
March 2001	Total of 241 patients	CSF Aβ42	Increased CSF	Andreasen et al.

Table 1: A β - and Tau-based biomarker studies in AD. A compilation of previous studies that investigated A β and tau as potential biomarkers in the context of AD.

	with probable AD (105), possible AD (58), vascular dementia (23), MCI (20), DLB (9), other neurological disorders (3), psychiatric disorders (5) and nondemented individuals (18)	and CSF Tau	tau and decreased CSF Aβ42 levels for possible and probable AD patients	
June 2023	Total of 132 patients with AD (55), DLB (47) and healthy controls (HC) (30)	P-tau181 and Plasma Aβ42	P-tau181 was lower in DLB compared to AD and HC while Aβ42 was higher in AD compared to DLB and HC	Yu et al.
July 2009	750 MCI patients, 529 AD patients and 304 controls	CSF Aβ42, total tau and P-tau	CSF Aβ42, total tau and P-tau could all identify AD	Mattson et al.
January 2003	22 AD patients	CSF Aβ42, CF Aβ40 and CSF Tau	CSF Aβ42 and CSF Tau can accurately predict AD	Lewczuk et al.
February 2006	180 MCI patients and 39 healthy individuals	CSF Aβ42, CSF total Tau and P-tau181	CSF Aβ42, total Tau and P-tau181 are associated with future AD development	Hansson et al.
November 2007	312 patients with early dementia and MCI	CSF Aβ42, CSF Aβ40, total tau and	Low CSF Aβ42 and Aβ40 and high tau and	Wiltfang et al.

		P-tau181	P-tau 181 predicts AD Aβ42/Aβ40 ratio is best at predicting AD	
September 2001	408 total patients	Plasma Aβ42 and Aβ40	Aβ42/Aβ40 ratio is the best at predicting AD	Janelidze et al.
October 2019	158 cognitively normal patients	Plasma Aβ42 and Aβ40	Aβ42/Aβ40 ratio with the presence of the APOE genotype can predict AD well	Schindler et al.
January 2018	53 patients (28 AD and 25 non-AD patients)	Tau PET, CSF Aβ42, total tau and P-tau	Tau PET and P-tau were able to diagnose AD	La Joie et al.
September 2017	39 AD patients, 14 prodromal AD patients and 30 healthy patients	Tau PET, CSF total tau and P-tau	Tau PET is associated with cognitive decline and appears early in AD	Mattsson et al.
March 2003	AD, FTD and CJD patients	CSF P-tau and total tau	CSF P-Tau/total tau ratio helps discriminate CJD from other diseases	Riemenschneider et al.
September 2017	458 total patients	Plasma total tau	Plasma total tau levels are associated with cognitive	Mielke et al.

			decline and AD	
March 2019	1453 participants in Framingham Heart Study and 367 individuals in the Memento Study	Plasma total tau	Plasma total tau can predict AD	Pase et al.
September 2006	26 total patients	P-tau231	P-tau231 is correlated with INTs and plaques	Buerger et al.
February 2022	171 patients in different stages of AD	P-tau181, P-tau217 and P-tau231	CSF P-tau231 increases early in AD pathology	Ashton et al.
January 2021	103 AD patients, 107 MCI patients and 99 cognitively unimpaired individuals	P-tau181, total tau and CSF Aβ42/Aβ40	P-tau181 detected AD in MCI patients	Simren et al.
March 2020	362 total participants	P-tau181	P-tau181 is helpful at detecting AD	Thijssen et al.
August 2020	1402 total participants	P-tau217	P-tau217 was able to discriminate AD from other diseases	Palmqvist et al.
September 2022	135 MCI patients	P-tau181, P-tau217 and P-tau231	P-tau217 performs the best at discriminating AD from other diseases	Janelidze et al.
April 2020	65 control patients,	P-tau181 and	P-tau217 might	Janelidze et al.

43 AD patients and	P-tau217	be more useful	
57 non-AD patients		at P-tau181 at	
		diagnosing AD	

Works Cited

- Alzheimer's Association. "2021 Alzheimer's Disease Facts and Figures", Alzheimer's Association, 23 Mar. 2021, alz-journals.onlinelibrary.wiley.com/doi/10.1002/alz.12328.
- Andreasen, Niels, et al. "Evaluation of CSF-Tau and CSF-AB42 as Diagnostic Markers for Alzheimer Disease in Clinical Practice." *Archives of Neurology*, JAMA Network, 1 Mar. 2001, jamanetwork.com/journals/jamaneurology/fullarticle/778729.

Antonioni, Annibale, et al. "Frontotemporal Dementia, Where Do We Stand? A Narrative Review." *MDPI*, Multidisciplinary Digital Publishing Institute, 21 July 2023, www.mdpi.com/1422-0067/24/14/11732.

Ashton, Nicholas J, et al. "Cerebrospinal Fluid P-TAU231 as an Early Indicator of Emerging Pathology in Alzheimer's Disease." *EBioMedicine*, U.S. National Library of Medicine, Feb. 2022, www.ncbi.nlm.nih.gov/pmc/articles/PMC8850760/.

Atri, Alireza. "The Alzheimer's Disease Clinical Spectrum: Diagnosis and Management." *Medical Clinics of North America*, Elsevier, 29 Jan. 2019, www.sciencedirect.com/science/article/pii/S0025712518301317?via%3Dihub.

- Ayodele, Temitope, et al. "Early-Onset Alzheimer's Disease: What Is Missing in Research?" *Current Neurology and Neuroscience Reports*, U.S. National Library of Medicine, 19 Jan. 2021, www.ncbi.nlm.nih.gov/pmc/articles/PMC7815616/.
- Barthélemy, Nicolas R, et al. "Blood Plasma Phosphorylated-Tau Isoforms Track CNS Change in Alzheimer's Disease." *The Journal of Experimental Medicine*, U.S. National Library of Medicine, 2 Nov. 2020, www.ncbi.nlm.nih.gov/pmc/articles/PMC7596823/.
- Becker, Robert E, and Nigel H Greig. "Alzheimer's Disease Drug Development: Old Problems Require New Priorities." CNS & Neurological Disorders Drug Targets, U.S. National Library of Medicine, Dec. 2008, www.ncbi.nlm.nih.gov/pmc/articles/PMC5175454/.
- Blennow, K, and H Zetterberg. "Biomarkers for Alzheimer's Disease: Current Status and Prospects for the Future." *Wiley Online Library*, Wiley Online Library, 26 July 2018, onlinelibrary.wiley.com/doi/10.1111/joim.12816.
- Bondi, Mark W, et al. "Alzheimer's Disease: Past, Present, and Future." *Journal of the International Neuropsychological Society : JINS*, U.S. National Library of Medicine, Oct. 2017, www.ncbi.nlm.nih.gov/pmc/articles/PMC5830188/.
- Briggs, Robert, et al. "Drug Treatments in Alzheimer's Disease." *Clinical Medicine (London, England)*, U.S. National Library of Medicine, June 2016, www.ncbi.nlm.nih.gov/pmc/articles/PMC5922703/.
- Buerger, Katharina, et al. "CSF Phosphorylated Tau Protein Correlates with Neocortical Neurofibrillary Pathology in Alzheimer's Disease ." *Brain*, Brain, 29 Sept. 2006, academic.oup.com/brain/article/129/11/3035/293326?login=false.
- Cahan, Joshua G, et al. "Lower Cerebrospinal Fluid Amyloid-β42 Predicts Sooner Time to Antipsychotic Use in Alzheimer's Disease." *Journal of Alzheimer's Disease Reports*, U.S. National Library of Medicine, 19 June 2023, www.ncbi.nlm.nih.gov/pmc/articles/PMC10357113/.

- Chen, Yijun, and Yang Yu. "Tau and Neuroinflammation in Alzheimer's Disease: Interplay Mechanisms and Clinical Translation." *Journal of Neuroinflammation*, U.S. National Library of Medicine, 14 July 2023, www.ncbi.nlm.nih.gov/pmc/articles/PMC10349496/.
- Cheng, G, et al. "Diabetes as a Risk Factor for Dementia and Mild Cognitive Impairment: A Meta-Analysis of Longitudinal Studies." *Wiley Online Library*, Internal Medicine Journal, 28 Feb. 2012, onlinelibrary.wiley.com/doi/10.1111/j.1445-5994.2012.02758.x.
- Cvetkovska, Vedrana, et al. "Neurexin-β Mediates the Synaptogenic Activity of Amyloid Precursor Protein." *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, U.S. National Library of Medicine, 30 Nov. 2022, www.ncbi.nlm.nih.gov/pmc/articles/PMC9732828/.
- Dubois, Bruno, et al. "Clinical Diagnosis of Alzheimer's Disease: Recommendations of the International Working Group." *The Lancet. Neurology*, U.S. National Library of Medicine, June 2021, www.ncbi.nlm.nih.gov/pmc/articles/PMC8339877/#G01.
- eBioMedicine. "The Need for Early Detection and Treatment in Alzheimer's Disease." *EBioMedicine*, U.S. National Library of Medicine, July 2016, www.ncbi.nlm.nih.gov/pmc/articles/PMC4972571/.
- Fagan, Anne M., et al. "Inverse Relation between in Vivo Amyloid Imaging Load and Cerebrospinal Fluid Aβ42 in Humans." *Wiley Online Library*, Wiley Online Library, 17 Feb. 2006, onlinelibrary.wiley.com/doi/10.1002/ana.20730.
- Fitzgerald, G S, et al. "Insulin-like Growth Factor-2 Is a Promising Candidate for the Treatment and Prevention of Alzheimer's Disease." CNS Neuroscience & Therapeutics, U.S. National Library of Medicine, June 2023, www.ncbi.nlm.nih.gov/pmc/articles/PMC10173726/.
- Galasko, D., et al. "High Cerebrospinal Fluid Tau and Low Amyloid B42 Levels in the Clinical Diagnosis of Alzheimer Disease and Relation to Apolipoprotein E Genotype." *Archives of Neurology*, JAMA Network, 1 July 1998,

jamanetwork.com/journals/jamaneurology/fullarticle/774064.

- Gallardo, Gilbert, and David M. Holtzman. "Amyloid-β and Tau at the Crossroads of Alzheimer's Disease." *SpringerLink*, Springer Singapore, 1 Jan. 1970, link.springer.com/chapter/10.1007/978-981-32-9358-8 16.
- Gendreau, Kerry L, and Garth F Hall. "Tangles, Toxicity, and Tau Secretion in Ad New Approaches to a Vexing Problem." *Frontiers in Neurology*, U.S. National Library of Medicine, 21 Oct. 2013, www.ncbi.nlm.nih.gov/pmc/articles/PMC3801151/.
- Gibbs, Daniel M. "Alzheimer's Dementia or Alzheimer's Disease What's the Difference and Why Should We Care?" *Ageing Research Reviews*, Elsevier, 1 Nov. 2022, www.sciencedirect.com/science/article/pii/S1568163722002215?via%3Dihub.
- Gotla, Suhas, and Silvina Matysiak. "Mechanistic Insights into the Inhibition of Amyloid-β Aggregation by Chitosan." *Physical Chemistry Chemical Physics*, The Royal Society of Chemistry, 22 Mar. 2023, pubs.rsc.org/en/content/articlelanding/2023/CP/D3CP00162H.

Greenberg, Barry D., et al. "Improving Alzheimer's Disease Phase II Clinical Trials." *Alzheimer's Association*, Alzheimer's Association, 19 Nov. 2012, alz-journals.onlinelibrary.wiley.com/doi/10.1016/j.jalz.2012.02.002.

- Grundke-Iqbal, I, et al. "Abnormal Phosphorylation of the Microtubule-Associated Protein Tau (Tau) in Alzheimer Cytoskeletal Pathology." *Proceedings of the National Academy of Sciences of the United States of America*, U.S. National Library of Medicine, July 1986, www.ncbi.nlm.nih.gov/pmc/articles/PMC323854/.
- Halder, Aditi, and Eleanor Drummond. "Outline Images Download Cite Share Favorites Permissions REVIEW Strategies for Translating Proteomics Discoveries into Drug Discovery for Dementia." *Neural Regeneration Research*, Neural Regeneration Research, Jan. 2023,

journals.lww.com/nrronline/Fulltext/2024/01000/Strategies_for_translating_proteomics_discoveries.19.aspx.

- Hampel, Harald, Filippo Caraci, et al. "A Path toward Precision Medicine for Neuroinflammatory Mechanisms in Alzheimer's Disease." *Frontiers in Immunology*, U.S. National Library of Medicine, 31 Mar. 2020, www.ncbi.nlm.nih.gov/pmc/articles/PMC7137904/#B2.
- Hampel, Harald, M-Marsel Mesulam, et al. "The Cholinergic System in the Pathophysiology and Treatment of Alzheimer's Disease." *Brain : A Journal of Neurology*, U.S. National Library of Medicine, 1 July 2018, www.ncbi.nlm.nih.gov/pmc/articles/PMC6022632/.
- Hansson, Oskar, et al. "Prediction of Alzheimer's Disease Using the CSF AB42/AB40 Ratio in Patients with Mild Cognitive Impairment." *Karger Publishers*, S. Karger AG, 19 Mar. 2007,

karger.com/dem/article-abstract/23/5/316/98116/Prediction-of-Alzheimer-s-Disease-Usin g-the-CSF-A?redirectedFrom=fulltext.

- Horie, Kanta, et al. "CSF MTBR-Tau243 Is a Specific Biomarker of TAU Tangle Pathology in Alzheimer's Disease." *Nature News*, Nature Publishing Group, 13 July 2023, www.nature.com/articles/s41591-023-02443-z.
- Isik, Ahmet Turan. "Late Onset Alzheimer's Disease in Older People." *Clinical Interventions in Aging*, U.S. National Library of Medicine, 11 Oct. 2010, www.ncbi.nlm.nih.gov/pmc/articles/PMC2981103/.
- Janelidze, Shorena, Charlotte E Teunissen, et al. "Head-to-Head Comparison of 8 Plasma Amyloid-β 42/40 Assays in Alzheimer Disease." *JAMA Neurology*, U.S. National Library of Medicine, 1 Nov. 2021, www.ncbi.nlm.nih.gov/pmc/articles/PMC8453354/.
- Janelidze, Shorena, Divya Bali, et al. "Head-to-Head Comparison of 10 Plasma Phospho-Tau Assays in Prodromal Alzheimer's Disease." *Brain : A Journal of Neurology*, U.S. National Library of Medicine, 19 Apr. 2023, www.ncbi.nlm.nih.gov/pmc/articles/PMC10115176/.
- Janelidze, Shorena, Erik Stomrud, et al. "Cerebrospinal Fluid P-TAU217 Performs Better than P-Tau181 as a Biomarker of Alzheimer's Disease." *Nature Communications*, U.S.

National Library of Medicine, 3 Apr. 2020,

www.ncbi.nlm.nih.gov/pmc/articles/PMC7125218/.

- Jeong, Sangyun. "Molecular and Cellular Basis of Neurodegeneration in Alzheimer's Disease." *Molecules and Cells*, U.S. National Library of Medicine, 30 Sept. 2017, www.ncbi.nlm.nih.gov/pmc/articles/PMC5638769/.
- Jin, Boru, et al. "Identification of Diagnostic Biomarkers in Alzheimer's Disease by Integrated Bioinformatic Analysis and Machine Learning Strategies." *Frontiers in Aging Neuroscience*, U.S. National Library of Medicine, 26 June 2023, www.ncbi.nlm.nih.gov/pmc/articles/PMC10331604/.
- Karaahmet, Berke, et al. "Inconsistent Effects of Glatiramer Acetate Treatment in the 5xFAD Mouse Model of Alzheimer's Disease." *MDPI*, Multidisciplinary Digital Publishing Institute, 24 June 2023, www.mdpi.com/1999-4923/15/7/1809.
- Kavungal, Deepthy, et al. "Artificial Intelligence-Coupled Plasmonic Infrared Sensor for Detection of Structural Protein Biomarkers in Neurodegenerative Diseases." Science Advances, U.S. National Library of Medicine, 14 July 2023, www.ncbi.nlm.nih.gov/pmc/articles/PMC10337894/.
- Kazim, Syed Faraz, et al. "Neuronal Network Excitability in Alzheimer's Disease: The Puzzle of Similar versus Divergent Roles of Amyloid β and Tau." *eNeuro*, U.S. National Library of Medicine, 23 Apr. 2021, www.ncbi.nlm.nih.gov/pmc/articles/PMC8174042/.
- La Joie, Renaud, et al. "Associations between [18F]AV1451 Tau Pet and CSF Measures of Tau Pathology in a Clinical Sample." *Neurology*, U.S. National Library of Medicine, 23 Jan. 2018, www.ncbi.nlm.nih.gov/pmc/articles/PMC5798657/.
- Lee, Sukwon, et al. "Endogenous Amyloid-β Mediates Memory Forgetting in the Normal Brain." *Biochemical and Biophysical Research Communications*, Academic Press, 23 Oct. 2018, www.sciencedirect.com/science/article/abs/pii/S0006291X18322800?via%3Dihub.
- Lester, Evan, and Roy Parker. "Tau, RNA, and RNA-Binding Proteins: Complex Interactions in Health and Neurodegenerative Diseases." *Sage Journals*, Sage Journals, 9 Mar. 2023, journals.sagepub.com/doi/10.1177/10738584231154551.
- Lewczuk, Piotr, et al. "Neurochemical Diagnosis of Alzheimer's Dementia by CSF AB42, AB42/AB40 Ratio and Total Tau." *Neurobiology of Aging*, Elsevier, 4 June 2003, www.sciencedirect.com/science/article/abs/pii/S0197458003000861?via%3Dihu
- Li, Li, et al. "Synthesis and Evaluation of Curcumin-Based near-Infrared Fluorescent Probes for Detection of Amyloid β Peptide in Alzheimer Mouse Models." *Bioorganic & Medicinal Chemistry*, Pergamon, 7 July 2023,

www.sciencedirect.com/science/article/abs/pii/S0968089623002584?via%3Dihub

Liu, Kathy Y, et al. "Key Questions for the Evaluation of Anti-Amyloid Immunotherapies for Alzheimer's Disease ." *Brain Communications*, Brain Communications, 2 June 2023, academic.oup.com/braincomms/article/5/3/fcad175/7188710?login=false.

- Long, Justin M, and David M Holtzman. "Alzheimer Disease: An Update on Pathobiology and Treatment Strategies." *Cell*, U.S. National Library of Medicine, 3 Oct. 2019, www.ncbi.nlm.nih.gov/pmc/articles/PMC6778042/.
- Ma, Lina, et al. "Traditional Chinese Medicine for the Treatment of Alzheimer's Disease: A Focus on the Microbiota–Gut–Brain Axis." *Biomedicine & Pharmacotherapy*, Elsevier Masson, 28 July 2023,

www.sciencedirect.com/science/article/pii/S0753332223010351?via%3Dihub.

- Mattsson, Niklas, Henrik Zetterberg, et al. "CSF Biomarkers and Incipient Alzheimer Disease in Patients with Mild Cognitive Impairment." *JAMA*, JAMA Network, 22 July 2009, jamanetwork.com/journals/jama/fullarticle/184311.
- Mecocci, Patrizia, et al. "Brain Aging and Late-Onset Alzheimer's Disease: A Matter of Increased Amyloid or Reduced Energy?" *Journal of Alzheimer's Disease*, IOS Press, 1 Jan. 2018, content.iospress.com/articles/journal-of-alzheimers-disease/jad179903.
- Mendez, Mario F. "Early-Onset Alzheimer Disease." *Neurologic Clinics*, U.S. National Library of Medicine, May 2017, www.ncbi.nlm.nih.gov/pmc/articles/PMC5407192/.
- Mielke, Michelle M, et al. "Association of Plasma Total Tau Level with Cognitive Decline and Risk of Mild Cognitive Impairment or Dementia in the Mayo Clinic Study on Aging." *JAMA Neurology*, U.S. National Library of Medicine, 1 Sept. 2017, www.ncbi.nlm.nih.gov/pmc/articles/PMC5710182/.
- Molinuevo, José Luis, et al. "Current State of Alzheimer's Fluid Biomarkers." *Acta Neuropathologica*, U.S. National Library of Medicine, Dec. 2018, www.ncbi.nlm.nih.gov/pmc/articles/PMC6280827/.
- Morley, John E., and Susan A. Farr. "The Role of Amyloid-Beta in the Regulation of Memory." *Biochemical Pharmacology*, Elsevier, 4 Jan. 2014, www.sciencedirect.com/science/article/abs/pii/S0006295213008022?via%3Dihub.
- Morris, John C, et al. "Autosomal Dominant and Sporadic Late Onset Alzheimer's Disease Share a Common in Vivo Pathophysiology." *Brain : A Journal of Neurology*, U.S. National Library of Medicine, 21 Oct. 2022, www.ncbi.nlm.nih.gov/pmc/articles/PMC9989348.
- Motter, R., et al. "Reduction of β-Amyloid Peptide42 in the Cerebrospinal Fluid of Patients with Alzheimer's Disease." *Wiley Online Library*, Wiley Online Library, Oct. 1995, onlinelibrary.wiley.com/doi/abs/10.1002/ana.410380413.
- Mueller, Rebecca L, et al. "Tau: A Signaling Hub Protein." Frontiers in Molecular Neuroscience, U.S. National Library of Medicine, 19 Mar. 2021, www.ncbi.nlm.nih.gov/pmc/articles/PMC8017207/.
- Naskar, Soumick, and Nidhi Gour. "Realization of Amyloid-like Aggregation as a Common Cause for Pathogenesis in Diseases." *MDPI*, Multidisciplinary Digital Publishing Institute, 7 July 2023, www.mdpi.com/2075-1729/13/7/1523.
- Nikolac Perkovic, Matea, et al. "Epigenetics of Alzheimer's Disease." *Biomolecules*, U.S. National Library of Medicine, 30 Jan. 2021, www.ncbi.nlm.nih.gov/pmc/articles/PMC7911414/.

Normando, Eduardo Maria, et al. "Focus on: Amyloid β." *Experimental Eye Research*, Academic Press, 21 May 2009,

www.sciencedirect.com/science/article/abs/pii/S0014483509001468?via%3Dihub

- Palmqvist, Sebastian, et al. "Discriminative Accuracy of Plasma Phospho-Tau217 for Alzheimer Disease vs Other Neurodegenerative Disorders." *JAMA*, U.S. National Library of Medicine, 25 Aug. 2020, www.ncbi.nlm.nih.gov/pmc/articles/PMC7388060/.
- Pase, Matthew P, et al. "Assessment of Plasma Total Tau Level as a Predictive Biomarker for Dementia and Related Endophenotypes." *JAMA Neurology*, U.S. National Library of Medicine, 1 May 2019, www.ncbi.nlm.nih.gov/pmc/articles/PMC6515589/.
- Reiss, Allison B, et al. "Alzheimer's Disease Treatment: The Search for a Breakthrough." *Medicina (Kaunas, Lithuania)*, U.S. National Library of Medicine, 4 June 2023, www.ncbi.nlm.nih.gov/pmc/articles/PMC10302500/.
- Riemenschneider, M, et al. "Phospho-Tau/Total Tau Ratio in Cerebrospinal Fluid Discriminates Creutzfeldt–Jakob Disease from Other Dementias." *Nature News*, Nature Publishing Group, 27 Mar. 2003, www.nature.com/articles/4001220.
- Ronning, Kaitryn E., et al. "The P2X7 Receptor, a Multifaceted Receptor in Alzheimer's Disease." *MDPI*, Multidisciplinary Digital Publishing Institute, 21 July 2023, www.mdpi.com/1422-0067/24/14/11747.
- Rudenko, Lauren K, et al. "Intraneuronal Tau Misfolding Induced by Extracellular Amyloid-β Oligomers." *Journal of Alzheimer's Disease : JAD*, U.S. National Library of Medicine, 2019, www.ncbi.nlm.nih.gov/pmc/articles/PMC7464573/.
- Rukmangadachar, Lokesh A, and Pradeep C Bollu. "Amyloid Beta Peptide Statpearls NCBI Bookshelf." *National Library of Medicine*, National Library of Medicine, 29 Aug. 2022, www.ncbi.nlm.nih.gov/books/NBK459119/.
- Sadleir, Katherine R, and Robert Vassar. "Connections between Apoe, Sleep, and AB and Tau Pathologies in Alzheimer's Disease." *The Journal of Clinical Investigation*, U.S. National Library of Medicine, 17 July 2023, www.ncbi.nlm.nih.gov/pmc/articles/PMC10348763/.
- Schindler, Suzanne E, et al. "High-Precision Plasma β-Amyloid 42/40 Predicts Current and Future Brain Amyloidosis." *Neurology*, U.S. National Library of Medicine, 22 Oct. 2019, www.ncbi.nlm.nih.gov/pmc/articles/PMC6946467/.
- Serrano-Pozo, Alberto, et al. "APOE and Alzheimer's Disease: Advances in Genetics, Pathophysiology, and Therapeutic Approaches." *The Lancet. Neurology*, U.S. National Library of Medicine, Jan. 2021, www.ncbi.nlm.nih.gov/pmc/articles/PMC8096522/.
- Seubert, Peter, et al. "Isolation and Quantification of Soluble Alzheimer's β-Peptide from Biological Fluids." *Nature News*, Nature Publishing Group, 24 Sept. 1992, www.nature.com/articles/359325a0.
- Sharari, Sanaa, et al. "Screening for Novel Inhibitors of Amyloid Beta Aggregation and Toxicity as Potential Drugs for Alzheimer's Disease." *MDPI*, Multidisciplinary Digital Publishing Institute, 11 July 2023, www.mdpi.com/1422-0067/24/14/11326.

- Sharma, Abhinav, et al. "Electrochemical Immunosensors Developed for Amyloid-Beta and Tau Proteins, Leading Biomarkers of Alzheimer's Disease." *Biosensors*, U.S. National Library of Medicine, 17 July 2023, www.ncbi.nlm.nih.gov/pmc/articles/PMC10377038/.
- Soria Lopez, Jose A, et al. "Alzheimer's Disease." *Handbook of Clinical Neurology*, Elsevier, 18 Nov. 2019,

www.sciencedirect.com/science/article/abs/pii/B9780128047668000133?via%3Dihub.

- Stakos, Dimitrios A, et al. "The Alzheimer's Disease Amyloid-Beta Hypothesis in Cardiovascular Aging and Disease: JACC Focus Seminar." *Journal of the American College of Cardiology*, U.S. National Library of Medicine, 3 Mar. 2020, www.ncbi.nlm.nih.gov/pmc/articles/PMC7042886/.
- Strozyk, D., et al. "CSF AB 42 Levels Correlate with Amyloid-Neuropathology in a Population-Based Autopsy Study." *Neurology*, Wolters Kluwer Health, Inc. on behalf of the American Academy of Neurology, 25 Feb. 2003, n.neurology.org/content/60/4/652.long.
- Tahami Monfared, Amir Abbas, et al. "The Humanistic and Economic Burden of Alzheimer's Disease." *Neurology and Therapy*, U.S. National Library of Medicine, June 2022, www.ncbi.nlm.nih.gov/pmc/articles/PMC9095804/#CR4.
- Takahashi, R.H., et al. "Histology and Histopathology." *Histol Histopathol, Vol 17, Takahashi et Al.*, 2002, www.hh.um.es/Abstracts/Vol_17/17_1/17_1_239.htm.
- Tapiola, Tero, et al. "Cerebrospinal Fluid β-Amyloid 42 and Tau Proteins as Biomarkers of Alzheimer-Type Pathologic Changes in the Brain." *Archives of Neurology*, JAMA Network, 1 Mar. 2009, jamanetwork.com/journals/jamaneurology/fullarticle/796677.
- Tellechea, P, et al. "Early- and Late-Onset Alzheimer Disease: Are They the Same Entity?" *Neurologia*, U.S. National Library of Medicine, 3 Nov. 2015, pubmed.ncbi.nlm.nih.gov/26546285/.
- Thijssen, Elisabeth H, et al. "Diagnostic Value of Plasma Phosphorylated Tau181 in Alzheimer's Disease and Frontotemporal Lobar Degeneration." *Nature Medicine*, U.S. National Library of Medicine, Mar. 2020, www.ncbi.nlm.nih.gov/pmc/articles/PMC7101073/.
- Trevisan, Kaynara, et al. "Theories of Aging and the Prevalence of Alzheimer's Disease." *BioMed Research International*, U.S. National Library of Medicine, 16 June 2019, www.ncbi.nlm.nih.gov/pmc/articles/PMC6601487/.
- Wang, Zhi-Bo, et al. "Associations of the A/T/N Profiles in PET, CSF, and Plasma Biomarkers with Alzheimer's Disease Neuropathology at Autopsy." *Alzheimer's Association*, Alzheimer's Association, 28 July 2023, alz-journals.onlinelibrary.wiley.com/doi/full/10.1002/alz.12068.
- Watwood, Carol. "Alzheimer's Disease." *TopSCHOLAR*®, Jan. 2011, digitalcommons.wku.edu/dlps fac pub/39/.
- Wegiel, Jerzy, et al. "Clinicopathological Staging of Dynamics of Neurodegeneration and Neuronal Loss in Alzheimer Disease." *Journal of Neuropathology and Experimental*

Neurology, U.S. National Library of Medicine, 1 Jan. 2021, www.ncbi.nlm.nih.gov/pmc/articles/PMC7749716/.

- Weller, Jason, and Andrew Budson. "Current Understanding of Alzheimer's Disease Diagnosis and Treatment." *F1000Research*, U.S. National Library of Medicine, 31 July 2018, www.ncbi.nlm.nih.gov/pmc/articles/PMC6073093/.
- Wiltfang, Jens, et al. "Amyloid β Peptide Ratio 42/40 but Not Aβ42 Correlates with Phospho-Tau in Patients with Low- and High-CSF Aβ40 Load." *Journal of Neurochemistry*, Journal of Neurochemistry, 2007, onlinelibrary.wiley.com/doi/epdf/10.1111/j.1471-4159.2006.04404.x.
- Yan, Xu, et al. "The Interaction of α-Synuclein and Tau: A Molecular Conspiracy in Neurodegeneration?" Seminars in Cell & Developmental Biology, Academic Press, 10 May 2018,

www.sciencedirect.com/science/article/abs/pii/S1084952117303890?via%3Dihub.

- Young, Zapporah T, et al. "Therapeutic Strategies for Restoring Tau Homeostasis." *Cold Spring Harbor Perspectives in Medicine*, U.S. National Library of Medicine, 2 Jan. 2018, www.ncbi.nlm.nih.gov/pmc/articles/PMC5540800/.
- Yu, Yueyi, et al. "Plasma Phosphorylated TAU181 and Amyloid-B42 in Dementia with Lewy Bodies Compared with Alzheimer's Disease and Cognitively Healthy People." *Journal of Alzheimer's Disease*, IOS Press, 1 Jan. 2023,

content.iospress.com/articles/journal-of-alzheimers-disease/jad230085.

- Zetterberg, H. "Review: Tau in Biofluids Relation to Pathology, Imaging and Clinical Features." *Wiley Online Library*, Wiley Online Library, 5 Jan. 2017, onlinelibrary.wiley.com/doi/10.1111/nan.12378.
- Zhang, Yun, et al. "Amyloid β-Based Therapy for Alzheimer's Disease: Challenges, Successes and Future." *Signal Transduction and Targeted Therapy*, U.S. National Library of Medicine, 30 June 2023, www.ncbi.nlm.nih.gov/pmc/articles/PMC10310781/.

The Impact of Anti-Asian Discrimination in Social Media and the News on EA/SEA Asian American Adolescents' Well-Being During the COVID-19 Pandemic By Kaitlyn Yhun

Literature Review

The COVID-19 pandemic has had a tremendous impact on numerous aspects of public health including mental health, which has had a significant decline globally (*New CDC*, 2022). According to data from the Centers for Disease Control and Prevention (CDC), "in 2021, more than a third (37%) of high school students reported they experienced poor mental health during the COVID-19 pandemic, and 44% reported they persistently felt sad or hopeless during the past year." Another notable statistic that has emerged since the beginning of the pandemic is that adolescents' social media use has continued to rise, with 33% of teens reporting more than five hours of daily social media use (Marciano, 2022). This can be largely attributed to the fact that, during health crises, people tend to more actively seek information about the ongoing event and recent updates about the circumstances (Austin, 2012). Since the pandemic has been "a time of psychological vulnerability and uncertainty" for virtually the entire population worldwide, the impact of COVID-related media content on mental health and well-being is prevalent, specifically among adolescents, whose levels of social media use continue to rise (Johnson et al., 2021).

Notably, this major health crisis has had significant impacts on people of color through the perpetuation of systemic racism in structural disparities in healthcare, law, education, employment, and more (Liu et al., 2020; Bailey et al., 2017). These structural forms of racism deeply rooted in society then further encourage racist beliefs and behavior (Bailey et al., 2017). Since the beginning of the COVID-19 pandemic, anti-Asian discrimination and hate, in particular, have surged significantly (Cheah et al., 2020). In a study to determine the correlation between racial discrimination against Asian Americans and their mental health, Cheah et al. used survey questions and scales of self-perceived information and discovered that 25% of participants endured indirect racial discrimination on a daily basis and almost all participants had witnessed racial discrimination against other Chinese or Asian Americans at least once before. Additionally, Johnson et al. conducted a study with findings that reveal that Asian Americans are "particularly vulnerable to the negative mental health effects of media use" during COVID-19, whereas media use had no such significant effect on the subjective well-being of white Americans (Johnson et al., 2021). These results suggest that the effects of social media on mental well-being have a connection to race/ethnicity and are not a general occurrence that has impacted different racial/ethnic groups similarly across categories. Thus, the research question arises: To what extent has social media and the news impacted the psychological well-being of East/Southeast Asian American adolescents during the COVID-19 pandemic?

To better examine the impacts of racial discrimination in social media and the news on the well-being of Asian Americans, it is essential to first understand the deeply ingrained discrimination against Asians in American society. Examining anti-Asian discrimination in the U.S. reveals that it has been consistently present throughout history. For instance, "yellow peril," a term coined in the 19th century, is a xenophobic metaphor meant to depict Asians as a threat to the Western world (Wu and Nguyen, 2022). Later in the 19th century, the spread of racist propaganda labeling Chinese people as unclean led to the Chinese Exclusion Act, "the first law in the United States that barred immigration solely based on race" (Leon, 2020). American officials in the early 20th century criticized Filipinos for their "unclean" and "uncivilized" bodies, using their supposed medical uncleanliness as an excuse to maintain U.S. colonization of the Philippines (Leon, 2020). In 1942, President Franklin D. Roosevelt approved the passing of Executive Order 9066, which would incarcerate individuals suspected to be spies (Leon, 2020). A significant majority of those who were moved to internment camps were Japanese despite many of them being second or third generation Americans who had had citizenship since birth. Such instances of anti-Asian racism throughout history have contributed to its perpetuation through modern times.

Today, anti-Asian discrimination continues, largely in the form of different aspects of the model minority myth, which encourages the misconceived notion that Asian Americans are collectively successful and not in need of any extra help (Jin, 2021). It supports misconceptions such as the ideas that they are a monolithic group, receive higher education and are well-earning, and experience less racism and discrimination than other ethnic groups. In reality, statistics suggest that Asian Americans are extremely diverse in ethnicities, vary greatly in both income and education, and face more systemic racism and discrimination than other ethnic groups in some aspects. For instance, a study by the Pew Research Center found that 32% of Asian American adults (more than any other racial/ethnic group studied) reported in April 2021 fearing that they might be threatened or physically attacked (Ruiz et al., 2021). Despite several such studies suggesting the considerable rise in anti-Asian discrimination since the beginning of the pandemic, a LAAUNCH survey showed that 37% of white Americans were unaware of increasing rates of anti-Asian hate crimes (LAAUNCH, 2021). This is a noteworthy statistic as it reveals the lack of knowledge that many Americans have regarding racial discrimination against Asians, even with the prevalence that it has gained as a result of the COVID-19 pandemic.

The nature of COVID-19's origin played a significant role in the rapid increase in discrimination against Chinese Americans and other EA¹ and SEA² Americans alike. Since the virus was first detected in Wuhan, China, discriminatory terms have been used to refer to the coronavirus, such as the "Chinese virus" or the "Wuhan virus" (Banerjee and Meena, 2021). Daily life for Asian individuals has gained a sense of judgment, as some people feel that, due to the virus' origin, the Chinese are more likely to have COVID-19. As a result, they assume that they must be more careful around Asian individuals who they perceive to be Chinese based on their physical appearances (Pedrosa et al., 2020). Since people tend to perceive individuals with EA or SEA features as Chinese and sometimes fear that they are more likely to have the coronavirus, it is important to consider everyone in these groups as potential victims when discussing the implications of anti-Asian hate during the pandemic.

¹ EA: East Asian

² SEA: Southeast Asian

Hate crimes against Asian Americans have become notably more prevalent since the beginning of the COVID-19 pandemic as well, which has resulted in a lack of a sense of safety in public for these individuals (Viladrich, 2021). The NYPD³ reported a 361% increase in anti-Asian hate crimes from 2020 to 2021, directly following the beginning of the pandemic (Ying, 2021). According to the Stop AAPI⁴ Hate National Report for 2020 to 2021, anti-Asian hate incidents were a total of 9,081 from March 19, 2020 to June 30, 2021, 2,748 of which were reported from April 2021 to June 2021 (Yellow Horse, 2021). Thus, many develop feelings of distress and anxiety for their own security and physical well-being, especially due to the news' coverage of events surrounding the rise in violent and aggressive hate crimes being committed against Asian Americans. Social media browsing in general was also found to be correlated with poorer subjective well-being as a result of more worrying about discrimination during the pandemic, likely due to the fact that anti-Asian hate was so prevalent and such information or reported incidents about these experiences was so easily accessible.

The gap addressed by this research study lies in the population as well as the survey questions that the researcher asked the participants in the study. There is already research that currently exists regarding Asian Americans' social media use, discrimination, and subjective well-being, but these existing studies conduct research surveys involving survey questions that only address subjective well-being, but not specific forms of media content and different ways in which they have impacted their well-being (Cheah et al., 2020; Yang et al., 2020). In this study, the researcher will be sending out online surveys to Asian American adolescents, who have been studied considerably less than Asian American adults. The survey questions will serve to show results answering how social media and the news have each impacted respondents' encounters with experiencing or witnessing experiences of discrimination through both forms of media, as well as to what extent these are correlated with their perceived well-being. This is a significant research gap due to the focus on adolescents of EA and SEA ethnicity as well as the distinct measurements of social media use and news consumption both included in a single study. *Hypothesis*

Based on the work of Cheah et al., whose study found that higher levels of perceived racism correlated with poorer mental well-being, the researcher hypothesized that both social media use and news consumption would be positively correlated with experiences of discrimination. The researcher also predicted that experiences of discrimination would have a negative correlation with both subjective well-being and perceived social support.

Method-Procedure

The research method is a survey, chosen as the method utilized in Yang et al.'s study. More specifically, the researcher conducted online surveys by having school officials send out a Google Forms link to school emails of recruited middle school and high school students in Cumberland County, PA. The alternative option of interviews was less ideal than online surveys

³ NYPD: New York Police Department

⁴ AAPI: Asian American and Pacific Islander

because conducting face-to-face interviews involving sensitive questions such as those regarding experiences of discrimination would make the study more susceptible to inaccurate data as a result of unintended pressure on participants. The researcher sent out surveys to students of only Cumberland County because this gave her a definite limit for the reach of the study population. Additionally, it was unrealistic to expect many survey responses from students across other areas of the state of Pennsylvania or in the U.S. as a whole when time constraints and the lack of a high school student researcher's credibility were taken into consideration. If possible, the researcher had school officials post an update on Schoology, the learning management system used up to high school in many schools of Cumberland County, to encourage students to check their emails so that the researcher could receive a larger sample size of responses from students, who might not often check their school emails.

The survey measured ethnicity to confirm each respondent's eligibility to participate in the study. The survey was sent out to students between 12 and 19 years of age (those in grades 7 to 12). At the beginning of the survey, the researcher verified their ages and grade levels because there might have been students who were younger or older than most others in their grade. The researcher eliminated any survey responses from students outside of the 12-19 age range. She was looking for responses from students between the ages of 12 and 19 because she was studying adolescents; although the age range of adolescents differs according to different sources, she chose an age range that is appropriate for the study, which prompts them to answer questions about their experiences of discrimination. Additionally, since it will be more difficult to reach out to college students for survey responses and they would be overall less responsive than students in high school and under, the researcher decided on an age range in which most students are still in high school or below. The researcher did not reach out to college or university students for this study. She referred to Yang et al.'s scholarly article Discrimination and Well-Being Among Asians/Asian Americans During COVID-19: The Role of Social Media as the model study because, similarly to this study's design, it utilizes the survey method to gather data on the subjective well-being of Asians and Asian Americans based on their experiences with racial discrimination on social media.

Ethics

The proposed method included both parent consent forms and child assent forms in the study, verifying that the researcher had consent to record and collect their survey responses for research. The method purposely avoided the population of individuals 11 and under because the survey contained questions about mental health and discrimination they have experienced in the past, which can be sensitive topics, especially because the time period is within the COVID-19 pandemic, a very recent period. By targeting an appropriate age range that will best ensure that the researcher did not inquire students who are too young about mental health/well-being struggles in relation to experiences of discrimination, the proposed method complied with ethical research practices. The method also practiced confidentiality, so the researcher was aware of the identities of the participants but excluded any identifying information in the project. The

researcher could not offer anonymity because she had to verify that each respondent was within the age range of 12 to 19 years. Also, since she reached out to them and sent them the online survey through email, their identities had to be known to her. Although the study did not involve deception, the researcher included a debriefing form for participants to read after they had completed the survey to provide them with information about the study and research. After fully completing the research project, the researcher discarded any and all information collected from the participants in the study and ensured that their confidentiality remained protected in the process.

Measures

Participants were asked about their social media use with the Social Media Engagement Scale for Adolescents to determine how often they use social media (e.g., "Using social media is my daily habit" and "I browse social media whenever I have time"). There were multiple choice-style answer choices from 1 *(Strongly Disagree)* to 5 *(Strongly Agree)*.

Participants' news consumption habits were measured using the Relative Response Scale to determine how frequently they viewed/read the news and what forms of news they consumed most commonly (e.g., "How often have you gotten news from television?" and "How often have you gotten news from the radio?"). There were multiple choice-style answer choices from 1 *(Often)* to 4 *(Never)*.

Participants' experiences of discrimination were measured using the Everyday Discrimination Scale to evaluate how frequently they experienced discrimination directly or witnessed others being discriminated against (e.g., "You are treated with less courtesy than other people" and "You are treated with less respect than other people"). There were multiple choice-style answer choices from 1 *(Never)* to 6 *(Almost Everyday)*.

Participants' subjective well-being was measured using the Satisfaction With Life Scale to determine their self-reported psychological wellness (e.g., "In most ways, my life is close to my ideal" and "The conditions of my life are excellent"). There were multiple choice-style answer choices from 1 *(Strongly Disagree)* to 7 *(Strongly Agree)*.

Participants' perceived social support was measured using the Multidimensional Scale of Perceived Social Support to determine their self-reported levels of social support, which higher social support tends to correspond with better well-being (e.g., "I get the emotional help and support I need from my family" and "I can count on my friends when things go wrong"). There were multiple choice-style answer choices from 1*(Strongly Disagree)* to 5 *(Strongly Agree)*.

Results/Discussion

The survey yielded a total of 36 responses from 3 different schools in Cumberland County, PA. The researcher had reached out to 14 other schools in Cumberland County, but they either did not respond or did not approve the study.





Graph 1: Survey respondents were of 7 different ethnicities, with 1 participant who reported being a mix of 2 ethnicities that were both already represented in the survey demographics. Significantly more respondents were Vietnamese, Chinese, Korean, or Filipino.



Social Media Use

Graph 3: Responses regarding social media use reported high levels of social media usage. There were significantly more responses ranging from 4 (*Agree*) to 5 (*Strongly Agree*) than those from 1 (*Strongly Disagree*) to 2 (*Disagree*) for all items except items 6, 8, 9, 10, and 11. *Item 1:* There were 33 responses from 4 (*Agree*) to 5 (*Strongly Agree*) and 2 responses from 1 (*Strongly Disagree*) to 2 (*Disagree*). *Item 2:* There were 30 responses from 4 (*Agree*) to 5

(Strongly Agree) and 1 response from 1 (Strongly Disagree) to 2 (Disagree). Item 3: There were 23 responses from 4 (Agree) to 5 (Strongly Agree) and 8 responses from 1 (Strongly Disagree) to 2 (Disagree). Item 4: There were 26 responses from 4 (Agree) to 5 (Strongly Agree) and 6 responses from 1 (Strongly Disagree) to 2 (Disagree). Item 5: There were 16 responses from 4 (Agree) to 5 (Strongly Agree) and 7 responses from 1 (Strongly Disagree) to 2 (Disagree). Item 6: There were 8 responses from 4 (Agree) to 5 (Strongly Agree) and 7 responses from 1 (Strongly Disagree) to 2 (Disagree). Item 6: There were 8 responses from 4 (Agree) to 5 (Strongly Agree) and 16 responses from 1 (Strongly Disagree) to 2 (Disagree). Item 7: There were 22 responses from 4 (Agree) to 5 (Strongly Agree) and 3 responses from 1 (Strongly Disagree) to 2 (Disagree). Item 8: There were 7 responses from 4 (Agree) to 5 (Strongly Agree) and 15 responses from 1 (Strongly Disagree) to 2 (Disagree) to 2 (Disagree). Item 9: There were 16 responses from 4 (Agree) to 5 (Strongly Agree) and 13 responses from 1 (Strongly Disagree) to 2 (Disagree) and 26 responses from 1 (Strongly Disagree) to 2 (Disagree). Item 11: There were 5 responses from 4 (Agree) to 5 (Strongly Agree) and 33 responses from 1 (Strongly Disagree) to 2 (Disagree). Item 11: There were 5 responses from 4 (Agree) to 5 (Strongly Agree) and 33 responses from 1 (Strongly Disagree) to 2 (Disagree). Item 11: There were 5 responses from 4 (Agree) to 5 (Strongly Agree) and 33 responses from 1 (Strongly Disagree) to 2 (Disagree).

Outliers in the trend of considerably more responses ranging from 4 (Agree) to 5 (Strongly Agree) than those from 1 (Strongly Disagree) to 2 (Disagree) appear in Items 6, 8, 9, 10, and 11. The outliers in responses to Item 6 can be explained by the fact that it prompts respondents to answer to what extent others' support and encouragement on social media is important to them, which is something they might not want to admit truthfully if it is on the higher end of the scale due to feelings of embarrassment or shame. The outliers in Items 8, 9, 10, and 11 are also valid and were expected because these involve inquiries suggesting more extreme levels of social media use, involving feelings of boredom or anxiety in the absence of social media as well as feeling that social media makes respondents feel happier or more comfortable than they do in real life. Despite these outliers, based on the majority of the results, it can be concluded that respondents report overall high social media use, which aligns with the original hypothesis.



News Consumption

A significant majority of respondents report social media being their main news source. *Item 1 (Television):* 5 respondents answered "Often" and 15 respondents answered "Sometimes." *Item 2 (Radio):* 4 respondents answered "Often" and 5 respondents answered "Sometimes." *Item 3 (Print Publications):* No respondents answered "Often" and 5 respondents answered "Sometimes." *Item 4 (News Sites/Apps):* 14 respondents answered "Often" and 9 respondents answered "Sometimes." *Item 5 (Social Media):* 27 respondents answered "Often" and 7 respondents answered "Sometimes." *Item 6 (Another Source):* 8 respondents answered "Often" and 6 respondents answered "Sometimes." *Item 7 (For the previous question: What other sources?):* 14 respondents answered the open-ended question with some variation of "Friends/Family." Both social media and news sites/apps received significantly more responses from "Often" to "Sometimes" than other choices, but social media is still rated significantly higher as a frequented news source than other options, with only 2 respondents answering "Rarely" or "Never" when asked about social media.



Experiences of Discrimination

Reports on experiences of discrimination were less than originally expected but still present, in some cases more often and in others less so. *Item 1:* 8 respondents answered "A Few Times a Month" and 16 respondents answered "A Few Times a Year." *Item 2:* 9 respondents answered "A Few Times a Month" and 11 respondents answered "A Few Times a Year." *Item 3:* 5 respondents answered "A Few Times a Month" and 8 respondents answered "A Few Times a

Year." *Item 4:* 3 respondents answered "Almost Everyday," 4 respondents answered "At Least Once a Week," 2 respondents answered "A Few Times a Month," and 7 respondents answered "A Few Times a Year." *Item 5:* 1 respondent answered "A Few Times a Month" and 4 respondents answered "A Few Times a Year." *Item 6:* 5 respondents answered "A Few Times a Month" and 8 respondents answered "A Few Times a Year." *Item 7:* 2 respondents answered "Almost Everyday," 7 respondents answered "At Least Once a Week," 8 respondents answered "A Few Times a Month," and 5 respondents answered "A Few Times a Year." *Item 8:* 2 respondents answered "A Few Times a Month," and 10 respondents answered "A Few Times a Year." *Item 9:* 2 respondents answered "A Few Times a Month" and 3 respondents answered "A Few Times a Year." Overall, the frequency of reports on experiences of discrimination raise concern.



Subjective Well-Being

Item 1: Responses were most commonly "Somewhat Agree" or "Somewhat Disagree." Item 2: Responses were most commonly "Agree," "Somewhat Agree," or "Neither Agree Nor Disagree." Item 3: Responses were most commonly "Neither Agree Nor Disagree" or "Somewhat Disagree." Item 4: Responses were most commonly "Neither Agree Nor Disagree," "Somewhat Agree," or "Agree." Item 5: Responses were most commonly "Disagree" or "Somewhat Disagree." The mean score on the Satisfaction with Life scale was 20.75, which is toward the lower end of the "Slightly Satisfied" range (21-25) and close to "Neutral" (20). This indicates that, on average, participants scored slightly above Neutral. However, results varied greatly, as there were considerably many respondents with overall high scores in the "Satisfied" (25-29) or "Extremely Satisfied" category (30-35) as well as those with overall low scores in the "Dissatisfied" category (10-14). No respondents scored in the "Extremely Dissatisfied" category (5-9).



Perceived Social Support

Item 1: Responses were most commonly "Neither Agree Nor Disagree," "Agree," or "Strongly Agree." Item 2: Responses were fairly evenly distributed across all five categories. Item 3: A significant majority of responses were "Strongly Disagree." Item 4: Responses were most commonly "Strongly Agree" or "Agree." Item 5: A significant majority of responses were "Agree." Item 6: A significant majority of responses were "Agree." Item 7: Responses were most commonly "Agree" or "Strongly Agree." Item 8: Responses were most commonly "Agree" or "Neither Agree Nor Disagree." Item 9: Responses were most commonly "Strongly Agree." Item 9: Responses were most commonly "Strongly Agree." Item 10: Responses were fairly evenly distributed across all five categories, but responses were most commonly "Strongly Agree." Item 11: Responses were most commonly "Strongly Agree." Item 12: Responses were most commonly "Strongly Agree." Item 11: Responses were most commonly "Strongly Agree." Item 12: Responses were most commonly "Strongly Agree." Item 12: Responses were most commonly "Strongly Agree." Item 11: Responses were most commonly used to family in comparison to friends or potential significant others. Most notably, Items 2 and 3 yielded particularly low reports of social support.

To analyze these results, the researcher calculated the mean of each participant's responses for each individual scale of survey questions (Social Media Use, Experiences of Discrimination, Subjective Well-Being, Perceived Social Support). For News Consumption, the

researcher utilized each participant's response to the inquiry regarding social media for the calculations. A Pearson's correlation coefficient⁵ was calculated to determine the extent of correlation between social media use and experiences of discrimination; social media news consumption and experiences of discrimination; experiences of discrimination and subjective well-being; and experiences of discrimination and perceived social support. This method was chosen because the data being analyzed is quantitative and on an interval scale.

The researcher found that social media use and experiences of discrimination had a strong correlation with each other (r = +0.955). The positive r value indicates that responses with a higher number value in social media use (5 = Strongly Agree) corresponded with responses of a higher number value in experiences of discrimination (6 = Almost Everyday). From these results, it can be concluded that more social media use is highly correlated with more frequent experiences of discrimination.

For social media news consumption and experiences of discrimination, there was almost no correlation between these two variables (r = -0.023). There was no meaningful relationship between social media news consumption and experiences of discrimination, so no conclusions can be made about their correlation with each other.

A highly negative correlation between experiences of discrimination and subjective well-being was identified (r = -0.922). The negative r value indicates that responses with a higher number value in experiences of discrimination (6 = Almost Everyday) corresponded with responses of a lower number value in subjective well-being (1 = Strongly Disagree). This suggests that more frequent exposure to discrimination is highly correlated with lower subjective well-being.

There was no significant correlation found between experiences of discrimination and perceived social support (r = +0.079). There are no particular conclusions to be made about any relationship between exposure to discrimination and perceived social support.

Social media news consumption had no relationship with experiences of discrimination, and the same was found between experiences of discrimination and perceived social support. However, extremely strong correlations were identified between social media use and experiences of discrimination, and experiences of discrimination and perceived social support. News and perceived social support cannot be considered in the conclusions made based on the results of this study. Higher social media use was found to correspond with more frequent exposure to discrimination and more frequent exposure to discrimination had a correlation with lower subjective well-being. Thus, the results of this study suggest that Asian American adolescents who more frequently use social media experience more discrimination and have a lower subjective well-being.

⁵ Pearson's correlation coefficient: A statistic measuring the linear interdependence between two variables or two sets of data

Limitations

Despite the findings of this study, some limitations must be considered when examining the results. The study would have more effectively measured participants' psychological well-being with questions measuring multiple aspects of well-being rather than being confined to satisfaction with life and social support. These are both scales measuring ego-syntonic aspects of psychosocial well-being, which involve behaviors that correspond to one's personal goals or ideal self-image (Ian, 2022). In future research, it would be helpful to also utilize measures of ego-dystonic behavior for a more thorough means of evaluating participants' overall psychological well-being. Ego-dystonic behavior was not measured in this study because the researcher purposely limited the number of questions in hopes of collecting more responses with a shorter survey.

The survey population itself was limited because the majority of the population consists of minors, so IRB approval from each school was needed in order to recruit participants. This was not feasible for schools outside of the researcher's school district, as they required a longer period of time to process the approval than other schools within the district. Thus, only students from within the district were surveyed. This might have affected the study results because the small sample size was an inadequate representation of all EA/SEA Americans. The fact that all participants were from the same area likely impacted the conclusions of the study due to less diverse experiences and perceptions regarding the research topic. Due to the lack of anonymity, respondents might also have been hesitant to answer questions truthfully, especially concerning sensitive topics or experiences such as racial discrimination as well as psychological well-being.

Conclusion

Some hypotheses were confirmed, while others were contradicted by the study results. Most responses regarding social media use ranged from 3-5 ("Neither Agree Nor Disagree" to "Strongly Agree"), but Items 6, 8, 9, 10, and 11 were outliers in this trend. A majority of respondents reported social media being their main news source. News sites/apps were also reported as being a common news source, but not as commonly as social media. Experiences of discrimination were not reported as occurring as frequently as expected. However, there were still reports of discrimination whose frequency was concerning. Participants reported higher overall perceived social support from friends and potential significant others than from family. Higher social media use correlated with more frequent experiences of discrimination, while more frequent exposure to discrimination corresponded with lower subjective well-being. However, there was no significant correlation between social media news consumption and experiences of discrimination, and no notable relationship between experiences of discrimination and perceived social support.

Although the study's findings seem to suggest that social media news consumption and perceived social support have no significant relationship to the other variables tested, there is previous research that contradicts these results. Due to the complexity of the matter and the recency of the pandemic, namely the numerous aspects of anti-Asian discrimination.

Works Cited

- Austin, L. (2012). How Audiences Seek Out Crisis Information: Exploring the Social-Mediated Crisis Communication Model. *Journal of Applied Communication Research*, 40(2), 188-207. <u>https://doi.org/10.1080/00909882.2012.654498</u>.
- Bailey, Z. D. et al. (2017). Structural Racism and Health Inequities in the USA: Evidence and Interventions. *The Lancet*, *389*(10077). <u>https://doi.org/10.1016/S0140-6736(17)30569-X</u>.
- Banerjee, D., & Meena, K. S. (2021). COVID-19 as an "Infodemic" in Public Health: Critical Role of the Social Media. *Frontiers in Public Health*, 9(6). <u>https://doi.org/10.3389/fpubh.2021.610623</u>
- Cheah, C. S. L. et al. (2020). COVID-19 Racism and Mental Health in Chinese American Families. *Pediatrics*, *146*(5). <u>https://doi.org/10.1542/peds.2020-021816</u>
- Ian. (2022, February 15). Egosyntonic and Egodystonic Behaviors in Psychotherapy. FHE Health. <u>https://fherehab.com/learning/ego-syntonic-and-ego-dyntonic#:~:text=What%20are%20E</u> <u>go%2DDystonic%20Behaviors.are%20inconsistent%20with%20your%20ego</u>.
- Johnson, J. M. et al. (2021). Media Use During COVID-19: An Investigation of Negative Effects on the Mental Health of Asian Versus White Americans. *Frontiers in Communication*, 6. <u>https://doi.org/10.3389/fcomm.2021.638031</u>.
- Liu, S. R., & Modir, S. (2020). The Outbreak That Was Always Here: Racial Trauma in the Context of COVID-19 and Implications for Mental Health Providers. *Psychological Trauma: Theory, Research, Practice, and Policy, 12*(5), 439–442. <u>https://doi.org/10.1037/tra0000784</u>.
- Marciano, L. et al. (2022). Digital Media Use and Adolescents' Mental Health During the COVID-19 Pandemic: A Systematic Review and Meta-Analysis. *Frontiers in Public Health*, 9. <u>https://doi.org/10.3389/fpubh.2021.793868</u>
- More Than 9,000 Anti-Asian Incidents Have Been Reported Since The Pandemic Began. NPR. (2021, August 12). Retrieved from <u>https://www.npr.org/2021/08/12/1027236499/anti-asian-hate-crimes-assaults-pandemic-incidents-aapi</u>
- New CDC Data Illuminate Youth Mental Health Threats During the COVID-19 Pandemic. Centers for Disease Control and Prevention. (2022, March 31). Retrieved from <u>https://www.cdc.gov/media/releases/2022/p0331-youth-mental-health-covid-19.html</u>
- NYPD Reports 361 Percent Increase in Anti-Asian Hate Crimes Since Last Year. NBC News. (2021, December 10). Retrieved from <u>https://www.nbcnews.com/news/asian-america/nypd-reports-361-percent-increase-anti-as</u> <u>ian-hate-crimes-last-year-rcna8427</u>
- One-Third of Asian Americans Fear Threats, Physical Attacks and Most Say Violence Against Them is Rising. Pew Research Center. (2021, April 21). Retrieved from <u>https://www.pewresearch.org/fact-tank/2021/04/21/one-third-of-asian-americans-fear-thre</u> <u>ats-physical-attacks-and-most-say-violence-against-them-is-rising/</u>

- Pedrosa, A. L. et al. (2020). Emotional, Behavioral, and Psychological Impact of the COVID-19 Pandemic. *Frontiers in Psychology*, *11*. <u>https://doi.org/10.3389/fpsyg.2020.566212</u>
- The Long History of Racism Against Asian Americans in the U.S. PBS News Hour. (2020, April 9). Retrieved from https://www.pbs.org/newshour/nation/the-long-history-of-racism-against-asian-americans -in-the-u-s
- Viladrich, A. (2021). Sinophobic Stigma Going Viral: Addressing the Social Impact of COVID-19 in a Globalized World. *American Journal of Public Health*, 111(5), 876–880. <u>https://doi.org/10.2105/ajph.2021.306201</u>
- Wu, L., & Nguyen, N. (2022). From Yellow Peril to Model Minority and Back to Yellow Peril. AERA Open, 8. <u>https://doi.org/10.1177/23328584211067796</u>.
- Yang, C. et al. (2020). Discrimination and Well-Being Among Asians/Asian Americans During COVID-19: The Role of Social Media. *Cyberpsychology, Behavior, and Social Networking*, 23(12). <u>https://doi.org/10.1089/cyber.2020.0394</u>.

Juvenile Arthritis' Effects on GPA: an Exploration on the Efficiency and Equity of 504 Plans in the American Special Education System By Maria A. Fernandez

Abstract

Juvenile Arthritis (JA) is the term used to describe when symptoms of Rheumatoid Arthritis (RA) present themselves in children or adolescents 16 or under. Rheumatoid arthritis is a chronic autoimmune disorder that primarily affects the joints, but can have profound effects throughout the body. Due to the prevalence of RA, adults in the U.S. with RA can apply for Social Security Association (SSA) benefits and qualify under the Americans with Disabilities Act (ADA), which federally requires employers to provide assistance and accommodations to aid adults with this disorder. However, research on the prevalence and efficiency of 504 accommodations plans for children diagnosed with JA is lacking. This sparked the goal for this study, to evaluate the effects of JA on schooling as a means to evaluate the efficacy of accommodations currently in place.

To assess this within the American special education system, data on GPA's, accommodations, attitudes and severity, was collected via survey, as means to compare correlations and academic performance of students receiving accommodations, with a particular focus on students reporting JA.

It was concluded that students with JA report generally lower academic performance in comparison to their peers receiving accommodations for other issues, and even lower when compared to their peers reporting no health impediments, and no accommodations. It was additionally concluded that accommodations currently in place for JA have a minimal effect on academic performance when comparing students with JA receiving accommodations, and students with JA not receiving accommodations.

Introduction

Juvenile arthritis (JA), also known as pediatric rheumatic disease, isn't one common experience, It's an umbrella term to describe the inflammatory and rheumatic diseases that develop in children under the age of 16⁶. The most common, Juvenile Idiopathic Arthritis, describes a clinically heterogeneous group of arthritides of unknown cause.⁷. This term encompasses several other disease categories, the main 6 oligoarthritis, polyarthritis, systemic, enthesitis-related, juvenile psoriatic arthritis and undifferentiated. JA also includes Juvenile Lupus, Juvenile myositis, Juvenile scleroderma, Vasculitis and Fibromyalgia. These varying conditions affect nearly 300,000 kids and teens in the United States⁸. While the term is broad, the subcategories do share some common symptoms, like joint stiffness and fatigue, which are

⁶ Gare, B. A. (1999). Juvenile arthritis—who gets it, where and when? A review of current data on incidence and prevalence. *Clin Exp Rheumatol*, *17*(3), 367-374.

⁷ Gare, B. A. (1999)

⁸ Ravelli, A., & Martini, A. (2007). Juvenile idiopathic arthritis. *The Lancet*, 369(9563), 767-778.

reported to be the most debilitating of the many symptoms associated with the disorder⁹. Another common factor is that these diseases are mostly idiopathic, unidentifiable to the untrained eye, and seriously underdiagnosed¹⁰. Rheumatoid arthritis– the adult diagnosis– has been widely reported as disabling in workplace settings¹¹. Yet research is lacking on the possible effects on Juvenile arthritis (JA) affecting school performance, and what accommodations are the most effective. Several programs exist in the United States to help specially aid school age children with disabling conditions ¹²— but JA stands alone. If accommodating systems are not set in place for children suffering from such conditions they'll fall behind in school work and have decreased learning abilities ¹³. In order to analyze what can be done to aid students diagnosed with this condition, there must be further analysis on what proves the most effective in aiding students with JA. There exist many comprehensive explorations on what accommodations aid kids with other disabilities¹⁴, that teachers are trained upon to help accommodate these students, and it has proven successful¹⁵. Considering the sudden rise of JA diagnosis throughout the nation¹⁶, it is empirical that teachers are further informed on how to aid students with this complex condition.

It can be quite a challenge to even truly evaluate how severe or what symptoms children with JA experience, making it an even bigger challenge to accommodate them—however, here are different ways of measuring arthritis severity, such as the BRAF MCQ¹⁷, which will be similar to what will be used to conduct symptom severity analysis in this study. Development and validation of a composite disease activity score for juvenile idiopathic arthritis has been a challenge for physicians worldwide, but certain pillars remain consistent on what proves practically efficient in quantifying symptoms.

⁹ Weiss, P. F., Beukelman, T., Schanberg, L. E., Kimura, Y., & Colbert, R. A. (2012). Enthesitis-related arthritis is associated with higher pain intensity and poorer health status in comparison with other categories of juvenile idiopathic arthritis: the Childhood Arthritis and Rheumatology Research Alliance Registry. *The Journal of rheumatology*, *39*(12), 2341-2351.

¹⁰ Koos, B., Twilt, M., Kyank, U., Fischer-Brandies, H., Gassling, V., & Tzaribachev, N. (2014). Reliability of clinical symptoms in diagnosing temporomandibular joint arthritis in juvenile idiopathic arthritis. *The Journal of rheumatology*, *41*(9), 1871-1877.

¹¹ van Vilsteren M, Boot CR, Knol DL, van Schaardenburg D, Voskuyl AE, Steenbeek R, Anema JR. Productivity at work and quality of life in patients with rheumatoid arthritis. BMC Musculoskelet Disord. 2015 May 6;16:107. doi: 10.1186/s12891-015-0562-x. PMID: 25940578; PMCID: PMC4425924.

¹² Cook, B. G., & Schirmer, B. R. (2003). What is special about special education? Overview and analysis. *The Journal of Special Education*, *37*(3), 200-205.

¹³ Cook, B. G., & Schirmer, B. R. (2003).

¹⁴ Reid, R., & Maag, J. W. (1998). Functional assessment: A method for developing classroom-based accommodations and interventions for children with adhd. *Reading & Writing Quarterly Overcoming Learning Difficulties*, *14*(1), 9-42.

¹⁵ Lovett, B. J., & Nelson, J. M. (2021). Systematic review: Educational accommodations for children and adolescents with attention-deficit/hyperactivity disorder. *Journal of the American Academy of Child & Adolescent Psychiatry*, *60*(4), 448-457.

¹⁶ Vincent, H. K., Sharififar, S., Abdelmalik, B., Lentini, L., Chen, C., & Woolnough, L. U. (2022). Gait parameters, functional performance and physical activity in active and inactive Juvenile Idiopathic Arthritis. *Gait & Posture*, *98*, 226-232

¹⁷ Bardwell, W. A., et al. "Rheumatoid Arthritis Severity Scale: a brief, physician-completed scale not confounded by patient self-report of psychological functioning." *Rheumatology* 41.1 (2002): 38-45.

Disability accommodation scale differs from official severity scales such as RASS (Rheumatoid Arthritis Severity Scale) which focuses on 3 points¹⁸, Disease Activity, Functional Impairment and Physical Damage. By this logic, a kid could have a high RASS score due to high disease activity in internal organs, but not report many physical impairments during school, and be considered within the level 1 mild disability accommodations.

There is Level 1, (mild), which refers to a child that is not currently handicapped, and their disorder isn't something that interferes with everyday learning. For kids in this category it is recommended to establish 504 plans, which are designed to aid a kid in case of a flare-up or emergency. Then there is Level 2, (mild to moderate), which is defined as a kid that is possibly handicapped, but their health impairment does not interfere with learning, although there is a possibility of unusual episodes or crises. For this kids are still recommended to seek a 504 plan, meant to accommodate them in a discussed possibility of crisis. Accommodations usually include but are not limited to, designed stretch breaks, extended testing periods, extra bathroom breaks, access to a school nurse, and reduced penalties on late assignments due to medical impairments¹⁹.

Next is moderate, which is defined as a kid that is handicapped and their health impairment either presents frequent crises or so limits the child's opportunity to participate in activities that learning is interrupted. For this kids are recommended to seek out a 504 as well as an IEP (Individual Education Plan) which is defined as a written educational plan that is constructed for each student who qualifies under the moderate to severe disability categories²⁰. This is eligible only to students who have certain specified conditions, if conditions require specialized educational programming. The development and implementation of the IEP falls under the responsibility of the special education program within each school district. The next category is Severe, which is defined as a handicapped child whose health impairment is so severe that special medical attention is regularly needed. The child's opportunity for activity is so limited that he or she may not be able to participate in a regular classroom. For this level of severity, IEP are exclusively recommended. This is the most rare qualification, and it applies to children who might be physically crippled, have severe bowel problems due to conditions such as ulcerative colitis, are considered legally blind due to conditions such as Uveitis, etc. It is important to note that IEP and 504 plans, as well as the disability ranking scale, do not only apply to children with conditions classified under JA, but to any chronic health conditions²¹.

¹⁸ W. A. Bardwell, P. M. Nicassio, M. H. Weisman, R. Gevirtz, D. Bazzo, Rheumatoid Arthritis Severity Scale: a brief, physician-completed scale not confounded by patient self-report of psychological functioning, Rheumatology, Volume 41, Issue 1, January 2002, Pages 38–45,

 ¹⁹ Whitehouse, R., Shope, J. T., Sullivan, D. B., & Kulik, C. L. (1989). Children with juvenile rheumatoid arthritis at school: Functional problems, participation in physical education. *Clinical pediatrics*, *28*(11), 509-514.
²⁰ Whitehouse, R.

²¹Nordal, E., Rypdal, V., Arnstad, E. D., Aalto, K., Berntson, L., Ekelund, M., ... & Nordic Study Group of Pediatric Rheumatology (NoSPeR) Gudmund Marhaug Freddy Karup Pedersen Pekka Lahdenne Boel Anderson-Gäre. (2019). Participation in school and physical education in juvenile idiopathic arthritis in a Nordic long-term cohort study. *Pediatric Rheumatology*, *17*, 1-10.

504 and IEP plans are personalized and curated child by child through a series of parent, child, and teacher conferences. Important to note that the teachers input is heavily valued in these conferences²², which might limit the reach of the accommodations as JA is an invisible disability, which teachers are not aware of. Most kids live most of their life with this disease and by high school have adjusted to controlling and concealing pain and medication side effects²³. Also important to note is that accommodations should also encompass JA treatment side effects. The top reported side effect from most common JA treatments (methotrexate, biologics, and steroids²⁴) is Fatigue and general Malaise²⁵²⁶— which happen to be the least visible and most disqualifiable symptoms to teachers²⁷, making it hard for children to get proper accommodations for such disabilities. Proper accommodations to this symptom include, but are not limited to, extended assignment time and breaks²⁸.

It has been well reported in the past that students suffering from "invisible disabilities" struggle the most in receiving proper accommodations, and having a "normal" school experience²⁹. Helping accommodate these students requires fundamental understanding of the symptoms being experienced, and a conscious effort from teachers³⁰.

Past Research/Literary Gap

JA can greatly impact children's quality of life, limiting them in many aspects, due to the complex and hard to treat symptoms. As reported by the Arthritis Journal of Care and Research "items most frequently rated as adolescents' biggest psychological problems were "felt frustrated" and "felt depressed," rated by 30.2% and 23.4%, respectively. These were particularly problematic for the 17-year-olds, with 39% reporting frustration as one of their biggest problems and 63.6% reporting depression. Variation in the adolescent JAQQ scores was explained by functional disability, pain, and disease activity." Meaning JA can go as far as impacting mental

²² Milatz, F., Klotsche, J., Niewerth, M., Geisemeyer, N., Trauzeddel, R., Weißbarth-Riedel, E., ... & Minden, K. (2019). Participation in school sports among children and adolescents with juvenile idiopathic arthritis in the German National Paediatric Rheumatologic Database, 2000–2015: results from a prospective observational cohort study. *Pediatric Rheumatology*, *17*, 1-10.

²³Whitehouse, R., Shope, J. T., Sullivan, D. B., & Kulik, C. L. (1989). Children with juvenile rheumatoid arthritis at school: Functional problems, participation in physical education. *Clinical pediatrics*, *28*(11), 509-514.

²⁴ Singh, J. A., Wells, G. A., Christensen, R., Ghogomu, E. T., Maxwell, L. J., MacDonald, J. K., ... & Buchbinder, R. (2011). Adverse effects of biologics: a network meta-analysis and Cochrane overview. *Cochrane database of systematic reviews*, (2).

²⁵Singh, J. A., Wells, G. A., Christensen, R., Ghogomu, E. T., Maxwell, L. J., MacDonald, J. K., ... & Buchbinder, R. (2011).

²⁶ Weinblatt ME, Coblyn JS, Fox DA, Fraser PA, Holdsworth DE, Glass DN, Trentham DE. Efficacy of low-dose methotrexate in rheumatoid arthritis. N Engl J Med. 1985 Mar 28;312(13):818-22.

²⁷Baum, S., & Owen, S. V. (1988). High ability/learning disabled students: How are they different?. *Gifted Child Quarterly*, *32*(3), 321-326.

²⁸ Tollit, M., Politis, J., & Knight, S. (2018). Measuring school functioning in students with chronic fatigue syndrome: a systematic review. *Journal of School Health*, 88(1), 74-89.

²⁹Maxam, S., & Henderson, J. E. (2013). Inclusivity in the Classroom: Understanding and Embracing Students With "Invisible Disabilities." *Journal of Cases in Educational Leadership*, *16*(2), 71–81.

³⁰ Kattari, S. K., Olzman, M., & Hanna, M. D. (2018). "You look fine!" Ableist experiences by people with invisible disabilities. *Affilia*, *33*(4), 477-492.

health. Having poor mental health is already correlated with poor school performance³¹, therefore students with JA are already at a predisposed position to struggle in school. Kids with JA/JA treatment related fatigue report the most absences, lowered test scores, and falling behind in their course work³². A study by BMC Pediatrics in Morocco³³ reported that 33% of children with JIA were unable to attend school due to their condition. The students with JIA who were able to attend school were absent much more often than controls (63% compared to 20%), with a highly significant p value (p<0.0001). Slightly less than half of the JIA patients (48.5%) failed in their schooling in contrast to 7% in the control group.

There's clearly an undressed limitation in the aid being provided in the school system for this discrepancy to occur. There is limited research even reporting on this discrepancy–particularly in the American special education system– which should be the first step to fixing the issue. To address this gap, a larger more comprehensive study discussing the actual limits of the accommodations, and impact on grade point average is necessary, as it proves relevant to high school students particularly seeking higher education. Such study will serve as a a stepping stone to improving JA students' school life. As elaborated earlier, JA is complicated and varied, which makes it challenging to reach a comprehensive conclusion on how to move forward in aiding these students, however, an exploration into the current state of the Special Ed. system should be the first step in narrowing down this issue.

Research Design and Methodology

Responses were collected via survey, which was administered at Juvenile Arthritis awareness events hosted by the Arthritis Foundation®. Responses were also collected from students that have 504 plans for alternative reasons, as well as students with no accommodations or health issues, which were collected at school grounds around the state of Florida. These groups were also included to work as a control when comparing the quantitative data gathered from the GPA inquiries.

Students were asked to report on their attendance, respondents indicating significantly below average attendance (more than 5 absences a month), were excluded from the data set. This is because students missing school significantly due to hospitalization and such, generally already report lower school performance, and it is not something that can be address by in-classroom accommodations³⁴.

³¹ DeSocio, J., & Hootman, J. (2004). Children's mental health and school success. *The Journal of School Nursing*, *20*(4), 189-196.

³²Bouaddi I, Rostom S, El Badri D, Hassani A, Chkirate B, Amine B, Hajjaj-Hassouni N. Impact of juvenile idiopathic arthritis on schooling. BMC Pediatr. 2013 Jan 7;13:2. doi: 10.1186/1471-2431-13-2. PMID: 23289498; PMCID: PMC3544633.

³³ Bouaddi I, Rostom S, El Badri D, Hassani A, Chkirate B, Amine B, Hajjaj-Hassouni N.

³⁴ Steinke, S. M., Elam, M., Irwin, M. K., Sexton, K., & McGraw, A. (2016). Pediatric Hospital School Programming: An Examination of Educational Services for Students who are Hospitalized. *Physical Disabilities: Education and Related Services*, *35*(1), 28-45.
Once students indicated that they are diagnosed with JA, they were asked "*How severe would you classify your disability levels? (0 would be asymptomatic, 5 would be visible accommodations/impediments such as a wheelchair, blindness due to uveitis, etc.)*" This question, while simple, works as a simplified form of the RASS scale, which focuses on 3 pillars Disease Activity, Functional Impairment and Physical Damage. This was applied through a simple Likert Scale, which can prove simple and efficient when collecting non-specific data. This was particularly chosen due to the known complexities and uncertainties when it comes to Arthritis symptoms that could possibly interfere with collecting responses particularly via. survey. All that was particularly needed was a general idea of the demographics partaking in this study, to make sure the responses were actually reflective of the average student with JA, and not focusing on exceptional cases of particularly low or high functionality. Additionally, when crafting 504 accommodation plans, functional impairment proves most

relevant, as these are usually the symptoms that interfere with school functioning. This scale would work as a simplified version of what is usually evaluated in schools to accommodate students.

Students were asked to report what treatment they are currently receiving, as while RA itself might be under control, different treatments might still affect quality of life, as well as what particular accommodations they receive. While not necessarily used to evaluate the correlations reported, it is still crucial to report the demographics of the students whose academic performance is being evaluated, when looking to make practical improvements in the field.

All students partaking in the survey were asked to report their GPA on a weighted and unweighted scale. Weighted GPA takes course intensity/level into account, and it can prove more substantial when analyzing a students academic performance as it gives a deeper insight on the students true academic performance. Unweighted GPA provides a raw average of a student's grades, without taking course intensity/level into consideration. Students reported both. GPA was chosen due to the simplicity of comparing academic performance through a single, generalized reporting on a student's success. Additionally, particularly with high school students, GPA proves relevant in situations such as college admissions, therefore it is relevant to acknowledge discrepancies caused by outside situations. GPA particularly focuses on schoolwork, rather than learning, which can reflect how students with JA might be simply impaired in participating in schoolwork, rather than not learning.

Qualitative Data/Attitude Exploration

Since past literature suggested the fact that invisible disabilities such as JA are specially not accommodated due to teacher's attitudes to unseen medical problems, students were asked to rate their dissatisfaction levels with the extent that their school goes to accommodate them. Dissatisfaction was measured through a series of questions on the Likert Scale, which is commonly used in surveys of the field to measure participants' attitudes.

The Likert scale asks participants to rate their attitude towards a statement as 1 = strongly agree, 2 = agree, 3 = neutral, 4 = disagree, and 5 = strongly disagree.

Students were given the following statements to rate as such:

"My GPA would be higher if I didn't have this condition."

"My teachers don't do a good enough job accommodating me."

"My teachers disregard my condition."

These statements were crafted based on past explorations on students with invisible disabilities, attitudes and perceptions of their educational environment. They are meant to reflect students' perspectives on their educational environment as a means to provide contextualization to any found correlations.

Results

The survey was administered to middle-high school students, they were asked to identify their grade level, 5.4 percent of the participants identified with grade level below 9th. These responses were removed from the data. 94.6 percent of responses identified with grade 9-12, these responses are the ones being reported on.

	Reported Juvenile Arthritis diagnosis	Reported other Diagnosis	Reported no Diagnosis	Total
Reported accommodations	254	165	0	423 (49.7%)
Reported no accommodations	64	9	342	428 (50.3%)
	318	174	342	851

Within the students that reported receiving no accommodations, 15% reported a Juvenile arthritis diagnosis, 2% reported other conditions that they think deserve accommodation, and 83% reported having no significant or active medical condition. In total, 37.8% of responses reported a Juvenile arthritis diagnosis.

Results: Severity



The average score was 2.6 on a scale of 5.

Treatment The top reported treatments were as follows

Methotrexate	37.5%
Biologics	62%
NSAIDs	51.2%
Corticoids	5.3%

Results: Demographics: Accommodation The top reported accommodations were as follows

Extended time for testing/assignments	77%
Extended breaks during class/testing	51%
Typing usually written assignments	33%
Accommodated seating	52%

Results: GPA

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	AVERAGE UNWEIGHTED GPA (0.0-4.0)	AVERAGE WEIGHTED GPA (0.0-6.0)
No accommodations reported and no reported conditions	3.110	3.823
Reported accommodations	2.821	3.532
Reported Juvenile Arthritis Diagnosis with accommodations	2.741	3.232
Reported Juvenile arthritis with no accommodations	2.612	3.144

:

Average student dissatisfaction:





"AGREE OR DISAGREE? My GPA would be higher if I didn't have this condition" 1- Strongly Disagree 5- Strongly Agree"

Average response for participants that reported Juvenile Arthritis: 3.47 Average response for other conditions: 3.21

"AGREE OR DISAGREE? My teachers don't do a good enough job accommodating me or following my 504 plan. 1- Strongly Disagree 5- Strongly Agree" Average response for participants that reported Juvenile arthritis : 4.67 Average response for other conditions : 3.21

"AGREE OR DISAGREE? My teachers disregard my condition 1-Strongly Disagree 5-Strongly Agree"

Average response for participants that reported Juvenile arthritis : 4.32 Average response for other conditions : 2.3. ÷

Discussion

The most evident discrepancy to be evaluated in these findings is the slight, but significant variance in GPA from the different groups. Students that reported accommodations not specific to JA, had generally lower GPAs than students with no reported accommodations and no conditions, suggesting that 504 plans in general are not fully efficient in providing students with the same educational experience as their peers. In an ideal world, there would be little to no discrepancy between these two groups as the "advantages" provided to students through accommodations would make up for the disadvantages the student experiences through their condition. In practice, this goal can be very hard to achieve, as schools are generally geared towards the majority of students who do not need any particular accommodations. Still, when looking to improve the special education system in general, noting these discrepancies is crucial to making progress in improving such programs.

When observing the results particular to JA, we can draw particular comparisons between students receiving accommodations with JA, and students not receiving them at all. We found a surprising near 20% of students with JA reported receiving no accommodations at all, and when comparing this 20% to the 80% receiving accommodations, we found only a very slight difference in GPA, as the accommodated group barely surpassed the one receiving accommodations. This suggests accommodations barely make a significant difference in actually improving students with JA performance.

When comparing students with JA to the general populace, the hypothesis was proven correct, as they had generally lower GPAs.

When it comes to students' personal attitudes about their accommodations, we found yet another discrepancy, as students with JA accommodations reported significantly more dissatisfied with their accommodations (see figure 3.). This can be attributed to the priorly reported phenomenon of invisible disabilities being specially harder to accommodate to. It suggests teachers particularly write off JA accommodations. This makes logical sense with the results of the demographics average severity (see figure 1.), as the average reported severity on 0-5 was 2.6, suggesting the great majority of students who partake in this study have symptoms, however don't have visible impediments that make it evident to school officials that they do in fact require extra help. When observing the distribution in responses, the great majority of students considered themselves within the 2-3 range of severity, meaning their disability is in fact not visible.

Nearly 98% of JA-diagnosed students reported being under some sort of treatment, which carries their own functional burdens. The top reported treatments (methotrexate and biologics), have common symptoms of general malaise and fatigue, a symptom that is completely unidentifiable to the average observer, and especially difficult to quantify. This suggests the average student with JA struggles with just a general lack of energy, that can be severely debilitating, but also easily written off as "laziness". However, the most appropriate accommodation for this symptom is extended time and breaks, which was reported by a 77% of total respondents with JA, suggesting the accommodations set in place are not being carried out

efficiently, which coincides with the responses from JA students stating that their accommodations that are set in place are not properly respected by teachers. This prompts further exploration on how these accommodations work within the classroom, and how they can be fully efficient. Previous research reports that a huge pillar of making 504 plans work is teacher conscientiousness and awareness of a students symptoms³⁵. This must be considered when applying this new understanding practically, as the issue might not be the written 504 accommodations, but how they are carried out in the classroom particularly. This concedes with past research reporting students with invisible disabilities struggle the most in receiving proper respect of their written and required accommodations.

Fulfillment of the Gap in Research

This study serves as a direct follow up to the one previous exploration on these discrepancies (Bouaddi, I., Rostom, S., El Badri, D.). This study concluded that a larger pool of students was necessary to confirm these findings. This study studied 32 students in contrast to the 851 students who took part in this survey. The findings support the previous study's general idea that JA has a negative impact on schooling.

However, this study was specific to American high school schooling, where 504 plans are legally required to be carried out.

Implications and Limitations

Some limitations carried with this choice of methodology is the reporting bias that comes with surveys generally, as students might inflate their responses. A more comprehensive analysis could instead directly report this data from school records, detailing GPA and received accommodations.

A limitation is the attempt to quantify students' attitudes through the use of the Likert scale. This can lead to overgeneralized results that don't particularly reflect the participants true attitudes.

Another is sample size, because while larger than past reports, an even larger data pool could provide more comprehensive data.

Reporting exclusively on GPA can have its downsides as it does not necessarily provide a holistic view of s as students educational experience. GPA can be influenced by other outside factors that do not particularly correlate with accommodations, therefore a more holistic view of a students educational experience and performance can prove beneficial. It must be noted that GPA focuses on school participation, as a students GPA can be dragged down due to not for example, turning in homework, while they might maintain high test scores due to still learning proficiently³⁶. This means these results do not necessarily suggest students with JA are not

³⁵ Spiel, C. F., Evans, S. W., & Langberg, J. M. (2014). Evaluating the content of Individualized Education Programs and 504 Plans of young adolescents with attention deficit/hyperactivity disorder. *School Psychology Quarterly*, *29*(4), 452.

³⁶ Hensley, W. E. (1995). What Do Grades Mean?: A Pilot Study Using Sex, GPA and Cognitive/Semantic Consistency.

learning, but that the school system simply does not serve them fairly. This is relevant to high school students as GPA is taken into account in college admissions, and a student with JA equally proficient as a student without, could be ridden off as "lazy" by college admissions due to their lowered GPA, while this assumption lacks context³⁷.

Areas for Future Research

what can actually be improved.

In order to further confirm these findings, a larger more comprehensive study is needed. A study that shifts the focus from student-responses in the form of a survey to empirical pre-existing data analysis can eliminate the reporter's bias or uncertainty. Such study would directly analyze school records, and explore similar correlations. It could also draw comparisons between school performance and satisfaction between the different reported accommodations being provided. This could provide applicable insight into what works, and what does notmaking it simpler for one to apply such results into empirical improvements. Another potential area of research would be shifting the focus away from GPA based analysis and instead focusing on other quantitative measures such as standardized test scores. This could provide a more holistic perspective of students' academic performance. A dual comparison of test scores and GPA could show further issues in the educational environment to be addressed. Another possible area of study would be to gather responses from teachers' particular attitudes towards student accommodations. This could help provide insight into why these accommodations do not work, and eliminate reporter's bias from students. A cross comparison between teachers and students' attitudes could highlight differences in attitudes. Similarly, a qualitative study could be performed, in comparison to the quantitative analysis that was performed. This could eliminate issues with the Likert scale. It could consist of a series of

Overall, there is much more research to be done to be able to confirm these findings, and many more ways to approach the issue of these discrepancies. In order to be able to holistically improve the American special education system, not limited to JA, more applicable insight is needed. There are many factors and uncertainties to be taken into account regarding this issue. Other research suggests ableist attitudes, or even financial issues might be what truly limits these accommodations from working³⁸. A comprehensive analysis on how other more efficient systems carry out accommodations might help point out the differences and faults of the American special education system.

interviews to teachers, students, and school officials, as a means to gather further insight into

³⁷ Sawyer, R. (2013). Beyond correlations: Usefulness of high school GPA and test scores in making college admissions decisions. *Applied measurement in education*, *26*(2), 89-112.

³⁸ Kattari, S. K., Olzman, M., & Hanna, M. D. (2018).

Works Cited

- Bardwell, W. A., et al. "Rheumatoid Arthritis Severity Scale: a brief, physician-completed scale not confounded by patient self-report of psychological functioning." Rheumatology 41.1 (2002): 38-45
- Baum, S., & Owen, S. V. (1988). High ability/learning disabled students: How are they different?. Gifted Child Quarterly, 32(3), 321-326.
- Bouaddi I, Rostom S, El Badri D, Hassani A, Chkirate B, Amine B, Hajjaj-Hassouni N. Impact of juvenile idiopathic arthritis on schooling. BMC Pediatr. 2013 Jan 7;13:2. doi: 10.1186/1471-2431-13-2. PMID: 23289498; PMCID: PMC3544633.
- Cook, B. G., & Schirmer, B. R. (2003). What is special about special education? Overview and analysis. The Journal of Special Education, 37(3), 200-205.
- DeSocio, J., & Hootman, J. (2004). Children's mental health and school success. The Journal of School Nursing, 20(4), 189-196.
- Gare, B. A. (1999). Juvenile arthritis—who gets it, where and when? A review of current data on incidence and prevalence. Clin Exp Rheumatol, 17(3), 367-374.
- Hensley, W. E. (1995). What Do Grades Mean?: A Pilot Study Using Sex, GPA and Cognitive/Semantic Consistency.
- Kattari, S. K., Olzman, M., & Hanna, M. D. (2018). "You look fine!" Ableist experiences by people with invisible disabilities. Affilia, 33(4), 477-492.
- Koos, B., Twilt, M., Kyank, U., Fischer-Brandies, H., Gassling, V., & Tzaribachev, N. (2014). Reliability of clinical symptoms in diagnosing temporomandibular joint arthritis in juvenile idiopathic arthritis. The Journal of rheumatology, 41(9), 1871-1877.
- Lovett, B. J., & Nelson, J. M. (2021). Systematic review: Educational accommodations for children and adolescents with attention-deficit/hyperactivity disorder. Journal of the American Academy of Child & Adolescent Psychiatry, 60(4), 448-457.
- Maxam, S., & Henderson, J. E. (2013). Inclusivity in the Classroom: Understanding and Embracing Students With "Invisible Disabilities." Journal of Cases in Educational Leadership, 16(2), 71–81.
- Milatz, F., Klotsche, J., Niewerth, M., Geisemeyer, N., Trauzeddel, R., Weißbarth-Riedel, E., ... & Minden, K. (2019). Participation in school sports among children and adolescents with juvenile idiopathic arthritis in the German National Paediatric Rheumatologic Database, 2000–2015: results from a prospective observational cohort study. Pediatric Rheumatology, 17, 1-10.
- Nordal, E., Rypdal, V., Arnstad, E. D., Aalto, K., Berntson, L., Ekelund, M., ... & Nordic Study Group of Pediatric Rheumatology (NoSPeR) Gudmund Marhaug Freddy Karup Pedersen Pekka Lahdenne Boel Anderson-Gäre. (2019). Participation in school and physical education in juvenile idiopathic arthritis in a Nordic long-term cohort study. Pediatric Rheumatology, 17, 1-10.

Ravelli, A., & Martini, A. (2007). Juvenile idiopathic arthritis. The Lancet, 369(9563), 767-778.

- Reid, R., & Maag, J. W. (1998). Functional assessment: A method for developing classroom-based accommodations and interventions for children with adhd. Reading & Writing Quarterly Overcoming Learning Difficulties, 14(1), 9-42.
- Sawyer, R. (2013). Beyond correlations: Usefulness of high school GPA and test scores in making college admissions decisions. Applied measurement in education, 26(2), 89-112.
- Singh, J. A., Wells, G. A., Christensen, R., Ghogomu, E. T., Maxwell, L. J., MacDonald, J. K., ... & Buchbinder, R. (2011). Adverse effects of biologics: a network meta-analysis and Cochrane overview. Cochrane database of systematic reviews, (2).
- Spiel, C. F., Evans, S. W., & Langberg, J. M. (2014). Evaluating the content of Individualized Education Programs and 504 Plans of young adolescents with attention deficit/hyperactivity disorder. School Psychology Quarterly, 29(4), 452.
- Steinke, S. M., Elam, M., Irwin, M. K., Sexton, K., & McGraw, A. (2016). Pediatric Hospital School Programming: An Examination of Educational Services for Students who are Hospitalized. Physical Disabilities: Education and Related Services, 35(1), 28-45.
- Tollit, M., Politis, J., & Knight, S. (2018). Measuring school functioning in students with chronic fatigue syndrome: a systematic review. Journal of School Health, 88(1), 74-89.
- Van Vilsteren M, Boot CR, Knol DL, van Schaardenburg D, Voskuyl AE, Steenbeek R, Anema JR. Productivity at work and quality of life in patients with rheumatoid arthritis. BMC Musculoskelet Disord. 2015 May 6;16:107. doi: 10.1186/s12891-015-0562-x. PMID: 25940578; PMCID: PMC4425924.
- Vincent, H. K., Sharififar, S., Abdelmalik, B., Lentini, L., Chen, C., & Woolnough, L. U. (2022). Gait parameters, functional performance and physical activity in active and inactive Juvenile Idiopathic Arthritis. Gait & Posture, 98, 226-232
- Weinblatt ME, Coblyn JS, Fox DA, Fraser PA, Holdsworth DE, Glass DN, Trentham DE. Efficacy of low-dose methotrexate in rheumatoid arthritis. N Engl J Med. 1985 Mar 28;312(13):818-22.
- Weiss, P. F., Beukelman, T., Schanberg, L. E., Kimura, Y., & Colbert, R. A. (2012). Enthesitis-related arthritis is associated with higher pain intensity and poorer health status in comparison with other categories of juvenile idiopathic arthritis: the Childhood Arthritis and Rheumatology Research Alliance Registry. The Journal of rheumatology, 39(12), 2341-2351.
- Whitehouse, R., Shope, J. T., Sullivan, D. B., & Kulik, C. L. (1989). Children with juvenile rheumatoid arthritis at school: Functional problems, participation in physical education. Clinical pediatrics, 28(11), 509-514.
- W. A. Bardwell, P. M. Nicassio, M. H. Weisman, R. Gevirtz, D. Bazzo, Rheumatoid Arthritis Severity Scale: a brief, physician-completed scale not confounded by patient self-report of psychological functioning, Rheumatology, Volume 41, Issue 1, January 2002, Pages 38–45,

The Impact of Stress on Development and Cognition: Effects Across the Lifespan By Esther Kreisberger

Abstract

Stress is a response to adverse circumstances that creates tension and emotional strain within the individual. There are two types of stress: chronic (a consistent apprehension toward a situation) and acute (a discrete response toward an adverse situation). Stress triggers the activation of the hypothalamus-pituitary-adrenal (HPA) axis, culminating in the production of glucocorticoids by the adrenals. They can act as transcription factors and so regulate gene expression. Thus, glucocorticoids can have long-lasting effects on the functioning of the brain regions that regulate their release.

In young children and early adolescents, stress reduces the volume of the hippocampus, and hence it negatively modulates the development of brain structures compared to healthy controls. Additionally, stress has been shown to adversely affect cognitive performance in test achievements and applies to tasks beyond educational administered tests.

In adults, stress impairs memory due to increased hippocampus function. In addition, stress is known for enhancing fearful memory, thus creating an abnormal fearful state. Furthermore, it causes changes in the dendrites and takes ten days to regulate them. It also impairs spatial learning and can be reversed 21 days later. The effects of chronic stress in adulthood are reversible, whereas, for infants, it is permanent.

Introduction

Stress is the body's response to physical, mental, or emotional pressure. Stress causes chemical changes in the body, raising blood pressure, heart rate, and blood sugar levels ("Definition of Stress," 2023). During acute stress, an individual will generally develop a short physiological response to the presented stressor, while chronic stress exposure will elicit a sustained maladaptive psychological response (Sparrenberger et al., 2009). Additionally, unlike acute stress, where the initial response to the stressor is phasic, an individual who experiences chronic stress is generally exposed to the stressor over an extended period (Bryant, 2019).

Clinical and basic science research has provided strong evidence that prolonged exposure to psychological stress can lead to behavioral deficits and psychiatric illnesses, specifically depression and anxiety (Duric et al., 2016). Additionally, elevated stress has been linked to other psychiatric disease states, such as depression, anxiety, and obsessive-compulsive disorder (OCD)(Hunting Pompon et al., 2018). Regarding systemic disorders, meaning people who suffer from bodily illnesses, such as heart failure, cancer, diabetes, and obesity, sufferers also experience elevated levels of stress (Afrisham et al., 2019). Thus, it can be concluded that stress could be a powerful driver for developing these diseases (Salleh et al., 2008). Exposure to chronic stress increases the risk of hypertension (Liu et al., 2017), heart attack, or stroke (Sparrenberger et al., 2019). Specifically, when an individual experiences repeated acute and persistent chronic stress, it can contribute to inflammation in the circulatory system. After prolonged stress, whether acute or chronic, the coronary veins (arteriole receiving deoxygenated blood from the heart, the heart can collapse (Levine, 2022), increasing an individual's chance of having a stroke or heart attack (American Psychological Association, 2023). This can put an individual at increased risk for a variety of physical and mental health problems, including anxiety, depression, digestive issues (Duric et al., 2013), headaches (Krishnan et al., 2012), muscle tension (American Psychological Association. 2023), heart disease (Levine et al., 2022; "Anxiety and Heart Disease," 2023), heart attack ((Levine, et al. 2022; "Anxiety and Heart Disease," 2023), high blood pressure (Pruthi, 2022), sleep problems (Dusang, 2019), weight gain (American Psychological Association, 2023), and memory and concentration impairment (American Psychological Association, 2022).

Cortisol is a steroid hormone in the glucocorticoid class of hormones, (Selye, 1973). When used as a medication, it is known as hydrocortisone (Schimmer, et al. 2006). It is produced in many animals, mainly by the zona fasciculata of the adrenal cortex in the adrenal gland (Rege, et al. 2014). It is produced in other tissues in lower quantities, (American Psychological Association, 2023), such as the liver, skin, and adipose tissue, and can also produce cortisol in smaller amounts (Lightman et al., 2020). This review article aims to inform and raise awareness of the effects of stress on the human body through the different stages of development.

Chronic Versus Acute Stress

Chronic and acute stress have different effects and connotations on the body. Chronic stress impairs memory because of decreased hippocampal function (Kleen et al., 2006). The hippocampus is involved in memory formation, and chronic stress has been shown to affect this region of the brain (Vogel and Schwabe, 2016). Stress hormones, such as cortisol, can have a toxic effect on the hippocampus, leading to impaired spatial and declarative memory (Yaribeygiet al., 2017; Vogel and Schwabe, 2016). Acute stress is pervasive and can profoundly influence cognitive functions. One critical function modulated by stress is cognitive flexibility, which refers to adapting behaviorally to situational demands (Gabrys et al., 2018). It also regulates the functioning of mechanisms such as the immune system (Segerstrom et al., 2004) and cardiovascular system and helps maintain homeostasis (Knauft et al., 2021). A threat stimulus triggers a fear response in the amygdala ("Understanding the Stress Response," 2011), a known node for integrating associative fear cues (Sun et al., 2020). After the amygdala detects the sensory threat cues, it activates downstream areas in preparation for motor functions involved in fight or flight (Hashemi et al., 2019; Swain et al., 2020; Stowers et al., 2013). In addition, threatening cues are perceived as stressful (Figure 1 A), and thus, triggers the release of stress hormones, such as cortisol and adrenaline (Figure 1 B), and activates the sympathetic nervous system (Yau and Potenza, 2013; Sherin and Nemeroff, 2022).



Figure 1. The image above shows what happens to the human body while they go through stress. (A) An individual crowded over is in visible distress next to a cobra snake. This stressful situation activates the sympathetic nervous system. (B) The colored areas of the brain show the hypothalamus, hippocampus, and amygdala, all areas of the brain triggered by the stressful situation and activating "fight or flight" mode. (C) The human body undergoes a number of changes when the sympathetic nervous system is active.

This leads to bodily changes that prepare us to be more efficient in danger: The brain becomes hyperalert (Fry, 2020), pupils dilate (Chen and Miller, 2007), the bronchi dilate (American Psychological Association. 2023), breathing accelerates (Amugongo and Hlusko, 2014), heart rate and blood pressure rise (Figure 1 C) (Davidovic et al., 2013; Mitchell and Everly, 2005). The skeletal muscles experience increased blood flow and a surge of glucose. Meanwhile, non-essential organs like the gastrointestinal system undergo a deceleration in their activity levels (Van der Valk et al., 2018).

In Utero and childhood consequences of stress exposure

Any stress has consequences on the prenatal stage of development. It alters the baby's dopaminergic system, (Lupien et al., 2009; Cattane et al., 2021), which is involved in reward- or

drug-seeking behavior, and they become more susceptible to acquiring addictive behaviors (Arain et al., 2013). Stress during pregnancy is also linked to lower weight and size (Coussons-Reed, 2013), in the baby, and it manifests its effects through the child's developmental stages (Lupien et al., 2009; Buss et al., 2012). A single or repeated exposure to stress affects the hypothalamic-pituitary-adrenal (HPA) axis (Stephens and Wand, 2012). It passes to the placenta, affects the baby's serotonin levels, and modifies development (Lupien et al., 2009; Lester et al., 2013) (Figure 2 A). Glucocorticoids are essential for normal brain maturation: they initiate terminal maturation, remodel axons and dendrites and affect cell survival. It alternates neural structure (De Bellis et al., 2014; Miranda et al., 2019). Cortisol is known to cross the placenta and consequently influence various aspects of development in the human fetus (Amugongo and Hlusko, 2018; Graham et al., 2019). The effects of elevated cortisol levels on the fetus may vary from defective development to spontaneous abortion (Amugongo and Hlusko, 2018). The first trimester is characterized by rapid organ development (Gillmore et al., 2018). Therefore, stress exposure in this period leads to widespread, global effects like cognitive dysfunction (Talge et al., 2007), heart malformation, (Carmichael et al., 2014) cataracts, (Minassian, et al., 2002) deafness (Swain et al., 2020), and genital and intestinal abnormalities (Amugongo and Hlusko, 2018) (Figure 2 A). In the second and third trimesters, the organs mainly enlarge and undergo refinement (National Research Council, 2000). Stress exposure in this period leads to low birth weight, skeletal abnormalities, and hearing loss (Amugongo, et al 2014; Wadwha, 2005) (Figure 2 B).

 A) Stress during the first trimester could lead to cognitive dysfunction, malformation, cataracts, deafness and genital and intestinal abnormalities



B) Stress during the second and third trimester can lead to low birth weight, skeletal abnormalities and hearing loss.



Figure 2. The image depicts what can happen to the human body if the individual experiences stress while pregnant. (A) A number of fetal organs are susceptible to impairment during development if a pregnant individual experiences repeated extreme stressful stimuli during their first trimester. (B) The possible consequences of experiencing repeated stress during the 2nd and 3rd trimesters of pregnancy include low birth weight, skeletal abnormalities, and hearing loss. All panels in the figure were created with BioRender.

Acute and Chronic Exposure to Stress in Adulthood

Stress during adulthood can impact most of the body's organisms. While it can impair memory due to increased hippocampus function (Yaribeygi, et al. 2017, Lupien et al., 2009), others have reported enhanced memories regarding events experienced during high-stress levels (Yaribeygi, et al. 2016, Lupien et al., 2009). Stress causes changes in the dendrites (debranching and shortening), which take ten days to change to their usual size. It also impairs spatial learning and is reversed 21 days later (Lupien et al., 2009, McEwen et al., 2016). In addition to neuronal changes that occur after a stressor, an individual's body is also affected. Mainly, when stress becomes chronic, our diets cannot quickly replace the calcium depletion, so our bones are constantly being leached of calcium, as shown in Figure 3, leading to potentially more porous bones, brittle bones, and osteoporosis (Epel et al, 2004). There is a strong association of obesity with chronic low-grade inflammation in premenopausal women (Benson et al, 2009). This proinflammatory state and altered neuroendocrine and cardiovascular stress responsiveness may conceivably constitute one of the mechanisms linking psychological stress and the long-term health risks associated with obesity (Duric et al., 2016) (Figure 3).



Figure 3. The image above shows bodily responses to stress in an adult human. They include: reduced bone strength, memory impairment, changes in the dendrites, impairment of spatial learning, inflammation in the stomach, and a propensity to obesity. All panels in the figure were created with BioRender.

The research study investigating the effects of stress on physiological variables in obese women compared to non-obese women found that obese women exhibited a more robust cortisol stress response and higher heart rate and diastolic blood pressure following stress than their non-obese counterparts. Additionally, obese women had higher levels of the inflammatory marker IL-6 before and after stress and higher baseline levels of circulating leukocytes, granulocytes, CD3+ cells, and hs-CRP (Van der Valk et al., 2018). However, the study also noted that stress led to a significant increase in IL-6 concentrations in non-obese women, thus suggesting a possible link that stress can induce changes in pro-inflammatory pathways regardless of body composition (Van der Valk et al., 2018; Benson et al, 2009).

Discussion

This review article explores the effects of stress during various stages of development and its impact on cognition. Stress can be categorized as chronic, which is a prolonged exposure to adverse circumstances, or acute, which is a response to specific stressful situations. The activation of the hypothalamus-pituitary-adrenal (HPA) axis and the release of glucocorticoids play a significant role in the stress response (Lester et al., 2013).

In young children and during early adolescence, research has shown that stress can lead to a decrease in the size of the hippocampus, (De Bellis et al., 2014) which can have detrimental effects on brain development when compared to individuals who are not exposed to similar stress ("American Psychological Association". 2023). Additionally, stress has been observed to have negative impacts on cognitive performance, including academic achievements and tasks that go beyond traditional educational assessments (Yaribeygi, et al. 2017). In adults, chronic stress impairs memory due to increased hippocampal function (Yaribeygi, et al. 2017, Lupien et al., 2009). Furthermore, changes in the size of dendrites and arborization enhance fearful memory, which take time to regulate (Yaribeygi, et al. 2016, Yaribeygi, et al. 2017). Chronic stress can impair spatial learning, but these effects can be reversed after a certain period (Lupien et al., 2009). The effects of chronic stress in adulthood are generally reversible, while for infants, they tend to be permanent (Lupien et al., 2009; Coussons-Read, 2013; Buss et al., 2012).

The review also highlights the impact of stress during pregnancy, which can affect the dopaminergic system of the baby, making them more susceptible to addictive behaviors (Lupien et al., 2009; Cattane et al., 2021). Stress exposure during pregnancy can lead to lower weight and size in the baby and have long-lasting effects on the child's physical development (Amugongo and Hlusko, 2018; Wadhwa, 2005).

Furthermore, stress in adulthood can have various impacts on the body, including impaired memory (McEwen et al., 2016), changes in dendrites (Lupien et al., 2009), and

negative effects on bone health (Epel et al, 2004), cardiovascular function, and obesity-related inflammation (Benson et al., 2009). Overall, this review emphasizes the detrimental effects of stress on different stages of development and cognition. Understanding these effects can help raise awareness and inform strategies for managing and reducing stress-related risks.

Although researchers have tried to understand the wide-ranging impacts of fetal stress on cognition, there are still many questions left unanswered. One of particular importance may be the specific mechanisms that underlie long-term consequences of stress during pregnancy. It is unknown how chronic stress impacts the volume of different brain regions indicated in stress, and how dendrites change in response to stress. Understanding the specific mechanisms involved in stress as it relates to cognition could allow researchers to study ways to reverse these negative effects, or at least to better manage them.

It would be important to further investigate the effect of chronic stress and its relation to the volume of the hippocampus, especially in young children and adolescents, and later investigate the long-term consequences of stress exposure on the adult brain. Another pressing topic to investigate is the reversibility of the negative effects of stress in the body, especially in cognition, since it is known that chronic stress impair memory in adults, it would be beneficial to learn what are the mechanisms behind the enhancement of fearful memory. It would be of great significance to discover what changes occur in dendrites in response to stress, and how long does it take for them to regulate? It would be of specific significance to know the cognitive deficits associated with stress exposure in young children and adolescents and, if reversible, which effects persist through adulthood. Other topics that are significant are the contribution of stress to obesity-related inflammation, and what are the long-term health risks associated with it. Are there effective strategies for managing and reducing the negative effects of stress on development and cognition? Although many studies have lead to a better understanding regarding the detrimental effects of stress during various stages of development, a greater focus is now necessary to better understand how persistent physiological responses can be mitigated in not only adults but all developing children. Within this review, the purpose is to have elucidated the current knowledge regarding acute and chronic stress and within the scope of in utero through adulthood.

Works Cited

- Afrisham, Reza, et al. "The influence of psychological stress on the initiation and progression of diabetes and cancer." *International journal of endocrinology and metabolism* 17.2 (2019).
- American Psychological Association. (2023, March 8). *Stress effects on the body*. <u>https://www.apa.org/topics/stress/body</u>
- American Psychological Association. (2022, October 31). *How stress affects your health*. <u>https://www.apa.org/topics/stress/health</u>
- Amugongo, Sarah K., and Leslea J. Hlusko. "Impact of maternal prenatal stress on growth of the offspring." *Aging and disease* 5.1 (2014): 1.
- "Anxiety and Heart Disease." *Johns Hopkins Medicine*, 5 Jan. (2023), <u>https://www.hopkinsmedicine.org/health/conditions-and-diseases/anxiety-and-heart-dise</u>
- Arain, Mariam et al. "Maturation of the adolescent brain." *Neuropsychiatric disease and treatment* vol. 9 (2013): 449-61. doi:10.2147/NDT.S39776
- Benson, S., et al. "Effects of obesity on neuroendocrine, cardiovascular, and immune cell responses to acute psychosocial stress in premenopausal women." *Psychoneuroendocrinology* 34.2 (2009): 181-189.
- Bryant, Richard A. "Post-traumatic stress disorder: a state-of-the-art review of evidence and challenges." *World psychiatry* 18.3 (2019): 259-269.
- Buss, Claudia, et al. "The role of stress in brain development: the gestational environment's long-term effects on the brain." *Cerebrum: the Dana forum on brain science*. Vol. 2012. Dana Foundation, (2012).
- Carmichael, Suzan L., et al. "Maternal stressors and social support as risks for delivering babies with structural birth defects." *Paediatric and perinatal epidemiology* 28.4 (2014): 338-344.
- Chen, Edith, and Gregory E. Miller. "Stress and inflammation in exacerbations of asthma." *Brain, behavior, and immunity* 21.8 (2007): 993-999.
- Coussons-Read, Mary E. "Effects of prenatal stress on pregnancy and human development: mechanisms and pathways." *Obstetric medicine* vol. 6,2 (2013): 52-57. doi:10.1177/1753495X12473751
- Cattane, Nadia, et al. "Depression, obesity and their comorbidity during pregnancy: effects on the offspring's mental and physical health." *Molecular Psychiatry* 26.2 (2021): 462-481.
- Davidovic, Goran, Violeta Iric-Cupic, and Srdjan Milanov. "Associated influence of hypertension and heart rate greater than 80 beats per minute on mortality rate in patients with anterior wall STEMI." *International journal of clinical and experimental medicine* 6.5 (2013): 358.
- Duric, Vanja et al. "Comorbidity Factors and Brain Mechanisms Linking Chronic Stress and Systemic Illness." *Neural plasticity* vol. 2016 (2016): 5460732. doi:10.1155/2016/54607321.

- Duric, Vanja, and Ronald S. Duman. "Depression and treatment response: dynamic interplay of signaling pathways and altered neural processes." *Cellular and molecular life sciences* 70 (2013): 39-53.
- "Definition of Stress NCI Dictionary of Cancer Terms." *National Cancer Institute*, https://www.cancer.gov/publications/dictionaries/cancer-terms/def/stress. Accessed 26 July 2023.
- De Bellis, Michael D, and Abigail Zisk. "The biological effects of childhood trauma." *Child and adolescent psychiatric clinics of North America* vol. 23,2 (2014): 185-222, vii. doi:10.1016/j.chc.2014.01.002
- Dusang, Kaylee. "How Stress Can Affect Your Sleep." *Baylor College of Medicine*, 9 May (2019),

https://www.bcm.edu/news/how-stress-can-affect-your-sleep#:~:text=%E2%80%9CHigh %20levels%20of%20stress%20impair,disrupts%20sleep%2C%E2%80%9D%20Wilson% 20explained.

- Epel, Elissa S., et al. "Accelerated telomere shortening in response to life stress." *Proceedings of the National Academy of Sciences* 101.49 (2004): 17312-17315.
- Fry, Alexa. "Stress and Insomnia." *Sleep Foundation*, 15 Sept. (2020), https://www.sleepfoundation.org/insomnia/stress-and-insomnia.
- Gabrys, Robert L., et al. "Cognitive control and flexibility in the context of stress and depressive symptoms: The cognitive control and flexibility questionnaire." *Frontiers in psychology* 9 (2018): 2219.
- Gilmore, John H., Rebecca C. Knickmeyer, and Wei Gao. "Imaging structural and functional brain development in early childhood." *Nature Reviews Neuroscience* 19.3 (2018): 123-137.
- Graham, Alice M., et al. "Maternal cortisol concentrations during pregnancy and sex-specific associations with neonatal amygdala connectivity and emerging internalizing behaviors." *Biological psychiatry* 85.2 (2019): 172-181.
- Hashemi, Mahur M., et al. "Neural dynamics of shooting decisions and the switch from freeze to fight." *Scientific reports* 9.1 (2019): 4240.
- Hunting Pompon, Rebecca, et al. "Modifying and validating a measure of chronic stress for people with aphasia." *Journal of Speech, Language, and Hearing Research* 61.12 (2018): 2934-2949.
- Kleen, Jonathan K., et al. "Chronic stress impairs spatial memory and motivation for reward without disrupting motor ability and motivation to explore." *Behavioral neuroscience* 120.4 (2006): 842.
- Knauft, Katherine, et al. "Perceived chronic stress influences the effect of acute stress on cognitive flexibility." *Scientific Reports* 11.1 (2021): 23629.
- Krishnan, Vaishnav, and Eric J. Nestler. "Linking molecules to mood: new insight into the biology of depression." *American Journal of Psychiatry* 167.11 (2010): 1305-1320.

- Lester, Barry M., Elisabeth Conradt, and Carmen J. Marsit. "Epigenetic basis for the development of depression in children." *Clinical obstetrics and gynecology* 56.3 (2013): 556.
- Levine, Glenn N. "Psychological Stress and Heart Disease: Fact or Folklore?." *The American journal of medicine* 135.6 (2022): 688-696.
- Lightman, Stafford L., Matthew T. Birnie, and Becky L. Conway-Campbell. "Dynamics of ACTH and cortisol secretion and implications for disease." *Endocrine reviews* 41.3 (2020): bnaa002.
- Liu, Mei-Yan, et al. "Association between psychosocial stress and hypertension: a systematic review and meta-analysis." *Neurological research* 39.6 (2017): 573-580.
- Lupien, Sonia J., et al. "Effects of stress throughout the lifespan on the brain, behaviour and cognition." *Nature reviews neuroscience* 10.6 (2009): 434-445.
- McEwen, Bruce S., Carla Nasca, and Jason D. Gray. "Stress effects on neuronal structure: hippocampus, amygdala, and prefrontal cortex." *Neuropsychopharmacology* 41.1 (2016): 3-23.
- Minassian, D. C., V. Mehra, and A. Reidy. "Childbearing and risk of cataract in young women: an epidemiological study in central India." *British journal of ophthalmology* 86.5 (2002): 548-550.
- Miranda, Magdalena, et al. "Brain-derived neurotrophic factor: a key molecule for memory in the healthy and the pathological brain." *Frontiers in cellular neuroscience* (2019): 363.
- Mitchell, Jeffrey T., and George S. Everly. *Critical incident stress management*. Stumpf & Kossendey, (2005).
- (US), National Research Council, et al. "The Developing Brain." *NCBI Bookshelf*, 1 Jan. 2000, https://www.ncbi.nlm.nih.gov/books/NBK225562/.
- Pruthi, Sandhya, M. D. "Stress and High Blood Pressure: What's the Connection?" *Mayo Clinic*, 10 Dec. (2022)
- Rege, Juilee, et al. "Transcriptome profiling reveals differentially expressed transcripts between the human adrenal zona fasciculata and zona reticularis." *The Journal of Clinical Endocrinology & Metabolism* 99.3 (2014): E518-E527.
- Salleh, Mohd Razali. "Life event, stress and illness." *The Malaysian journal of medical sciences: MJMS* 15.4 (2008): 9.
- Segerstrom, Suzanne C., and Gregory E. Miller. "Psychological stress and the human immune system: a meta-analytic study of 30 years of inquiry." *Psychological bulletin* 130.4 (2004): 601.
- Selye, Hans. "The Evolution of the Stress Concept: The originator of the concept traces its development from the discovery in 1936 of the alarm reaction to modern therapeutic applications of syntoxic and catatoxic hormones." *American scientist* 61.6 (1973): 692-699.
- Schimmer, Bernard P., and Keith L. Parker. "Adrenocorticotropic hormone; adrenocortical steroids and their synthetic analogs; inhibitors of the synthesis and actions of

adrenocortical hormones." Goodman & Gilmans the pharmacological basis of therapeutics, 11th ed. New York: McGraw Hill (2006): 1587-612.

- Sherin, Jonathan E., and Charles B. Nemeroff. "Post-traumatic stress disorder: the neurobiological impact of psychological trauma." *Dialogues in clinical neuroscience* (2022).
- Stephens, Mary Ann C, and Gary Wand. "Stress and the HPA axis: role of glucocorticoids in alcohol dependence." *Alcohol research : current reviews* vol. 34,4 (2012): 468-83.
- Stowers, Lisa, Peter Cameron, and Jason A. Keller. "Ominous odors: olfactory control of instinctive fear and aggression in mice." *Current opinion in neurobiology* 23.3 (2013): 339-345.
- Sparrenberger, Felipe, et al. "Does psychosocial stress cause hypertension? A systematic review of observational studies." *Journal of human hypertension* 23.1 (2009): 12-19.
- Swain, Santosh Kumar, Basanta Kumar Pati, and Jatindra Nath Mohanty. "Otological manifestations in pregnant women-A study at a tertiary care hospital of eastern India." *Journal of Otology* 15.3 (2020): 103-106.
- Sun, Yajie et al. "Fear conditioning and the basolateral amygdala." *F1000Research* vol. 9 F1000 Faculty Rev-53. 28 Jan. 2020, doi:10.12688/f1000research.21201.1
- Talge, Nicole M., et al. "Antenatal maternal stress and long-term effects on child neurodevelopment: how and why?." *Journal of Child Psychology and Psychiatry* 48.3-4 (2007): 245-261.
- "Understanding the Stress Response." *Harvard Health*, 1 Mar. 2011, <u>https://www.health.harvard.edu/staying-healthy/understanding-the-stress-response</u>.
- Van der Valk, Eline S., Mesut Savas, and Elisabeth FC van Rossum. "Stress and obesity: are there more susceptible individuals?." *Current obesity reports* 7 (2018): 193-203.
- Vogel, Susanne, and Lars Schwabe. "Learning and memory under stress: implications for the classroom." *npj Science of Learning* 1.1 (2016): 1-10.
- Wadhwa, Pathik D. "Psychoneuroendocrine processes in human pregnancy influence fetal development and health." *Psychoneuroendocrinology* 30.8 (2005): 724-743.
- Yaribeygi, Habib, et al. "The impact of stress on body function: A review." *EXCLI journal* 16 (2017): 1057.
- Yau, Y H C, and M N Potenza. "Stress and eating behaviors." *Minerva endocrinologica* vol. 38,3 (2013): 255-67.

Evaluating Shifts in Canadian Public Opinion on Immigration Policies and Their Impact on Governmental Decisions By Gudisa Tufa and Kangyun Kim

Abstract

In Canada's current diverse and multicultural landscape, immigration policy has always been pivotal in shaping the nation's identity and social fabric. Within Canada's existence, the Canadian public's voice of opinion concerning immigration has always fluctuated, influenced by various factors such as economic conditions, global events, and the state of domestic political discourse, as well as immigration itself changing who constitutes Canadians. This article aims to explore the ever-shifting perspectives of Canadians toward immigration policy and how these perspectives by the public have influenced governmental policies in Canada. By tracing the history of public sentiment and attitude towards immigration, analyzing prevalent perspectives and events, and examining the implications of governmental decisions, we gain valuable insight into the intricate relationship between public opinion and immigration policies within Canada. Moreover, we delve into the recent developments in public opinion and the corresponding governmental decisions on this topic, as well as discuss the immediate repercussions of these policies. Discussing these modern ramifications can lead to a critical understanding of the effectiveness of past policies and their repercussions in Canada's future. Therefore, within the scope of this paper, we seek to contribute to the ongoing discourse on immigration by fostering an informed dialogue for a more inclusive and prosperous Canada.

Introduction

Throughout its history, Canada has prided itself upon being a land of opportunity and a haven for immigrants seeking refuge and better living standards. Though the nation's so-called "commitment" to multiculturalism and diversity has played a decisive role in shaping its immigration policies, no such policy remains static, and immigration has always been a topic of debate and contention among the Canadian populace. From its early beginnings as a "white man's country" aiming to expand European settlers westward to the multicultural nation as it proudly calls itself today, Canadian opinions have shifted in response to war and macroeconomic pressures, foreign crises that caused refugee influx, and the nature of media and government in related political discourse (Triadafilopoulos). Understanding the dynamics and history of public opinion on this issue is crucial in dealing with the motivations and rationale of the Canadian government within this realm of politics.

From the start, immigration has always remained a critical institution of the Canadian economy, originally meant to fulfill labour needs for resource extraction, industrialization, and agriculture in Canada's vast territory. In the late 19th century, Canadian opinions on immigration were determined by who was then considered Canadians and on what basis people were considered valid immigrants. This brings to light how most of the Canadian establishment at this time was foreign-born, namely from the United Kingdom and other parts of Europe, who looked favourably upon settling their left-behind counterparts from their cradlelands as opposed to other

people's immigration. Their opinions on the matter, however, did not represent the Indigenous population, who initially welcomed the settlers with open arms and engaged in fur trade, among other forms of interaction, though mainly economic interaction through businesses such as the Hudson's Bay Company (HBC). At that time, Canada's formal immigration policies were mainly based upon racial hierarchies, as evidenced by the discriminatory Chinese Head Tax and the Komagata Maru Incident. We will examine how immigration functioned as a necessary institution in Canada's early development and how it changed going forward, along with changing public sentiments as the population grew in number and diversity.

Furthermore, within the context of the early 20th century onwards, different points of interest in Canada's timeline must be noted and discussed. Here, domestic and global economic and humanitarian events are analyzed vis-a-vis their influence on policy and opinion under the circumstances of evergrowing centralized media and broadcast, alongside the emergence of intergovernmental organizations such as the United Nations (UN) and their agendas regarding the matter. Within this timeline of immigration in Canada, some early catalysts for change are global wars such as World War 2 (WW2), wherein family reunifications and skillful labour came to play a stronger role in immigration policy rather than race. Subsequently, the UN came to have the 1951 Refugee Convention, where the term "refugee" was defined as "someone unable or unwilling to return to their country of origin owing to a well-founded fear of being persecuted for reasons of race, religion, nationality, membership of a particular social group, or political opinion," (UNHCR). Canada accepted that definition in its policies, giving heed to the coming conventions and protocols concerning the international treatment of refugees and their rights, among other declarations regarding the classification of immigrants in Canada. Thereafter, influxes of immigration from Africa, Asia, and Latin America rose primarily due to their respective crises, coincidently with a rise in public debate on the topic of immigration in Canada. However, this paper deals with certain fitting examples from the geographic regions of the Middle East, South Asia, and East Asia, as these places comprise the vast majority of immigrants in Canada today, as well as provides vivid examples of public opinion on immigration since Canada's inception. The influx of diverse immigration led to Canada implementing its first Multiculturalism Policy in 1971, and the ethnic backgrounds of the people representing public opinion would significantly change. Now accepting of this pluralistic statehood and being the only country ever to be awarded the Nansen Refugee Award in 1986, Canada as a state continued using immigration as a tool to develop the country in all facets (Los Angeles Times). In more recent memory, we have seen the Harper Immigration Reforms in the early 2010s attempts to address conservative concerns regarding immigration and emphasis on streamlining the immigration process to prioritize economic immigrants. Today, we see how the culmination of these events and policy changes has shaped Canada's social cohesion and identity as a nation.

Historical Shifts in Canadian Immigration Policy

The paradigm shift in Canadian public opinion on the ornate subject of immigration is a tapestry woven with divergent and convergent threads of historical events, societal trends, and

policy changes. During Canadian history, Canada has significantly shifted how it perceives immigration and newcomers to its territorial bounds. From the early waves of European settlement that intertwined with the Indigenous populace to the discriminatory Chinese Head Tax, which reflected prevailing anti-Asian sentiments in Canada, each era of Canadian history has left its mark on the immigration landscape. The transformative Immigration Act of 1952 would then mark a historically significant turning point, steering Canada away from its race-based policies established in previous Acts and into a more nuanced policy, considering skills and family reunification, following the aftermath of WW2. In the ensuing decades in Canada, we have witnessed further debates and discussions, marked notably by those revolving around the diversified nature of immigrants in the 1980s and 90s, which shed light on integration and cultural concerns for immigration within Canada. Similarly, the Syrian Refugee Crisis of 2015-2016 brought the forefront questions of immigration forward regarding humanitarian response, security considerations, the Canadian ethos of moral duty, and cultural integration concerns. By exploring these critical chapters of Canadian immigration history, we can unravel the complex, woven fabric of Canadian public opinion on immigration while shedding light on how these historical eras/events have caused a domino effect that can still be observed in modern politics.

To begin with, it is vital to acknowledge the pre- and post-Confederation background to immigration in the land mass of modern-day Canada. The first interactions between European travellers and the Indigenous people followed a booming fur trade facilitated in significant part by the HBC first operating in Rupert's Land at the tail-end of the 17th century, alongside colonial agendas from Britain and France that found the former effectively ousting the latter in terms of territorial jurisdiction and influence. The HBC, then a London-based transnational corporation, dominated a fur trade that changed the lifestyles of many people (Ray). European traders would come to settle in Canada and set up shop permanently. The indigenous people of the fur-trapping area would abandon their traditional livelihoods to become dependent on this trade to obtain goods from European traders. Slowly, sedentary communities would develop with the Indigenous people's welcoming the Europeans to settle alongside them, creating the Metis, people of both European and Indigenous heritage (Gaudry).

Naturally, as the number of settlers grew and animal populations declined, the fur trade became less lucrative, and the British expanded their borders westward. Post-Confederation, Canada would launch a westward expansion for European settlement, predominantly for the sake of agriculture, and the extraction of natural resources such as timber and minerals available beyond the prairies in British Columbia would become of increased interest once incorporated in 1871. With that, more Europeans would be welcomed to populate the country as the 1869 Immigration Act, among others, promoted while discouraging other immigrants (Immigration Act, 1869). Additionally, the nature of the treaties between the dispersed Indigenous people and the Europeans that formed Canada was that which forced the hands of the former because of the systemic bison massacres instigated by the latter, which would destroy the livelihoods of the

Indigenous people, forcing them to agree to treaties that placed them on small reserves and organized them into decentralized bands (Borrows).

Focusing on public opinion, this chronology of events gives insight into Indigenous and European attitudes towards immigration and how they shifted during this period. The socioeconomic potencies of the HBC's operation reveal how the Indigenous people initially welcomed immigrants, accepted them into their communities, and built a new way of life with them, in addition to creating a new culture in the Metis. Conversely, it also depicts the European traders and settlers as in support of their counterparts back home finding new lives in Canada and the members of their ruling class as having ulterior motives of expansion that act against the interests of those who welcomed them with open arms. As the Indigenous people became more aware that the newcomers were not egalitarian in how they were to live, they began resisting colonial attempts that undermined their existence and upheld European settlers, such as in the infamous Red River Resistance (Bumsted). In the end, the bison massacre was used by the ruling class as a way to make a profit off of hides while also coercing the Indigenous people to comply with unfair treaties, all not to be respected by the Canadian government that proposed them in the first place (A History of Treaty-Making) The Indigenous people's resented the European settlers. They frowned upon the white immigration that the Canadian government would endorse.

As we delve deeper into the historical shifts in Canadian public opinion on immigration, it becomes evident that the sinuous interactions between the Indigenous populations and European settlers during the early stages of Canada's framework as a country and, perhaps more importantly, lays the groundwork for the Canadian opinion on immigration as a central focus. The coinciding socioeconomic practices of the fur trade, the emergence of Metis communities, and the composite negotiations over land and resources would provide further nuance into this stage-setting dynamic on immigration in Canada. The initial openness of Indigenous communities toward European settlers and their subsequent resistance as the latter's intentions became more and more specified would serve as an ironic paradox in the later years of Canadian public immigration policy.

This backdrop would set the tone for understanding the overlapping era of the Chinese Head Tax, which would see a significant shift in Canadian public opinion regarding immigration. Between the late 19th century and the early 20th century, Canada underwent a series of economic developments, one of which would be known as the Canadian Pacific Railway. Within the building of this railway, the arrival of Chinese immigrants into Canada comes into focus. However, the movement of Chinese immigrants into Canada became a point of contention among the Canadian populace once the Canadian Pacific Railway, built primarily along the lines of cheap Chinese immigrant labour, was complete. Conclusively, this dispute within the Canadian populace would result in a discriminatory head tax on an ethnic basis towards Chinese people. Between 1885 and 1923, Chinese immigrants had to pay sums of money to enter Canada in a shameless act by the Canadian government to restrict Chinese Immigration into Canada. The severity of this head tax can be denoted by the fact that by 1923, the year the act was removed, Chinese immigrants had paid 23 million Canadian dollars in head tax (Chan). In 1923 however, although the Chinese head tax was lifted, there was an even harsher crackdown on Chinese immigrants entering Canada. The Chinese Immigration Act of 1923 forbade all Chinese immigrants from entering Canada until it was ultimately revoked in 1947 after a successful appeal.

The significance of understanding the Chinese Head Tax within the context of understanding Canadian public opinion is profound. It showcased how prejudices and fears manifested within the government of Canada and its general populace and how these phobias became a basis for the suffering of the immigrant populace. By examining this era, we can gain valuable insight into how the populace and the government can work cooperatively to create a shift in opinion and foster a specific environment within Canada. Conclusively, the Chinese Head Tax serves as a crucial point in understanding historical shifts in Canadian public opinion as, much like the European settlement and colonization, it would set the stage for future discussions on the spectre of Canadian Immigration.

Of equal significance are the practices and effects of WW2 that created conditions of urgent necessity post-WW2, which gave way to a paradigm shift in Canadian immigration. Among them, the massive displaced population emigrating from a devastated Europe and their returning Canadian service members and dependents are noteworthy. Canada would receive about 1.5 million immigrants from Europe in the decade following the war's end in 1945 (Post War Immigration). This is partly heavily attributed to Canada's post-war recovery and economic flourishment. Effectively, Canadians experienced immigration as a beneficial institution that brought more labour for the workforce and better settlement of the country. As mentioned, the government would even go on to revoke the Chinese Immigration Act, steadily changing its immigration policy to be more inclusive and rid of racial quotas. The end of the war would also conclude with the creation of the UN, which would go on to have the 1951 Refugee Convention, which made international guidelines Canada keenly followed in its hallmark 1952 Immigration Act, which promoted economic immigrants, family reunification, and a non-racial categorization of immigrants that later accepted the practice of non-refoulement when Canada officially signed the convention's 1967 Protocol in 1969 (A History of Refuge).

Inherently, the 1952 Immigration Act within Canada would be a reflection of the changing global socio-political environment post-WW2. The devastation caused by the war prompted a reassessment of immigration policies, recognizing that the nation's global prosperity and growth could be enhanced by attracting individuals with various skills and talents, regardless of their ethnic background. This act would depart from racially motivated politics, attesting to the evolving societal attitudes that saw the potential benefits of a diverse and skillful workforce (Immigration Act, 1952). Cohesively, the Immigration Act of 1952 exemplified how policy decisions can exhibit, influence, and shape public sentiment. The shift towards skills and family reunification post-war would be denoted as the foundation for future immigration policy in Canada, all the while serving as a resonator with the growing societal recognition of the value of cultural diversity. Ultimately, the Act would pave the way for a more inclusive and equitable

immigration system that would conclusively shift public attitudes toward newcomers in years to come.

In due course, Canada would enact the keystone 1971 Multiculturalism Policy under the Pierre Trudeau government, which bellowed an irreversible shift in the socio-cultural makeup of the country by creating a conducive environment for all people within Canada's borders. Ultimately, this policy promoted four key ideas: providing support for all cultural groups to develop, aiding full socio-cultural citizenship, encouraging intercultural exchanges for national unity, and increasing support to aid immigrants to learn English or French. The action taken to implement this act was also quite large, at a time when Canada's population would barely reach 25 million, a total of \$200 million would be allocated by the federal government over the following ten years (Raska). The effects of this Act alongside other events, such as the Vietnamese War that caused 60 000 'Boat People' to find refuge in Canada, the influx of 85 000 immigrants from the Caribbean and Bermuda, and over a million immigrants from East Asia in coming decades (Statistics Canada). With this huge surge of immigration, the government of Canada officially embraced the pluralist identity it preaches today and promoted Canada as a beacon of humanitarian excellence.

Nonetheless, this would not come without some turmoil with future refugee settlement efforts. Especially after 9/11 and the wars occurring in the Middle East during the 2000s, public and state sentiments from the West began to perceive those from these places and, generally, those of Islamic faith in an increasingly worse light (Cesari). Of course, this had and continues to affect immigration today profoundly. During the 2015-2016 Syrian Refugee Crisis, Canada accommodated their target goal of 25,000 refugees in February 2016, but in a fashion some found questionable (Tyyskä et al.). Firstly, there lacked much logistical planning on the part of the government in light of the fundamentally frantic nature of refugee crises. Apart from the arbitrarily set target, there was little set agenda, and many refugees were settled via private sponsorship. The 2016 Census demonstrates that from January 1, 2015, to May 10, 2016, about 47% of refugees were either privately sponsored or settled through the Blended Visa Office-Referred Program that operates on a volunteer basis of permanent residents (Houle). Some media criticized the exclusion of isolated young men seeking refuge on the basis that they were security threats, whereas others justified it by referring to recent affairs. Amidst the Paris terrorist attacks in late 2015, the Canadian government decided to prioritize vulnerable women and children for settlement. Inadvertently, this made for a circumstance where some mothers and their children arrived in Canada without a mature male figure, fostering continued vulnerability due to the traditional gender roles practiced in Syria (Maktabi). Public opinion would fluctuate on this issue due to changing government policy and other issues that would surface with time.

Factors Influencing Canadian Public Opinion on Immigration

In the increasingly interconnected and rapidly transforming socioeconomic landscape of Canada, immigration has emerged as a vital yet contentious issue for the Canadian government and its citizens alike. The multifaceted nature of immigration, encompassing developing topics such as humanitarian concerns, economic implications, and cultural interplay, allows immigration to be subject to various contemporary factors. The media's portrayal of specific refugee crises, such as the poignant Syrian Refugee Crisis, can invoke empathic responses or fuel existing apprehensions toward immigration, ergo impacting the level of support for humanitarian immigration. Furthermore, economic recessions, such as that of the early 1990s and the seismic 2008 global financial crisis, can sway public opinions by intertwining economic anxieties and national security considerations regarding immigration. Moreover, the emergence and proliferation of far-right and populist movements in Canada inject an additional layer of influence, often moulding anti-immigration sentiments and policy stances within governmental decisions. To comprehensively understand the subtleties of Canadian attitudes toward immigration and according to governmental reactions, it is imperative to delve into these critical intricacies and nuances between many interwoven factors.

As aforementioned, the media played the role of a powerful purveyor of information and narratives, often wielding a considerable influence over public perceptions and policy discussions surrounding immigration, particularly in the context of the Syrian Refugee Crisis. The Syrian Refugee Crisis still stands as a vivid metaphor for how media coverage can sway public sentiment and catalyze support for humanitarian immigration policies. During this crisis, media outlets worldwide played a crucial role in capturing and disseminating stories of Syrian refugees fleeing the newly sprung Syrian Civil War in search of asylum. Images of war-torn Syrian families undertaking perilous journeys across seas, combined with heart-wrenching stories of families separated and personal struggles evoked empathy and compassion from the global audience (Wallace). Among these stories and images was a tragic image of Alan Kurdi, a young Syrian boy whose lifeless body had been caught on camera washed ashore would become an indelible symbol of the crisis's human toll and generated an outpouring of sympathy from a global audience (Walsh). An important detail pertaining to this specific case, however, was the fact that the Kurdi family had filed for refugee sponsorship for a pathway into Canada to rejoin their relatives residing in Vancouver but was rejected by the Department of Citizenship and Immigration Canada following a no-exit visa via Turkish authorities (Hynie). This would cause immense outrage as the Canadian populace saw this tragic image and gut-wrenching details appear on media networks.

Media coverage would go on to not only spotlight the immediate suffering of the refugees but also highlight the potential benefits of humanitarian immigration policies. Stories highlighting successful refugee integration, instances of refugee individuals making valuable contributions to Canadian society, and heartwarming stories of local support headlined the mainstream media. However, many media outlets were quick to discuss concerns with Syrian refugees regarding the integration of Syrian refugees into Canadian society, bringing up the impact that these refugees could have on Canada's economic and logistical infrastructure. Often keywords or phrases such as "planeloads of Syrian Refugees" and references to Syrian refugees as those to "be housed" or to "be distributed" often left an imprint on Canadian citizens' minds that they were just numbers of people that Canadians had to deal with and viewed as competition (Msefer). Inherently, this gave way to the 'othering' of the refugees, and some dispute that the media's coverage of the Syrian Refugee Crisis gave leeway to modern-day islamophobia, anti-refugee, and racist sentiment in Canada.

Consequently, the media's portrayal of the Syrian Refugee Crisis shaped Canadian public immigration by affirming an existing fear/sentiment of immigrants or providing and striking sympathy into hearts. These portrayals continue to have a resounding effect today, shaping modern Canadian political views on immigration and the existing hegemony surrounding immigrants.

With that said, media narratives that shape social issues cannot be discussed without framing them within the adequate scope of economic pressures, which serve as intrinsic motivators for change. At this juncture, it is crucial to invoke the dichotomy of the exemplary recessions of the early 1990s and late 2000s, with the former enduring more significant immigrant economic implications and the latter exhibiting more emphasis on the perceived notions of the recession as opposed to its effects. Outlined by a time of world political repositioning -Soviet influence collapsing in conjunction with the Persian Gulf Crisis-the first recession disproportionately affected immigrant employment and earnings, particularly recent immigrants (residing for less than five years). This is to the extent that, from 1993 to 1994, recent immigrant men experienced a 14% drop below pre-recession levels in employment incidence, whereas their comparison group only dropped 6%; throughout the recession, they also suffered a 24% drop in median annual earnings (Hou and Picot). Indicating a "scarring" effect on their financial capacity following the recession, it is notable that the jobs that were either lost or reduced in opportunity for full-time work during that time coincided with the jobs of many recent immigrants, including manufacturing and construction. Conversely, the 2008 financial crisis produced less enunciated economic detriments as in the case of Canada; it was a "relatively mild" recession that affected recent immigrants partly due to the immigrants selected around this time being economic immigrants (Hou and Picot). Notwithstanding, relative to their Canadian-born counterparts, immigrants are still recorded to have been inordinately affected by unemployment, a decline in full-time work, and the severed good-producing sector (Kelly et al.). Economically, these two occurrences unveil tangible evidence of immigrants receiving the short end of recessions, correlatable with their pre-established social status and their perceived role in Canada's development with reference to concurrent media and citizen perspectives on immigration.

Undoubtedly, notions concerning such economic downfalls exacerbate takes and demands from groups previously less amplified or ignored during times of prosperity. Of course, this encapsulates consensus on the central issue, but in that agreement exists the pointing of fingers and scapegoating to find solutions driven by self-interest. To illustrate, a 1991 CBC news report highlighted that Canadians were pessimistic about the government's recovery and that they were spending less when the economy required the opposite to run as usual (When Canadians Weren't Buying). This demonstrates economic constraints, creating widespread suspicions and mistrust among people at a time when immigration was planned to be more frequent.

Simultaneously, there are figures in entertainment who occasionally give their political takes; Don Cherry, an outspoken hockey coach, in 1990 said that some Canadians are "ticked off" that foreigners are entering the country and making considerable money, also calling himself a "Pro-Canadian" (Don Cherry on Immigration). On the other hand, the general trend seems to show the opposite of this view, irrespective of slight geographic exceptions such as Alberta. According to an Environics survey, 56% of Canadians in 1993 agreed that immigrants have a positive economic impact, growing to 80% of Canadians in 2019 (Neuman). Despite the correlation and possible causation between increased support for immigration and the number of immigrants representing Canadians, it nonetheless is a strong indicator of public opinion.

Although Canadians have been increasingly supportive of immigration and remain much more socially open to immigrants than their other Western counterparts. Canada is not absent from extreme right-wing populist groups that lobby for reducing immigration. Though forming a small fragment of the population, this vocal yet divided cluster of groups is represented politically in the People's Party of Canada (PPC) and geographically concentrated in Alberta. Their prime motivators stem from varying sources, such as ideology, identity, or from a place of socioeconomic frustration, leading to concerns about cultural integration, public service feasibility, and economic benefit, alongside security matters. On its website, the PPC affirms such concerns, claiming that immigration policy should only go as far as to gain economic benefit, not to transform the country's social fabric or financially stress Canadians with humanitarian endeavours (People's Party of Canada). Despite this juxtaposition of interests pointing to political candidacy, the PPC does not currently have a seat in the parliament. Out of phase with the rest of Canada, polls show that 43% of Albertans agree that immigration levels are too high, telling of the general anti-immigration sentiments that exist (Neuman). Additionally, an anonymous member of the Proud Boys suggests mass immigration should be much more regulated because some immigrants in Canada are not "contributive" to society. Others also cite terrorism in Europe as evidence for Canada to tighten borders and be more aware of security threats posed by militant Islamic groups camouflaging themselves among refugees and other immigrants (Munk School of Global Affairs & Public Policy). Despite being minority opinions, the concerns raised by far-right Canadians showcase what extremes are possible among usual conservatives and the need for proper discourse in governing immigration policy.

All in all, Canadian public opinion on immigration policy is subject to the required accommodation of humanitarian crises such as the Syrian Refugee Crisis, along with economic recessions such as those of the early 1990s and late 2000s, their consequent media coverage, and the opinions of loud small sects that display the extremes of public opinion. In this relationship, practically felt change such as the governmental action taken in response to domestic and humanitarian crises, serves as the central origin that media coverage and audible groups revolve around to foster attitudes such as panic, disarray, frustration, and apprehensiveness from Canadians.

Impact of Shifting Public Opinion on Governmental Decisions and Immigration Policies

The evolution of governmental decisions and immigration policies in response to shifting public opinion evinces the intricate interplay between Canada's sociopolitical horizon and its correlating immigration framework. Four distinct instances exemplify the significant impact of public sentiment on shaping immigration policies in Canada. The Komagata Maru incident of 1914 highlights the Canadian government's refusal to admit Indian passengers on a ship and, in due course, the policy changes that would reflect the interface of public attitudes and immigration regulations toward South Asians. The landmark adoption of the Multiculturalism Policy serves as a shifting point and pivotal juncture marked by the Canadian government's commitment to adopting a more multiculturalist society amid a diverse, opinionated Canadian public. Transitioning to the Harper Immigration Reforms spanning from 2008 to 2015, a comprehensive examination unfolded that would highlight the convoluted balance between alleviating public concerns and enhancing the efficiency of immigration systems, pertaining specifically to the nuances involved with economic-driven immigration. Lastly, the Temporary Foreign Worker Program (TFWP) reforms illustrate the Canadian government attempting to take a proactive approach in addressing public outcry and refining the frameworks of political policy to alleviate concerns about program abuse among Canadian citizens.

Delving further into these focal moments and periods of Canadian history provides a more comprehensive understanding of how the dynamics of public sentiment and opinion have influenced government decisions. Each moment allows us to not only showcase the sensitivity of immigration policies to the prevailing societal attitudes but also underscore the government's adaptive capacity to respond to public concerns and aspirations while also trying to maintain the integrity of its immigration objectives. A panoramic view emerges through meticulous analysis of these instances, giving way to the complicated relationship between public opinion and immigration policies in the Canadian context.

Again, revisiting history, we look towards the Komagata Maru Incident with a critical eye to analyze how shifts in public opinion translate to real policy reform. The incident would spark a government response on its own, but a change in public ideals would also bring this piece of history into focus for the sake of a due apology not given in due time. On May 23rd, 1914, a ship called the *Komagata Maru* would arrive at the Vancouver harbour with 376 South Asians hoping to immigrate to Canada. Outraged, the local population would attempt to deport the ship's passengers under the justification of certain racial rhetoric. In defence of the passengers, the local South Asian community, who were barred from communicating with the passengers stranded on the ship, would put up an unfruitful legal action, which ended in the ship being sent back (Johnston). At the time, two order-in-council decrees, one mandating all Asians to carry 200 dollars upon entry to Canada and the other requiring nonstop direct travel from the country of origin–unavailable for South Asians at the time–, were measures put in place to restrict South Asian immigration. The ill-treatment of the passengers of this ship went as far as the government's initial refusal to give the ship provisions for their return trip and military involvement as a response. Still, the local community would convince the governor to provide

the rations. On July 23rd, most passengers returned to India and faced violent political persecution from the British government, which viewed it as an act of rebellion (The Komagata Maru Incident).

This story provides a fitting example of how public opinion creates policy. The racial discrimination perpetuated and white nationalism shared by Canadian citizens is what prompted the overtly racist laws to exist and allowed for them to persist unabated until 1921 when both mentioned laws were revoked. The motive for backtracking was specifically spearheaded by local South Asian communities who rallied against racist laws, with their peaceful integration and co-existence in Canada, alongside the Komagata Maru Incident contributed to a longstanding fight for equality among all Canadians. However, the Canadian government did not address this incident until nearly a century later, in 2008, when Stephen Harper offered apologies at a Sikh event in British Columbia. Still, it was returned with backlash from the Sikh community because it was not a formal apology at the House of Commons in Ottawa as other wronged people have received (Harper Apologizes in B.C). In 2012, the government of British Columbia officially apologized for how it handled the incident (Husser). In 2016, Prime Minister Justin Trudeau would officially apologize for the incident on behalf of the government (Trudeau Gives Komagata Maru Apology). These apologies reflect a change in public opinion on that historical event and the horizons their opinions have come open to, making such apologies palatable by many Canadians.

Considering this, exploring what changed for these horizons to be opened for successive generations in Canada is rational. Among the many policies regarding immigration that shifted towards a less racialized immigration system post-WW2, the Multiculturalism Policy would be the first codified and implemented policy that promoted cultural diversity as a valuable asset to the social fabric of Canada. Though it can be contended that multiculturalism in Canada arose from this singular policy, a more based argument is that the zeitgeist this policy came out of is what opened new horizons in Canadian plurality—leading up to Pierre Trudeau's introduction of the policy, discourse and debate among politicians and academics surrounding Canada's national identity brew amidst more diverse immigrants in the 1960s following post-WW2 immigration reform. Two blocs emerged during this period: one favouring multiculturalism and the other for biculturalism. The distinction is that whereas multiculturalism embraced an ethnocultural mosaic formed through immigration and integration with Canada's identity in constant metamorphosis, biculturalism was established upon the principle that Canada was of English and French origin; hence, it argued that Canada's identity should be consolidated in its original cultural and linguistic makeup. This debate was especially poignant in Quebec as francophone nationalists aimed to maintain their language and culture, yet they were still fully incorporated in politico-economic decision-making. In response, the federal government created the Royal Commission on Bilingualism and Biculturalism (referred to as the Bi-Bi Commission), which operated from 1963-1969 to investigate bilingualism and cultural relations in Canadian institutions, and at a far lesser extent engaging in the study of other groups as an appendage objective. In its concluding report, the Bi-Bi Commission recommended that Canada undertake a multicultural approach to progressing the country, which the federal Cabinet discussed. Members expressed concern about how certain groups would receive it, trying to balance opposed existing and potential demands regarding official recognition, government priority, cultural absorption, and economic consequences, among others (Raska). Ultimately, Canada formulated the policy in response to the detailed demands and interests behind the general surface of public opinion.

In this contemporary atmosphere, we must discuss the intricate interplay between public sentiment, policy evolution, and Canada's socioeconomic environment, now known as the Harper Immigration Reforms of 2008-2015. During this period, comprehensive reforms were introduced to recalibrate immigration responses, driven by a dual objective: addressing public concerns and optimizing economic-driven immigration. While specific policies aimed to derive a successful outcome from these aims, the era also experienced notable challenges that underscored the complexity of managing public opinion vis-a-vis policy implementation.

Among the era's notable successes in immigration policy, a significant main point in dialogue would be the introduction of the Canadian Experience Class (CEC) in 2008, which aimed to capitalize on immigrants' existing connections to the Canadian workforce, thereby mitigating fears of labour market integration by the Canadian populace (Chase). Furthermore, this policy sought to alleviate public concerns regarding job displacement by prioritizing already well-established candidates within the Canadian employment horoscope. Similarly, the Federal Skilled Worker Program (FSWP) reforms in 2013 centred on language proficiency and work experience and reflected a strategic alignment of immigration selection with economic goals (Desiderio and Hooper).

However, the Harper Immigration Reforms came with significant challenges that exposed the growing pains of policy implementation and the complexities of managing public opinion. One such example was the TFWP, an initiative by the Harper government designed to address short-term labour shortages in industries that could not find Canadian workers to fill specific job positions (Nakache and Kinoshita). Under this program, employers were allowed to hire foreign workers temporarily to meet their immediate labour needs. However, while addressing legitimate concerns about program abuse under the conditions of the previously implemented FSWP, it faced criticism for unintended consequences, which included the negative impact on businesses heavily reliant on temporary foreign labour, particularly the agriculture and hospitality sectors (Government of Canada Announces Workforce Solutions). This would serve as a highlight of the shortcoming within the context of Harper's Immigration Reforms. Furthermore, the Harper Governmental Reforms faced general criticism from the Canadian public for potentially exacerbating social tensions and fostering an environment where questions were raised regarding cultural diversity, influencing Harper's eventual defeat in the 2015 Canadian Federal election to Liberal Candidate Justin Trudeau.

Inherently, the Harper Immigration Reforms comprised successes and failures in managing public sentiment while pursuing policy objectives. The introduction of policies such as the CEC and FSWP reforms demonstrated the government's ability to proactively address the public's concerns regarding immigration and also advance economic goals. However, the TFWP

reforms and general policy approach also highlighted the shortcomings of the Reforms in a broader setting, while laying down a blueprint model for the nuanced balance required to navigate the complexities of public opinion, economic imperatives, and social cohesion. Conclusively, this era in Canadian history serves as an everlasting reminder that shaping immigration policies not only requires an understanding of the economic imperatives of the nation but also a nuanced engagement with the changing attitudes of the Canadian public, which can shape these policies.

Conclusion

In its totality, this academic exploration provides a gradated understanding of the historical shifts and contemporary factors that have moulded Canadian public opinion on immigration and the consequential impact on governmental decisions and policies.

Throughout Canadian history, a plethora of events properly embody the public opinions of their time on immigration policy. From Canada's early settlement and establishment to discriminatory laws such as the Chinese Head Tax, leading up to the new circumstantial needs of the post-WW2 era and foreign humanitarian responsibilities taken as in the case of the 2015-2016 Syrian Refugee Crisis. With regards to Canada's early days, public opinion was mostly of the European settlers who ruled the government, who believed that Canada was to be a "white man's country" and that the immigrants who did come should be of European descent. This would be followed by continued immigration of people from Europe, to which the Indigenous people who came to co-exist with newcomers were complicit. To prevent other groups from entering Canada, the government would impose certain racist laws as an assuring appendage to already racially ascribed immigration policies. In the case of the Chinese, and anti-Asian sentiment at large, the Chinese Head Tax served as an additional limitation to ensure fewer Asian immigrants in western Canada, following the construction of the Canadian Pacific Railway that heavily utilized Chinese labour. These racist attitudes would soften in the post-WW2 era, as the 1952 Immigration Act, alongside other reforms, would respond to the recent international humanitarian standards set by the UN and a heavy influx of immigrants with more focus placed on the skills and qualities of immigrants. Canadian immigration, though still not rid of racial consideration, would become more diversified in the 1960s and more discussion would open up for new developments. Fast-forwarding to the 21st century, the Syrian Refugee Crisis would attest to a significant shift in public opinion surrounding refugees towards that of a country that acknowledges its foundations are built upon immigration and claims moral responsibility for aiding the international effort to settle vulnerable refugees. Considering these shifts in public opinion, we also explored the factors that brought them about.

In the contemporary milieu of Canadian history, the paradigm of events can be astutely recognized and described in the context of the factors that have influenced Canadian public opinion on immigration. The media's portrayal of refugees, exemplified vividly by the 2015 Syrian Refugee Crisis, exercises a formidable agency, employing emotive imagery and poignant narratives to deftly sway public sentiments in favour of action regarding the crisis.

Simultaneously, the reverberation of global events, typified by the convulsions of the 2008 financial crisis and the more locally impactful recession in the early 1990s, intertwine economic uncertainties with the prism of refugee acceptance, yielding a nuanced tapestry of fluctuating public inclinations. Amidst this serpentine mural, the ascension of far-right movements such as the PPC assumes a catalytic role in amplifying their influence through resonating messages of fervent nationalism and strident calls for stringent immigration controls. The orchestration of these diverse elements, including the media's emotional resonance, global economic undercurrents, and the ideological resurgence of far-right ideologies, synergistically crafts the contours of Canadian immigration discourse, unravelling a compounded dynamic where narratives, events, and sociopolitical forces converge to sculpt prevailing public attitudes and, subsequently, mould the course of governmental responses.

Nonetheless, this leads back to the counterbalance in government action. From the Komagata Maru Incident to the biculturalism versus multiculturalism debates leading up to the Multiculturalism Policy, the Canadian government has always made policies apropos of Canadian sentiments up to the immigration reforms of the Harper administration. The Komagata Maru Incident exposes the racial norms that permeated throughout Canadian immigration policy in addition to the transformation of public opinion that drove an official apology over a century later. Regarded today as an aberration of Canadian etiquette, the nature of the incident, constituted of both the local response and the legal framework that supported them, conveys an elusive goal of maintaining long-standing legality due to ever-changing social norms. As such, the case of the Multiculturalism Policy presents the same message; debates and discourse that take place over several years produce satisfactory policy when considerate of all perspectives, as the Bi-Bi Commission came to resolve in the late 1960s. Contrarily proving the same point, the immigration reforms of the Harper government and their consequent developments and damages display an instance where proper accounting of public concerns was not taken for. Whereas the programs were focused on solving economic shortcomings –which were not solved in the long run-, they neglected their social implications, raising criticism about diversity and the deteriorated relationships within it. Essentially, policy cannot exist in a democracy such as Canada without affirmation or check from the people.

Amidst the elaborate interweaving of historical echoes, contemporary nuances, and government decisions, a discernible pattern appears to emerge: Canadian immigration policy appears to serve as an effective reflection of the ever-evolving currents of public sentiment, whilst exhibiting a reciprocal effect on public opinion. The trajectory from early colonization to the present-day responses to the refugee crisis unravels this apparent truth. This exploration aimed to underscore the nuanced intricacy inherent in immigration policy - a pivotal convergence where historical legacies merge with modern influences, coalescing to shape the multifaceted visage of Canadian identity and its approach to those seeking a home within its lands.

Works Cited

- "A History of Treaty-Making in Canada." *Government of Canada*, 2 Sept. 2011, www.rcaanc-cirnac.gc.ca/eng/1314977704533/1544620451420. Accessed 15 Jul. 2023
- Borrows, John, and Michael Coyle. *The Right Relationship: Reimagining the Implementation of Historical Treaties*. University Of Toronto Press, 2017.
- Bumsted, J.M. "Red River Resistance". *The Canadian Encyclopedia*, 08 July 2021, www.thecanadianencyclopedia.ca/en/article/red-river-rebellion. Accessed 17 Aug. 2023
- "Canada: A History of Refuge." *Government of Canada*, 20 June 2011, www.canada.ca/en/immigration-refugees-citizenship/services/refugees/canada-role/timeli ne.htm. Accessed 09 Aug. 2023.
- CBC. "Don Cherry on Immigration, Hockey Fighting in 1990 CBC Interview." *YouTube*, 6 Apr. 2015. www.youtube.com/watch?v=2-sG6u_Sats. Accessed 16 Aug. 2023.
- Cesari, Jocelyne. Muslims in the West after 9/11. Routledge, 2009.
- Chan, Arlene. "Chinese Head Tax in Canada." *The Canadian Encyclopedia*, 8 Sept. 2016, www.thecanadianencyclopedia.ca/en/article/chinese-head-tax-in-canada. Accessed 28 Jul. 2023.
- Chase, Steven. "Canada Needs to Get Competitive to Attract Skilled Immigrants: Harper." *The Globe and Mail*, 10 Nov. 2012,

www.theglobeandmail.com/news/politics/canada-needs-to-get-competitive-to-attract-skill ed-immigrants-harper/article5179369/. Accessed 16 Aug. 2023.

- "Convention and Protocol Relating to the Status of Refugees." *United Nations High Commissioner for Refugees UNHCR*, 1951, <u>https://www.unhcr.org/media/convention-and-protocol-relating-status-refugees</u>. Accessed 24 Jul, 2023.
- Desiderio, Maria, and Kate Hooper. "The Canadian Expression of Interest System." *Migration Policy Institute*, Mar. 2016,

www.migrationpolicy.org/sites/default/files/publications/MPIE-Canada-ExpressEntry-FI NAL.pdf. Accessed 30 Jul. 2023.

Gaudry, Adam. "Métis." *The Canadian Encyclopedia*, 7 Jan. 2009, www.thecanadianencyclopedia.ca/en/article/metis. Accessed 20 Aug. 2023.

"Government of Canada Announces Workforce Solutions Road Map – Further Changes to the Temporary Foreign Worker Program to Address Labour Shortages across Canada." *Government of Canada*, 2 Apr. 2022,

www.canada.ca/en/employment-social-development/news/2022/04/government-of-canad a-announces-workforce-solutions-road-map--further-changes-to-the-temporary-foreign-w orker-program-to-address-labour-shortages-ac.html. Accessed 20 Aug. 2023.

"Harper Apologizes in B.C. For 1914 Komagata Maru Incident." *CBC*, 3 Aug. 2008, www.cbc.ca/news/canada/british-columbia/harper-apologizes-in-b-c-for-1914-komagatamaru-incident-1.747120. Accessed 05 Aug. 2023.
- Hou, Feng, and Garnett Picot. "Immigrant Labour Market Outcomes during Recessions: Comparing the Early 1990s, Late 2000s and COVID-19 Recessions ." *Statistics Canada*, 23 Feb. 2022, https://doi.org/10.25318/36280001202200200003-eng. Accessed 06 Aug. 2023.
- Houle, René. "Results from the 2016 Census: Syrian Refugees Who Resettled in Canada in 2015 and 2016." *Statistics Canada*, 12 Feb. 2019, www150.statcan.gc.ca/n1/pub/75-006-x/2019001/article/00001-eng.htm. Accessed 18 Aug. 2023.
- Husser, Amy. "Komagata Maru Apology: Ship's Story Represents 'Dark Chapter' of Canada's Past." *CBC*, 18 May 2016, www.cbc.ca/news/canada/komagata-maru-backgrounder-apology-1.3584372. Accessed
- 20 Aug. 2023. Hynie, Michaela. "Canada's Syrian Refugee Program, Intergroup Relationships and Identities." *Canadian Ethnic Studies*, vol. 50, no. 9, 2018, pp. 4–5, km4s.ca/wp-content/uploads/Syrian-refugee-youth-use-social-media-Building-transcultur al-spaces-and-connections-for-resettlement-in-Ottawa-Canada-Veronis.pdf.
- "Immigration." *People's Party of Canada*, 2023, www.peoplespartyofcanada.ca/immigration. Accessed 13 Aug. 2023.
- Johnston, Hugh. "Komagata Maru." *Canadian Encyclopedia*, 2021, www.thecanadianencyclopedia.ca/en/article/komagata-maru#:~:text=At%20the%20time %2C%20few%20Canadians. Accessed 05 Aug. 2023.
- Kelly, Philip, Stella Park, and Laura Lepper. "Economic Recession and Immigrant Labour Market Outcomes in Canada, 2006-2011." *Toronto Immigrant Employment Data Initiative*, 2011. http://www.yorku.ca/tiedi/doc/AnalyticalReport22.pdf
- Maktabi, Rania. "Gender, Family Law and Citizenship in Syria." *Citizenship Studies*, vol. 14, no. 5, Oct. 2010, pp. 557–572, https://doi.org/10.1080/13621025.2010.506714.
- Meister, Daniel, et al. "Immigration Act, 1952." *Canadian Museum of Immigration at Pier 21*, 2023, <u>https://pier21.ca/research/immigration-history/immigration-act-1952</u>. Accessed 10 Aug. 2023
- Mesiter, Daniel, et al. "Immigration Act, 1869." *Canadian Immigration Museum at Pier 21*, 2019, https://pier21.ca/research/immigration-history/immigration-act-1869. Accessed 10 Aug. 2023
- Msefer, Farah. "Impact of Media Narratives on the Inclusion of Refugees in Canada." *Social Connectedness*, 2017,

Www.socialconnectedness.org/Wp-Content/Uploads/2019/10/Impact-of-Media-Narrative s-On-The-Inclusion-of-Refugees-In-Canada.pdf.

Nakache, Delphine, and Paula Kinoshita. "The Canadian Temporary Foreign Worker Program Do Short-Term Economic Needs Prevail over Human Rights Concerns?" *IRPP Study*, vol. 5, no. 5, 2010, pp. 1-52, https://irpp.org/wp-content/uploads/assets/research/diversity-immigration-and-integration /new-research-article-3/IRPP-Study-no5.pdf.

Neuman, Keith. "Canadian Public Opinion on Immigration and Refugees." *Environics Institute*, 5 Nov. 2019,

www.environicsinstitute.org/projects/project-details/canadian-public-opinion-on-immigra tion-and-refugees. Accessed 31 Jul. 2023.

- "150 Years of Immigration in Canada." *Statistics Canada*, 29 June 2016, www150.statcan.gc.ca/n1/pub/11-630-x/11-630-x2016006-eng.htm. Accessed 10 Aug. 2023
- "Post War Immigration National Historic Event." *Parks Canada*, www.pc.gc.ca/apps/dfhd/page nhs eng.aspx?id=1737. Accessed 06 Aug. 2023
- "Radical Right in Canada and Their Views on Immigration." Munk School of Global Affairs & Public Policy, 2023,

https://munkschool.utoronto.ca/harney/radical-right-canada-and-their-views-immigration. Accessed 02 Aug. 2023.

- Raska, Jan. "Early Political and Public Responses to Canada's Official Multiculturalism Policy, 1971-1972." *Canadian Museum of Immigration at Pier 21*, 4 Nov. 2020, https://pier21.ca/research/immigration-history/canadas-official-multiculturalism-policy. Accessed 06 Aug. 2023
- Ray, Arthur J. "Hudson's Bay Company." *The Canadian Encyclopedia*, 2023, www.thecanadianencyclopedia.ca/en/article/hudsons-bay-company. Accessed 06 Aug. 2023
- "The Komagata Maru Incident of 1914." *Parks Canada*, 7 Aug. 2016, www.canada.ca/en/parks-canada/news/2016/08/the-komagata-maru-incident-of-1914.htm 1. Accessed 09 Aug. 2023
- Triadafilopoulos, Triadafilos. "Good and Lucky." *Policy Success in Canada: Cases, Lessons, Challenges*, edited by Evert Lindquist, et al., Oxford Academics, 21 July 2022, pp. 161–82, https://doi.org/10.1093/oso/9780192897046.003.0009.
- "Trudeau Gives Komagata Maru Apology in House of Commons." *CBC*, 18 May 2016, <u>www.cbc.ca/news/politics/komagata-maru-live-apology-1.3587827</u>. Accessed 01 Aug. 2023.
- Tyyskä, Vappu, et al. "The Syrian Refugee Crisis in Canadian Media." *RCIS Working Papers*, no. 3, Apr. 2017, https://doi.org/10.32920/ryerson.14669130. Accessed 3 Aug. 2023.
- "U.N. Awards Medal to Canada for its Contributions to Cause of Refugees." *Los Angeles Times*, 7 Oct. 1986, www.latimes.com/archives/la-xpm-1986-10-07-mn-5066-story.html. Accessed 16 Aug. 2023.
- Wallace, Rebecca. "How the News Media Framed the Syrian Refugee Crisis." *Policy Options*, 7 Mar. 2018,

policyoptions.irpp.org/fr/magazines/march-2018/how-the-news-media-framed-the-syrian-refugee-crisis/. Accessed 25 Jul. 2023.

- Walsh, Bryan. "Alan Kurdi's Story: Behind the Most Heartbreaking Photo of 2015." *Time*, 29 Dec. 2015, time.com/4162306/alan-kurdi-syria-drowned-boy-refugee-crisis/. Accessed 31 Jul. 2023.
- "When Canadians Weren't Buying the News That Bad Times Were Ending." *CBC*, 16 Oct. 2020,

www.cbc.ca/archives/when-canadians-weren-t-buying-the-news-that-bad-times-were-end ing-1.5761576. Accessed 16 Aug. 2023.

New York City Reimagined Without Cars By Srivanth Reddy

Abstract

While cities today are dominated by forms of privatized transportation, such as personal vehicles and taxis, an alternative is needed to this normalized form of transportation in order to maximize the potential of cities and their inhabitants. Car free cities today are the product of their geographical surroundings, such as Venice, but here we will be implementing this car-free city infrastructure in a city with already profound and deeply rooted automobile activity: New York City. There are countless ways in which the city would benefit from the removal of motor vehicles from the street; for example, this manuscript details how by modifying the current infrastructure of the city reduces superfluous expenses and the amount of space that cars create and take up in the city. The infrastructure also greatly increases the efficiency of public transportation in terms of carrying capacity and reliability while also greatly reducing Co2 emissions and transportation costs, as well as also greatly contributing to the health and environment of the city as a whole. Keywords: Infrastructure, Transportation, Cars, New York City

Introduction

The automobile has been a staple of American society ever since the industries first domestic conception in Detroit Michigan through the likes of Henry Ford. Spurred by the accessibility that it provided with the Model T, Ford soon became a household name, providing everyone with the perfect balance of efficiency and reliability along with a reasonable price. By the 1910s, the government had realized the potential of cars as a dominant mode of transportation and issued the first Federally funded roadways such as the Federal Road Aid act in 1916 and the Federal Aid Highway Act in 1921¹. Automobiles have since then dominated transportation as a whole in America, with 90% of all US adults, about 232.48 million people, being licensed drivers as of 2021². It's clear why many of the older cities would adjust their existing infrastructure to account for this new global phenomenon, but the environmental consequences associated with the excessive use of automobiles necessitates that we have to once again reevaluate our city models into one that relies much more heavily on public and active transportation.

In the U.S, transportation accounts for about 38% of total emissions, which represents the largest sector of greenhouse gas emissions in 2021 and amounts to about 1.75 billion metric tons of CO2 in 2021 ³. In addition, in 2019 58% of emissions produced from the transportation sector were from personal vehicles, about 1.04 billion metric tons, which is almost 25% of all emissions created in the transportation sector ³. With U.S. car ownership having increased by 3.66% from 2017 to 2021, CO2 emissions will continue to rise unless there is a major shift in its production ⁴.

As a way to combat this rise of Greenhouse Gases, cities can drastically reduce their CO2 output by removing car infrastructure or modifying it to accommodate for much more sustainable practices. Cities like San Francisco have already implemented such measures by using signage and barriers to limit traffic and speeds on about 30 corridors in order to make roads more pedestrian and cyclist friendly; as a result, 50% of vehicle traffic was reduced while pedestrian and cyclist traffic increased by 17% and 65% respectively ⁵. Internationally, cities like Paris and Bogota have implemented various programs such as 15-minute city and widening sidewalks and biking lanes ⁵. However, this paper will take a more radical approach to reducing cars by eliminating them all together by creating a car free infrastructure.

This paper will specifically look at New York city as a basis for how a car-free city can be made from an already existing city in order to achieve these desired results. The major actions of adjusting a city like New York into a car-free city will be outlined while also establishing the significant effects that come from the outcomes of these actions.

Implementation

The first stage of infrastructure implementation would be the creation of a road conversion system for various road sizes ⁶. Single lane roads would be completely stripped of asphalt and converted into a bicycle path. Buses and other public transport will not have any dedicated lanes on single lane roads because bus routes will not focus on the more insignificant roadways compared to other, more larger, roads. Roadways will also be stripped and converted into a bicycle lane(preferably in the middle) with an extended walkway surrounding it. There will be no designated buffer zone for bike lanes on these types of roads. 4 lane roads with 2 lanes on each side will be split so the 2 lanes closest to the middle would be converted into a bus lane(if not already one), while the other 2 lanes would be converted into extended walkways. Roads with 6 lanes will be split so that the lanes closer to the middle will be converted to bus lanes, the second closest to the middle will become a walkway to allow bus rider to get down, as well as a bike lane between the added walkway and the extended walkway, leaving 6 ft to remain for the bikers to use(assuming that lane widths are approximately 10 ft)⁷. For 8 lane roads, the middle 2 lanes will be dedicated bus lanes, the next lane being an additional walkway for bus passengers, the 3rd lane being a biking lane with a width of 8ft, and 4th lane on each side being a combined extended walkway as well as a designated vending area to help organize street vendors. By creating this system it will be easier to integrate these different roads into the new infrastructure.

Furthermore, we will also have to integrate various spaces dedicated to vehicle parking. As part of the system previously discussed, certain parking space types can have certain changes. Residential area parking spaces can be changed into extended walkways and bike lanes while parking garages can be completely dismantled and sold off again. In total there are about 1100 off-street parking garages in Manhattan and 100,000 parking spaces in outdoor parking lots ⁸. In total this can come up to about 5,361,550 parking spaces or, assuming a parking space length ranges from 16ft-18ft while its width ranges from 7.9ft - 9ft, 24.3 to 31.2 square miles ^{9,10}. If the

average cost of New York City land is about \$5.2 million per acre, the area of all the parking spaces amounts to about \$8.09-\$10.4 billion dollars ¹¹.

The removal of parking spaces and roads in NYC may prompt many to sell their car, but quite a few may still want to keep their vehicles, therefore prompting to build parking lots outside of the city for either short term or long term parking. The parking may also be funded by various corporations and groups, allowing for new industries to grow in the region.

Furthermore, many people's livelihood comes from serving cars, whether serving as a mechanic or a manager at a gas station. With about 697 gas stations and numerous auto repair shops, many of these locations will go out of business ¹². Therefore, before development of this infrastructure may start, the city government will have to provide the option for financial compensation for all businesses that may go out of business. The financial compensation will provide for the workers' job as well as the owner's. However, if the owner or worker refuses the financial compensation in favor of keeping their job and they do end up losing their job after the no-car system has been completely implemented, then they are not entitled to financial compensation.

Effects on Efficiency

Once implementing the no-car infrastructure the effects would be evidently seen through various increases in efficiencies of public transportation.

With the removal of the automobiles for the 400,730 car riders will come a new surge of demand for public transportation. In 2019, ridership per weekday totalled at about 5,493,875 on the subway as well as close to 2,158,469 on the bus ¹³. This decreases the amount of traffic commonly found with cars. By congesting 50 people who would have owned individual cars into one bus, you are cutting the amount of space per person from 55 square feet to 9 square feet ⁶. This allows for the remaining space to be converted to parks, walkways, and bike lanes. Some detractors of my proposition may claim that the influx of



depicted in the following picture

previously car driving commuters may create congestion that may be uncomfortable for some people. Fortunately enough, improvements in recent history have already been made to public transportation. Projects such as the 42nd st connection have provided easier access to metro stations by building more escalators and elevators as well as increasing metro car capacity from 4 cars to 6 cars, increasing passenger capacity by 20% ¹⁴. Furthermore, access to stations in Manhattan will be provided to residents of Long island with the induction of East Side Access, a

project that provides long island residents with 40 miles of new tracks, a new terminal beneath Grand Central station, as well as train line modernization ¹⁴. With this project train capacity to and from Manhattan will increase by 50% ¹⁴.

Energy efficiency will also increase dramatically with the ban of private vehicles in Manhattan. According to the U.S Department

of Energy, annually cars consume 474 gasoline gallon equivalents(GGEs) per year compared to a transit bus's 13,329 GGEs ¹⁵. However, as it was previously mentioned, 50 single passenger cars can account for a single transit bus, so we are essentially comparing 50 different cars and motorcycles to a single transit bus ¹⁵. Therefore, we can multiply 50 by 474 GGEs, totalling at 23,700 GGEs, about 2x more GGEs used compared to one transit bus. Greater energy efficiancy is also

Figure 2 | Depicts the expansion of the MTA into queens via. the east side access





achieved through the removal of asphalt during the road conversion phase. Due to the color of asphalt, which is black, the albedo of the material is 0.05, meaning that Asphalt only reflects 5% of solar radiation while absorbing the rest of the 95% ¹⁶. Consequently, cities heat up much more quickly, especially in the summer, increasing costs and energy use in air conditioning. If the 6,300 miles of roads and highways that make up New York City are made up of asphalt, and Asphalt absorbs about 900 J/Kg-K per, paved areas can reach up from 120°F to 150°F during the summer ^{17,18}. If this trend continues, New Yorkers may demand as much as 80% more electricity on some days to keep themselves cool ¹⁹. Air conditioning already accounts for 9% of electricity consumption during the summer so 80% of the current amount may severely impact the distribution of energy in the city ²⁰. By removing the pavement and instead replacing it with sidewalks, which have an albedo of 0.4, as well as installing more green space for natural cooling, AC energy consumption will be reduced considerably in the coming years ²¹.

Additionally, with the removal of roads the local government will not have to pay as much money for the maintenance of roads. According to the Department of Transportation(DOT), in 2016 the city of New York had set aside \$1.1 billion dollars for the DOT ²². If the no-car infrastructure is implemented, we can essentially be removing at most 76%, about 762 million dollars, of the money allocated in the budget, which in turn can be used to fund public transportation and the construction of various green spaces around the city ²².

CO2 emissions will also drastically reduce once automobiles are banned. On average, a car produces 411 grams of CO2 per mile traveled for one person; however, by using public transportation, it reduces a person's CO2 emissions by 27% to 299 grams ^{23,24}. If the average NYC commuter spends 79.6 minutes roundtrip and the average car speed is 12 mph while the average bus travels at 7.9mph, a single person can reduce the amount of CO2 they produce by

7.5 pounds per day if they choose to switch from car to public transportation ^{25,26,27}. If we were to use this statistic and apply it to the 400,730 car riders who would switch to public transportation if this new system was applied, then possibly carbon emission can be reduced by 3,005,475 pounds per day.

With the implementation of the no-car system there will be a decrease in travel time in public transportation. Currently the worst city in the US for traffic congestion, NYC drivers average at just 12 mph, which is slower compared to other forms of transportation ²⁵. If automobiles were banned, other public transportation such as buses would be able to travel at much faster paces. Furthermore, bike routes will be able to be expanded to accommodate more space and therefore more bikers once roads are removed, also decreasing travel time for bikers. Also, with tax money diverted from road management and safety, more money can be invested in other public transportation systems such as the transit and buses in order to decrease the travel time. This has already been seen with the creation of East Side access, which will reduce the amount of time by as much as 40 minutes for 160,000 passengers ¹⁴.

Cost of travel can also be decreased or taken out entirely for public transportation. Instead of removing the money used to maintain roads in NYC from the DOT budget, the money can instead be used to fund MTA, so that residents can use the metro without pay. Tallinn, the capital of Estonia, made public transportation free for all its residents and saw the increase in

public transportation usage, effectively making public transport more efficient. New York City can expect similar effects as seen in Tallinn if they were to implement a car-free infrastructure. Travel costs are also reduced by the efficiency of public transportation in comparison to cars ²⁸. According to the DOE, the average person annually drives about 15,000 miles, costing as much as \$8,000 in gas annually, which is much more expensive than the \$1,524 dollars spent annually to pay for public transportation in New York ²⁹. Furthermore the annual costs of a car will also include maintenance costs, parking passes, and taxes as well.



Figure 4 | Annual fuel cost of light duty vehicles in 2022

Effects on City Environment

In 2022, traffic accidents with injuries from 2020 to 2021 have increased by 16% to a total of 67,467 car collisions in NYC with 31,735 accidents resulting in injury; about 171 of those car accidents resulted in fatalities ³⁰. Banning cars will almost guarantee a decrease in the

number of street accidents and fatalities, though accidents may still happen with bus collisions. However in comparison, there have been about 1,870 metro accidents during 2021 with only 50 people killed on tracks . Furthermore, according to the APTA(American Public Transportation Association), it is ten times safer per mile to travel by public transportation instead of by car ³¹. Cars are also deadly when it comes to pollution as well, with about 1,400 lives being claimed due to car pollution ³². With the integration of the no-car system, deaths previously resulting from car pollution would dramatically decrease creating a much safer city environment.

The city environment will also be bolstered as many people are incentivized to walk and bike for the sake of faster travel and greater amount of green spaces. In New York City, for the past few years, childhood obesity has become an increasing problem with 15%-19.4% of children being overweight while 22-27% are obese ³³. Adults are even worse, with more than half(57%) of the adult population in New York City being overweight or obese ³⁴. By removing car infrastructure and providing bigger walkways and bike lanes it gives people much more of a reason to exercise and lose weight as well as reduce the risk of various cardiovascular diseases. According to one study in 2011, researchers found that by increasing the bikeability(access to biking space in cities), bikers were able to save almost \$146 million dollars per year ³⁵.

Removing cars can also provide more space to build green spaces which can provide vital exercise to both children and adults alike. Creation of Green Spaces as replacement of roads will also serve as a source of fresh oxygen for a city with 48 AQI(Air Quality Index)³⁶. According to centralparknyc.org, central parks trees remove about one million pounds of CO2 per year, proving to be an integral part of NYC air quality ³⁷. By creating more parks NYC has a possibility of increasing its air quality by 5 AQI.

Removing cars also provides the possibility of providing more space for the creation of new businesses. With parking spaces taking up more than 4 times the area of central park, much of that area can be dedicated to new local business or companies which can generate much needed revenue for the local government as well as bolster the economy ⁶. Also, with the removal of cars taxpayer money can be distributed to different sectors of need such as garbage disposal or homeless shelters. Additionally, as of 2025, the New York transit system will be facing a \$2.5 billion dollar deficit, which is 12% of their normal operational budget ³⁸. If this no-car system is implemented now then the possible money that can be diverted and generated in the future can help alleviate the future disaster.

Conclusion

Car transportation in New York city, specifically Manhattan, is wildly inefficient and causes numerous problems ranging from pollution to inefficient travel practices. Car transportation in New York city proves as a hindrance towards creating better solutions as well as getting rid of old problems. By eliminating the possibility of private transportation, with the exception of commercial vehicles, and installing a new infrastructure that promotes walkability and public transportation, many of the problems that plague New York City may be alleviated or possibly altogether eliminated. There are essentially 2 questions that we have to ask ourselves

before even implementing the plan. First is whether or not it is even possible to do so. As I had outlined, it is indeed possible. By creating a planned system that creates a general layout for how different types of roads should be altered to fit the new car free infrastructure as well as considering the different dependencies of people on driving cars, creating the car free infrastructure would be well within reach. The second question we have to ask ourselves is whether it is worth even changing a whole city ground layout to restrict cars. As seen throughout the paper, there are many different benefits that come with banning private vehicles: Public transportation becomes more efficient, CO2 emissions decrease, Car accidents decrease, businesses have more room to grow, more green spaces can be made, and new ways of making money can also be found. As a final emphasis, I want readers of this paper to keep in mind that we are simply sacrificing an inefficient mode of travel and part of the infrastructure needed to maintain it for the betterment of the lives of all New Yorkers. By understanding the tradeoff that this solution provides can usher greater prosperity in the lives of new yorkers and can serve as an example for cities around the world of how the removal of the automobile can positively affect a city.

Works Cited

- Weingroff, R. F. (1996). Federal aid road act of 1916: Building the foundation. Federal Aid Road Act of 1916: Building The Foundation. FHWA, 60, 10-18. https://highways.dot.gov/public-roads/summer-1996/federal-aid-road-act-1916-building-f oundation
- Carlier, M. (2023, March 14). *Total number of licensed drivers in the U.S. by State*. Statista. <u>https://www.statista.com/statistics/198029/total-number-of-us-licensed-drivers-by-state/#:</u> <u>~:text=Licensed%20drivers%20in%20the%20U.S.%20%2D%20total%20number%20by</u> <u>%20state%202021&text=In%202021%2C%20there%20were%20almost,in%20the%20co</u> <u>untry%20that%20year</u>.
- Shirley, C., Gecan, R., Kile, J., Adler, D., Austin, D., Chase, N., Hopkins, B., Krupkin, A., Prendergast, T., Resse, R., Rosenberg, J., Tawil, N., Willie, S., & Rebach, R. L. (2022). *Emissions of carbon dioxide in the Transportation Sector*. Congressional Budget Office. https://www.cbo.gov/publication/58861#:~:text=In%202019%2C%20CO2%20emissions, all%20lower%20per%20passenger%2Dmile.
- Tilford, A. (2023, August 17). Car Ownership Statistics 2023. *Forbes Advisor*. <u>https://www.forbes.com/advisor/car-insurance/car-ownership-statistics/#:~:text=U.S.%20</u> <u>in%202021.-,The%20number%20of%20registered%20vehicles%20in%20the%20United</u> <u>%20States%20increased,upward%20trend%20in%20car%20ownership</u>.
- Galloway, L. (2022, September 13). Four health-conscious cities putting pedestrians first. BBC Travel.

https://www.bbc.com/travel/article/20220912-four-health-conscious-cities-putting-pedest rians-first

Manjoo, F. (2020, July 12). Opinion | I've Seen a Future Without Cars, and It's Amazing. *The New York Times*.

https://www.nytimes.com/2020/07/09/opinion/sunday/ban-cars-manhattan-cities.html

- Ink, S. (2015, July 24). *Lane width*. National Association of City Transportation Officials. https://nacto.org/publication/urban-street-design-guide/street-design-elements/lane-width/
- Skillings, P. (2019). Where to Park in New York City. *TripSavvy*. <u>https://www.tripsavvy.com/guide-to-nyc-parking-garages-2286763</u>

Team, M. (2020, August 12). *How large is a parking space*?. Franklin Street. <u>https://franklinst.com/how-large-is-a-parking-space/</u>

too many cars.nyc. Jehiah, (n.d.). https://toomanycars.nyc/

- Cohen, M., & Cohen, M. (2023). Study shows huge disparity in U.S. urban land value, with NYC making up 10% | 6sqft. 6sqft | NYC Real Estate News and Information. https://www.6sqft.com/study-shows-huge-disparity-in-u-s-urban-land-value-with-nyc-ma king-up-10/#:~:text=The%20New%20York%20metro%20area,at%20%242.7%20million %20per%20acre.
- Bell, S. (2022, October 3). Manhattan Now Has 11 Times As Many EV Charging Sites As Gas Stations | Carscoops. Carscoops.

https://www.carscoops.com/2022/10/its-now-10-times-easier-to-find-an-ev-charger-in-ma nhattan-than-a-gas-station/#:~:text=Although%20charging%20sites%20outnumber%20g as,it%20has%20697%20gas%20stations.

- Subway and bus ridership for 2021. MTA. (2021). https://new.mta.info/agency/new-york-city-transit/subway-bus-ridership-2021
- East Side Access. (2023). MTA.

https://new.mta.info/project/east-side-access

- U.S. Department of Energy. (2020). *Maps and data average annual fuel use by vehicle type*. Alternative Fuels Data Center: Maps and Data - Average Annual Fuel Use by Vehicle Type. <u>https://afdc.energy.gov/data/10308</u>
- Aletba, S. R. O., Hassan, N. A., Jaya, R. P., Aminudin, E., Mahmud, M. Z. H., Mohamed, A. K., & Hussein, A. A. (2021). Thermal performance of cooling strategies for asphalt pavement: A state-of-the-art review. *Journal of Traffic and Transportation Engineering*, 8(3), 356–373. <u>https://doi.org/10.1016/j.jtte.2021.02.001</u>

Rodriguez, Y. (2022). *About NYC DOT*. NYC DOT. https://www.nyc.gov/html/dot/html/about/about.shtml

(2013). Pavement Thermal Performance And Contribution To Urban And Global Climate. U.S. Department of Transportation/Federal Highway Administration.

https://www.fhwa.dot.gov/pavement/sustainability/articles/pavement_thermal.cfm

Ravilious, K. (2018, November 7). New York Air Con set to spike electricity demand by 80%. Physics World.

https://physicsworld.com/a/new-york-air-con-set-to-spike-electricity-demand-by-80/

Ortiz, L., González, J. E., & Lin, W. . *IOPscience*. Environmental Research Letters, **13**, 094008 (2018, August 3).

Albedo. GCCA, (2021, April 30).

https://gccassociation.org/sustainability-benefits-of-concrete/albedo/#:~:text=Albedo%20 is%20the%20fraction%20of,%2C%20the%20higher%20the%20reflectivity).

The Council of the City of New York. (2017). *Report of the Finance Division on the Fiscal 2018 Preliminary Budget and the Fiscal 2017 Preliminary Mayor's Management Report for the Department of Transportation*. Department of Transportation. Retrieved May 12, 2023, from

http://council.nyc.gov/budget/wp-content/uploads/sites/54/2017/03/841-DOT.pdf

Environmental Protection Agency. (2014). *Greenhouse gas emissions from a typical passenger vehicle*. EPA.

https://nepis.epa.gov/Exe/ZyNET.exe/P100JPPH.TXT?ZyActionD=ZyDocument&Client =EPA&Index=2011%2BThru%2B2015&Docs=&Query=&Time=&EndTime=&SearchM ethod=1&TocRestrict=n&Toc=&TocEntry=&QField=&QFieldYear=&QFieldMonth=&Q FieldDay=&IntQFieldOp=0&ExtQFieldOp=0&XmlQuery=&File=D%3A%5Czyfiles%5 CIndex+Data%5C11thru15%5CTxt%5C00000011%5CP100JPPH.txt&User=ANONYM OUS&Password=anonymous&SortMethod=h%7C-&MaximumDocuments=1&FuzzyDe gree=0&ImageQuality=r75g8%2Fr75g8%2Fx150y150g16%2Fi425&Display=hpfr&Def SeekPage=x&SearchBack=ZyActionL&Back=ZyActionS&BackDesc=Results+page&M aximumPages=1&ZyEntry=1&SeekPage=x&ZyPURL

- Blumgart, J. (2022, February 11). *Are trains or buses better for the environment?*. Governing. https://www.governing.com/next/are-trains-or-buses-better-for-the-environment#:~:text= Mathews%20points%20to%20research%20showing,to%20cars%20at%20371%20grams.
- Morphet, J., & Crane, E. (2023, March 13). *NYC ranked Us's most congested city as motorists spend 10 full days in rush-hour traffic per year*. New York Post. https://nypost.com/2023/03/13/nyc-drivers-travel-just-12-mph-during-rush-hour/
- Duggan, K. (2021, November 15). Crawling along: MTA bus speeds are down in all five boroughs, agency stats show. amNewYork. https://www.amny.com/transit/mta-bus-speeds-slow-down-in-all-five-boroughs/
- Perry, B. (2023, February 24). *NYC workers have the longest commutes in the U.S.* Secret NYC. https://secretnyc.co/nyc-longest-commutes/#:~:text=In%20a%20new%20survey%20cond ucted,in%20at%2079.6%20minutes%20roundtrip.
- The Economist Newspaper. (2022). *Better, cheaper, faster: Improving public transport in cities*. The Economist. https://impact.economist.com/sustainability/social-sustainability/better-cheaper-faster-im
- proving-public-transport-in-cities FOTW #1245, July 4, 2022: EPA estimated annual fuel cost for model year 2022 light-duty vehicles ranges from \$500 to \$8,250. Energy.gov. (2022). https://www.energy.gov/eere/vehicles/articles/fotw-1245-july-4-2022-epa-estimated-annu al-fuel-cost-model-year-2022-light
- Rosenbaum & Rosenbaum, P.C. (2023, February 20). New York Car Accident Statistics -Rosenbaum & Rosenbaum, P.C.

https://www.rosenbaumnylaw.com/new-york-car-accident-lawyer/statistics/

- Hughes-Cromwick, M. (2021, April 8). *Public Transit's Safety Benefits American Public Transportation Association*. American Public Transportation Association. https://www.apta.com/research-technical-resources/research-reports/public-transit-is-key-strategy-in-advancing-vision-zero/
- Cuba, J, Kessler, E, Wilson, K, Schmitt, A, Goffman, E, Goodyear, S. (2021, June 8). *Harvard Study: Car Pollution in NYC Claims 1,400 Lives, Billions in Costs*. Streetsblog New York City.

https://nyc.streetsblog.org/2021/06/08/harvard-study-car-pollution-in-nyc-claims-1400-lives-billions-in-costs/

Obesity. Columbia University Mailman School of Public Health. (2023, March 8). https://www.publichealth.columbia.edu/research/centers/columbia-center-childrens-envir onmental-health/our-research/health-effects/obesity#:~:text=New%20York%20City%20h as%20particularly,those%20followed%20to%20age%207.

- Centers for Disease Control and Prevention. (2013). *Obesity and Tobacco Use Prevention*. Centers for Disease Control and Prevention. https://www.cdc.gov/nccdphp/dch/programs/communitiesputtingpreventiontowork/comm unities/profiles/both-ny_newyorkcity.htm
- Stewart, S. K., Johnson, D. C., & Smith, W. P. (2013). Bringing Bike Share to a Low-Income Community: Lessons Learned Through Community Engagement, Minneapolis, Minnesota, 2011. Centers for Disease Control and Prevention. https://www.cdc.gov/pcd/issues/2013/12_0274.htm#:~:text=Active%20transportation%2 0(ie%2C%20biking%20and,diabetes%20(6%2C7).
- AccuWeather. New York, NY Air Quality Index | AccuWeather. https://www.accuweather.com/en/us/new-york/10021/air-quality-index/349727
- Sain-Baird, J. (2022, March 15). *How Central Park Keeps New York City Healthy*. Central Park Conservancy. <u>https://www.centralparknyc.org/articles/park-city-healthy</u>
- Ley, A. (2022, August 15). The Pandemic Wasn't Supposed to Hurt New York Transit This Much. *The New York Times*. <u>https://www.nytimes.com/2022/08/15/nyregion/mta-nyc-budget.html</u>

Combination of mRNA Vaccines and Immune Checkpoint Inhibitors for Cancer Treatment By Claire Zhu

Abstract

Messenger RNA (mRNA) vaccines have emerged as one of the most promising immunotherapies for cancer due to their treatment efficacy, safety profile, and low development costs. Through the mRNA vaccine, cells are instructed to produce proteins associated with specific mutations in tumors, prompting the immune system to identify and attack these mutations. While mRNA vaccines are considered a rising solution in the field of cancer research, monotherapy trials in general have yet to show significant clinical success. Due to tumors' ability to evade detection by the immune system, including impairing immune cell function and developing resistance to drugs, monotherapies are believed to be insufficient to treat multiple types of cancers. As a result, many scientists have shifted their strategies to prioritize the concept of combination therapy in order to maximize the benefits of clinical trials. The purpose of this paper is to evaluate the potential benefits of combining mRNA vaccines with immune checkpoint inhibitors for cancer treatment. Using data from past clinical trials combining mRNA vaccines with immune checkpoint inhibitors, as well as reviewing trials using immunotherapies alone, we will examine the design and procedures of the trials, as well as the results and data collected. Studies have demonstrated promising results from combining mRNA vaccines with immune checkpoint inhibitors, including improved distant metastasis-free survival (DMFS). These discoveries are vital to opening up a number of new avenues for the treatment of cancers of many types.

Tumor Immunity & Immunotherapy

Immunotherapy is a type of cancer treatment designed to strengthen a patient's immune system. These therapies aid in the detection and destruction of cancerous cells (*What Is Immunotherapy*?, 2022). Over time, the study of immunotherapy has progressed into just about every type of cancer, and immunotherapy has proven effective in treating certain cancers, such as skin, lung, and bladder (Bondhopadhyay, 2020). Unlike traditional, nonspecific cancer treatments such as chemotherapy, which target all dividing cells in the body including healthy tissues (S. Lee, 2021), immunotherapy works more directly and specifically at the level of the immune system (Mheslinga, 2023). This mitigates off-target toxicity and minimizes negative side effects (Mheslinga, 2023). Despite immunotherapy having few side effects, it is possible to experience side effects triggered by an overly active immune response that may affect the tissue or organs. The severity of side effects can range from mild to moderate to severe, and in rare circumstances, they can be life-threatening. Fortunately, immunosuppressive drugs such as steroids can safely manage most side effects when recognized early and treated effectively (Mheslinga, 2023). Consequently, every patient receiving immunotherapy should be appropriately monitored during and after treatment (Mheslinga, 2023).

While an increasing number of cancer patients are eligible to receive immunotherapy and experience effective and durable responses (Cercek et al., 2022), the vast majority of cancer

patients do not respond (Bai et al., 2020). There are many differences between individuals, so people may not respond to the same treatments in the same manner (Sambi et al., 2019). Depending on their genetic makeup, some people metabolize drugs too slowly, causing the drug to accumulate in their bodies and be toxic (Lynch, 2023). In the case of others, the body may process drugs so quickly that even when they take a normal dose, the amount of drugs in the blood never reaches a level sufficient for the drug to be effective, potentially resulting in inadequate treatment (Lynch, 2023).

Additionally, drug resistance may also contribute to failed treatments, as seen in some patients with melanoma (Thornton et al., 2022). In some patients, immunotherapy for melanoma has been resisted by cancer cells over time (Thornton et al., 2022). Other times, scientists are unable to determine the exact reason why patients are not responding to immunotherapy (Bai et al., 2020).

Despite this, immunotherapy remains as a viable option for eradicating cancer since it addresses factors such as cancer evasion from the immune system more effectively. (Koury et al., 2018).

For example, the illustration shown in Figure 1 is just one way tumors may evade the immune system to multiply and grow.

Figure 1



Note. Using cytokines and granzymes, CD8+ T cells combat cancer cells containing IDH (Figure 1A). When IDH is mutated, D-2HG is produced and begins to alter the DNA of cancer cells.

Then, the T cell absorbs D-2HG (illustrated in red) (Figure 1B). When D-2HG is absorbed, it deactivates the T cell and the cancer cell divides and grows (Figure 1C).

In cancer cells, a metabolic enzyme called isocitrate dehydrogenase (IDH), is often mutated, causing cancer cells to produce an oncometabolite known as D-2HG (Harvard Medical School, 2022). Research has demonstrated that D-2HG causes epigenetic dysregulation inside cancer cells, altering their DNA (Harvard Medical School, 2022). Normally, cytotoxic CD8+ T cells release cytokines and granzymes, which are molecules that kill cancerous cells. T cells can also absorb D-2HG produced by cancerous cells (Harvard Medical School, 2022). Once inside, D-2HG disrupts the release of cytokines and granzymes, and reduces T cells' ability to fight cancer (Harvard Medical School, 2022). In this way, cancer cells can grow and evade immune cells.

Types of Immunotherapies

There are a variety of immunotherapies that can improve the immune system's overall ability to fight cancer, including chimeric antigen receptor (CAR) T-cell therapy (*T-cell Transfer Therapy - Immunotherapy*, 2022). As part of CAR T-cell therapy, T cells from a patient are engineered in the lab to produce CAR proteins before they are expanded and reinfused back into the patient (*T-cell Transfer Therapy - Immunotherapy*, 2022). These CARs enable T cells to better identify and attach to specific proteins on the surface of cancer cells, thereby increasing the effectiveness of their attack (*T-cell Transfer Therapy - Immunotherapy*, 2022).

Another type of immunotherapy, cytokine therapy, uses cytokines to enhance the immune system's capability to fight cancer (S. Lee, n.d.). Cytokines are chemicals produced by the body that activate the immune system to combat disease or germs that enter the body (S. Lee, n.d.). They can also be engineered in a laboratory to be used as cancer treatments (S. Lee, n.d.). Cytokines stimulate immune effector cells that elicit an immune response at tumor sites (Lee & Margolin, 2011). Effector cells, such as those of cytotoxic CD8+ T cells, can identify and target cancerous cells that bear specific antigens while sparing neighboring healthy cells (Janeway, 2001).

A specific class of cytokines made by the body are called interferons (Zaidi & Merlino, 2011). Interferons play a crucial role in initiating a stronger immune response against cancer cells as well as slowing their growth or inducing cell death (Di Franco et al., 2017). There are two types of interferon approved by the FDA for adjuvant treatment of cancers such as melanoma: interferon α -2b (Intron A) and a pegylated version of α -2b (Sylatron) (Chiarion-Sileni et al., 2006; Sondak & Kudchadkar, 2012). Due to this pegylation, Sylatron remains in the blood for a longer period of time, which allows it to be administered at lower doses (*Interferon for Melanoma Adjuvant Therapy*, n.d.).

Among the other types of immunotherapy, immune checkpoint inhibitors are also important for the treatment of cancer (Carlino et al., 2021). An immune checkpoint protein in the body assists in preventing the immune system from overreacting and destroying healthy cells (Stirling et al., 2022).

Figure 2

PD1/PDL1 Antibodies: How They Work



Note. By binding PD-L1 to PD-1, T cells are prevented from killing tumor cells (left image). An immune checkpoint inhibitor (anti-PD-L1 or anti-PD-1) can block the PD-L1-PD-1 interaction and allow T cells to kill tumor cells (right image).

For instance, the cell surface receptor programmed death-1 (PD-1) on T cells and its corresponding ligand PD-L1 on tumor cells are examples of checkpoint proteins that assist to prevent and/or tune an immune response (Ghosh et al., 2021). When PD-L1 binds to its receptor PD-1 on the surface of a T cell, this can suppress T cell activation and prevent it from killing tumor cells (Ghosh et al., 2021). This is another mechanism by which tumors evade the immune system, thereby allowing cancer to grow and spread.

Immune checkpoint inhibitors prevent checkpoint proteins from binding with their cognate ligands by forming a barrier between them (Stirling et al., 2022). By blocking the interaction between PD-L1 and PD-1, for example, immune checkpoint inhibitors allow T cells to exert their effector function and kill the malignant tumor cells (Yi et al., 2022).

At present, eight immune checkpoint inhibitors are approved by the FDA, including atezolizumab, pembrolizumab, and ipilimumab (J. B. Lee et al., 2022). Atezolizumab is a monoclonal antibody that targets PD-L1 on cancer cells (Herbst et al., 2020); pembrolizumab is an anti-PD-1 humanized monoclonal antibody (Khoja et al., 2015); and ipilimumab is anti-CTLA-4 (i.e. another immune checkpoint protein) (Touboul & Bonavida, 2021). Several immune checkpoint inhibitors are being tested for cancers such as head and neck, aiming to

improve long-term survival rates and extend progression-free survival times in early stages (Kwapisz, 2020).

Messenger RNA (mRNA) vaccines

An mRNA vaccine can encode for any protein, for instance, it may introduce a piece of mRNA that corresponds to a viral protein or cancer-specific antigen (Sockrider & Krishnan, 2021; Vishweshwaraiah & Dokholyan, 2022). Shown in Figure 3 is a step-by-step illustration of how an mRNA vaccine encoding a cancer-specific protein works.

Figure 3

mRNA Vaccine: Step by Step



Note. Dendritic cells, a type of immune cell, take up mRNA wrapped in a fat particle layer (Figure 3A). After entering these cells, mRNA remains in the cytoplasm, where ribosomes read it to produce cancer-associated proteins (Figure 3B). Then, on the surface of dendritic cells, these proteins are displayed (Figure 3C). As the dendritic cells migrate to nearby lymph nodes, they present the proteins they possess to other immune cells. The cells will then produce antibodies in order to fight the cancer (Figure 3D).

A special type of immune cell called a dendritic cell takes up mRNA, and once inside the dendritic cell, the mRNA remains in the cytoplasm - it does not enter the nucleus of the cell (Children's Hospital Of (C.H.O.) Philadelphia, n.d.). Following this, the ribosome reads the mRNA to create pieces of cancer-associated proteins (Children's Hospital Of (C.H.O.) Philadelphia, n.d.). The dendritic cells will have pieces of the protein on their surfaces and travel to a lymph node nearby, where they will present the proteins to other immune cells (Children's Hospital Of (C.H.O.) Philadelphia, n.d.). In response, other immune cells will begin to produce antibodies (Children's Hospital Of (C.H.O.) Philadelphia, n.d.). In order to protect the body against infection, antibodies recognize individual viruses or other pathogens, attach to them, and mark them for destruction by the immune system (Sockrider & Krishnan, 2021). After the body has rid itself of the pathogen, antibodies remain in the body, allowing the immune system to rapidly respond to a potential subsequent infection (Sockrider & Krishnan, 2021).

For some time, researchers have studied and worked with mRNA vaccines due to their potential to treat cancer and their convenience for clinical trials (Vishweshwaraiah & Dokholyan, 2022). However, despite promising results in clinical trials, no mRNA vaccine has yet received FDA approval for treating cancer (Lorentzen et al., 2022). As noted by Vishweshwaraiah and Dokholyan (2022), mRNA can be produced using readily available materials and as a result can be developed much more quickly than traditional methods. Once developed, this enables large-scale clinical trials to be conducted for experimental purposes. As an additional benefit, since mRNA vaccines are versatile, they can quickly be adapted to prevent new variants, enabling clinical trials to be done as soon as possible to evaluate the immune response to the variant (Vishweshwaraiah & Dokholyan, 2022).

In recent years, scientists have explored the efficacy of mRNA vaccines against various types of cancers including melanoma ("Precision Medicine Meets Cancer Vaccines," 2023), pancreatic cancer (Huang et al., 2022), and other advanced solid tumors. In addition, personalized mRNA cancer vaccines are currently being studied in different clinical trials in combination with other immunotherapies as they may improve in distant metastasis-free survival (DMFS) (Khattak et al., 2023). In personalized mRNA cancer vaccines, a patient's own neoantigens are encoded, which are proteins that form on cancer cells when mutations occur (Huang et al., 2022). Manufacturing begins with the identification of genetic mutations in tumor cells of a patient that may give rise to neoantigens (Huang et al., 2022). Using computer algorithms, it is possible to predict which neoantigens will most likely bind to receptors on T cells and stimulate the immune system (Huang et al., 2022).

As an example, mRNA-5671 is a personalized KRAS-targeted vaccine that codes for four of the most common mutations in KRAS: G12D, G12V, G13D, and G12C (Asimgil et al., 2022). According to Xu et al. (2019), the KRAS mutation occurs in normal cells as a result of an error in the protein. KRAS controls the proliferation of healthy cells by acting as an on-off switch. To do this, it binds the KRAS-activating molecule GTP and converts it to GDP, which inactivates the protein. Mutations of the KRAS gene, however, can allow cells to grow uncontrolled, ultimately resulting in cancer (Xu et al., 2019). KRAS mutations are found in about 25% of

tumors, making them one of the most commonly occurring mutations in cancer and colorectal cancer in particular (Beganovic, 2010). Additionally, other mRNA vaccines, like CV9104 encode for prostate cancer encode antigens such as PSA, PSMA, PSCA, STEAP1, PAP, and MUC1 (Stenzl et al., 2017).

Researchers have tested the effectiveness of immune checkpoint inhibitors alone or combined with mRNA vaccines. For example, mRNA-5671 in combination with pembrolizumab is under clinical development by Moderna for colorectal cancer. It is necessary to note that drug resistance is often apparent in monotherapy (*Benefits of Combination Immunotherapy and Reducing Harms*, n.d.). In some cases, cancer cells may adapt to a drug while it is administered, acquiring molecular changes that allow them to evade its effects (*Why Do Cancer Treatments Stop Working?*, 2016). Thus, many researchers believe combining different drugs to treat patients may be an effective way to overcome or delay resistance (*Why Do Cancer Treatments Stop Working?*, 2016). With combination therapy, pathogens or tumors are less likely to resist multiple drugs at the same time (*Why Do Cancer Treatments Stop Working?*, 2016). Because of this, many trials are still being conducted to determine whether combination therapy will result in better outcomes for cancer patients than monotherapy.

Clinical Trials Evaluating mRNA Vaccines in Cancer: Two Case Study Methods

Phase I/IIB trial of the novel mRNA-based prostate cancer vaccine CV9104 in patients with metastatic castration-resistant prostate cancer:

According to Stenzl et al. (2017), patients with mCRPC who were asymptomatic or oligosymptomatic were randomized 2:1 to receive intradermal CV9104 or a placebo. A 2:1 randomization, for example, would mean that for every three patients, two would receive CV9104 and one would receive a placebo. A double-blind trial, in which neither the experimenters nor the participants knew which treatment was given (David, 2022), was continued beyond initial progression until progression under a subsequent standard of care (SOC) or toxic effects occurred (Stenzl et al., 2017). The primary endpoint was overall survival, while secondary endpoints included radiographic progression-free survival (rPFS), time to symptom progression (TTSP) (Stenzl et al., 2017). According to Halabi et al. (2021), rPFS is measured from the date of random assignment to death from any cause or disease progression on CT or TC scan, whichever occurs first. The time to symptomatic progression (TTSP) refers to the period of time before symptoms worsen (Bouchard et al., 2018).

Phase 2 mRNA-4157-P201/KEYNOTE-942 distant metastasis-free survival results:

As stated by Khattak et al. (2023), mRNA-4157-p201 is currently being tested in a multicenter, open-label, randomized Phase II study in patients with high-risk Stage IIIB/C/D and IV cutaneous melanoma that has been completely resected. Patients were stratified, that is, divided into subgroups based on shared characteristics or attributes, in this case cancer stage. Within each subgroup, patients were then assigned to receive either mRNA-4157 in combination with pembrolizumab (anti-PD-1) or pembrolizumab alone within each subgroup using a 2:1 randomization. 157 patients were randomized to receive mRNA-4157 and pembrolizumab

together (n = 107) or pembrolizumab monotherapy (n = 50). Every three weeks, mRNA-4157 (1 mg) was administered intramuscularly for a total of nine doses, and pembrolizumab (200 mg) was given intravenously for up to eighteen cycles. In this study, the primary endpoint was recurrence-free survival (RFS) (Khattak et al., 2023), which is the time from the date of curative surgery until the date of recurrence or death (Yan et al., 2018). After determining a positive RFS, the secondary endpoint of DMFS was pre-specified and hierarchically tested. In the context of DMFS, it is the period of time between randomization and the development of distant metastases or death (Amabile et al., 2021).

Two Case Study Results

Phase I/IIB trial of the novel mRNA-based prostate cancer vaccine CV9104 in patients with metastatic castration-resistant prostate cancer (mCRPC):

CV9104 represents an advancement of CV9103 (which encodes for the antigens PSA, PSCA, PSMA, and STEAP1) (Rausch et al., 2014). As part of CV9104 immunotherapy, two additional antigens are encoded, namely PAP and Mucin 1 (MUC1) (Rausch et al., 2014).

In the majority of cases, cancer treatments cause cancer cells to undergo apoptosis (Nath & Mukherjee, 2014). However, cancer cells may acquire defects in the apoptosis pathway and, as a consequence, do not respond to these treatments (Nath & Mukherjee, 2014). MUC1 is a glycoprotein that will prevent the activation of the intrinsic apoptotic pathway in cancer cells, which helps them evade cell death (Nath & Mukherjee, 2014). The overexpression of MUC1 will result in cancer cells to spread (Hosseinzadeh et al., 2022). In this regard, it is important to determine whether combining CV9104, which targets specific genes like MUC1, with standard of care (SOC) might result in a longer overall survival for patients with metastatic CRPC than placebo and standard of care (Stenzl et al., 2017).

Table 1

Group	# of Patients	Median OS (months)	Incidence of grade >= 3 AEs (%)	Incidence of serious AEs (%)
mRNA vaccine CV9104	134	35.5	51.1	44.5
Placebo	63	33.7	59.7	43.5

Summary Table of mCRPC Study Results

Note. This table compares the treatment of mCRPC patients with CV9104 versus placebo.

As part of the trial, 197 patients were randomly assigned 2:1 to receive CV9104 (n = 134) or placebo (n = 63) (Stenzl et al., 2017). In terms of sample size, the 197 patients represented in

the study are an appropriate and sufficient number, since normal Phase I trials need a total of around 20-80 subjects, and phase II trials that investigate the treatment's effects seldom require more than 100-200 subjects (Pourhoseingholi, 2013).

In addition, the characteristics of the patients, the median number of administrations, and the first subsequent SOC therapy were also well balanced within the arms (Stenzl et al., 2017). No significant differences were observed in overall survival (Stenzl et al., 2017). The median overall survival in the CV9104 arm was 35.5 months compared to 33.7 months in the placebo arm (Stenzl et al., 2017). Although the treatment group had a median overall survival of 1.8 months longer, the study indicated a hazard ratio (HR) of 1.1. A hazard ratio represents the ratio of the hazard rates in the treated group to the control group (Barraclough et al., 2011). According to Barraclough et al. (2011), a HR of 1 implies equal risks for both groups; the HR is less than 1 if the experimental treatment group performs better than the control group, and greater than 1 if the experimental group performs worse. This trial's HR of 1.1 indicates that the HR in the treatment group is 10% higher than the rate in the control group. This suggests that those who died in the treatment group did so sooner than those in the control group. In the study, researchers were also 95% confident that the true hazard ratio would fall between 0.70 and 1.76 (Stenzl et al., 2017). As indicated by the confidence interval of the hazard ratio, the hazard ratio may fall below one or above one, indicating that the results of effectiveness between the two groups are not significantly different. Further, the study concluded with a p-value of 0.33 (Stenzl et al., 2017). Since the p-value was greater than 0.05, this also suggests that there were no significant differences between the treatment and control groups in terms of overall survival (Stenzl et al., 2017).

As for the rPFS endpoints and time to symptom progression, no notable differences were observed (Stenzl et al., 2017). The results revealed that grade \geq 3 adverse events (AEs) (51.1% vs. 59.7%) and serious AEs (44.5% vs. 43.5%) were similar between the two arms, while injection site reactions and flu-like symptoms were more frequent in the CV9104 arm (Stenzl et al., 2017). The study concluded that CV9104 did not improve overall survival in comparison to a placebo (Stenzl et al., 2017).

Phase 2 mRNA-4157-P201/KEYNOTE-942 distant metastasis-free survival results:

mRNA-4157 encodes at least 34 neoantigens that are uniquely tailored to a patient's tumor mutations (Khattak et al., 2023). Neoantigen-directed therapy can enhance endogenous neoantigen T-cell responses, resulting in epitope spread to novel antigens that can drive antitumor activity and maintain memory with cytolytic properties (Seymour, 2023). In this way, disease control can be more effectively maintained (Seymour, 2023).

Table 2

Summary Table of Melanoma Study Results

Group	# of Patients	Median follow-up RFS events	18-month RFS rates	18-month DMFS rates	Distant recurrence or death
Combination (mRNA-4157 + Pembrolizumab)	107	22.4% (24/107) in 23 months	78.6% 95% CI: (69.0%, 85.6%)	91.8% 95% CI: (84.2%, 95.8%)	8.4 % (9/107)
Pembrolizumab	50	40% (20/50) in 24 months	62.2% 95% CI: (46.9%,74.3%)	76.8% 95% CI: (61.0%, 86.8%)	24% (12/50)

Note. This table compares monotherapy versus combination therapy for melanoma patients.

In this study, a total of 157 patients were treated with mRNA-4157, either in combination with pembrolizumab (n = 107) or as a monotherapy with pembrolizumab (n = 50) (Khattak et al., 2023). There is a statistically significant and clinically meaningful improvement in RFS in combination therapy compared to pembrolizumab monotherapy, with a reduction in the risk of recurrence or death of 44% (Khattak et al., 2023). Based on the trial, the HR was calculated at 0.561 with a 95% confidence interval between 0.309 and 1.017 for the true HR (Khattak et al., 2023). The p-value of 0.0266 (Khattak et al., 2023) indicates that there are significant differences in RFS between the combination and monotherapy groups, as it is less than 0.05. Upon completion of a minimum of 12 months on study, the primary analysis of the primary endpoint was conducted and 44 RFS events were observed (Khattak et al., 2023). In the primary analysis, there were 22.4% (24/107) RFS events reported in the combination arm at a median follow-up of 23 months and 40% (20/50) events reported in the monotherapy arm at a median follow-up of 24 months (Khattak et al., 2023). As of 18 months, the overall RFS rate was 78.6%, and researchers were 95% confident that the RFS rate in the combination arm would be between 69%-85.6%, compared to 62.2% (46.9%,74.3%) in the monotherapy arm (Khattak et al., 2023).

Furthermore, combination therapy improved DMFS compared to pembrolizumab monotherapy both statistically and clinically (Khattak et al., 2023). With a hazard ratio of 0.347 (Khattak et al., 2023), this indicates that the combination arm has 65.3% less chance of developing distant metastases or death than the monotherapy group. A 95% confidence interval was also provided for the hazard ratio, suggesting that the true hazard ratio would likely lie between 0.145 and 0.828 (Khattak et al., 2023). As the hazard ratio range remained below 1.0, the combination therapy group was achieving better DMFS rates than the monotherapy group. In addition, there was a p-value of 0.0063, and any p-value below 0.05 indicates a statistically significant difference between the combination and monotherapy groups (Khattak et al., 2023).

In the combination arm, the DMFS rates were 91.8% with 95% confidence that the true rate would be between 84.2% and 95.8%, while in the monotherapy arm, DMFS rates were 76.8% (61.0%, 86.8%) (Khattak et al., 2023). Viewing the combination arm, patients experienced a distant recurrence, which means cancer spread far from its original site, or died in 8.4% (9/107) of cases, and in 24% (12/50) of cases in the monotherapy group (Khattak et al., 2023).

Researchers concluded that mRNA-4157, in combination with pembrolizumab, significantly prolonged DMFS in patients with resected high-risk melanoma compared to pembrolizumab alone (Khattak et al., 2023). Accordingly, these findings support the hypothesis that combining mRNA vaccines with immune checkpoint inhibitors may be beneficial to outcomes for cancer patients (Khattak et al., 2023). Patients with melanoma will soon be enrolled in a phase 3 randomized trial (Khattak et al., 2023).

Conclusion

In this paper, two major trials were examined, which supported the idea that mRNA vaccines combined with immune checkpoint inhibitors offer greater potential than monotherapy alone. In the trial of mCRPC patients receiving CV9104 vaccine or a placebo, CV9104 did not improve OS in comparison to the placebo group (Stenzl et al., 2017). While the median overall survival rate in the treatment group was 1.8 months longer, the study indicated a hazard ratio of 1.1 (Stenzl et al., 2017), which indicates that the hazard rate is 10% higher than the rate in the control group. Further evidence of the non-significant difference between the treatment and control groups was provided by statistics such as the 95% confidence interval for the hazard ratio (0.70 and 1.76) and the p-value (0.33) (Stenzl et al., 2017). In the study with melanoma patients, combination therapy improved the RFS statistically significantly compared to pembrolizumab monotherapy, resulting in a 44% reduction in recurrence or death (Khattak et al., 2023). Additionally, researchers found that patients with resected high-risk melanoma who received pembrolizumab along with mRNA-4157 had a better DMFS rate than patients who received pembrolizumab alone (Khattak et al., 2023). With a hazard ratio of 0.347 (Khattak et al., 2023), the combination arm has 65.3% fewer chances of developing distant metastases or dving compared to the monotherapy group.

While mRNA vaccines combined with immune checkpoint inhibitors are more effective than monotherapy in the two examined studies, further trials are needed. As there are few detailed clinical trials evaluating mRNA vaccines and immunotherapy for cancer treatment, finding appropriate studies to compare combination therapy with monotherapy was challenging. We were therefore limited to early-stage trials. Phase 3 trials, where more patients are included in the study to verify the benefits of combination and monotherapy, are necessary to further compare the effectiveness of these therapies (Cancer Research UK, 2023). Moreover, these therapies should be investigated in diverse types of cancer, since different cancers may respond differently to different treatments. By doing so, a clearer picture will emerge of whether mRNA vaccines in combination with immune checkpoint inhibitors are more effective than either alone. mRNA vaccines for cancer may have a role outside of immunotherapy as well. Research is ongoing regarding potential methods of using mRNA to induce cancer cell destruction without immune cells at Tel Aviv University (Tasleem & Tasleem, 2023). mRNA vaccines are an important area of active cancer research with the potential for significant benefits to patients.

Works Cited

- Amabile, S., Roccuzzo, G., Pala, V., Tonella, L., Rubatto, M., Merli, M., Fava, P., Ribero, S., Fierro, M. T., Queirolo, P., & Quaglino, P. (2021). Clinical Significance of Distant Metastasis-Free Survival (DMFS) in Melanoma: A Narrative Review from Adjuvant Clinical Trials. *Journal of Clinical Medicine*, *10*(23), 5475. https://doi.org/10.3390/jcm10235475
- Asimgil, H., Ertetik, U., Çevik, N. C., Ekizce, M., Doğruöz, A., Gökalp, M., Arık-Sever, E., Istvanffy, R., Friess, H., Ceyhan, G. O., & Demir, I. E. (2022). Targeting the undruggable oncogenic KRAS: the dawn of hope. *JCI Insight*, 7(1). https://doi.org/10.1172/jci.insight.153688
- Bai, R., Chen, N., Li, L., Du, N., Bai, L., Lv, Z., Tian, H., & Cui, J. (2020). Mechanisms of cancer resistance to immunotherapy. *Frontiers in Oncology*, 10. https://doi.org/10.3389/fonc.2020.01290
- Barraclough, H., Simms, L., & Govindan, R. (2011). Biostatistics Primer: What a clinician ought to know: hazard ratios. *Journal of Thoracic Oncology*, 6(6), 978–982. https://doi.org/10.1097/jto.0b013e31821b10ab
- Beganovic, S. (2010). Clinical significance of the KRAS mutation. *Bosnian Journal of Basic Medical Sciences*, 9(1), S17–S20. https://doi.org/10.17305/bjbms.2009.2749
- *Benefits of combination immunotherapy and reducing harms*. (n.d.). Melanoma Research Alliance.

https://www.curemelanoma.org/blog/article/the-next-frontier-of-combination-immunother apy-maximizing-the-benefits-and-reducing-harms

- Bondhopadhyay, B. (2020). *Cancer immunotherapy: a promising dawn in cancer research*. PubMed Central (PMC). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7811907/
- Bouchard, L. C., Aaronson, N. K., Gondek, K., & Cella, D. (2018). Cancer symptom response as an oncology clinical trial end point. *Expert Review of Quality of Life in Cancer Care*, 3(2–3), 35–46. https://doi.org/10.1080/23809000.2018.1483193
- Cancer Research UK. (2023, February 24). *Phases of clinical trials*. https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/what-clinical-trials-ar e/phases-of-clinical-trials#:~:text=Phase%203%20trials%20usually%20involve,hospitals %20and%20even%20different%20countries.
- Carlino, M. S., Larkin, J., & Long, G. V. (2021). Immune checkpoint inhibitors in melanoma. *The Lancet*, *398*(10304), 1002–1014. https://doi.org/10.1016/s0140-6736(21)01206-x
- Cercek, A., Lumish, M., Sinopoli, J., Weiss, J., Shia, J., Lamendola-Essel, M. F., Dika, I. H. E., Segal, N. H., Shcherba, M., Sugarman, R., Stadler, Z. K., Yaeger, R., Smith, J. J., Rousseau, B., Argilés, G., Patel, M., Desai, A. M., Saltz, L., Widmar, M., . . . Diaz, L. (2022). PD-1 blockade in mismatch Repair–Deficient, locally advanced rectal cancer. *The New England Journal of Medicine*, *386*(25), 2363–2376. https://doi.org/10.1056/nejmoa2201445

- Cheng, F., Wang, Y., Bai, Y., Liang, Z., Mao, Q., Liu, D., Wu, D. D., & Xu, M. (2023). Research advances on the stability of mRNA vaccines. *Viruses*, 15(3), 668. https://doi.org/10.3390/v15030668
- Chiarion-Sileni, V., Del Bianco, P., Romanini, A., Guida, M., Paccagnella, A., Palma, M. D., Naglieri, E., Ridolfi, R., Silvestri, B., Michiara, M., & De Salvo, G. L. (2006).
 Tolerability of intensified intravenous interferon alfa-2b versus the ECOG 1684 schedule as adjuvant therapy for stage III melanoma: a randomized phase III Italian Melanoma Inter-group trial (IMI Mel.A.) [ISRCTN75125874]. *BMC Cancer*, 6(1). https://doi.org/10.1186/1471-2407-6-44
- Children's Hospital Of (C.H.O.) Philadelphia. (n.d.). *How mRNA vaccines work*. Children's Hospital of Philadelphia. https://www.chop.edu/video/how-mrna-vaccines-work
- David, S. (2022, July 18). *Double-Blind study*. StatPearls NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK546641/
- Di Franco, S., Turdo, A., Todaro, M., & Stassi, G. (2017). Role of type I and II interferons in colorectal cancer and melanoma. *Frontiers in Immunology*, 8. https://doi.org/10.3389/fimmu.2017.00878
- Ghosh, C., Luong, G., & Sun, Y. (2021). A snapshot of the PD-1/PD-L1 pathway. *Journal of Cancer*, *12*(9), 2735–2746. https://doi.org/10.7150/jca.57334
- Guo, L., Zhang, H., & Chen, B. (2017). Nivolumab as programmed death-1 (PD-1) inhibitor for targeted immunotherapy in tumor. *Journal of Cancer*, 8(3), 410–416. https://doi.org/10.7150/jca.17144
- Halabi, S., Roy, A., Yang, Q., Xie, W., Kelly, W. K., & Sweeney, C. J. (2021). Radiographic progression-free survival as a surrogate endpoint of overall survival in men with metastatic castrate-resistant prostate cancer. *Journal of Clinical Oncology*, 39(15_suppl), 5057. https://doi.org/10.1200/jco.2021.39.15_suppl.5057
- Harvard Medical School. (2022, October 24). *T cell Take Down: Researchers discover how cancer cells manipulate the immune system* [Video]. YouTube. https://www.youtube.com/watch?v=ge6jyIqeXm8
- Herbst, R. S., Giaccone, G., De Marinis, F., Reinmuth, N., Vergnenègre, A., Barrios, C. H., Morise, M., Felip, E., Andric, Z., Geater, S. L., Ozguroglu, M., Zou, W., Sandler, A., Enquist, I., Komatsubara, K. M., Deng, Y., Kuriki, H., Wen, X., McCleland, M. L., . . . Spigel, D. R. (2020). Atezolizumab for First-Line Treatment of PD-L1–Selected Patients with NSCLC. *The New England Journal of Medicine*, *383*(14), 1328–1339. https://doi.org/10.1056/nejmoa1917346
- Hosseinzadeh, A., Merikhian, P., Naseri, N., Eisavand, M. R., & Farahmand, L. (2022). MUC1 is a potential target to overcome trastuzumab resistance in breast cancer therapy. *Cancer Cell International*, 22(1). https://doi.org/10.1186/s12935-022-02523-z
- Huang, X., Zhang, G., Tang, T., Gao, X., & Liang, T. (2022). Personalized pancreatic cancer therapy: from the perspective of mRNA vaccine. *Military Medical Research*, 9(1). https://doi.org/10.1186/s40779-022-00416-w

- Interferon for melanoma adjuvant therapy. (n.d.). Melanoma Research Alliance. https://www.curemelanoma.org/patient-eng/melanoma-treatment/adjuvant-therapy/interfe ron-intron-a-or-sylatron#:~:text=Interferon%20is%20an%20adjuvant%20therapy,destroy %20any%20remaining%20tumor%20cells
- Janeway, C. A., Jr. (2001). *T cell-mediated cytotoxicity*. Immunobiology NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK27101/#:~:text=Cytotoxic%20T%20cells%20k ill%20target,only%20infected%20cells%20are%20killed.
- Khattak, A., Weber, J. S., Meniawy, T., Taylor, M. H., Ansstas, G., Kim, K. B., McKean, M., Long, G. V., Sullivan, R. J., Faries, M. B., Tran, T., Cowey, C. L., Medina, T. M., Segar, J. M., Atkinson, V., Gibney, G. T., Luke, J. J., Buchbinder, E. I., Meehan, R. S., & Carlino, M. S. (2023). Distant metastasis-free survival results from the randomized, phase 2 mRNA-4157-P201/KEYNOTE-942 trial. *Journal of Clinical Oncology*, *41*(17_suppl), LBA9503. https://doi.org/10.1200/jco.2023.41.17_suppl.lba9503
- Khoja, L., Butler, M. O., Kang, S. P., Ebbinghaus, S., & Joshua, A. M. (2015). Pembrolizumab. *Journal for ImmunoTherapy of Cancer*, 3(1). https://doi.org/10.1186/s40425-015-0078-9
- Koury, J., Lucero, M., Cato, C., Chang, L., Geiger, J., Henry, D., Hernandez, J., Hung, F., Kaur, P., Teskey, G., & Tran, A. (2018). Immunotherapies: Exploiting the immune system for cancer treatment. *Journal of Immunology Research*, 2018, 1–16. https://doi.org/10.1155/2018/9585614
- Kwapisz, D. (2020). Pembrolizumab and atezolizumab in triple-negative breast cancer. *Cancer Immunology, Immunotherapy*, 70(3), 607–617. https://doi.org/10.1007/s00262-020-02736-z
- Lee, J. B., Kim, H. S., & Ha, S. Y. (2022). Immune Checkpoint Inhibitors in 10 years: Contribution of basic research and clinical application in cancer immunotherapy. *Immune Network*, 22(1). https://doi.org/10.4110/in.2022.22.e2
- Lee, S. (n.d.). *Immunotherapy*. Canadian Cancer Society. https://cancer.ca/en/treatments/treatment-types/immunotherapy#:~:text=Non%2Dspecific %20immunotherapy%20uses%20cytokines,that%20get%20into%20the%20body.
- Lee, S. (2021, February 1). *Precision medicine*. Canadian Cancer Society. https://cancer.ca/en/research/understanding-cancer-research/precision-medicine#:~:text=P ersonalizing%20treatment%20in%20this%20way,that%20are%20right%20for%20them
- Lee, S., & Margolin, K. (2011). Cytokines in cancer immunotherapy. *Cancers*, *3*(4), 3856–3893. https://doi.org/10.3390/cancers3043856
- Lorentzen, C. L., Haanen, J. B., Met, Ö., & Svane, I. M. (2022). Clinical advances and ongoing trials of mRNA vaccines for cancer treatment. *Lancet Oncology*, 23(10), e450–e458. https://doi.org/10.1016/s1470-2045(22)00372-2
- Lynch, S. S. (2023, July 18). *Genetic makeup and response to drugs*. MSD Manual Consumer Version.

https://www.msdmanuals.com/home/drugs/factors-affecting-response-to-drugs/genetic-m

akeup-and-response-to-drugs?query=Genetic%20makeup%20and%20response%20to%2 0drugs

- Mheslinga. (2023, April 6). Cancer immunotherapy, explained. *University of Chicago News*. https://news.uchicago.edu/explainer/what-is-immunotherapy#benefits
- Nath, S., & Mukherjee, P. (2014). MUC1: a multifaceted oncoprotein with a key role in cancer progression. *Trends in Molecular Medicine*, 20(6), 332–342. https://doi.org/10.1016/j.molmed.2014.02.007
- Pourhoseingholi, M. A. (2013, January 1). *Sample size calculation in medical studies*. PubMed Central (PMC).

```
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4017493/#:~:text=Initial%20trials%20m ight%20require%20a,%2D200%20patients%20(8).
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- Precision medicine meets cancer vaccines. (2023). *Nature Medicine*, 29(6), 1287. https://doi.org/10.1038/s41591-023-02432-2
- Rausch, S., Schwentner, C., Stenzl, A., & Bedke, J. (2014). mRNA vaccine CV9103 and CV9104 for the treatment of prostate cancer. *Human Vaccines & Immunotherapeutics*, 10(11), 3146–3152. https://doi.org/10.4161/hv.29553
- Sambi, M., Bagheri, L., & Szewczuk, M. R. (2019). Current challenges in cancer immunotherapy: Multimodal approaches to improve efficacy and patient response rates. *Journal of Oncology*, 2019, 1–12. https://doi.org/10.1155/2019/4508794
- Seymour, C. (2023, June 16). Cancer vaccine mRNA-4157 improves Recurrence-Free survival for patients with High-Risk Melanoma. *Oncology Nursing News*. https://www.oncnursingnews.com/view/cancer-vaccine-mrna-4157-improves-recurrencefree-survival-for-patients-with-high-risk-melanoma
- Sockrider, M., & Krishnan, J. A. (2021). How vaccines work to prevent infections. American Journal of Respiratory and Critical Care Medicine, 203(6), P16–P17. https://doi.org/10.1164/rccm.2021c1
- Sondak, V. K., & Kudchadkar, R. R. (2012). Pegylated interferon for the adjuvant treatment of melanoma: FDA approved, but what is its role? *Oncologist*, 17(10), 1223–1224. https://doi.org/10.1634/theoncologist.2012-0368
- Stenzl, A., Feyerabend, S., Syndikus, I., Sarosiek, T., Kübler, H., Heidenreich, A., Cathomas, R., Grüllich, C., Loriot, Y., Gracia, S. L., Gillessen, S., Klinkhardt, U., Schröder, A., Schönborn-Kellenberger, O., Reus, V., Koch, S. D., Hong, H. S., Seibel, T., Fizazi, K., & Gnad-Vogt, U. (2017). Results of the randomized, placebo-controlled phase I/IIB trial of CV9104, an mRNA based cancer immunotherapy, in patients with metastatic castration-resistant prostate cancer (mCRPC). *Annals of Oncology*, *28*, v408–v409. https://doi.org/10.1093/annonc/mdx376.014
- Stirling, E., Bronson, S. M., Mackert, J., Cook, K. L., Triozzi, P. L., & Soto-Pantoja, D. R. (2022). Metabolic implications of immune checkpoint proteins in cancer. *Cells*, 11(1), 179. https://doi.org/10.3390/cells11010179

- Tasleem, R., & Tasleem, R. (2023). Israeli researchers discover breakthrough method to induce cancer cells' Self-Destruction. *BNN Breaking*. https://bnn.network/breaking-news/israeli-researchers-discover-breakthrough-method-to-i nduce-cancer-cells-self-destruction/
- *T-cell transfer therapy immunotherapy*. (2022, April 1). National Cancer Institute. https://www.cancer.gov/about-cancer/treatment/types/immunotherapy/t-cell-transfer-thera py#:~:text=TIL%20therapy%20uses%20T%20cells,grow%20to%20large%20numbers% 20quickly.
- Thornton, J., Chhabra, G., Singh, C. K., Guzmán-Pérez, G., Shirley, C. A., & Ahmad, N. (2022). Mechanisms of immunotherapy resistance in cutaneous melanoma: Recognizing a shapeshifter. *Frontiers in Oncology*, 12. https://doi.org/10.3389/fonc.2022.880876
- Touboul, R., & Bonavida, B. (2021). YY1 expression and PD-1 regulation in CD8 T lymphocytes. In *Elsevier eBooks* (pp. 289–309). https://doi.org/10.1016/b978-0-12-821909-6.00003-1
- Vishweshwaraiah, Y., & Dokholyan, N. V. (2022). mRNA vaccines for cancer immunotherapy. *Frontiers in Immunology*, 13. https://doi.org/10.3389/fimmu.2022.1029069
- *What is immunotherapy*? (2022, May 26). Cancer.Net. https://www.cancer.net/navigating-cancer-care/how-cancer-treated/immunotherapy-and-v accines/what-immunotherapy
- *Why do cancer treatments stop working?* (2016, December 21). National Cancer Institute. https://www.cancer.gov/about-cancer/treatment/research/drug-combo-resistance
- Xu, K., Park, D., Magis, A. T., Zhang, J., Zhou, W., Sica, G. L., Ramalingam, S. S., Curran, W. J., & Deng, X. (2019). Small molecule KRAS agonist for mutant KRAS cancer therapy. *Molecular Cancer*, 18(1). https://doi.org/10.1186/s12943-019-1012-4
- Yan, W.-T., Quan, B., Xing, H., & Wu, M.-C. (2018). Time to recurrence, but not recurrence-free survival, should be the endpoint used to predict early recurrence after HCC resection. *Journal of Hepatology*, *70*(3), P570-571. https://www.journal-of-hepatology.eu/article/S0168-8278(18)32509-1/fulltext
- Yi, M., Zheng, X., Niu, M., Zhu, S., Ge, H., & Wu, K. (2022). Combination strategies with PD-1/PD-L1 blockade: current advances and future directions. *Molecular Cancer*, 21(1). https://doi.org/10.1186/s12943-021-01489-2
- Zaidi, M. R., & Merlino, G. (2011). The two faces of interferon-Γ in cancer. *Clinical Cancer Research*, *17*(19), 6118–6124. https://doi.org/10.1158/1078-0432.ccr-11-0482

Identifying Optimal Variables for Stock Price Prediction By Isaac Chu

Abstract

Stock price prediction is a difficult task that, when done accurately, could yield great rewards. If one is able to know the future of a stock, they would be able to invest wisely and make good profits. One strategy of stock prediction is the use of computers and machine learning. This paper examines potential variables that would be helpful in predicting stock prices through the use of neural networks. Models of different input variables were compared in performance (using the R² metric) to determine how helpful said variable was to predicting next day's closing stock price. This evaluation resulted in the conclusion that the test variables—opening share price, related stock prices, and United States Dollar index—were not conducive to the neural network in predicting the next day's closing price. While the control experiment yielded test and train performances of 0.96, all other test experiments had lower R² scores.

Introduction

The stock market is a complex entity where parts of companies, known as "shares," are traded. The prices of these shares are determined by how much the company is valued [1]. For example, if many investors believe that a company will do well in the near future, they may be compelled to buy the stock. Historically speaking—during the Great Depression, for example—the stock market has been a way for some people to get rich quickly since some share prices can change drastically in a relatively short time period [2]. Because the stock market can be very lucrative, many investors have evolved strategies to try to predict the future of stock prices. Some examples of these strategies are fundamental analysis and technical analysis. Fundamental analysis is the qualitative examination of the company's business to see how it will evolve in the economy. Technical analysis, on the other hand, is a strategy that focuses on the company's statistics, patterns, and uses that to predict the future prices [3].

A recent strategy of stock trading is using machine learning to optimize trading decisions—buying, selling, shorting, etc [4]. My project compared the performance of a neural network model for predicting the next day's closing price depending on its input factors: opening price, closing price, United States Dollar price, other related stock prices, and more. Doing so may reveal the level of impact of certain factors on the share prices. For instance, a certain variable may increase or decrease a model's prediction performance.

Algorithms

The model used in the experiments was a neural network. Neural networks take numbers as inputs, apply a function, and then output a number or multiple numbers. The inputted numbers are called the "input layer," while the last layer is called the "output layer." In between usually lies multiple in-between layers called "hidden layers," since they typically are not directly interacted with. These hidden layers are how a neural network maps from the input layer to the

output layer. Each layer, the neural network applies a weight to each of its inputs. This means that each node (value in the layer) is a linear combination of values from the previous layer.

Training neural networks involves giving it large amounts of data. Using this data allows the network to calibrate its weights, and therefore, become more accurate. To test for performance, the model is given a different data set. The testing data is data that the neural network has not been trained on. This allows us to evaluate the model's performance on new information.

In the case of stock price prediction, there will be multiple inputs and a single value output—the prediction. An example of a neural network is shown below:



The data used (300 previous days) were randomly split into training and testing data to allow the neural network to train itself while also having enough data to compute its performance in real world situations. The data for the train set and test set were not in chronological order in order to minimize any effect of the date on the model's prediction or test performance. For any picked date, the neural network would be tasked with predicting the closing stock price for that day, using the appropriate data given by the test and control variables. The same ratio of training data and testing data was used in the following test variables: opening prices, related stock closing prices, and United States Dollar index.

After training a model using inputs of the last three closing prices and one test variable, the R^2 metric was calculated. The R^2 test measures how close the model was to the actual prices. An R^2 of 1 means perfect performance, and the lower the R^2 , the worse the performance. R^2 values can be negative too. The R^2 test is defined by the following equations.

1.
$$R^{2} = 1 - \frac{SS_{res}}{SS_{tot}}$$
2.
$$SS_{res} = \sum_{i}^{n} (y_{i} - f_{i})^{2}$$
3.
$$SS_{tot} = \sum_{i}^{n} (y_{i} - \overline{y})^{2}$$
4.
$$\overline{y} = \frac{1}{n} \sum_{i}^{n} y_{i}$$

Equation 1: definition of R^2 .

Equation 2: definition of residual sum of squares, the sum of the squared difference between the actual and predicted values.

Equation 3: definition of total sum of squares, the sum of the squared difference between the actual and mean value.

Equation 4: definition of arithmetic mean of observed data, the sum of all actual values divided by the number of values.

100 separate neural networks were trained for each experiment in order to minimize the effects of outlier models. The R^2 value for each model was measured. After, the mean of all 100 R^2 values was taken to measure the performance of that experiment.

One potential concern for the training process of the neural networks was overfitting. Neural networks are prone to overfitting since they are able to model complex nonlinear relationships between variables—stock prices included [5]. Overfitting is when the model performs much better on training data compared to new/test data [6]. Overfit models are undesirable in this paper because the experiments are set up to have their testing performances compared. An overfit model would invalidate that comparison. To see if models were overfitting, both the test and train performances were calculated. These scores were then averaged across the 100 model sample for each experiment.

Closing price (control variable)

Using the last 3 closing prices to predict the next day's closing price, a neural network was trained on 210 days worth of data, and tested on 90 days in predicting the next day's closing share price (of NVDA). To measure performance, the R² metric was calculated.

Test variable #1, opening price: Data consists of the last three opening prices of Nvidia (NVDA) stock.

Test variable #2, AMD: Data consists of the last three closing prices of Advanced Micro Devices (AMD) stock.

Test variable #3, Intel:

Data consists of the last three closing prices of Intel (INTC) stock.

Test variable #4, United States Dollar:

Data consists of the last three closing prices of the United States Dollar index (DX-Y.NYB). Since the value of stocks are expressed in terms of the United States Dollar, the value of the US Dollar may impact stock prices.

Results

Control (Only last 3 close prices): Test performance (Mean R² error): 0.96 Train performance (Mean R² error): 0.96



Test variable #1, opening price (last 3 close prices and last 3 open prices): Test performance (Mean R² error): 0.95 Train performance (Mean R² error): 0.95 Closing prices (Opening Prices & Control)



Test variable #2, AMD closing price (last 3 close prices and last 3 AMD close prices): Test performance (Mean R² error): 0.89 Train performance (Mean R² error: 0.89



Test variable #3, Intel closing price (last 3 close prices and last 3 Intel close prices):
Test performance (Mean R² error): 0.85 Train performance (Mean R² error): 0.85

Closing prices (Intel Closing Prices & Control)



Test variable #4, US Dollar closing price (last 3 close prices and last 3 US Dollar index close prices): Test performance (Mean R² error): 0.86 Train performance (Mean R² error): 0.87



Conclusion

Since the performance of the model decreased when the test variables were introduced, it can be concluded that these variables do not benefit the model in predicting Nvidia's next day's closing share price. Because of this, one may infer that these elements are not correlated with the closing share price. However, there also could be alternate causes for this observed effect. For example, the model used six inputs for the test variable experiments—three for the previous closing prices, and three for the control variable. This is different from the control experiment of only three input variables. These extra variables that needed to be taken into account may have affected the performance.

Overfitting was another concern of the algorithm's and data's reliability. However, since the test and train performances do not significantly differ, it can also be concluded that the models did not overfit. Therefore, the performance of the models were reliable figures.

For future work, other machine learning models could be tested. An example of this may be a natural language processing model that reads news articles could be used as an input. Finally, other test variables and combinations can be measured.

Works Cited

[1] Bohl, Lee, and Randy Frederick. "How to Pick Stocks Using Fundamental and Technical Analysis." *Charles Schwab*,]

- [2] Charles Schwab. "Understanding Stocks." *Charles Schwab*, https://www.schwab.com/stocks/understand-stocks. Accessed 17 June 2023.
- [3] Davydov, Roman. "How Machine Learning Helps Predict Stock Prices." *Built In*, 5 January 2023, <u>https://builtin.com/machine-learning/machine-learning-stock-prediction</u>. Accessed 17 June 2023.
- [4] Guo, Yixin. "Stock Price Prediction Using Machine Learning By: Yixin Guo." *DiVA portal*, 2022, <u>https://www.diva-portal.org/smash/get/diva2:1672304/FULLTEXT01.pdf</u>. Accessed 24 June 2023.
- [5] PBS. "The First Measured Century: Timeline: Events Stock Market Crash." *PBS*, <u>https://www.pbs.org/fmc/timeline/estockmktcrash.htm</u>. Accessed 17 June 2023.
- [6] "What is Overfitting? Overfitting in Machine Learning Explained AWS." *Amazon AWS*, <u>https://aws.amazon.com/what-is/overfitting/</u>. Accessed 17 June 2023.

The United States v. United States Steel Corporation: A Justified Antitrust Lawsuit By Yichen Xing

Introduction

Founded in 1901, United States Steel Corporation became the world's largest corporation, producing 67% of all steel in America during its first year.³⁹ In 1900, Charles M. Schwab, the president of Carnegie Steel, approached Elbert H. Gary, founder of Federal Steel Company, with the idea of forming a giant consolidation.⁴⁰ As a result, prominent financier J. P. Morgan and other businessmen together bought Carnegie's interests for more than \$492 million.⁴¹ In 1901, US Steel formed out of the merger of Carnegie Steel Company, Federal Steel Company, National Steel Company, National Tube Works, American Steel & Wire, American Sheet Steel, American Steel Hoop, American Tin Plate, American Bridge, and the Lake Superior Consolidated Iron Mines.⁴²

The giant's birth attracted much public attention and, because of the antitrust movement of the time, induced fear of trusts becoming too powerful financially and politically. Trust in the late 19th-century referred to a group of businesses that merged together to form a monopoly to dictate the market. Antitrust, by definition, means legislation regulating trusts to promote competition and prevent monopolies. Major leaders of the antitrust movement included Presidents Theodore Roosevelt and William Howard Taft, Roosevelt's successor. Roosevelt earned a reputation as a "trustbuster" for launching the trust busting and government regulation of monopolies, filing monumental antitrust cases such as the 1904 *Northern Security Co. v. United States*. Taft, however, filed more antitrust cases than Roosevelt did and preferred to use judicial power over executive power to regulate businesses' behaviors.

One of the most controversial cases that Taft filed was the *United States v. United States Steel Corporation.* This paper explores the antitrust lawsuit of that case. In doing so, this paper argues that Taft's administration was correct in filing the *US v. USS* lawsuit because it exposed US Steel's monopolistic motives and increased competition. This paper will first present the context of the Progressive Era, the role of muckrakers in antitrust, other major antitrust cases at the time and background information for the *US v. USS* case. Then it will uncover US Steel's deceit in acquiring permission for the purchase of Tennessee Coal and Iron Company. Next, it will examine Theodore Roosevelt's involvement in the lawsuit. Subsequently, it will analyze the Taft administration's involvement in the court case. Finally, it will delve into the supreme court case and the implications of the final ruling in 1920.

³⁹ Steelmuseum, accessed June 4, 2023, https://steelmuseum.org/pais300_exhibit_2017/us_steel.cfm.

 ⁴⁰ Britannica, accessed June 4, 2023, https://www.britannica.com/topic/United-States-Steel-Corporation.
 ⁴¹ Ibid.

⁴² "The Founding of U.S. Steel and the Power of Public Opinion," *Harvard Business School*, accessed June 4, 2023,

https://www.library.hbs.edu/us-steel/exhibition/the-founding-of-u.s.-steel-and-the-power-of-public-opinion

Context

To understand US v. USS, it is crucial to learn about the Progressive Era and the beginning of antitrust. From 1878 to 1889, the United States experienced rapid economic growth and industrialization. However, underneath the expansion was blatant political corruption and widening wealth gap, leading to its name, The Gilded Age. The end of the 19th century marked the beginning of the Progressive Era, a period of widespread social and political reforms curbing corruption and monopoly. The Gilded Age gave rise to many big corporations such as Standard Oil and US Steel. These companies established trusts to reduce competition and standardize prices, reducing competition in the market. All of these benefited the companies but hurt consumers, workers, and smaller businesses. The muckrakers, a group of Progressives who were reform-minded journalists and novelists, sought to expose corruption in big business and government. An example of muckraking in the steel industry is William B. Hard's article "Making Steel and Killing Men" in the November 1907 issue of *Everybody's Magazine*.⁴³ In his article, Hard described "an accident in which a man was roasted alive by molten slag that spilled from a giant ladle when a hook from an overhead crane carrying it slipped."⁴⁴ In addition, Hard argued that "U.S. Steel had ample ability to reduce accidents but lacked strong incentive to do so."⁴⁵ Reading about the deadly working conditions and the disregard of the trusts, people feared for their families and sought to break up the trusts. Concurrently, the combination of economic and political power induced fear of decreasing economic and political opportunity. In time, public fear pressured the government to take action to control the practices of trust, passing the Sherman Antitrust Act of 1890, which prohibited activities that restrict competition and authorized the federal government to dissolve contravening trusts.

Many antitrust cases were filed under the Sherman Antitrust Act, with the most famous ones being *Standard Oil Co. of New Jersey v. United States* and *United States v. American Tobacco Company*. In *Standard Oil*, the Supreme Court found Standard Oil guilty of monopolizing the petroleum industry through anticompetitive actions such as underpricing and threatening suppliers of its competitors. In 1911, the Court ordered the dissolution of Standard Oil into 34 companies.⁴⁶ Similarly, the Supreme Court ruled that American Tobacco Company violated the Sherman Antitrust Act for seeking to monopolize all sectors of the tobacco industry, splitting the company into four competing entities to increase competition. Both cases resulted in the dissolution of the trusts and allowed for more competition in the market.⁴⁷ In an article in the

 ⁴³ DOL, accessed May 22, 2023, https://www.dol.gov/general/aboutdol/history/mono-regsafepart05.
 ⁴⁴ Ibid.

⁴⁵ Ibid.

⁴⁶ Library of Congress, accessed June 4, 2023,

https://guides.loc.gov/chronicling-america-standard-oil-monopoly#:~:text=In%201911%20the%20U.S.%20 Supreme,and%20split%20into%2034%20companies.

⁴⁷ Library of Congress, accessed May 22, 2023,

https://guides.loc.gov/chronicling-america-standard-oil-monopoly#:~:text=In%201911%20the%20U.S.%20 Supreme,and%20split%20into%2034%20companies. Ncpedia, accessed May 22, 2023,

https://www.ncpedia.org/american-tobacco-company#:~:text=On%2016%20Nov.,Lorillard.

American Historical Review, Robert H. Wiebe claims that the magnates read the decisions in *Standard Oil Co. of New Jersey v. United States* and *United States v. American Tobacco Company* as an "invitation" to [Attorney General George W.] Wickersham and Taft to investigate United States Steel and International Harvester.⁴⁸

One of the key allegations of the US v. US Steel case-that the acquisition of the Tennessee Coal and Iron Company (TCI) constituted illegal business activity under the Sherman Act-stemmed from the Panic of 1907. On October 16, 1907, two minor speculators, F. Augustus Heinze and Charles W. Morse, suffered huge losses after failing to corner the market on the stock of United Copper.⁴⁹ The panic on Wall Street led to runs by depositors on banks associated with the two speculators, such as the Knickerbocker Trust, New York City's third largest trust.⁵⁰ The collapse of Knickerbocker spread fear that resulted in regional banks withdrawing reserves from New York City banks and eventually people across the nation withdrawing deposits from regional banks.⁵¹ By November, the financial contagion ceased thanks to the help of J. P. Morgan and other New York bankers, who pledged their own money to support the banking system. Another crisis, however, loomed on November 2, when Moore & Schley, the largest brokerage firm on Wall Street, borrowed \$25 million using shares of TCI as collateral.⁵² If banks call the loans of Moore & Schley, the company would have to liquidate the stock to pay them off, which would tumble the price of TCI stock. Under a weak stock market, such a disruption could have been disastrous, triggering further panic in the market. In an attempt to save the market, J. P. Morgan convened with other financiers to formulate a plan concerning the plummeting price of the stock of the Tennessee Coal and Iron Company.⁵³ The group suggested that US Steel should purchase the stock of TCI and thus confirm its value, preventing the market from collapsing.⁵⁴

US Steel deceived Roosevelt

In a meeting in the White House, US Steel representatives Elbert Gary and Henry Frick fooled Roosevelt into approving US Steel's acquisition of TCI. The representatives lied about the amount of TCI stocks Moore & Schley owned. Roosevelt recounted that Gary and Frick said "there was a certain business firm which would fail if help should not be given, and that among

⁴⁸ Robert H. Wiebe, "The House of Morgan and the Executive, 1905-1913," *The American Historical Review* 65, no. 1 (1959): 59, https://doi.org/10.2307/1846601.

⁴⁹ Federal Reserve History, accessed May 22, 2023,

https://www.federalreservehistory.org/essays/panic-of-1907.

⁵⁰ Library of Congress, accessed May 22, 2023,

https://blogs.loc.gov/inside_adams/2021/03/united-copper-panic-of-1907/.

⁵¹ "The Panic of 1907," Federal Reserve History, last modified December 4, 2015, accessed July 31, 2023, https://www.federalreservehistory.org/essays/panic-of-1907.

⁵² "J. P. Morgan: The Panic of 1907 and the Federal Reserve," Crf-usa, accessed June 25, 2023,

https://www.crf-usa.org/images/pdf/jpmorgan.pdf. Ellis W. Tallman and Jon R. Moen, "Lessons from the Panic of 1907," Atlantafed, last modified 1990, accessed June 25, 2023,

https://www.atlantafed.org/-/media/documents/research/publications/economic-review/1990/orphans/l essons-from-panic-of-1907-tallman-moen-1990-may-june.pdf.

⁵³ James C. German, "Taft, Roosevelt, and United States Steel," *The Historian* 34, no. 4 (1972): 599, http://www.jstor.org/stable/24442959.

⁵⁴ Ibid.

its assets were a majority of the securities of the Tennessee Coal Company."⁵⁵ In contrast, Jacob Dickinson, Secretary of War under Taft, former assistant attorney general and creator of the suit, stated that "it was not true that among the assets of the firm were a majority of said securities."⁵⁶ Dickinson's point is verifiable because testimony at the trial and before the Stanley committee of the House of Representatives, who held hearings investigating US Steel, showed that Moore & Schley's holdings were 50,933 shares short of a majority, revealing that US Steel exaggerated the severity of the situation and the extent of help if it had purchased TCI.⁵⁷

Further, US Steel downplayed the benefits of the purchase. Dickinson said, "Judge Gary and Mr. Frick informed [him] that little benefit will come to the Steel Corporation from the purchase."⁵⁸ This statement was also misleading because US Steel, in its report to its stockholders of the purchase, said that "the Tennessee property was very valuable."⁵⁹ Financial expert John Moody estimated the ore owned by TCI alone had a potential value of "hardly less than \$1,000,000,000," making the \$45,000,000 US Steel paid for the purchase "the best bargain the Steel Corporation or any other concern or individual ever made in the purchase of a piece of property."⁶⁰ Even Judge Gary later admitted that a valuation of \$200,000,000 or even two or three times that much "is not very much too high."⁶¹ This huge difference between the paid amount and the evaluated amount indicates that US Steel benefited hugely from the purchase. Both lies show that US Steel hid its motives of removing TCI, its major competitor, and increasing market control from Roosevelt. In doing so, US Steel hoped to get permission for the purchase from Roosevelt, which would exempt US Steel from prosecution under the Sherman Antitrust Act. The act of avoiding prosecution hints at US Steel's monopolistic motive.

Besides providing false information, US Steel did not report the current financial status of TCI, which could potentially impede them from getting permission for the purchase. US Steel representatives failed to mention the competitive relationship between US Steel and TCI. Roosevelt testified that he did not know that TCI was the largest owner of commercial iron ore in the United States besides US Steel.⁶² Nor did Roosevelt know that TCI was beginning to emerge as a potential competitor to US Steel.⁶³ Though it is hard to tell if this lack of information was deliberate, it definitely helped US Steel acquire permissions for the purchase from Roosevelt because had Roosevelt known there exist competition between the two, antitrust law, specifically the illegality of reducing competition through harming competitors, might stand in the way of obtaining the approval of the purchase.

 ⁵⁵ William T. Alderson, "TAFT, ROOSEVELT, AND THE U. S. STEEL CASE: A LETTER of JACOB McGAVOCK DICKINSON," *Tennessee Historical Quarterly* 18, no. 3 (1959): 268, http://www.jstor.org/stable/42621438.
 ⁵⁶ Ibid.

⁵⁷ German, "Taft, Roosevelt," 611.

⁵⁸ Alderson, "TAFT, ROOSEVELT," 268.

⁵⁹ Alderson, "TAFT, ROOSEVELT," 268.

⁶⁰ German, "Taft, Roosevelt," 611.

⁶¹ German, "Taft, Roosevelt," 611.

⁶² Ibid.

⁶³ Ibid.

To conclude, US Steel obtained permission for its purchase of TCI by lying on the level of emergency, understating the benefit, and failing to disclose salient information. In agreement with American lawyer Elihu Root, who said "To show that Roosevelt was fooled you must show that either they lied or there was no emergency," this section of the essay proves that US Steel intentionally duped Roosevelt to avoid prosecution, suggesting that US Steel knew that their purchase of TCI was considered illegal under the Sherman Antitrust Act.⁶⁴

Roosevelt's Response

Roosevelt, however, refused to admit that US Steel fooled him. On August 11, 1907, Roosevelt explained that "his action was conditioned, not upon what [he] believed to be the motives actuating the Steel Corporation, but upon [his] belief that the action which [US Steel] proposed taking would be enormously to the benefit of the community at large at that particular moment."⁶⁵ Roosevelt defended himself arguing that his decision should be judged in the context of the panic and the calamitous consequences if he had not approved the purchase. Three months later, Roosevelt stated that the representatives of US Steel told him the truth regarding the effect of the TCI purchase.⁶⁶ Dickinson, on the contrary, believes that Roosevelt had been deceived and that if Roosevelt was told the truth, he would not have approved the purchase.⁶⁷ Given that US Steel failed to communicate the details of the purchase, it is obvious that Roosevelt was unable to accept that he had been deceived. With a strong reputation as a trustbuster, it is not hard for one to predict that Roosevelt would respond outrageously to his hand-picked successor questioning his judgment. Whether Roosevelt's decision was wise or not is of less importance in judging the legality of the purchase. What is more important is the fact that US Steel intended to deceive Roosevelt to benefit from the purchase, showing that the investigations following the lawsuit successfully exposed US Steel's attempt to control the market.

Taft's Response

On the other hand, President Taft innocently confided in his attorney general in filing the petition without much personal involvement, causing Roosevelt to respond aggressively. According to letters between Taft and Dickinson, Taft did not see a copy of the petition before it was submitted to the court on October 26, 1911.⁶⁸ He was surprised to learn that Roosevelt had been included specifically in the bill of particulars and, when they met in Chicago, asked Dickinson why Roosevelt's name had been "lugged" in.⁶⁹ Dickinson explained that the bill was a vindication of Roosevelt "no matter what view he might take of it."⁷⁰ Dickinson's guarantee

⁶⁴ German, "Taft, Roosevelt," 612.

⁶⁵ Theodore Roosevelt, "The Steel Corporation and the Panic of 1907," *Outlook*, August 19, 1911, https://dpl6hyzg28thp.cloudfront.net/media/Roosevelt_19_Aug_1911.pdf.

⁶⁶ Theodore Roosevelt, "The Trusts, the People, and the Square Deal," *Outlook*, November 18, 1911, https://dpl6hyzg28thp.cloudfront.net/media/Roosevelt_18_Nov_1911.pdf.

⁶⁷ German, "Taft, Roosevelt," 606.

⁶⁸ German, "Taft, Roosevelt," 608.

⁶⁹ German, "Taft, Roosevelt," 608.
⁷⁰ German, "Taft, Roosevelt," 608.

clearly shows that he has a misunderstanding about Roosevelt's extreme pride about his marvelous move to save the market. Even the original allegation in the petition itself shows the naivete of Dickinson's explanation:

The President was not made fully acquainted with the state of affairs in New York relevant to the transaction as they existed. If he had been fully advised to the transaction he would have known that a desire to stop the panic was not the sole moving cause, but that there was also the desire and purpose to acquire the control of a company that had recently assumed a position of potential competition of great significance. The President, taken as he was partially into confidence, and moved by his appreciation of the gravity of the situation and the necessity for applying what was represented to him to be the only

known remedy, stated that he did not feel it to be his duty to prevent the transaction.⁷¹ The main point is this part of the petition is that US Steel deceived Roosevelt into permitting the purchase of TCI. First of all, it is hard to believe that Dickinson did not understand that the mere fact of being misled could mortify and infuriate Roosevelt. On top of that, Dickinson stated Roosevelt's blind confidence as the first reason why he was unable to discover that the representatives of US Steel were lying. Though he tried to counteract it by mentioning Roosevelt's consideration of the gravity of the situation, just like historian James C. German Jr. saw it, "no matter how friendly, reasonable or just the accusation was, it would have the same effect on Roosevelt."⁷²

Surprisingly, Taft was satisfied with the explanation and encouraged his attorney to continue pressing the legal actions, infuriating Roosevelt.⁷³ As mentioned earlier, Taft knew little to nothing about the allegations against Roosevelt in the petition before its submission, potentially hinting that he was not as interested in the details of the lawsuit and trusted his Attorney General Wickersham fully to file and review the petition before submitting it to the court. Taft's minimal involvement and his trust in Wickersham potentially explains why he did not have a problem with Roosevelt's name being in the petition. However, the two reasons above alone do not seem to be enough for Taft to overlook the implications of charging Roosevelt publicly had he known that Roosevelt was already displeased with his limited-government form of Republicanism approach. This assumption shed light on a third reason why Taft saw it acceptable to leave Roosevelt's name in the petition. As historian George Mowry put it, Taft was "an incredibly dull student of human reactions."⁷⁴ Another possible reason for mentioning Roosevelt's name is that Wickersham and Dickinson wanted to use every piece of evidence to attest US Steel's violation of antitrust laws. Since both men were lawyers, it is possible that they either treated the US Steel case like any other cases or they valued successfully prosecuting US Steel over the relations between the two presidents. After Roosevelt responded angrily to the suit, Taft's administration did not respond or explain to Roosevelt why and how the decision to

⁷¹ German, "Taft, Roosevelt," 605.

⁷² German, "Taft, Roosevelt," 608.

⁷³ German, "Taft, Roosevelt," 608.

⁷⁴ George E. Mowry, The Era of Theodore Roosevelt, 1900-1912 (New York: Harper, 1958), 290.

include him in the petition had been made.⁷⁵ Ultimately, the inclusion of Roosevelt's name was a mistake by all three men because it compounded deteriorating relations between Taft and Roosevelt to the place where there is no return, contributing to Roosevelt running against Taft in the election of 1912.

The Court Case

Taft's administration filed the petition for *US v. USS* on October 26, 1911, and the case resulted in a Circuit Court decision in 1915 and a Supreme Court decision in 1920, both in favor of US Steel. The full petition from 1911 and details of the 1915 Circuit Court decision, unfortunately, are not accessible for research, making the court case in 1920 the only federal account available. To assess the relevance of the arguments of Taft's administration to the legality of US Steel, while it is reasonable to assume that the continuation of the suit by President Wilson's administration indicates that they to some degree believed in the contentions of Taft's administration against US Steel, one cannot assume the arguments presented to the Supreme Court in 1920 were the same as the opinions made by Taft's administration in 1911.

In the final court case *US v. USS* (1920), the allegations from Wilson's administration against US Steel prove that filing the suit was the right decision. The court case summarized the charges into two points: 1. The combinations formed in various branches of the iron and steel trade were not "incidents of normal growth," but were created with "the purpose and effect of unduly restricting competition," and that their existence violated the Sherman Antitrust Act.⁷⁶ 2. In 1901, by the means of a holding company, US Steel brought together several illegal combinations to form "one super-combination of overwhelming power. . ., unduly restricting competition in the iron and steel trade," violating the Sherman Antitrust Act.⁷⁷

The government pointed at the monopolistic purpose of the formation of US Steel to show that it had the power to restrict competition. Past adjudications in cases such as *Addyston Pipe Co. v. United States* and *Swift & Co. v. United States* proved that combinations that satisfy two conditions, created with the purpose of suppressing competition and holding a dominant proportion of an industry, are illegal combinations in restraint of trade.⁷⁸ However, it was hard for the government to unearth evidence of monopolistic practices because the company and its leaders had been aware of the prosecution of other giant corporations such as Standard Oil and American Tobacco and adjusted their actions accordingly to avoid legal actions. An example of US Steel's change in practice due to fear of prosecution was the discontinuation of the Gary Dinner system, in which Elbert Gary assembled trade opponents by pools, associations, and trade meetings ostensibly to "stabilize" the industry, when in reality he exerted power to control and maintain prices.⁷⁹ When the system came under official scrutiny and public attention in 1911,

 ⁷⁵ Lewis L. Gould, *The William Howard Taft Presidency* (Lawrence: University Press of Kansas, 2009), 170.
 ⁷⁶ UNITED STATES v. UNITED STATES STEEL CORPORATION ET AL, 419, accessed July 19, 2023, https://tile.loc.gov/storage-services/service/ll/usrep/usrep251/usrep251417/usrep251417.pdf.
 ⁷⁷ Ibid.

⁷⁸ Ibid.

⁷⁹ Ibid.

Gary abandoned it nine months before the suit began, indicating that he recognized that the system was illegal and ended it to avoid litigation.⁸⁰ The Supreme Court, indeed, ruled that the Gary Dinners constituted unlawful combinations.⁸¹ The investigation concerning the suit pressured Gary to end his illegal practice and thus uncovered US Steel's monopolistic actions, proving that the filing of the suit was correct in controlling anticompetitive activities.

In addition, the government used US Steel's gigantic size as evidence for its illegal purposes and its ability to restrict competition. The argument in the court case stated that US Steel is a combination in restraint of trade because it is not a result of natural trade growth but is a combination of competing corporations which included "the largest and most powerful competitors in practically every branch of the iron and steel industry in rails; plates; structural shapes; wire rods and wire products; hoops, bands, and cotton ties; skelp; wrought pipe and tubular goods; seamless tubes; bars; billets and sheet bars."⁸² The overarching web of US Steel reaching every branch of the steel industry shows that they had the power to control prices. Further, US Steel's "capital as compared with that of competitors, its proportion of the total production, its proportion of the total production as compared with that of each of its principal competitors, its proportion of ore reserves, its control over transportation of ore, its effect upon prices, concerted maintenance of prices under its leadership, and opinion evidence as to its power" manifested its preponderance and dominance in the steel industry.⁸³ The list above shows US Steel's ability to influence price through potentially controlling ore portions and steel production. Specific figures also support US Steel's dominant position in the market: "Its total assets on December 31, 1913, were in excess of 1,800,000,000; its outstanding capital stock was \$868,583,600; its surplus \$151,798,428; Its cash on hand ordinarily was \$75,000,000."⁸⁴ There is no doubt that US Steel's "resources, strength, and comprehensive ownership of the means of production" together enabled it to control and dominate the market, corroborating the proposition that federal antitrust action was necessary to prevent the use of such power in restraint of trade.⁸⁵

The use of US Steel's size as an evidence for its illegal purposes, although dismissed by the courts, conveys that the final ruling does not necessarily mean that US Steel did not violate the law. In response, the Justices interpreted the Sherman Antitrust Act as not making the mere size an offense or the existence of exerted power an offense.⁸⁶ This interpretation is valid, as Justice Day stated, only "when the size and power have been obtained by lawful means and developed by natural growth," but does not apply to US Steel because it is not a product of

⁸⁰ "Business: Gary Dinners," Time, last modified November 9, 1925, accessed July 19, 2023, https://content.time.com/time/subscriber/article/0,33009,728689,00.html. William H. Page, *The Gary Dinners and the Meaning of Concerted Action*, 602, 610, 2009, accessed July 19, 2023, https://scholarship.law.ufl.edu/cgi/viewcontent.cgi?article=1075&context=facultypub.

⁸¹ Page, *The Gary*, 610.

⁸² UNITED STATES, 423.

⁸³ UNITED STATES, 423.

⁸⁴ UNITED STATES, 464.

⁸⁵ UNITED STATES, 464.

⁸⁶ UNITED STATES, 451.

natural growth.⁸⁷ The government's failure to provide supporting evidence for the corporation's unlawful practice weakened the evidence of its size as a supporting proof of its illegality. This failure, however, does not invalidate the filing of the petition because the government's lack of evidence and experience does not mean US Steel was legal and indeed hints that the failure to prosecute US Steel in 1920 has little value in determining the legality of US Steel. Concurring with Judge Learned Hand in the 1945 United States v. Aluminum Co. of America, the error in the final decision to dismiss the lawsuit "lay in requiring a showing of predatory acts," suggesting The Sherman Act lacked the power to rule trusts that consolidate a great deal before courts were able to find evidence of monopolistic actions.⁸⁸ The use of US Steel size failed to evince the corporation's illegality due to vagueness in antitrust laws concerning trusts that did not adopt an illegal degree of monopolization, advising that antitrust laws required further modifications and interpretations about its applications on trusts that are less of a complete monopoly.

Although the final ruling of *US v. USS* might be contradictory, the decreased market share of US steel from 1911 to 1920 shows that the lawsuit successfully increased competition and protected democratic economic interests. The turning point of the case came in 1920, when the Supreme Court, by a 4 to 3 vote, ruled that US Steel was not guilty of violating the Sherman Antitrust Act.⁸⁹ The Court saw no act of aggression against competitors of US Steel, deducing that there could not be any restraint of trade.⁹⁰ On the other hand, the case repeatedly referred to US Steel's loss of market share to support the decision that it did not violate the Sherman Antitrust Act.⁹¹ This use of evidence potentially suggests that US Steel moved towards a less monopolistic practice due to fear of prosecution. Similarly, Historian Thomas Mccraw and economist Forest Reinhardt stated that "had [US Steel's] share not dropped significantly from the 66 percent figure of 1901, it would have been dismembered."⁹² Data on U.S. Steel share of production shows a steady decrease in share from 66% in 1901 to 46% in 1920.⁹³ The decrease in market share suggests that over the period of the lawsuit, changes in US Steel's practice led to more shares of production in its competitors, resulting in more competition, indicating that the suit increased competition.

Conclusion

Taft's administration was correct in filing the US v. USS Supreme Court case because it successfully revealed US Steel's monopolistic motives and protected competition. Knowing that

⁸⁷ UNITED STATES, 460.

 ⁸⁸ William H. Page, Standard Oil and U.S. Steel: *Predation and Collusion in the Law of Monopolization and Mergers*, 85 S. Cal. L. Rev. 101 (2012), 674, http://scholarship.law.ufl.edu/facultypub/260.
 ⁸⁹ "Split between Taft and Roosevelt," Ehistory, accessed June 1, 2023,

https://ehistory.osu.edu/exhibitions/1912/trusts/trtaft.

 ⁹⁰ Cornell Law School, accessed May 22, 2023, https://www.law.cornell.edu/supremecourt/text/251/417.
 ⁹¹ Ibid.

⁹² Thomas K. Mccraw and Forest Reinhardt, "Losing to Win: U.S. Steel's Pricing, Investment Decisions, and Market Share, 1901-1938," *The Journal of Economic History* 49, no. 3 (1989): 613, http://www.jstor.org/stable/2122506.

nitp://www.jstor.org/stable/zizz

⁹³ Ibid, 608.

purchasing TCI would violate the Sherman Act, US Steel proceeded to obtain permission from Roosevelt by exaggerating the level of emergency, understating the benefit, and failing to disclose salient information. Roosevelt and Taft's response to the petition deepened the discord between them, leading to Roosevelt running to unseat Taft in 1912. Allegations in the court case, specifically the Gary Dinner system and US Steel's dominance in the steel industry served as evidence for US Steel's monopolistic purpose at its birth and its attempt to create a monopoly. Failure to prosecute the monopolistic US Steel shows that the Sherman Antitrust Act required further elaboration on its applications on trusts that intend to monopolize trade without any glaringly illegal actions. Due to fear of prosecution, the continuation of the case from 1911 to 1920 allowed US Steel to reduce its market share, implying that the suit increased and protected competition in the steel industry.

Throughout the history of antitrust, news laws such as the Clayton Act and the Federal Trade Commission Act of 1914 had been created to supplement the original Sherman Antitrust Act. The Clayton Act addressed practices untended by the Sherman Antitrust Act, such as interlocking directorates, which is when board directors serve on the boards of multiple corporations.⁹⁴ As corporations continue to find new ways to increase control of the market without violating the existing antitrust laws, revisions and amendments to antitrust laws are necessary to ensure that they continue to protect competition. *US v. USS* is an example of trust successfully avoiding prosecution by expanding its power, to the extent where it has the ability to control the market, without perpetrating obvious predatory actions. The question of whether predatory actions are required to deem a corporation anticompetitive remains to be discovered.

⁹⁴ Federal Trade Commission, accessed August 1, 2023,

https://www.ftc.gov/advice-guidance/competition-guidance/guide-antitrust-laws/antitrust-laws.

Works Cited

- Alderson, William T. "TAFT, ROOSEVELT, AND THE U. S. STEEL CASE: A LETTER of JACOB McGAVOCK DICKINSON." *Tennessee Historical Quarterly* 18, no. 3 (1959): 266-72. http://www.jstor.org/stable/42621438.
- Bork, Robert H. The Antitrust Paradox: A Policy at War with Itself. New York, 1978.
- Britannica. Accessed June 4, 2023.

https://www.britannica.com/topic/United-States-Steel-Corporation.

- Buenker, John D., and Joseph Buenker. *Encyclopedia of the Gilded Age and Progressive Era*. Vol. 1. Armonk, NY: Sharpe Reference, 2005.
- "Business: Gary Dinners." Time. Last modified November 9, 1925. Accessed July 19, 2023. https://content.time.com/time/subscriber/article/0,33009,728689,00.html.
- Cornell Law School. Accessed May 22, 2023.

https://www.law.cornell.edu/supremecourt/text/251/417.

Davenport, Spencer. "Antitrust: Taking on Monopoly Power from the Gilded Age to the Digital Age." *Cato Journal* 41, no. 3 (2021): 787-91.

https://ezproxy.bpl.org/login?url=https://www.proquest.com/scholarly-journals/antitrust-t aking-on-monopoly-power-gilded-age/docview/2640588427/se-2?accountid=9675.

DOL. Accessed May 22, 2023.

https://www.dol.gov/general/aboutdol/history/mono-regsafepart05.

Federal Reserve History. Accessed May 22, 2023. https://www.federalreservehistory.org/essays/panic-of-1907.

Federal Trade Commission. Accessed August 1, 2023.

https://www.ftc.gov/advice-guidance/competition-guidance/guide-antitrust-laws/antitrust-laws.

"The Founding of U.S. Steel and the Power of Public Opinion." *Harvard Business School*. Accessed June 4, 2023.

https://www.library.hbs.edu/us-steel/exhibition/the-founding-of-u.s.-steel-and-the-power-of-public-opinion.

- German, James C. "Taft, Roosevelt, and United States Steel." *The Historian* 34, no. 4 (1972): 598-613. http://www.jstor.org/stable/24442959.
- Goodwin, Doris Kearns. *The Bully Pulpit: Theodore Roosevelt, William Howard Taft, and the Golden Age of Journalism.* New York: Simon & Schuster, 2013.
- Gould, Lewis L. *The William Howard Taft Presidency*. Lawrence: University Press of Kansas, 2009.
- Guy B. Maseritz, "No Inventions, No Innovations": Reassessing the Government's Antitrust Case Against United States Steel Corporation, 7 J. Bus. & Tech. L. 247 (2012), https://digitalcommons.law.umaryland.edu/jbtl/vol7/iss2/1
- Jaycox, Faith. The Progressive Era. New York: Facts On File, 2005.
- "J. P. Morgan: The Panic of 1907 and the Federal Reserve." Crf-usa. Accessed June 25, 2023. https://www.crf-usa.org/images/pdf/jpmorgan.pdf.

- Keppler, Joseph. *The Bosses of the Senate*. Accessed May 22, 2023. https://www.senate.gov/art-artifacts/historical-images/political-cartoons-caricatures/38_0 0392.htm.
- Klobuchar, Amy. *Antitrust: Taking on Monopoly Power from the Gilded Age to the Digital Age.* New York: Alfred A. Knopf, 2021.
- Library of Congress. Accessed May 22, 2023.

https://blogs.loc.gov/inside_adams/2021/03/united-copper-panic-of-1907/.

Library of Congress. Accessed May 22, 2023.

https://guides.loc.gov/chronicling-america-standard-oil-monopoly#:~:text=In%201911% 20the%20U.S.%20Supreme,and%20split%20into%2034%20companies.

- Library of Congress. Accessed June 4, 2023. https://guides.loc.gov/chronicling-america-standard-oil-monopoly#:~:text=In%201911% 20the%20U.S.%20Supreme,and%20split%20into%2034%20companies.
- Mccraw, Thomas K., and Forest Reinhardt. "Losing to Win: U.S. Steel's Pricing, Investment Decisions, and Market Share, 1901-1938." *The Journal of Economic History* 49, no. 3 (1989): 593-619. http://www.jstor.org/stable/2122506.
- Mowry, George E. The Era of Theodore Roosevelt, 1900-1912. New York: Harper, 1958.
- Ncpedia. Accessed May 22, 2023.

https://www.ncpedia.org/american-tobacco-company#:~:text=On%2016%20Nov.,Lorild. *New York Times*, November 17, 1911. Accessed May 11, 2023.

https://timesmachine.nytimes.com/timesmachine/1911/11/17/104843000.html?pageNum ber=1.

Page, William H. *The Gary Dinners and the Meaning of Concerted Action*. 2009. Accessed July 19, 2023.

https://scholarship.law.ufl.edu/cgi/viewcontent.cgi?article=1075&context=facultypub.

- "The Panic of 1907." Federal Reserve History. Last modified December 4, 2015. Accessed July 31, 2023. https://www.federalreservehistory.org/essays/panic-of-1907.
- Roosevelt, Theodore. "The Steel Corporation and the Panic of 1907." *Outlook*, August 19, 1911. https://dpl6hyzg28thp.cloudfront.net/media/Roosevelt 19 Aug 1911.pdf.

Roosevelt, Theodore. "The Trusts, the People, and the Square Deal." *Outlook*, November/December 1911, 649.

https://dpl6hyzg28thp.cloudfront.net/media/Roosevelt_18_Nov_1911.pdf.

"Split between Taft and Roosevelt." Ehistory. Accessed June 1, 2023.

https://ehistory.osu.edu/exhibitions/1912/trusts/trtaft.

Steelmuseum. Accessed June 4, 2023.

https://steelmuseum.org/pais300_exhibit_2017/us_steel.cfm.

Tallman, Ellis W., and Jon R. Moen. "Lessons from the Panic of 1907." Atlantafed. Last modified 1990. Accessed June 25, 2023.

https://www.atlantafed.org/-/media/documents/research/publications/economic-review/19 90/orphans/lessons-from-panic-of-1907-tallman-moen-1990-may-june.pdf.

- UNITED STATES v. UNITED STATES STEEL CORPORATION ET AL. Accessed July 19, 2023. https://tile.loc.gov/storage-services/service/ll/usrep/usrep251/usrep251417/usrep251417.p df.
- Valentine, Rebecca, and Lawrence W. Baker. *Gilded Age and Progressive Era Reference Library*. Detroit: UXL, 2007.
- Wiebe, Robert H. "The House of Morgan and the Executive, 1905-1913." *The American Historical Review* 65, no. 1 (1959): 49-60. https://doi.org/10.2307/1846601.

The State of Convolutional Neural Networks in Today's Medical Practices By Prateek Hanumappanahalli

Abstract

In today's medical world, image analysis is one of the most vital skills to have. Medical images are taken to identify the issue and make a prognosis. These images are typically analyzed by medical professionals. This causes the image interpretation to vary based on the subjectivity of the specific individual. An alternative method, that is slowly revolutionizing the industry, is using Convolutional Neural Networks(CNNs). This network is mainly used for image processing due to its ability to detect image patterns. The primary objective of this article is to present an in-depth analysis of how CNNs are currently being applied to medical image analysis. This review should drive more people in the medical field to learn and apply CNN in image evaluation. We first provide a brief introduction to CNNs. We then discuss the gargantuan significance of image analysis in the medical field. An application of CNNs in image analysis is presented. These applications in image processing include various areas: detection, classification, and segmentation. Limitations of the application are also presented. By automating the interpretation of medical images, CNNs have proven to be powerful tools for healthcare professionals, ultimately leading to improved patient outcomes and more precise treatment planning.

Keywords: Convolutional neural networks, segmentation, detection, classification, localization, registration, image analysis

Introduction

In the realm of modern medicine, image analysis stands as a pivotal tool, allowing medical professionals to dramatically improve patient outcomes. Medical image analysis is a process of extracting and processing medical information from images. Image analysis helps professionals determine a treatment. The practice of medical image analysis encompasses a wide range of imaging modes, such as X-rays, magnetic resonance imaging (MRI), computed tomography (CT), and more[Sarvamangala and Kulkarni 1]. Each mode serves a unique purpose and allows medical professionals to gain insights into different aspects of the human body's structure and function. By selecting the most suitable imaging method for a specific case, healthcare experts can precisely analyze and interpret these images. Before the analysis, images are modified and processed to enhance the quality of the image. Radiologists, physicians, cardiologists, and other medical professionals in the field go through years of specialized training to accurately interpret medical images. Despite the extensive training, medical professionals have some limitations in certain situations. Human interpretation of medical images can be subjective and may vary among different medical professionals. Differences in experience, expertise, and individual biases can lead to varying diagnoses and treatment recommendations. Large datasets can impose an issue that could lead to gargantuan processing times. Additionally,

there is always space for human error. These drawbacks have led medical image analysis professionals to invest in the practice of using machine learning, specifically Convolutional Neural Networks(CNNs).

CNNs are one of the many neural networks in deep learning. This network is primarily used for image and video recognition tasks. The primary element of CNNs is convolutional layers. Each convolutional layer applies a learning filter over small sections of the input image. The filter runs through the designated receptive fields and creates feature maps[Sarvamangala and Kulkarni 1]. After feature maps are produced, activation functions are applied to introduce non-linearity. This principal step allows for the learning of more complex patterns and relationships. There are various activation functions available based on specific cases. Some of them include Rectified Linear Unit(ReLU), Sigmoid, and Tanh. Additionally, activation functions determine whether a neuron should be activated based on the addition of the weighted sum and bias[Apicella et al. 4]. The next step is to pool layers. This process reduces the sample size while still retaining areas with dense data. This minimizes the processing time and the number of parameters. The output from the convolutional and pooling layers is a 3-dimensional array and needs to be resized into a 1-dimensional array. The 1-D arrays are then passed into fully connected layers, and each neuron from the connected layers is connected to the neuron in the previous layer. This allows the paradigm to learn and adapt features extracted from previous models[Sarvamangala and Kulkarni 1, Yamashita et al. 5]. If medical professionals have the intention of classifying the medical image, a Softmax function is often applied to the last fully connected layer. During the classification process, the neural networks provide logits based on the probability of a certain element. To modify logits into a readable probability, a Softmax function is applied. The Softmax function makes the logits positive and makes the probabilities add up to The element with the highest probability is typically the accurate element that was detected in the image[Sarvamangala and Kulkarni 1].

Logits \rightarrow Probabilities

 $[3.7, 1.2, 0.1] \rightarrow [0.74, 0.24, 0.02]$

After the results have been determined, a loss function is used to measure the difference between the training and experimental results. A series of optimization techniques are then used to minimize the difference. Once the loss is calculated, backpropagation is used to update the weights of the network layers to minimize the loss. The gradients of the loss function concerning the weights are computed, and the weights are adjusted[Christoffersen and Jacobs 8].

The idea of CNNs can be traced back to the late 1980's. The model realization and the extensive research stage were started by Kunihiko Fukushima. Fukushima proposed Neocognitron, a self-organizing neural network designed for character recognition. In the early 1990s, Yann LeCun, along with other researchers, developed LeNet-5, one of the first CNN architectures. LeNet-5 was primarily used for handwritten digit recognition and consisted of

several convolutional layers, pooling layers, and fully connected layers. It was an early success in applying CNNs to practical pattern recognition tasks[Zhang 7]. This eventually led to the fully functional CNN. In the field of medical image analysis, CNNs provide many functionalities. CNNs are revolutionizing the field of medicine by allowing for the detection, classification, and segmentation of medical images. The following research paper will include information on how CNNs detect, classify, and segment medical images. It will also include a section on the limitations of CNNs in medical image analysis. Finally, a conclusion is presented which will include potential future studies.

Detection

Medical image detection is one of the many processes medical professionals use in medical image analysis. It involves detecting and assessing specific patterns, abnormalities, and structures. For decades image analysis was done by medical professionals. They manually detect the patterns through visual inspections, measurements, and consultations. Professionals can miss vital details, which can cause insufficient labeling. This can lead to inaccurate treatment plans[Ker et al. 9]. In 2017, the Kaggle Data Science Bowl required contestants to complete many image detection tasks, including detecting malignant skin cells. It was determined that CNNs accurately determined whether the cells were malignant or benign 72% of the time. It was also recorded that two dermatologists accurately recorded this information 65% and 66% of the time[Ker et al. 9]. The increase in accuracy from CNNs is causing a shift from manual medical image detection to computer-aided image detection(CADe).

In all the applications of CNNs, medical professionals are first required to collect data. In the case of medical imaging, data comes in the form of X-rays, magnetic resonance imaging (MRI), computed tomography (CT), and much more. Medical professionals then annotate these images with bounding boxes. The purpose of a bounding box may vary depending on the specific CNN application. In the study of feature detection, bounding boxes are used to identify certain abnormalities, structures, and patterns in medical images[Sarvamangala and Kulkarni 1].



Figure 1: Bounding Boxes Identifying a Brain Tumor

The dataset of images is then split into three sets: training, validation, and testing. The training dataset is typically the largest and is used to train the CNN model in detection processes. Images in the training dataset are modified to bring diversity to the CNN model. The augmenting

process can include processes like flipping and scaling. This will allow the model to experience various medical imaging situations, so it can be better adapted.



Normal

Zoomed

Rotated

A proper CNN object detection architecture must be selected. These architectures are required for the feature detection model. A CNN architecture serves as the foundation upon which the model learns to extract meaningful features from the input data. Selecting the appropriate architecture is a critical step in developing effective deep-learning models. The architecture heavily influences a model's performance, accuracy, and ability to detect specific patterns. It is especially important for medical tasks because professionals require models that can detect minor details[Shin et al. 6]. Some commonly used architectures include Faster R-CNN, YOLO, and more. Next, the object detection model has to be built. Building an object detection model involves creating a neural network architecture that can accurately identify objects in images and predict their locations using bounding boxes. Before the training, an optimizer must be selected and metrics must be defined. This will allow for the loss function to be minimized and the training performance to be monitored. The training process involves repeating through batches of images and their corresponding annotations. In each repetition there is a forward pass, compute loss, and backward pass. The forward pass process includes passing images through the model to predict bounding boxes. Many medical images have features that vary in size and location between pictures. This means that models will not be able to accurately detect varying features. This creates the need for predicting the size and location of a feature. Medical professionals do this through anchor boxes. Anchor boxes are predefined bounding boxes that are placed in several locations throughout the image to predict the feature positions. These professionals predict the bounding boxes by using anchor boxes as a reference. The next component in the training process is computing the loss. After the forward pass, the predicted output is compared to the actual target output using a loss function. A loss function is defined based on how accurately the bounding boxes fit the actual location and size as well as how well the model classifies objects [Zhang et al. 10]. The last component is the backward pass or backpropagation. The gradients are measured and the loss is minimized using parameter tuning. Parameter tuning includes processes like adjusting the learning rate and number of epochs[Yadhav and Jadhav 2]. During the validation stage, the dataset is monitored for the

detection accuracy. The testing stage includes an assessment of the CNN model to make sure of its performance[Oh et al. 11].

Classification

Image classification is one of the most important applications of image analysis. This process involves categorizing images into specific classes. The goal of this process is to automatically classify these images into different categories or classes based on the presence or absence of specific medical features and structures found in medical images. The traditional, manual method of medical image classification has reached its cap. Additionally, it takes a great amount of time and effort to put into a simple visual inspection of a medical image. CNNs are a widely used tool for image classification, as it is specialized for visual feature extraction. A study was done where the InceptionV3, an image recognition model, with the ImageNet database performed a weight and transfer learning training on a dataset, containing 108,312 optical coherence tomography (OCT) images. Through this study, they determined that the CNN model had an accuracy of 96.6%, a sensitivity of 97.8%, and a specificity of 97.4%. These results were compared with six experts, and it was found that they had a high sensitivity but low specificity. This means that humans aren't able to detect the instance of a negative class as well as the InceptionV3 model did[Hossian and Sajib 3]. This increase in accuracy from CNN models is bringing a change to the process of medical classification.

The process of training a CNN model for medical image classification is similar to the process of medical object detection training. Medical professionals start by collecting a dataset of images. It is important to obtain a variety of images, including negative classes. As done in all medical image applications, images are augmented to bring different variations of an image. Image classification tasks don't require bounding boxes as whole images are classified instead of specific feature detections. The next step is to choose a CNN architecture. Determining a proper CNN architecture for image classification depends on the network complexity, output layer, loss function, and model size. Image classification models focus primarily on learning features that help discriminate between different classes. These models are typically less complex than image detection models. Some examples include LeNet, ResNet, and AlexNet. The output layer is a major factor in choosing the right architecture[Shin et al.6]. Depending on the image analysis application, different CNN models have various outputs. For image classification, the last layer includes a Softmax function that calculates the class probabilities[Cardarilli et al. 14]. Next, the CNN model has to be built. Building a classification model involves creating a neural network architecture that can accurately separate images based on their classes. Before training any model it is important to select and define loss functions, optimizers, and metrics. Models are trained, validated, and tested in the same process as medical feature detection. The results of a classification model output the probability of an image fitting into categories. The class with the highest probability is usually where the image belongs[Cardarilli et al. 14].

Segmentation

Image segmentation is a crucial technique in image analysis that involves dividing an image into distinct regions. This process is essential for identifying specific objects or structures within a medical image. Unlike image classification which assigns an entire image to a single category, segmentation focuses on labeling, enabling precise identification of boundaries and individual components[Feng et al. 15]. Traditional manual segmentation methods are time-consuming and prone to human errors. This prompted the adoption of advanced approaches such as CNNs for automated segmentation tasks. In the medical field, image segmentation plays a vital role in tasks like feature extraction and abnormality assessment[Sarvamangal and Kulkarni 1]. Segmenting an image helps medical professionals track diseases as they spread and assign a treatment plan according to that. CNNs have revolutionized medical image segmentation. These networks are trained on labeled datasets to accurately map pixels to corresponding classes, creating detailed and accurate segmentations[Yin et al. 16]. One notable CNN architecture for biomedical image segmentation is the U-Net. U-Net's unique encoding and decoding structure allows it to capture intricate spatial information while maintaining high-resolution features. This architecture is well-suited for medical imaging due to its ability to precisely segment structures with complex shapes.



The encoder part of the architecture extracts important features from the image, and the decoder processes the input into a segmented output. This two-way process allows neural networks like U-Net to effectively segment complex structures in medical images. In Figure 3, the 3 x 3 convolution operation performs feature extraction, and the ReLU activation introduces non-linearity to the model, making it capable of learning complex patterns and features in the input data. The max pooling operation helps in reducing complexity and controlling overfitting by capturing the most dominant features in an image. The up-sampling operation is often used to restore the lost spatial information caused by downsampling operations, such as pooling. The 1 x 1 convolution is used at the end to maintain efficiency by controlling the number of parameters[Yin et al.16]. The segmentation process, like object detection and classification,

typically involves obtaining a labeled dataset, augmenting images to enhance variability, designing an appropriate CNN architecture, training the model using loss functions specific to segmentation tasks, and parameter tuning. The model is then tested[Sarvamangala and Kulkarni 1].

Limitations

CNNs have revolutionized the field of medical imaging by allowing for automated detection, classification, and segmentation. Despite the major benefits CNNs provide, they come with notable limitations. One primary challenge is that Convolutional Neural Networks (CNNs) exhibit limitations in terms of their generalization abilities, particularly when exposed to medical images acquired using different machines. While CNNs have shown remarkable performance in image recognition tasks, they often lack adaptability to changes in external factors, such as variations in imaging devices, scanner settings, and acquisition protocols. These models heavily rely on the data they are trained on, which can lead to issues when presented with images that differ significantly from the training data in terms of imaging parameters and characteristics. The interpretability of CNNs is a major issue in the medical world. Understanding the reasoning behind the CNN decision is vital to progressing the advancement of deep learning in the medical field. It is also important for the patient's safety and other medical decisions[Perone and Adad 12]. Another issue that medical professionals face is the amount of images they need in the training dataset to train a CNN model. This can lead to enormous processing times, which may be a limiting factor for small healthcare organizations or research groups [Yang and Yu 13]. Medical professionals must address these limitations and disadvantages of using a CNN model for image analysis. Addressing these disadvantages involves a combination of strategies, including proper data collection and interpretation techniques.

Conclusion

Convolutional Neural Networks have revolutionized modern medical imaging. Their application in medical practices has redefined image analysis, offering automated solutions that enhance diagnostic precision and treatment planning. This review paper highlights the significant advancements of CNNs in modern medical imaging. These networks have shown impressive potential in enhancing diagnostic precision, disease identification, and patient care. By learning complex features from extensive datasets, CNNs surpass conventional medical imaging with advanced computational techniques. The discussion of detection, classification, and segmentation showcased CNNs' versatility. CNNs are often superior to humans in medical imaging due to their ability to accurately and consistently recognize intricate patterns and anomalies within images while minimizing subjective biases. In classification, CNNs consistently outperformed traditional methods with higher accuracy. Additionally, segmentation demonstrated the networks' precision in outlining regions of interest. While CNNs offer significant advantages, they are not immune to challenges. The issue of generalization across different imaging settings remains, as does the question of interpretability in critical medical

decisions. The resource-intensive nature of CNN development and training also poses challenges. Overall, CNNs have reshaped medical image analysis, promising more accurate diagnoses and improved patient care. While challenges persist, ongoing research and development hold the potential to further refine CNN models for specific medical needs. As technology continues to progress, it will be crucial to overcome limitations and effectively utilize their potential to advance contemporary medical procedures.

Works Cited

- [1] Sarvamangala, D. R., and Raghavendra V. Kulkarni. "Convolutional Neural Networks in Medical Image Understanding: A Survey." *Evolutionary Intelligence*, vol. 15, no. 1, Mar. 2022, pp. 1–22. *Springer Link*, <u>https://doi.org/10.1007/s12065-020-00540-3</u>.
- [2] Yadav, Samir S., and Shivajirao M. Jadhav. "Deep Convolutional Neural Network Based Medical Image Classification for Disease Diagnosis." *Journal of Big Data*, vol. 6, no. 1, Dec. 2019, p. 113. *BioMed Central*, <u>https://doi.org/10.1186/s40537-019-0276-2</u>.
- [3]Hossain, Md. Anwar, and Md Sajib. "Classification of Image Using Convolutional Neural Network (CNN)." *Global Journal of Computer Science and Technology*, vol. 19, May 2019, pp. 13–18. *ResearchGate*, <u>https://doi.org/10.34257/GJCSTDVOL19IS2PG13</u>.
- [4] Apicella, Andrea, et al. "A Survey on Modern Trainable Activation Functions." Neural Networks, vol. 138, June 2021, pp. 14–32. ScienceDirect, https://doi.org/10.1016/i.neunet.2021.01.026.
- [5] Yamashita, Rikiya, et al. "Convolutional Neural Networks: An Overview and Application in Radiology." *Insights into Imaging*, vol. 9, no. 4, 4, Aug. 2018, pp. 611–29. *insightsimaging.springeropen.com*, <u>https://doi.org/10.1007/s13244-018-0639-9</u>.
- [6] Shin, H.-C., et al. Deep Convolutional Neural Networks for Computer-Aided Detection: CNN Architectures, Dataset Characteristics and Transfer Learning | IEEE Journals & Magazine | IEEE Xplore. <u>https://ieeexplore.ieee.org/abstract/document/7404017</u>. Accessed 18 Aug. 2023.
- [7] Zhang, Quan. Convolutional Neural Networks. 2018.
- [8] Christoffersen, Peter, and Kris Jacobs. "The Importance of the Loss Function in Option Valuation." *Journal of Financial Economics*, vol. 72, no. 2, May 2004, pp. 291–318. *ScienceDirect*, <u>https://doi.org/10.1016/j.jfineco.2003.02.001</u>.
- [9] Ker, Justin, et al. "Deep Learning Applications in Medical Image Analysis." *IEEE Access*, vol. 6, 2018, pp. 9375–89. *IEEE Xplore*, <u>https://doi.org/10.1109/ACCESS.2017.2788044</u>.
- [10] Zhang, Yi-Fan, et al. "Focal and Efficient IOU Loss for Accurate Bounding Box Regression." *Neurocomputing*, vol. 506, Sept. 2022, pp. 146–57. *ScienceDirect*, <u>https://doi.org/10.1016/j.neucom.2022.07.042</u>.
- [11] Oh, Shu Lih, et al. "Deep Convolutional Neural Network Model for Automated Diagnosis of Schizophrenia Using EEG Signals." *Applied Sciences*, vol. 9, no. 14, 14, Jan. 2019, p. 2870. www.mdpi.com, <u>https://doi.org/10.3390/app9142870</u>.
- [12] Promises and Limitations of Deep Learning for Medical Image Segmentation Perone -Journal of Medical Artificial Intelligence. https://jmai.amegroups.org/article/view/4659/html. Accessed 18 Aug. 2023.
- [13] Yang, Ruixin, and Yingyan Yu. "Artificial Convolutional Neural Network in Object Detection and Semantic Segmentation for Medical Imaging Analysis." Frontiers in Oncology, vol. 11, 2021. Frontiers, https://www.frontiersin.org/articles/10.3389/fonc.2021.638182.

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- [14] Cardarilli, Gian Carlo, et al. "A Pseudo-Softmax Function for Hardware-Based High Speed Image Classification." *Scientific Reports*, vol. 11, no. 1, 1, July 2021, p. 15307. *www.nature.com*, https://doi.org/10.1038/s41598-021-94691-7.
- [15] Feng, Yong, et al. "Learning What and Where to Segment: A New Perspective on Medical Image Few-Shot Segmentation." *Medical Image Analysis*, vol. 87, July 2023, p. 102834. *ScienceDirect*, <u>https://doi.org/10.1016/j.media.2023.102834</u>.
- [16] Yin, Xiao-Xia, et al. "U-Net-Based Medical Image Segmentation." Journal of Healthcare Engineering, vol. 2022, Apr. 2022, p. e4189781. www.hindawi.com, <u>https://doi.org/10.1155/2022/4189781</u>.

Extensive Review of Allergic Rhinitis and Overview of Treatment Options By Shan Hsieh

Abstract

Allergic Rhinitis (AR) is the most common clinical type of allergy, presenting itself via symptoms in upper respiratory tract locations, most commonly the nose. It is characterized by the 4 central symptoms of watery rhinorrhea, nasal itching, nasal obstruction, and sneezing. The prevalence of AR has also been increasing globally, with 60 million people affected in the U.S. alone, and is present in between 10-30% of adults and a staggering 40% of children. For these affected patients, risk factors may take the form of environmental, genetic, or even diet. This paper aims to explore the unknowns of AR and its relevance in a broad scheme of the population.

Epidemiology

In terms of the Epidemiology of Allergic Rhinitis (AR), prevalence of the disease has increased significantly since the late 1990s. AR is known to comorbid with asthma, atopic disease, sinusitis, conjunctivitis, and otitis media. Globally, it affects between 25-40% of children and adults, respectively.^{1,2} In 80% of AR cases, symptoms develop before the age of 20 and peaks at ages between 20-40. In children, the incidence rate of peak AR diagnoses was between 24-29 months of age.^{1,2} Further meta-analysis studies have concluded that male AR is predominant in childhood while females demonstrate a predominance in adolescence. Increased Levels of pollutants in urban environments has led to an increased prevalence in said urban areas when compared to rural areas. In addition, Smoking is actually not associated with severe nasal symptoms in patients with AR but does impact patients with chronic rhinitis. Usually, maternal smoking confers the greatest risk to the development of pediatric AR. However, novel smoking technologies such as vapes and e-cigarettes increase risk of AR in adolescents. This widespread prevalence of AR has an economic impact estimated to be up to \$20.9 billion in the United States.^{1,2}

Risk Factors

Unfortunately, as is the case with many inflammatory diseases, there is no one root cause for the appearance and persistence of AR-rather, it results from an apotheosis of a variety of factors, including genetic, environmental, immunological, and even lifestyle factors. This section will expound upon some of the major risk factors that may culminate in the development of AD in individuals.

2.1 - Environmental Risks

Increased levels of pollutants in outdoor urban environments is known to increase prevalence of AR in such urban areas when compared to rural areas. Pollution is widely known to be one of, if not the largest environmental risk to personal health. Such pollution is often associated with AR, asthma, and autoimmunity, and can have detrimental effects on an individual's immune system.^{3,4} When atopic individuals are exposed to allergens and pollutants, they develop specific Immunoglobulin E (IgE) antibodies on the surface of mast cells and other such immune cells.⁵ This ligand-receptor interaction mediates the release of histamines, arachidonic acid metabolites (which stimulates the further formation of prostanoids such as prostaglandin and leukotrienes, which play major roles in inflammatory responses). This results in the typical battery of AR symptoms such as sneezing, nasal congestion, and watery rhinorrhea.⁶ In addition, novel smoking technologies such as vapes and e-cigarettes increase risk of AR in adolescents. Maternal smoking also confers the greatest risk to the development of pediatric AR. However, smoking is actually not associated with severe nasal symptoms in patients with AR but does impact patients with chronic rhinitis.

Indoor allergens such as dust mites, pet dander, molds, and potentially pollen all also contribute to the aggravation and exacerbation of symptoms. Many individuals in the western hemisphere spend the vast majority of their time indoors, and 90% of said individuals live in places where air quality does not meet World Health Organization (WHO) standards. Particulate matter with a diameter of between 2.5 -10 micrometers were found to be responsible for the exacerbation of AR symptoms by increasing levels of inflammatory cytokines such as interleukin (IL-8), which further stimulate the upregulation and expression of the histamine H1 receptor (H1R).⁷ At the same time, exposure to coarse particulate matter was also shown to increase the number of IL-5-secreting eosinophils in mice exposed to allergens. Another common indoor pollutant is known as Volatile Organic Compounds (VOCs). These are frequently released by indoor cooking and heating appliances, and are associated with the development of AR and aggravation of its symptoms.⁸

2.2 - Genetic Risks

Emerging studies show that the pathogenesis of AR can largely be driven by genetic factors. Genome-wide association studies (GWAS) have identified a wide number of genes involved in mediating the body's response to allergens and promote the development of AR.^{3,9} This article will explore 3 sets of genes: 1) IL-33, 2) PTPN22, and 3) microRNAs.

IL-33

Interleukin-33 (IL-33) is a cytokine that are primarily secreted by "first-line of defense cells," such as epithelial cells, in response to an exposure to an exogenous stimulus, including allergens. It has been shown that IL-33 represses pro-inflammatory signaling by sequestering nuclear NF-kB and preventing its subsequent translocation into the nucleus.¹⁰ This form of refractory inflammation is what consequently leads to the development of allergy.

Mechanistically, IL-33 binds to a target host cell receptor called IL-1R1, which then initiates a signal transduction cascade via recruitment of Myeloid differentiation factor 88 (MyD88). Further downstream signaling activities such as NF-kB and p38-associated mitogen-associated protein kinase (MAP Kinase) signaling.^{10,11} This signaling cascade eventually

leads to expression of genes related to polarization of Th2 cells, which play a prominent role in the development of allergic responses (See section on Molecular Pathophysiology).

The late-phase progression of AR (around 6-24h post-allergen exposure) is caused by presence of Th2 cytokines (e.g., IL-4, IL-5, and IL-13) and chemokines that actively recruits immune cells into the nasal mucosa. Studies have shown that when nasal epithelial cells (NECs) are stimulated with toll-like receptor (TLR)-9 ligand, a mimic of a bacterial infection, IL-33 expression is significantly upregulated by these NECs.¹² Likewise, in response to allergens, these NECs release IL-33 and subsequently induce the release of IgE-mediated histamine from mast cells and basophils. Finally, IL-33 induces Th2 cells to produce IL-4, IL-5, and IL-13, which further contributes to IgE release by plasma cells. Thus, genetic mutations that lead to elevated levels of IL-33 in the serum and sinus mucosa are highly correlated with the severity of AR.

PTPN22

A study focused on Han Chinese children found that specific single nucleotide polymorphism (SNPs) in the genes, protein tyrosine phosphatase non-receptor 22 (PTPN22) and cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) are associated with childhood development of AR. PTPN22 is a protein phosphatase that removes a phosphate group from a target protein, specifically the phosphorylated ZAP-70 and phosphorylated zeta chain of CD3 receptor.¹³ Both ZAP70 and CD3 plays an important role in T-cell activation in response to an antigen, and thus, the activation of PTPN22 prevents the full activation and differentiation of T-lymphocytes. This is to ensure that regulatory events are held in place to prevent over-maturation and activation of T-cells.^{13,14}

Likewise, CTLA-4 is an immune checkpoint membrane receptor protein that counteracts the stimulatory signals induced by its counterpart, CD28. Both CD28 and CTLA-4 binds to their target proteins presented on the surface of antigen presenting cells—CD80 and CD86. CTLA-4 exhibits a much stronger affinity for both CD80 and CD86, which then transmits inhibitory signals to T-cells to prevent downstream activation.¹⁵ The mechanisms at which CTLA-4 exerts this signal remains controversial, but some studies suggest that CTLA-4 activation leads to recruitment of phosphate molecules that help attenuate the TCR activation signal.

While meta-analyses have been performed and found that polymorphisms of PTPN22 and CTLA-4 genes are largely correlated with development of AR, the underlying mechanism is not fully understood. It could be possible that both PTPN22 and CTLA-4 SNPs are altering the expression of TCRs and CD28 to promote antigen presenting via cellular signaling or transcriptional regulation. More studies need to be performed to fully address how these polymorphisms are contributing to the progression of AR.^{14,16}

miRNA

Finally, recent studies have shown advances in the role of micro-RNAs (miRNA) in the regulation and progression of AR. miRNA are small, non-coding RNA molecules with ~18-24 nucleotides in length, and they have demonstrated many fundamental roles in the

post-translational regulation of gene expression. miRNAs carry complementary sequences against the 3' untranslated region (UTR) of mRNA. Binding of the miRNA to the 3' UTR leads to degradation of mRNA or inhibition of translation. A single miRNA can target numerous genes, and numerous miRNA can also target one gene.¹⁷

When comparing the transcriptional profile of 8 patients with perennial AR and 8 healthy control individuals, several miRNAs were downregulated. In particular, miR-224 downregulation was associated with inhibition of TGF β signaling, while the reduction of miR-498 showed decreasing levels of CD4+ T-cell. It is possible that the imbalance of these regulatory T-cells due to lack of TGF β signaling could be associated with the development of AR.^{18,19}

Furthermore, another group has investigated the expression of miRNAs in exosomes in nasal mucus in patients with severe AR and healthy control patients via quantitative real time PCR. Some of these differentially expressed miRNAs are involved in B-cell receptor signaling, NK-mediated cellular cytotoxicity, T-cell receptor signaling, leukocyte transendothelial migration, etc. These exosomes can be transferred between cell-to-cell, and transfer miRNAs within each other. One of the most upregulated miRNA was miR-233, which is specifically involved in eosinophil inflammation as well as lowered Treg cell counts. Therefore, it could be possible that heightened eosinophil activity due to increased miR-233 function contributes to the progression and pathogenesis of AR.^{18,19}

2.3 - Dietary Risks and The Presence of Sex-based Discrepancy

While the most abundantly researched aspects when it comes to AR or asthma often include genetic and environmental risk factors, diet is an often overlooked yet fundamentally critical aspect that influences atopic individuals. A study by Rosenkranz et al. (2012) on the identification of dietary risk factors was able to accurately pinpoint which factors actually contributed to the development and diagnosis of either asthma (AS) or hay fever (HF).²⁰ The study concluded that for men, the dietary presence of meat and cheese posed a strong, positive association in an unadjusted model of an Australian male (average age, 62.2 years), as well as an adjusted model, with the risk of diagnosis of AS and HF. Poultry and Seafood also demonstrated a strong positive association as a risk factor for already diagnosed AS/HF.^{20,21} Generally, this factor also conclusively demonstrated a positive monotonic relationship with the diagnoses of AS/HF, if somewhat inconsistently. Fruits and vegetables as a factor showed the weakest relationship between consumption and diagnoses of AS/HF, as a weak, inconstant protective relationship in the unadjusted as well as adjusted models were demonstrated. In men, other dietary factors were not considered, as they had no known effect on AS/HF diagnosis.

In women, the factor of cheese and brown bread demonstrated an inverse association in the unadjusted model, however, for diagnosed AS/HF, the cheese and brown bread factor in the adjusted model showed a consistent protective factor for AS, while being somewhat less consistent for HF. Meat on its own also put forth a positive monotonic association with the adjusted and unadjusted models of diagnosed AS/HF. Similarly, poultry and seafood show

significant association in both adjusted and unadjusted models in this study, demonstrating itself to be a risk factor in all 4 of the models used. Somewhat unexpectedly, fruits and vegetables showed a significant relationship with diagnosed asthma, and intake appeared to show higher levels of diagnosed AS/HF.^{20,21}

The general conclusion of this study when it came to dietary risk factors, diets marked by greater intakes of meat, poultry, and seafood were associated with diagnosed AS as well as HF in Australian adults.

Signs and Symptoms

Allergic rhinitis is characterized by the presence of multiple nasal, upper respiratory, and non-nasal symptoms. Generally, nasal and upper respiratory symptoms can include (ranging from mild to severe) sneezing, nasal congestion and/or itching of the nose (pruritus), and anterior or posterior watery rhinorrhea.^{1,22} These symptoms often persist for hours after initial exposure and subsequent reaction to allergens, and mucosa is consequently rendered more reactive to the triggering allergen, other allergens, and even to potentially non-allergenic stimuli (which may include but is not not limited to: strong odors, smoke, pet dander, and other such irritants). Non-nasal symptoms often manifest in ocular symptoms such as allergic rhinoconjunctivitis (itchy or swollen red eyes supplemented by tear gland overexpression), or in symptoms such as an itchy upper palate, postnasal drip, and coughing. At least 30% of AR patients suffer from debilitating or even life threatening symptoms that can lead to severe disability and conditions such as anaphylaxis, bronchospasm, laryngeal edema, cyanosis, or hypotension.^{1,22}

AR can be classified as mild, moderate, or severe based upon the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines. The measurement is based on four aspects, of which are sleep abnormality, impairment in daily activities, impairment in school or work performance, and troublesome symptoms. Patients that do not have any of the aforementioned aspects with relation to their AR are considered as mild cases, however the presence of one or more of these symptoms can elevate the identification to moderate or severe, with the distinction becoming clearer based on further classification. This classification separates AR into intermittent and persistent based on the duration of the symptoms present in an AR patient. The intermittent classification is usually defined as the occurrence of symptoms for less than 4 days per week or less than 4 consecutive weeks. Persistent symptoms occur more than 4 days per week and for more than 4 consecutive weeks.²³

Diagnosis

The diagnosis of AR relies on an analysis on the typical history of allergic symptoms as well as a battery of diagnostic tests. Typically, when watery rhinorrhea, sneezing, nasal obstruction or nasal pruritus persist for a greater time period than one hour on days, AR is suspected as a likely diagnosis.²⁴ In this case, disease severity should be classified according to Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines. Furthermore, the battery of tests

previously mentioned would also be conducted at this time to determine whether or not AR is present.²³ These tests include the skin prick test or the serum specific IgE level test. In terms of symptoms that may initially seem to indicate the presence of AR, Unilateral nasal stiffness, mucopurulent rhinorrhea, mucoid postnasal drip, pain, recurrent epistaxis and anosmia are usually not associated with AR.

Skin testing, with the most common of which being the skin prick test, is usually recommended in clinical practice, despite the potential for false-positive or false-negative results. These tests involve the scratching, pricking, or puncturing of the surface layer of the skin to introduce an allergen. Other methods of skin testing, though less common, involve the intradermal injection of allergen into the skin and waiting for a reaction to display itself. Unfortunately, the criteria for positive results differ from clinic to clinic, and individual professionals' interpretations of these results vary further. Furthermore, skin tests may be influenced by external factors such as drugs (particularly antihistamines), age of the patient, and even location of the testing site on the body of the patient. Despite all these apparent flaws, skin testing is regarded as a reliable and safe diagnostic method.²⁵

Allergen specific IgE testing is a method of blood testing that measures levels of Immunoglobulin E (hence IgE) in the blood. Immunoglobulin E is an antibody heavily involved in the allergic inflammatory processes that are especially prevalent in diseases such as AR. The test measures levels of IgE in the blood, and can aid in the detection of common allergens such as dust mites, mold, pollen, and animal fur.²⁶

Pathophysiology

The cellular and molecular mechanism of AR is complex. In order to first understand the specific pathophysiology of AR, it is important to discuss the general basis of allergic reactions.

Most forms of allergy begin with the innate immune system. In short, the immune system is subdivided into two broad categories: innate/non-specific immunity and adaptive/acquired immunity. When an organism is first exposed to a microbial pathogen, they need to quickly and effectively eradicate this microbial threat before it starts to permeate across the body and damage other tissues and organs.^{27,28} Innate immune system is composed of various cell types such as macrophages, dendritic cells, neutrophils, and natural killer cells, and each of these cells possess unique effector functions that facilitate pathogen clearance. For example, macrophages have the unique ability to transcytose across epidermal barriers by "squeezing" in-between tight junctions and engulfing microbes via phagocytosis.^{27,28}

Innate immune system is also highly non-specific, meaning that it recognizes a broad range of microbial elements, also known as pathogen-associated molecular patterns (PAMPs). All innate immune cells express certain set of receptors called pattern-recognition receptors (PRRs) that recognize specific microbial components that are not found in the host (e.g., peptidoglycan from bacterial cell walls, double-stranded RNA from viruses, unmethylated CpG islands from bacteria, etc.). Upon recognition of these microbes, innate immune cells can either directly kill the pathogen, or help promote a long-lasting "memory" of the pathogen by

activating the adaptive immune system. In short, adaptive immunity involves primarily two cell types—T-cells and B-cells. Both cell types help "train" the body to "remember" the pathogen, should a secondary infection by the same pathogen occur in the future.²⁹

Allergic reactions involve a series of sequential events, starting with the recognition of the allergen, such as pollen, peanut, insect sting, medications, etc. Normally, the host organism will "ignore" the allergen. However, some individuals have a hypersensitive condition, in which their body views an allergen as a microbial threat. Consequently, the innate immune cells end up phagocytosing the allergen, process these allergens into tiny peptide-like antigens, and present these antigens via a transmembrane complex known as major histocompatibility complex (MHC).³⁰ MHC molecules are specifically recognized by naïve T-cells (T-cells that have not "encountered" an antigen yet), and upon recognition & binding, these naïve T-cells are activated and subsequently differentiate into specific effector T-cells, depending on the cytokine stimulation. One branch of T-cells is a cell-type called Th2 cells, which secretes a cytokine called interleukin-4 (IL-4).³¹ IL-4 goes on to activate another adaptive immune cell called B-cells. B-cells undergo rigorous maturation to differentiate into plasma cells, which are responsible for secreting a massive number of immunoglobulins/antibodies.³²

One type of immunoglobulin, called IgE, is primarily responsible for driving allergic reactions. Fully activated and differentiated plasma cells will secrete these IgE antibodies, and these antibodies are specific to the original allergen particle that was processed by the innate immune cells. Secreted IgE antibodies will then "coat" around the surface of another innate immune cell type, called mast cells. This "coating" of mast cells completes the first round of allergic reactions.³³ When the host organism contracts the same allergen in a secondary exposure, this is where the real allergic symptoms begin. This is because the allergen will bind onto the IgE antibodies that are coated on the surface of these mast cells. This antibody binding triggers a massive inflammatory reaction, in which mast cells begin to degranulate and relinquish large amounts of histamine particles. This large release of histamine molecules is what leads to the development of rashes and hives that start to disseminate throughout the skin. In a nutshell, this is how most allergic reactions are coordinated, from start to finish.^{33,34}

AR consists of two phases of allergic responses: early phase and late phase. The early phase of AR is characterized by massive degranulation of mast cells, upon activation of IgE-bound surface receptors. Early phase occurs within minutes to a first few hours post-exposure. This phase is associated with acute nasal symptoms, such as itching, redness, and watering, due to massive release of histamine within the nasal mucosa. In conjunction, the initial release of histamines is coupled to rapid secretion of pro-inflammatory molecules, such as leukotrienes, prostaglandins, and kinins. These molecules lead to an increased vascular permeability, which contributes to the formation of oedema.³⁵

Later phase occurs over several hours post-exposure. By this stage, a large influx of neutrophils, T-cells, monocytes, and eosinophils are trafficked towards the site of damage by following a chemokine gradient that has been set by pro-inflammatory mediators during the early phase. Subsequently, there is heightened inflammation that is characterized by deeper tissue

oedema, perpetuation of nasal congestion, and further mucosal inflammation that enables much more vigorous reaction to allergen exposure.³⁵



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Prevention

The prevention of AR usually is as simple as avoiding the allergen that causes it. However, allergens such as dust mites, pet dander (skin and waste particles) are particularly difficult to avoid, as dust mites are prolific breeders and family pets often require a great amount of care. Fortunately, these allergens can be limited within the household by changing atopic individuals' lifestyles. The National Health Society (NHS) recommends purchasing air-permeable occlusive bedding and covers, which provide barriers to both dust mites and their feces. Carpet flooring is also discouraged, as the insects thrive in dust-rich environments. Regularly cleaning said flooring, pillows, mattresses and other upholstered furniture can also prevent unnecessary allergen exposure. The most effective recommendation they give, however, is the use of high-efficiency particulate air (HEPA) filters in cleaning appliances and air filters. These not only help remove greater amounts of dust from furniture but also prevent the further spread of dust as a result of dry cleaning.^{36,37}

Pet fur, contrary to popular belief, is not the cause of allergic reaction; rather, it is exposure to dead skin matter, saliva, and dried urine or feces particles. The NHS recommends

removing the pet from the home entirely as the most secure option to prevent potential allergic reaction. However, this is not always possible. Aside from this option, other ones include the washing of pets at least once every two weeks, as well as not allowing pets inside bedrooms or onto upholstered furniture.³⁷

Pollen is another major allergen, contributing to roughly 26% of all allergic rhinitis cases in the U.S. Often, due to the flowering of a majority of plant species, pollen allergies are synonymous with seasonal allergies. However, the potential for individuals to suffer from these allergies at other times of the year may be dependent on what specific plant they are allergic to. During these specific seasons, the NHS recommends that atopicc individuals check pollen level counts daily, and to adjust their lifestyle accordingly. These adjustments may include staying at home if the given pollen level is too high, and avoiding line-drying clothing outdoors. Wearing extra protection is also recommended, such as masks and wrap-around glasses. Showering often and thoroughly prevents pollen from staying on individual bodies for too long, which aids in avoiding the allergen.³⁷

Treatment

The treatment of AR can be classified into three main categories, namely avoidance, pharmacological, and immunotherapy treatments.

6.1 - Avoidance Treatment

Avoidance of allergens that are known causes of AR in patients may be difficult, therefore the 2008 ARIA guidelines have reported there is a lack of evidence supporting the effectiveness of avoidance of house dust mites, animal dander, and other such allergens. However, previous studies have shown that cleaning with water at a temperature of 60 degrees celsius removes house dust mites and other allergens as effectively as water at 30 degrees celsius. While this may not be relevant to most sufferers of AR, avoidance is mandatory for occupational AR, which was supported by findings by the European Academy of Allergy and Clinical Immunology (EAACI).³⁸⁻⁴⁰

6.2 - Pharmacological Treatments

Pharmacological treatment is principally based on a stepwise approach based on the severity of the diagnoses as well as the duration of time the symptoms persist. The identification of diagnosis severity can be found in the previous sections under signs and symptoms. The 2008 ARIA guidelines describe the use of leukotriene receptor antagonists in all AR treatments, and that topical steroids are regarded as the most effective drugs for both adult and pediatric patients.

Antihistamines can be further subdivided into the oral and intranasal treatment categories. Oral antihistamines can be categorized into first and second generation antihistamines, with the latter having much more effectiveness in AR treatment. First-generation antihistamines have been in widespread medical use since the late 1940s, and though they provide sufficient relief, they also have numerous notable side effects, including but not limited to sedation, memory impairment, psychomotor dysfunction, and low blood pressure. These side effects can create many problems in clinical practice, which is why ARIA guidelines from 2008 recommend second-generation antihistamines in treatment. As compared to first-generation antihistamines, second-generation antihistamines penetrate the blood-brain barrier far less effectively, leading to a reduction in side effects regarding the central nervous system. Oral antihistamines are effective in the treatment of rhinorrhea, sneezing, nasal itching and eye symptoms but have proved less effective in the control of nasal congestion. In addition, they are proven to be safe and effective in children. Intranasal antihistamines have been shown to reduce nasal pruritus, sneezing, and rhinorrhea in patients, while at the same time effectively reducing eye symptoms in patients. The intranasal application of azelastine twice a day can reduce the symptoms of seasonal AR patients who do not respond to the less effective oral antihistamines. They do, however, present side effects such as sedation and reportedly have a metallic taste.^{39,40}

Since intranasal corticosteroids are not absorbed into the body in a systematic fashion, few side effects are presented through their use. After penetrating the cellular membrane and binding to the cytoplasmic steroid receptor sites, the steroid-receptor complex is then transferred to the nucleus and binds the specific DNA site. The anti-inflammatory effect then occurs through the modification of protein synthesis following the binding of the steroid-receptor complex to DNA or by affecting other transcriptional factors. These types of corticosteroid treatments inhibit early and late reactions of AR, and reduce Immunoglobulin E (IgE) production and eosinophilia by preventing cytokine IL-4, IL-5, and IL-13 secretion. This treatment is effective in all AR symptoms, particularly nasal obstruction and eye swelling and itching symptoms.^{39,40}

The role of leukotrienes in allergic reactions has been thoroughly studied, and Leukotriene receptor antagonists, or LTRAs, aim to take the same success the medicine demonstrated in asthma patients and replicate it in cases of AR. In asthma patients, the typical reaction pathway for leukotrienes involves its synthesis from arachidonic acid following the action of 5-lipoxygenase in many inflammatory airway cells (macrophages, dendritic cells, etc.). This arachidonic acid is then released by membrane phospholipase A2. Following the release, thromboxane and prostaglandins are produced from the acid via the cyclooxygenase pathway. LTRAs inhibit the function of phospholipase A2, thus preventing the formation of inflammatory compounds such as prostaglandin and leukotrienes.⁴¹ In 2008, ARIA guidelines re-evaluated the medicinal value of LTRAs. Currently, Pranlukast (commercially known as Onon), Montelukast (Singulair) are available as over-the-counter medication. Both, however, should be taken carefully in clinical and personal settings, as Pranlukast's serum concentration can be elevated if a patient is administered other medication such as terfenadine, astemizole, and others. And while Montelukast is effective in reducing nasal and ocular symptoms, the synergic effect of loratadine and montelukast has created controversy. Currently, in terms of effectiveness, these stand above antihistamines but below intranasal corticosteroids.

Anti- IgE antibodies commonly take the form of Omalizumab, a recombinant humanized monoclonal antibody, which interferes with the interactions between mast cells and IgE by
binding to the surface of free IgE, resulting in lower levels of serum IgE. These medications also suppress inflammatory reactions in blood or nasal mucosa. While effective in treating seasonal AR, side effects such as headaches, upper respiratory infections and sinusitis must be noted.⁴²

6.3 - Immunotherapy

Immunotherapy is an important therapeutic option because it is the only one that modifies the basic allergic reaction. It induces the desensitization of the body for offending allergens by producing an anergy (absence of immune response) state. Initially, Immunotherapy was proposed for seasonal AR due to pollen. However, its use has now been extended to other allergic diseases. The process is as follows. Initially, extracts of offending allergens are injected subcutaneously with increasing doses until a specific maintenance dose is discerned. Following this identification, this maintenance dose is administered for a time greater than or equal to 3 years. While subcutaneous immunotherapy is a common and relatively safe treatment option, the risk of anaphylaxis, a severe, potentially life-threatening allergic reaction, has led to the development of other administrative routes such as oral, nasal, or even sublingual routes.^{43,44}

Sublingual immunotherapy (SLIT) has been used for a significant period of time in European countries not only because of its non-invasive nature, but also because of the low incidence rate of adverse effects and convenience of the self - administration of the medication. More recently, SLIT has even replaced subcutaneous treatment. The mechanism of SLIT treatment begins with the regulation of antigen specific responses (increasing the IgG4/IgE ratio), inhibition of activation of inflammatory cells, and the shift of Th2/Th1 responses and activation of regulatory T cells. These regulatory T cells are known to play a crucial role in immune tolerance, which allow for high-dose extracts for SLIT to induce them.⁴⁵

Conclusion

Allergic Rhinitis along with other diseases in the hypersensitive immune disorder category, have been studied extensively over the course of the last several decades, not because of their lethality but because of their extensive and ever increasing prevalence. The significant increase in case number combined with its incurability pose major unmet needs to alleviate these issues and ameliorate the lives of patients that suffer from it. Despite this, major advancements have been made in the treatment of Allergic Rhinitis, and tools such as IgE antibody treatment and immunotherapy offers patients various effective choices for both symptom control and long term management. However, while significant progress has been made regarding the action of resulting treatment options of Allergic Rhinitis, there remain many important unresolved questions that warrant further research and development. Research on variation between allergen-mediated cellular mechanisms at local sites between AR patients, as well as the pathogenic mechanisms such as the breakdown of nasal epithelial barrier integrity, may lead to the development of more precise and targeted therapies, and may present improved strategies for allergen avoidance.

In closing, this review paper examines the characteristics of AR, starting with critical risk factors as well as diagnosis, followed by the pathophysiology of the disease and current understanding and recent therapeutic developments. No doubt with the completion of further research into some of the important, unanswered questions regarding AR, the increased mechanistic understanding of allergic diseases such as AR will help uncover new methods of combating the progression of the disease.

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Works Cited

- InformedHealth.org [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2006-. Hay fever: Overview. [Updated 2020 Apr 23]. Available from: <u>https://www.ncbi.nlm.nih.gov/books/NBK279488/</u>
- Wang X, Zhuang Y, Chen Y, Wang H, Wang X. Prevalence of adult eczema, hay fever, and asthma, and associated risk factors: a population-based study in the northern Grassland of China. Allergy Asthma Clin Immunol. 2021 Mar 9;17(1):27. doi: 10.1186/s13223-021-00532-7. PMID: 33750462; PMCID: PMC7941905.
- Wang DY. Risk factors of allergic rhinitis: genetic or environmental? Ther Clin Risk Manag. 2005 Jun;1(2):115-23. doi: 10.2147/tcrm.1.2.115.62907. PMID: 18360551; PMCID: PMC1661616.
- Wu AC, Dahlin A, Wang AL. The Role of Environmental Risk Factors on the Development of Childhood Allergic Rhinitis. Children (Basel). 2021 Aug 17;8(8):708. doi: 10.3390/children8080708. PMID: 34438599; PMCID: PMC8391414.
- Averbeck M, Gebhardt C, Emmrich F, Treudler R, Simon JC. Immunologic principles of allergic disease. J Dtsch Dermatol Ges. 2007 Nov;5(11):1015-28. English, German. doi: 10.1111/j.1610-0387.2007.06538.x. PMID: 17976144.
- InformedHealth.org [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2006-. Allergies: Overview. [Updated 2020 Apr 23]. Available from: <u>https://www.ncbi.nlm.nih.gov/books/NBK447112/</u>
- Gosset P, Tillie-Leblond I, Malaquin F, Durieu J, Wallaert B, Tonnel AB. Interleukin-8 secretion in patients with allergic rhinitis after an allergen challenge: interleukin-8 is not the main chemotactic factor present in nasal lavages. Clin Exp Allergy. 1997 Apr;27(4):379-88. PMID: 9146930.
- Nurmatov UB, Tagiyeva N, Semple S, Devereux G, Sheikh A. Volatile organic compounds and risk of asthma and allergy: a systematic review. Eur Respir Rev. 2015 Mar;24(135):92-101. doi: 10.1183/09059180.00000714. PMID: 25726560; PMCID: PMC9487771.
- Ferreira MA, Vonk JM, Baurecht H, Marenholz I, Tian C, Hoffman JD, Helmer Q, Tillander A, Ullemar V, van Dongen J, Lu Y, Rüschendorf F, Esparza-Gordillo J, Medway CW, Mountjoy E, Burrows K, Hummel O, Grosche S, Brumpton BM, Witte JS, Hottenga JJ, Willemsen G, Zheng J, Rodríguez E, Hotze M, Franke A, Revez JA, Beesley J, Matheson MC, Dharmage SC, Bain LM, Fritsche LG, Gabrielsen ME, Balliu B; 23andMe Research Team; AAGC collaborators; BIOS consortium; LifeLines Cohort Study; Nielsen JB, Zhou W, Hveem K, Langhammer A, Holmen OL, Løset M, Abecasis GR, Willer CJ, Arnold A, Homuth G, Schmidt CO, Thompson PJ, Martin NG, Duffy DL, Novak N, Schulz H, Karrasch S, Gieger C, Strauch K, Melles RB, Hinds DA, Hübner N, Weidinger S, Magnusson PKE, Jansen R, Jorgenson E, Lee YA, Boomsma DI, Almqvist C, Karlsson R, Koppelman GH, Paternoster L. Shared genetic origin of asthma, hay fever and eczema

elucidates allergic disease biology. Nat Genet. 2017 Dec;49(12):1752-1757. doi: 10.1038/ng.3985. Epub 2017 Oct 30. PMID: 29083406; PMCID: PMC5989923.

- Drake LY, Kita H. IL-33: biological properties, functions, and roles in airway disease. Immunol Rev. 2017 Jul;278(1):173-184. doi: 10.1111/imr.12552. PMID: 28658560; PMCID: PMC5492954.
- Cayrol C. IL-33, an Alarmin of the IL-1 Family Involved in Allergic and Non Allergic Inflammation: Focus on the Mechanisms of Regulation of Its Activity. Cells. 2021 Dec 30;11(1):107. doi: 10.3390/cells11010107. PMID: 35011670; PMCID: PMC8750818.
- Soyka MB, Holzmann D, Basinski TM, Wawrzyniak M, Bannert C, Bürgler S, Akkoc T, Treis A, Rückert B, Akdis M, Akdis CA, Eiwegger T. The Induction of IL-33 in the Sinus Epithelium and Its Influence on T-Helper Cell Responses. PLoS One. 2015 May 1;10(5):e0123163. doi: 10.1371/journal.pone.0123163. PMID: 25932636; PMCID: PMC4416791.
- Tizaoui K, Terrazzino S, Cargnin S, Lee KH, Gauckler P, Li H, Shin JI, Kronbichler A. The role of PTPN22 in the pathogenesis of autoimmune diseases: A comprehensive review. Semin Arthritis Rheum. 2021 Jun;51(3):513-522. doi: 10.1016/j.semarthrit.2021.03.004. Epub 2021 Mar 4. PMID: 33866147.
- Song SH, Wang XQ, Shen Y, Hong SL, Ke X. Association between PTPN22/CTLA-4 Gene Polymorphism and Allergic Rhinitis with Asthma in Children. Iran J Allergy Asthma Immunol. 2016 Oct;15(5):413-419. PMID: 27917628.
- Van Coillie S, Wiernicki B, Xu J. Molecular and Cellular Functions of CTLA-4. Adv Exp Med Biol. 2020;1248:7-32. doi: 10.1007/978-981-15-3266-5_2. PMID: 32185705.
- Botturi, K., Lacoeuille, Y., Cavaillès, A. *et al.* Differences in allergen-induced T cell activation between allergic asthma and rhinitis: Role of CD28, ICOS and CTLA-4. *Respir Res* 12, 25 (2011). <u>https://doi.org/10.1186/1465-9921-12-25</u>
- O'Brien J, Hayder H, Zayed Y, Peng C. Overview of MicroRNA Biogenesis, Mechanisms of Actions, and Circulation. Front Endocrinol (Lausanne). 2018 Aug 3;9:402. doi: 10.3389/fendo.2018.00402. PMID: 30123182; PMCID: PMC6085463.
- Specjalski K, Jassem E. MicroRNAs: Potential Biomarkers and Targets of Therapy in Allergic Diseases? Arch Immunol Ther Exp (Warsz). 2019 Aug;67(4):213-223. doi: 10.1007/s00005-019-00547-4. Epub 2019 May 28. PMID: 31139837; PMCID: PMC6597590.
- Weidner J, Bartel S, Kılıç A, Zissler UM, Renz H, Schwarze J, Schmidt-Weber CB, Maes T, Rebane A, Krauss-Etschmann S, Rådinger M. Spotlight on microRNAs in allergy and asthma. Allergy. 2021 Jun;76(6):1661-1678. doi: 10.1111/all.14646. Epub 2020 Nov 20. PMID: 33128813; PMCID: PMC8246745.
- Rosenkranz RR, Rosenkranz SK, Neessen KJ. Dietary factors associated with lifetime asthma or hayfever diagnosis in Australian middle-aged and older adults: a cross-sectional study. Nutr J. 2012 Oct 12;11:84. doi: 10.1186/1475-2891-11-84. PMID: 23057785; PMCID: PMC3544658.

- Rosenlund H, Kull I, Pershagen G, Wolk A, Wickman M, Bergström A. Fruit and vegetable consumption in relation to allergy: disease-related modification of consumption? J Allergy Clin Immunol. 2011 May;127(5):1219-25. doi: 10.1016/j.jaci.2010.11.019. Epub 2011 Jan 8. PMID: 21215999.
- Akhouri S, House SA. Allergic Rhinitis. [Updated 2023 Jul 16]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538186/
- Lourenço O, Bosnic-Anticevich S, Costa E, Fonseca JA, Menditto E, Cvetkovski B, Kritikos V, Tan R, Bedbrook A, Scheire S, Bachert C, Białek S, Briedis V, Boussery K, Canonica GW, Haahtela T, Kuna P, Novellino E, Samoliński B, Schünemann HJ, Wallace D, Bousquet J. Managing Allergic Rhinitis in the Pharmacy: An ARIA Guide for Implementation in Practice. Pharmacy (Basel). 2020 May 16;8(2):85. doi: 10.3390/pharmacy8020085. PMID: 32429362; PMCID: PMC7355936.
- Sheikh A, Singh Panesar S, Salvilla S, Dhami S. Hay fever in adolescents and adults. BMJ Clin Evid. 2009 Nov 18;2009:0509. PMID: 21726475; PMCID: PMC2907832.
- Birch K, Pearson-Shaver AL. Allergy Testing. [Updated 2023 Jul 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <u>https://www.ncbi.nlm.nih.gov/books/NBK537020/</u>
- Ansotegui IJ, Melioli G, Canonica GW, et. al., IgE allergy diagnostics and other relevant tests in allergy, a World Allergy Organization position paper. World Allergy Organ J. 2020 Feb 25;13(2):100080. doi: 10.1016/j.waojou.2019.100080. Erratum in: World Allergy Organ J. 2021 Jun 17;14(7):100557. PMID: 32128023; PMCID: PMC7044795.
- Alberts B, Johnson A, Lewis J, et al. Molecular Biology of the Cell. 4th edition. New York: Garland Science; 2002. Innate Immunity. Available from: <u>https://www.ncbi.nlm.nih.gov/books/NBK26846/</u>
- Janeway CA Jr, Travers P, Walport M, et al. Immunobiology: The Immune System in Health and Disease. 5th edition. New York: Garland Science; 2001. Principles of innate and adaptive immunity. Available from: <u>https://www.ncbi.nlm.nih.gov/books/NBK27090/</u>
- Janeway CA Jr, Travers P, Walport M, et al. Immunobiology: The Immune System in Health and Disease. 5th edition. New York: Garland Science; 2001. Principles of innate and adaptive immunity. Available from: <u>https://www.ncbi.nlm.nih.gov/books/NBK27090/</u>
- Janeway CA Jr, Travers P, Walport M, et al. Immunobiology: The Immune System in Health and Disease. 5th edition. New York: Garland Science; 2001. The major histocompatibility complex and its functions. Available from: https://www.ncbi.nlm.nih.gov/books/NBK27156/
- Berger A. Th1 and Th2 responses: what are they? BMJ. 2000 Aug 12;321(7258):424. doi: 10.1136/bmj.321.7258.424. PMID: 10938051; PMCID: PMC27457.
- Alberts B, Johnson A, Lewis J, et al. Molecular Biology of the Cell. 4th edition. New York: Garland Science; 2002. Helper T Cells and Lymphocyte Activation. Available from: <u>https://www.ncbi.nlm.nih.gov/books/NBK26827/</u>

- Hostoffer RW, Joseph N. Immunoglobulin E. [Updated 2022 Sep 9]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <u>https://www.ncbi.nlm.nih.gov/books/NBK482212/</u>
- Leung DY. Molecular basis of allergic diseases. Mol Genet Metab. 1998 Mar;63(3):157-67. doi: 10.1006/mgme.1998.2682. PMID: 9608537.
- Min YG. The pathophysiology, diagnosis and treatment of allergic rhinitis. Allergy Asthma Immunol Res. 2010 Apr;2(2):65-76. doi: 10.4168/aair.2010.2.2.65. Epub 2010 Mar 24. PMID: 20358020; PMCID: PMC2846743.
- Royal C, Gray C. Allergy Prevention: An Overview of Current Evidence. Yale J Biol Med. 2020 Dec 29;93(5):689-698. PMID: 33380931; PMCID: PMC7757062.
- Liu Y, Liu Z. Epidemiology, Prevention and Clinical Treatment of Allergic Rhinitis: More Understanding, Better Patient Care. J Clin Med. 2022 Oct 14;11(20):6062. doi: 10.3390/jcm11206062. PMID: 36294381; PMCID: PMC9605427.
- InformedHealth.org [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2006-. Hay fever: Which medications can relieve allergic rhinitis? [Updated 2020 Apr 23]. Available from:
 - https://www.ncbi.nlm.nih.gov/books/NBK279486/
- Wood SF. Treatment of hay fever. J R Coll Gen Pract. 1989 Jul;39(324):292-6. PMID: 2556545; PMCID: PMC1711909.
- Emeryk A, Emeryk-Maksymiuk J, Janeczek K. New guidelines for the treatment of seasonal allergic rhinitis. Postepy Dermatol Alergol. 2019 Jun;36(3):255-260. doi: 10.5114/ada.2018.75749. Epub 2019 Jun 18. PMID: 31333340; PMCID: PMC6640027.
- Ferreira MA. Cytokine expression in allergic inflammation: systematic review of in vivo challenge studies. Mediators Inflamm. 2003 Oct;12(5):259-67. doi: 10.1080/09629350310001619717. PMID: 14760932; PMCID: PMC1781628.
- Hu J, Chen J, Ye L, Cai Z, Sun J, Ji K. Anti-IgE therapy for IgE-mediated allergic diseases: from neutralizing IgE antibodies to eliminating IgE+ B cells. Clin Transl Allergy. 2018 Jul 18;8:27. doi: 10.1186/s13601-018-0213-z. PMID: 30026908; PMCID: PMC6050685.
- InformedHealth.org [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2006-. Hay fever: Allergen-specific immunotherapy (desensitization) in the treatment of allergies. [Updated 2020 Apr 23]. Available from: <u>https://www.ncbi.nlm.nih.gov/books/NBK279487/</u>
- Persaud Y, Memon RJ, Savliwala MN. Allergy Immunotherapy. [Updated 2023 May 1]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <u>https://www.ncbi.nlm.nih.gov/books/NBK535367/</u>
- Han DH, Rhee CS. Sublingual immunotherapy in allergic rhinitis. Asia Pac Allergy. 2011 Oct;1(3):123-9. doi: 10.5415/apallergy.2011.1.3.123. Epub 2011 Oct 11. PMID: 22053308; PMCID: PMC3206241.

Comprehensive Review of Brain-Computer Interfaces By Victor Zheng

Abstract

Immerse yourself into the world of Brain-Computer Interfaces (BCIs), a world where thoughts become actions. BCIs have great promise for reshaping mental health care, improving cognitive ability, increasing economic production, and restoring mobility. From healthcare to entertainment, BCIs are poised to revolutionize how we engage with technology and supercharge our mental faculties, but as they evolve they also bring forth significant problems, with security, privacy, and ethics at the forefront.

Introduction

A Brain-Computer Interface (BCI) is a computer-based system that acquires brain signals from the central nervous system (CNS), and peripheral nerves and muscles. It analyzes them and translates them into commands for an output device.¹ BCIs act as an external communication gateway for the human brain to an external device or application. They enable users to act on the world using brain signals instead of muscles. BCIs can translate brain activity into signals that a device can interpret. However, they are not mind-reading devices in the sense of extracting knowledge or mental intellect from the patient.^{1,2}

Currently, BCIs have medical applications, such as assisting people with nerve damage or detecting epilepsy. They can detect physiological states and intended movements, such as blinking and moving an arm, but they cannot read specific thoughts. BCIs can be invasive or non-invasive, with non-invasive systems being more patient-friendly, but they can lead to worse signals. For more clarification, an electroencephalogram (EEG) alone is not a BCI because it only records brain signals without generating an output.^{1,2}

This review article will provide a comprehensive understanding of BCI and its practical applications. First, it will start with the fundamental background of neuroanatomy and the physiological factors that govern the nervous system. It will then provide the basic components of BCI and factors that influence its performances. Furthermore, it will explore the current usages and applications of BCI, along with its associated benefits and disadvantages. Finally, it will lay out some of the current and prospective challenges that are associated with BCI's technology.

Background in Neuroanatomy

The nervous system is a complex and sophisticated system that coordinates nearly all body activities, such as mobility, cognition, metabolism, host defense, transport, growth, reproduction, and many more.³ The key player that drives the nervous system is called the neuron, which uses both electrical and chemical signals to facilitate cell-cell communication throughout the body. The neuron primarily consists of 3 components: (1) the dendrite, which receives information from adjacent neurons, (2) the cell body, which contains the neuron's

genetic information and provides energy to drive neuronal activities, and (3) the axon, which carries electrical signals across a thin fiber to neighboring neurons.^{3,4}



Figure 1. The Anatomy of a Neuron (Image adapted from CUSABIO)

One of the vital features of a neuron is the ability to communicate signals *very rapidly*. If someone were to accidentally place their hand on a hot stove, the pain receptors on their hands will deliver "pain" signals to the sensory neurons, which then convey the message directly to the brain. From there, the brain sends signals that travel back to the same hand to draw back their hand away from the hot stove. In order for the body to regulate these signaling, a rapid-relay mechanism is necessary to transmit signals both rapidly and efficiently.⁵

First, a series of <u>electrical signals</u> is conveyed and exchanged along the neuron's axon. The fundamental driver of these electrical signals is dependent on electric potential differences (i.e., voltage) between the cytosol and the extracellular environment.⁶ Voltage exists because there is an unequal distribution of ions across the plasma membrane. When cells are at rest (i.e., not actively sending neuronal signals), a cell's resting potential can be measured. Resting membrane potential in human neurons is between -70 to -80 mV. This is because when neurons are at rest, the sodium-potassium pump actively pumps 3 Na⁺ ions *out* of the cell and 2 K⁺ ions *into* the cell, which consequently results in more accumulation of positive charged ions *outside* the cell relative to the cell's interior. Furthermore, during rest potential, most ion channels are closed except for potassium channels, which further contributes to the negatively charged membrane potential as the cell spontaneously loses K⁺ ions.^{6,7}

When neurons receive signals (usually in the form of a neurotransmitter), the electric potential difference shifts from a negative resting membrane potential to a more positive membrane potential because more ion channels start to open up. This process is called depolarization, and the major contributor of membrane depolarization is the opening of sodium channels, which consequently allow rapid influx of Na⁺ ions across its concentration gradient (From outside to inside the cell). If the initial depolarization exceeds a specific threshold

potential, the impulse (aka action potential) will travel along the neuron's axon. The propagation of action potential follows a "domino" model. In other words, when one sodium channel opens to trigger depolarization, this sets the stage for the adjacent sodium channels to follow suit, which enables the action potential to permeate across the end of the neuron.^{6,7}

Eventually, the neuron will need to undergo repolarization, which is the process of closing the sodium channels and subsequently stopping the rush of positively charged ions into the cells. At the same time, potassium channels start to open, which enables the efflux of K^+ out of cells, restoring the membrane's resting potential. This prompts the neuron to make itself available for receiving another signal in the future.^{6,7}

These changes in electrical activities drive the nervous system to transmit different types of action potentials across the body, each producing a unique response. When a person accidentally touches a hot surface, the pain receptors will automatically trigger a movement away from the source. When a person hears the sound of loud fireworks, they will naturally jerk away from the source. Although both stimuli result in a similar response, the brain will interpret these signals differently because different receptors engage in different pathways, which is reflected by the unique propagation of action potential patterns. Altogether, BCI can either use an unintentional, cognitive state of the brain or brain waves generated as response to an external signal to evoke a physical response.⁸ It is important that BCI properly distinguishes specific electrical activities that don't have overlapping electrical signals led by another physiological event.^{1,2,8} The most commonly studied signals are the electrical signals produced via neuronal postsynaptic membrane polarity changes that occur in response to the activation of voltage-gated ion channels.



The Components of Brain-Computer Interface

Figure 2. Components of BCI (Image adapted from Nguyen et. al (IEEE, 2018))

1. Signal Acquisition

The foundation of utilizing EEG lies in the groundbreaking work of Hans Berger, who in 1924 first revealed the possibility to measure electrical brain signals from the scalp. In stark contrast to Invasive BCIs, which require neurosurgical implants within the skull, EEG electrodes placed on the scalp have emerged as more patient-friendly. These saline based electrodes capture signals, while refraining from causing any discomfort or sensory stimuli. To capture EEG signals, a technician attaches electrodes with a saline based adhesive which is held in place by an electrode cap attached to your head, which then connects to an electrical board amplifying and recording brain waves which then displays it on a BCI based software. During the test, lasting between 20 and 40 minutes, you remain at ease with closed eyes. Guided by the technician, you intermittently open and close your eyes, perform simple calculations, read a paragraph, view an image, practice deep breathing, or observe a flashing light. Once these signals are acquired, they undergo meticulous signal processing to eliminate electrical noise and irrelevant signals before being digitized.^{9,29}

2. Feature Extraction

The process of feature extraction enhances the interpretability of raw brain signals. The most prevalent techniques employed are the Fast Fourier Transform (FFT) and power spectral density analysis. By employing the fast Fourier transform, specific frequency bands of the user's brain waves are isolated. Also, artifacts are removed from the signals, 60 hz notch filtering is also used to remove other background interferences.^{9,29}

3. Feature Translation and Control of Devices

These features undergo translation and classification into control commands, enabling interaction with external devices. This translation process involves meticulously mapping these features to commands, actions. Robotic arm operation, cursor movement and control, are all examples of device feedback to the user.^{9,29}

Factors Influencing BCI Performances

There are three essential criteria that influence BCI's performance: (1) signal acquisition, (2) reliability, and (3) system validation and dissemination . As mentioned in the previous section, BCI needs to acquire unique, distinguishable signals that don't overlap with other physiological functions. Ideally, noninvasive, EEG-based BCIs consist of electrodes that do not require skin penetration, and it should be portable, convenient, cosmetically acceptable, easy to set-up and maintain, and perform well in all environments. But some BCI technology requires the electrodes to be implanted, which can result in a number of issues. It is essential that these implanted electrodes are safe, functional, and non-invasive to normal cellular functions. Furthermore, these implanted electrodes must be able to charge *in situ* or contain batteries that

comfortably last a few years or decades–otherwise, the patient would need frequent surgeries to replace the electrodes, which can be uncomfortable and burdensome.^{10,11}

It is also important to maintain an acceptable threshold of signal-to-noise ratio. There are many intrinsic factors that can influence the baseline performance of BCI technology (e.g., user's attention span, diet, single nucleotide polymorphism, and other psychophysiological traits). Because of these intrinsic signal variations, BCI systems require subject-specific training, during which subjects attend a calibration session-i.e., to "normalize" the BCI's integrative system across all patients. To circumvent these tedious training exercises, the concept of inter-subject associative modules for individuals who share common brain dynamics have been proposed.^{10,11} Perhaps one of the biggest factors that influences BCI's performance is its reliability-Is the BCI technology as reliable as natural muscle-based actions? Muscular movements can be extremely complex, and thus, the practical usefulness of BCI would remain limited to basic restorative functions appropriate for patients with severe mobility dysfunction. Normal muscle-based skills require coordination with the central nervous system, as well as continual activity-dependent plasticity throughout the brain and the spinal cord. In essence, this perpetual plasticity is what enables toddlers to walk, children to learn and speak, and adults to acquire athletic and intellectual skills. However, BCI operation relies on the binary junction between the central nervous system and BCI itself. Integrating the "learning" aspect, particularly in infants and children, can be a huge challenge, which makes BCI much less reliable as a long-term technology. To this day, this fundamental, dynamic interaction between the central nervous system and motor development remains obscure and requires more substantial research.^{10,11}

Finally, it is important to assess the <u>social validation</u> of BCI. Current BCIs are useful mainly for individuals with severe motor disabilities, which implies that the technology is nascent at best, and there isn't adequate incentive for commercial demand to mass produce them at large scale to promote their widespread dissemination. Initial cost burden for invasive BCIs can be massive, coupled with perpetual technical support. In the long term, BCI technology would require substantial increase in the number of users, as well as ensuring reimbursements from the federal government and/or insurance companies in order to become a practical, supportive application for its customers. This would require clear evidence that BCIs can indeed improve motor rehabilitation without significantly compromising the patient's spiritual health.^{10,11}

Current Usage and Applications

BCI technology is highly ubiquitous, and its application is widely applicable across multiple, diverse fields, such as medicine, education, games & entertainment, and neuromarketing & advertisement. The following sections describe the practical application of BCI in the aforementioned sections.

1. Medicine

One of the fundamental applications of BCI is the ability to help patients with severe disabilities to interact and communicate with their environment, fostering independence. For example, BCIs have eased pain from spinal cord injuries. A spinal cord injury interrupts the communication between the brain and the region of the spinal cord that produces walking, which leads to paralysis. BCI consists of fully implanted recording and stimulation systems that establish a direct link between cortical signals and the electrical stimulation targeting the spinal cord regions that regulate mobility.¹²

BCI has also shown promising signs of treatments for mental and sleep disorders, such as ADHD. The standard treatment for ADHD includes mainly medication and psychosocial or behavioral treatment. In one study, a new intensive BCI-based attention training game has monitored unmedicated ADHD children using headband and dry EEG sensors, which was used to drive a feed-forward game. These sensors were positioned to detect EEG patterns from the children's frontal sites (FP1 and FP2). Participants were then asked to play a training game, CogoLand, which is a game that involves moving an avatar based on how well participants "concentrate." The greater the participants were able to concentrate, the faster the avatar would move. During each game trial, the participant's EEG was heavily monitored. After several rounds of training exercise, these children started to develop greater concentration skills, and they were able to perform significantly better in assessment exams that involved recalling information.¹³

Finally, BCI has shown promising treatment benefits for migraines and other related headaches. Migraines can be painful because they involve the trigeminal nerve underneath the skin of the forehead. A BCI device can potentially alleviate pain by stimulating the trigeminal nerve and its innervating branches using a short electric current to redirect the motor nerve. Therefore, it may be possible that BCI technology can artificially alter the direction of electric current flow away from specific localities.¹⁴

2. Cognitive biometrics

Modern-day technology has enabled the emergence of many unique forms of biometric authentication, such as fingerprint, facial recognition, retina scan, and sound. However, many of these current biometric authentication methods can still be bypassed by a fraudulent party. However, BCI can provide a unique framework because BCI biometrics are performed through brain-oriented sensors where a Brainsense headband is used as Bluetooth through which we can capture brain signals via electrically charged beams. These electrical information transmitted by the brain are extracted, processed, and interpreted by a secondary platform, such as Matlab, which can finally send the processed signal for final authentication. Brain signals are innate and unique to a particular individual, and they do not have the problem of visibility to copy it.^{15,16}

First, a signal needs to be acquired using either invasive or non-invasive means. Some methods focus solely on EEG signals, but others rely on capturing specific neurological activity. Then, the signals need to be pre-processed by clearing off all external noise and artifacts (e.g., eye blinks, eye movements, heartbeats, and any other muscle movement). After preprocessing and filtering, EEG signals will pass through extraction procedures that rely on certain algorithms, and these signals will be interpreted by an authenticator to validate the user's identity.^{15,16}

3. Games and Entertainment

BCI technology doesn't necessarily have to be only applicable for medicine, biometrics, or other practical applications. Healthy individuals can also benefit from BCI gaming and entertainment. Studies have demonstrated examples of BCI applications in well-known games, such as Pacman, Pinball, Tetris, and World of Warcraft. BCI forms a closed loop on its framework consisting of 5 elements: 1) control paradigm; 2) measurement; 3) processing; 4) prediction; and 5) application. These 5 steps would interpret a user's intention or mental state and uses that information to run the application.^{17,18}

During control paradigm, a user would "imagine" body part movement or "concentrate" on a certain object to generate brain signals that include the user's intention. These parameters will be measured by BCI, with EEG being the most popular, noninvasive form. Then these brain signals are processed to maximize signal-to-noise ratio. Finally, these brain signals will be used to predict the next outcome of the application, and the output will be employed to change the environment of the application.^{17,18,19}

One example of BCI application in gaming is pinball. In one study, a pinball game employed BCI for control of left and right paddles. The purpose of this application is to discriminate between two classes of motor imagery: left or right hand movement. When a user imagines right-hand movement, the amplitude of the activity in the mu-rhythm in the sensory-motor area of the brain decreases in the left hemisphere and increases in the right hemisphere. For motor imagery on the left-hand movement, the converse occurs. Through signal processing, BCI can detect spatially distinct patterns and decide which direction the user intends. And subsequently, this information is used to control the application's paddles (left or right). In other words, the user initiates brain activity, and the information is captured and processed to control the movement of game paddles–all done through electrical signaling.¹⁹

Benefits and Advantages of BCI

It is clear that BCI offers practical applications and real-life usages that help improve the quality of life. This section will explore some of the benefits of BCI.

1. Restoration of Mobility and Motor Functions

As mentioned throughout the article, one of the practical applications of BCI is to enable patients with impaired motor function to restore normal life. These devices, whether it's invasive or non-invasive, can give patients direct motor control over exoskeletons and prosthetic limbs. BCI would read the electrical signals from the patient's brain, and effectively bypass the site of injury–severed spinal cord or loss of neuromuscular activity.

Furthermore, BCI applications can be extended to other severe forms of neurological disorders and pathologies, such as ALS, cerebral palsy, brainstem stroke, spinal cord injuries, muscular dystrophies, or chronic peripheral neuropathies.²⁰

2. Mental Health

Aside from physiological conditions, BCI can potentially one day be extended to quench psychiatric conditions, such as bipolar disorders, obsessive compulsive disorders, depression, and anxiety. This can be achieved by delivering targeted electrical stimulation to specific parts of the brain.

During the COVID-19 pandemic, there has been a rapid acceleration in the increased number of mental health concerns and illnesses. BCI can serve as a cornerstone to better support mental well-being and detect illnesses as early as possible, using neuronal signaling and electrical activities. Technologies like these do already exist–you can measure the concentration of serotonin levels in patients to evaluate their cognition and mental state. However, these tests often require expensive technologies such as positron emission tomography (PET), which may not be affordable for a lot of patients. Alternatively, if BCI can provide a cost-effective resolution to quickly measure the electrical activities of the patient that corresponds to serotonin/dopamine secretion, it can become a new frontier for early clinical diagnosis of mental disorders.²⁰

3. Cognitive Enhancement

As described in the "Games and Entertainment" section above, BCI users can train their brains–e.g., memory and processing speed–to the biofeedback they receive from a neural implant in real time. Emerging studies show that certain patterns of electrical impulses ("spikes") trigger a cascade of changes in neuronal circuits linked to learning, memory, and judgment.

One practical example of BCI-mediated cognitive enhancement is ChatGPT-4, which is an AI-driven BCI that promises to enhance human cognition and pave the way for a new era of cognitive enhancement. By leveraging advanced natural language processing algorithms, ChatGPT-4 is able to understand and interpret human thoughts with remarkable accuracy, allowing users to communicate with their device using only their minds. This groundbreaking technology has the potential to transform the way users interact with their computers, making it possible to perform complex tasks and access information with unparalleled speed and efficiency. ChatGPT-4 could be used to provide real-time assistance with problem-solving, decision making, and creative tasks, effectively amplifying our natural abilities.²¹

4. Economic Advantages

With the growing advancement in artificial intelligence, BCI could be one of these emerging technologies that could be a catalyst to supercharge productivity and efficiency for businesses. BCI technology can enable employees to focus their minds on a specific task that they want to achieve, and subsequently transmit these instructions to a secondary device or application. For example, individuals can use BCI to change channels on a TV, share screens back and forth during Zoom meetings, send messages on a platform like Slack, write and submit reports, etc. This means that individuals will not be "wasting time" typing out messages, manually switching between different modes during Zoom meetings, handwriting and/or typing progress reports, etc. Businesses can now utilize these extra time to expand and complete other projects, which can ultimately help increase both the top and bottom line of their income statement.

At the end of the day, higher business productivity equates to increased net gross domestic products (GDP), thereby fostering more innovative growth and expansion. If all businesses start adopting BCI as a form of artificial intelligence, worker's productivity would substantially increase, thus providing a positive externality toward society. At first of course, BCI adoption can be a costly investment burden for most businesses, which could initially hurt their cash flow statement. However, it is anticipated that within the next decade or so, BCI would be nearly an essential technology that needs to be adopted (i.e., BCI or any form of AI would be the "new normal," as companies realize that these technologies are vital to their growth and expansion).^{22,23}

Risks, Dangers, and Ethical Concerns Associated with BCI

While BCI provides huge benefits at large scale, this doesn't mean that BCI technology is perfect. This section will explore some of the risks, dangers, and ethical concerns associated with BCI.

1. BCI Security

Although the opportunities BCI has offered for us is substantial, the security of a BCI is mostly very elementary and susceptible to simple malware. During the process of signal output, a malicious hacker can intercept the process of sending brain signals to an external device such as an app or a prosthetic arm and could potentially tamper with that signal to do what the hacker intends or save it and translate it into the user's thoughts to obtain private information. As brain signals can be converted into numbers a hacker could know your passwords, pin numbers, area of living, knowledge of people that you have met. As mobile based BCI are becoming more common, there risk of the users being compromised is at a higher risk as attacks can originate from the mobile device. As BCI such as EEG require there to be a minimum amount of electromagnetic radiation in the surrounding a hacker could also generate enough radiation for the signal acquisition process done electrodes to be poor and inadequate. A new type of biometric authentication which consists of neuron signals specific to the user could be used to access private information could be intercepted and compromised by the hacker if there are not adequate security measures.^{15,16,24}

2. Legislations for BCI Technology

In 2019, the Organization for Economic Cooperation and Development (OECD) emphasized the significant risks associated with brain-computer interfaces. This caution was reiterated in 2021 by the UNESCO Bioethics Committee in a report stating that there is hardly any legislation in place for neurotechnology. However, despite these concerns, many countries have not taken sufficient steps in this realm. Currently, Chile is at the forefront of establishing comprehensive legislation to safeguard neurotech rights. The primary objective of this legislation is to grant personal brain data a status that prohibits its sale, trafficking, or manipulation.²⁴

Challenges

This section will conclude with some of the current and future challenges associated with BCI. Many of these challenges are related to BCI's technology.

1. Types of BCI and the challenges associated with them

a. Invasive

These types of BCI require craniotomy, which is a neurosurgical procedure done where the portion of the brain's skull is removed and the tissue is exposed. These BCI can track all of the action generated by the neurons as they are placed on the brain's cortex, which can lead to higher spatial resolution and higher quality signals. However neurosurgery has many flaws such as being prone to infection, bleeding complications, there is also a possibility of scar tissue formation which results in lower quality signals and tissue scarring. This procedure is very costly also, which is mostly used on blind, and paralyzed patients.^{1,2}

b. Semi-Invasive

To avoid scar tissue formation, the use of a semi-invasive BCI would be beneficial, one example of this would be ECoG, which is great against motion artifacts such as blinking and eye movement. The use of a semi-invasive BCI would still require brain surgery and electrode placement underneath the skull.^{1,2}

c. Non-invasive

The bulk of BCI related research has been conducted using non-invasive BCI such as EEG. These non-invasive EEG techniques are popular because they do not require any surgical setting.^{1,2} Here are some examples of non-invasive BCI:

i. Electroencephalogram (EEG)

Despite its high temporal resolution, safety, ease of use, and affordability, there are several issues needed to improve the accuracy and signal. One of the setbacks is the use of gel or saline based solutions, to improve the contact with the scalp of the patient, thereby reducing the resistance. A faraday cage is also needed to reduce the amount of electromagnetic interference. The use of the 10-20 international system is mandatory because each electrode has to be placed 10-20% total front–back or right–left distance of the skull at an anatomical landmark of a brain and are abbreviated (F for frontal, C for central, P for parietal, O for occipital) even numbers are on the right side and odd numbers are on the left. (10–20 system (EEG) - Wikipedia) Signal quality is more deficient compared to its invasive alternatives, and is more susceptible to background noise interference.²⁵

ii. Magnetoencephalography (MEG)

When neurons become active they generate small electrical currents via action potentials. These electrical currents, in turn, produce weak magnetic fields. MEG measures these extremely faint magnetic fields, which in turn produces a high temporal and spatial resolution of neural events. MEG adds more detail to EEG findings as it relies on magnetic signals rather than electrical ones. During these years, MEG has been more widely used for detecting epilepsy and brain tumors. Recently, improved MEG signals have elicited using more sensitive sensors such as superconducting quantum interference devices (SQUID). MEG systems are hard to maintain and construct, with few institutions having acquired them. Also, they are susceptible to movement which can cause disruption to signals and can be inappropriate for children and people who are diagnosed with motor disease.²⁶

iii. Functional Magnetic Resonance Imaging (fMRI)

This technique is used to measure the change in blood oxygenation levels (BOLD). When a specific region of a brain becomes active to correspond to an outside event, the blood becomes more oxygenated, which could be used for researchers to analyze the brain when the person is put through instances of different stimuli. As it can detect which parts of the brain are

active with high specificity, it can create images of high spatial resolution. It has contributed to research in psychiatric disorders such as depression, social phobia, psychopathy, and stroke. Currently, fMRI BCIs have certain limitations that need to be noted in order to improve them. Traditional imaging methods aim to understand how specific cognitive states are shown in brain activity. They do this by measuring brain activity at thousands of different locations repeatedly and then analyzing each of these locations separately (univariate analysis). If there's a difference in brain activity between two states, researchers can use the activity measurements from that location to decode the state. However, it is very challenging and time consuming to find specific brain locations where the differences between different mental states are significant enough to allow for accurate decoding.^{27,28}

d. Context of P300 ERPs

The most common neurological signal studied is known as the P300 ERP, which is a perceptible positive spike in microvolts which occurs after 300 milliseconds post outside stimulation provided by a P300 speller apparatus. This consists of a grid of alphabetical characters whose rows and columns flash simultaneously on a target character which prompts the patient to conjure a ding sound when it is his/her view. A person diagnosed with locked-in syndrome would operate with this paradigm. An ERP is known as an event related potential, which is the brain's response to a specific sensory event.³⁰

If P300 ERPs are target specific and rely on visual stimuli elicited by external devices, patients with impaired visual processing and locked in syndrome cannot communicate. Also motivation is related to the performance of a P300 BCI. Attention, memory load, fatigue, and competing cognitive processes, as well as individual characteristics such as lifestyle, gender, and age, have a significant impact on the immediate brain activities, and the performance of a P300 BCI.³⁰

Conclusion

In conclusion, brain-computer interfaces (BCIs) are an emerging field of technology with an abundance of potential for applications in a range of fields, such as healthcare, cognitive enhancement, entertainment, and productivity. However, as they evolve and advance, BCIs face difficult ethical concerns along the way. In order to fully realize the transformative potential of BCIs while proactively addressing their associated challenges, research and development initiatives are poised to prioritize improvements in signal quality, the implementation of strong security measures, and the nuanced exploration of ethical considerations.

Works Cited

- Shih JJ, Krusienski DJ, Wolpaw JR. Brain-computer interfaces in medicine. Mayo Clin Proc. 2012 Mar;87(3):268-79. doi: 10.1016/j.mayocp.2011.12.008. Epub 2012 Feb 10. PMID: 22325364; PMCID: PMC3497935.
- Mridha MF, Das SC, Kabir MM, Lima AA, Islam MR, Watanobe Y. Brain-Computer Interface: Advancement and Challenges. Sensors (Basel). 2021 Aug 26;21(17):5746. doi: 10.3390/s21175746. PMID: 34502636; PMCID: PMC8433803.
- InformedHealth.org [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2006-. How does the nervous system work? 2009 Oct 28 [Updated 2016 Aug 19]. Available from: <u>https://www.ncbi.nlm.nih.gov/books/NBK279390/</u>
- Ludwig PE, Reddy V, Varacallo M. Neuroanatomy, Central Nervous System (CNS) [Updated 2022 Oct 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK442010/
- Institute of Medicine (US) Committee on Pain, Disability, and Chronic Illness Behavior;
 Osterweis M, Kleinman A, Mechanic D, editors. Pain and Disability: Clinical,
 Behavioral, and Public Policy Perspectives. Washington (DC): National Academies Press
 (US); 1987. 7, The Anatomy and Physiology of Pain. Available from: https://www.ncbi.nlm.nih.gov/books/NBK219252/
- Grider MH, Jessu R, Kabir R. Physiology, Action Potential. [Updated 2023 May 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <u>https://www.ncbi.nlm.nih.gov/books/NBK538143/</u>
- Pirahanchi Y, Jessu R, Aeddula NR. Physiology, Sodium Potassium Pump. [Updated 2023 Mar 13]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <u>https://www.ncbi.nlm.nih.gov/books/NBK537088/</u>
- Batista A. Brain-computer interfaces for basic neuroscience. Handb Clin Neurol. 2020;168:233-247. doi: 10.1016/B978-0-444-63934-9.00017-2. PMID: 32164855.
- Salahuddin U, Gao PX. Signal Generation, Acquisition, and Processing in Brain Machine Interfaces: A Unified Review. Front Neurosci. 2021 Sep 13;15:728178. doi: 10.3389/fnins.2021.728178. PMID: 34588951; PMCID: PMC8475516.
- Nijboer F, Birbaumer N, Kübler A. The influence of psychological state and motivation on brain-computer interface performance in patients with amyotrophic lateral sclerosis - a longitudinal study. Front Neurosci. 2010 Jul 21;4:55. doi: 10.3389/fnins.2010.00055. PMID: 20700521; PMCID: PMC2916671.
- Hammer EM, Halder S, Kleih SC, Kübler A. Psychological Predictors of Visual and Auditory P300 Brain-Computer Interface Performance. Front Neurosci. 2018 May 14;12:307. doi: 10.3389/fnins.2018.00307. PMID: 29867319; PMCID: PMC5960704.
- Lorach, H., Galvez, A., Spagnolo, V. *et al.* Walking naturally after spinal cord injury using a brain–spine interface. *Nature* 618, 126–133 (2023). <u>https://doi.org/10.1038/s41586-023-06094-5</u>

- Lim CG, Lee TS, Guan C, Fung DS, Zhao Y, Teng SS, Zhang H, Krishnan KR. A brain-computer interface based attention training program for treating attention deficit hyperactivity disorder. PLoS One. 2012;7(10):e46692. doi: 10.1371/journal.pone.0046692. Epub 2012 Oct 24. PMID: 23115630; PMCID: PMC3480363.
- Daly, Janis J., and Ranganatha Sitaram, 'BCI Therapeutic Applications for Improving Brain Function', in Jonathan Wolpaw, and Elizabeth Winter Wolpaw (eds), *Brain–Computer Interfaces: Principles and Practice* (2012; online edn, Oxford Academic, 24 May 2012), https://doi.org/10.1093/acprof:oso/9780195388855.003.0022
- Zhang S, Sun L, Mao X, Hu C, Liu P. Review on EEG-Based Authentication Technology. Comput Intell Neurosci. 2021 Dec 24;2021:5229576. doi: 10.1155/2021/5229576. PMID: 34976039; PMCID: PMC8720016.
- Yap HY, Choo YH, Mohd Yusoh ZI, Khoh WH. Person authentication based on eye-closed and visual stimulation using EEG signals. Brain Inform. 2021 Oct 11;8(1):21. doi: 10.1186/s40708-021-00142-4. PMID: 34633582; PMCID: PMC8505588.
- Moreno-Calderón S, Martínez-Cagigal V, Santamaría-Vázquez E, Pérez-Velasco S, Marcos-Martínez D, Hornero R. Combining brain-computer interfaces and multiplayer video games: an application based on c-VEPs. Front Hum Neurosci. 2023 Aug 3;17:1227727. doi: 10.3389/fnhum.2023.1227727. PMID: 37600556; PMCID: PMC10435322.
- Chang D, Xiang Y, Zhao J, Qian Y, Li F. Exploration of Brain-Computer Interaction for Supporting Children's Attention Training: A Multimodal Design Based on Attention Network and Gamification Design. Int J Environ Res Public Health. 2022 Nov 15;19(22):15046. doi: 10.3390/ijerph192215046. PMID: 36429765; PMCID: PMC9690270.
- Ahn M, Lee M, Choi J, Jun SC. A review of brain-computer interface games and an opinion survey from researchers, developers and users. Sensors (Basel). 2014 Aug 11;14(8):14601-33. doi: 10.3390/s140814601. PMID: 25116904; PMCID: PMC4178978.
- Urwin, M. (2023, July 25). Builtin. https://builtin.com/hardware/brain-computer-interface-bci
- Frąckiewicz, M. (2023, April 12). ChatGPT-4 and the Future of Cognitive Enhancement: AI-driven Brain-Computer Interfaces. TS2 SPACE. <u>https://ts2.space/en/chatgpt-4-and-the-future-of-cognitive-enhancement-ai-driven-brain-computer-interfaces/</u>
- Simon C, Bolton DAE, Kennedy NC, Soekadar SR, Ruddy KL. Challenges and Opportunities for the Future of Brain-Computer Interface in Neurorehabilitation. Front Neurosci. 2021 Jul 2;15:699428. doi: 10.3389/fnins.2021.699428. PMID: 34276299; PMCID: PMC8282929.
- Howell, D. (2022, October 21). What the Brain-Computer Interface means for business [Review of What the Brain-Computer Interface means for business]. ITPro.

https://www.itpro.com/technology/369239/what-the-brain-computer-interface-bci-meansfor-business

- Uppal, R. (n.d.). Brain-computer interfaces (BCI) are vulnerable to cyber attacks and need security and safety measures. International Defense Security & Technology Inc. https://idstch.com/cyber/brain-computer-interfaces-bci-vulnerable-cyber-attacks-need-sec urity-safety-measures/
- Rayi A, Murr N. Electroencephalogram. [Updated 2022 Oct 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <u>https://www.ncbi.nlm.nih.gov/books/NBK563295/</u>
- Singh SP. Magnetoencephalography: Basic principles. Ann Indian Acad Neurol. 2014 Mar;17(Suppl 1):S107-12. doi: 10.4103/0972-2327.128676. PMID: 24791076; PMCID: PMC4001219.
- Chow MS, Wu SL, Webb SE, Gluskin K, Yew DT. Functional magnetic resonance imaging and the brain: A brief review. World J Radiol. 2017 Jan 28;9(1):5-9. doi: 10.4329/wjr.v9.i1.5. PMID: 28144401; PMCID: PMC5241538.
- Sitaram R, Caria A, Veit R, Gaber T, Rota G, Kuebler A, Birbaumer N. FMRI brain-computer interface: a tool for neuroscientific research and treatment. Comput Intell Neurosci. 2007;2007:25487. doi: 10.1155/2007/25487. PMID: 18274615; PMCID: PMC2233807.
- T. Nguyen, I. Hettiarachchi, A. Khatami, L. Gordon-Brown, C. P. Lim and S. Nahavandi, "Classification of Multi-Class BCI Data by Common Spatial Pattern and Fuzzy System," in *IEEE Access*, vol. 6, pp. 27873-27884, 2018, doi: 10.1109/ACCESS.2018.2841051
- Harwood V, Kleinman D, Puggioni G, Baron A. The P300 event related potential predicts phonological working memory skills in school-aged children. Front Psychol. 2022 Oct 12;13:918046. doi: 10.3389/fpsyg.2022.918046. PMID: 36312112; PMCID: PMC9599408.

Health Disparities within Diagnosis, Treatment, and Mental Health Care at the Intersection of Race/Ethnicity and Autism Spectrum Disorder (ASD) By Inika Mehta

Abstract

This research paper explores how individuals with Autism Spectrum Disorder (ASD) face disparities in the public health sector specifically within diagnosis, treatment, and mental health access based on their race/ethnicity. The study defines the target population and first establishes the benefits of diagnosis, treatment, and mental health care for individuals with ASD. Then, it focuses on the health disparities within the intersection of race/ethnicity and ASD specifically in those three categories. By assessing other studies and inferring what may cause these disparities, the research aims to shed light on the disparities of a minority group that often goes missed. The study uses data from various experiments done and thus provides a holistic review on the disparities that individuals with ASD may face. At the end, we discuss policy changes to advance health equity for individuals with disability thus this research opens a new path for us to explore the gaps within the healthcare system and what can be done to improve it.

Introduction

The American with Disabilities Act of 1990 prohibits discrimination against individuals with disabilities in all areas of public life. The purpose of this law is to make sure that people with disabilities have the same rights and opportunities as everyone else. However, the history of the ADA did not begin in 1990, instead long ago when people with disabilities began to challenge societal barriers that excluded them from their own communities. Over the last few decades, injustices faced by people with disabilities has



become increasingly evident and so the movement strengthened. The disability rights movement adopted many strategies used by the Civil Rights movement before it, and finally in 1973 *Fig 1: Symbol for the ADA* marked the first legal shift with the passage of Section 504 of the 1973 Rehabilitation Act which for the first time marked individuals with disabilities as a minority group. This was crucial in the moment to gain rights for individuals with disabilities. As time has passed, individuals with disabilities continue to fight for their individuals with disabilities, and though there has been some improvement, new research suggests that individuals with disabilities experience many differences within the public health space (Mayerson, n.d.).

This research will examine the health disparities of individuals with Autism Spectrum Disorder (ASD) a neurological developmental disability faced by about 1-2% of the world population (Mayerson, n.d.). Specifically, it will focus on the health disparities within diagnosis, treatment, and access to mental health resources based on the race and ethnicity of individuals with ASD. This research will end with ideas on how to improve these disparities in the public health sector.

By beginning with the definition of a disability, the history of ASD and carefully defining the scope of individuals with this disability, one will have a clear understanding of the target group that is being focused in this research. Next, this research will clearly define a health disparity and then explore the intersection of specific health disparities with race for individuals with autism. Thus, proving the injustices this minority group faces. Lastly, policy changes to advance health equity will be discussed to find gaps in the system currently in place that are working to improve the lives of this minority group and thus overall improve their quality of life.

Literary Analysis –What is a disability?

Today, there are over sixty seven federal definitions of the word "disability" today. This definition affects an individuals (with a disability) benefits, protection, prevalence estimates, social stigma, and even their personal identity. Although there is no single definition, the most frequently used are the medical and social concepts. The medical concept defines a disability as a problem within the mind that can be identified by scientific experiments and treated by experts so that the individual can conform to a more natural setting. However, the social model labels the lives of disabled individuals as inferior and thus they are a minority group with a unique story. In this paper, we will use a third approach which conceptualizes a disability as a combination of both the medical and social models (*Advancing Health*, 2022).

History of Autism and Autism Today

The term "autism" was first used by a psychiatrist, Eugen Bleuler in 1908 to describe a schizophrenic patient who had withdrawn into his individual world. In 1943, another psychiatrist, Leo Kanner studied the social interactions of 11 children. These children had trouble adapting to changes, difficulties in social interactions, allergies to several foods, and great intellectual potential. As more children continued to be studied, scientists believed that the problem within the children was due to their mothers. This theory was disproved in 1964 when Bernard Rimland published *Infantile Autism: The Syndrome and its Implications for a Neural Theory of Behavior*. Finally, in the 1970's Autism became more widely recognized as the Erica Foundation started therapy for children in the 80's (Mandal, n.d.).

Today, we define autism as not a single disease but rather a range of disorders known as ASD. These disorders begin in childhood and can last through adulthood. It is a neurological developmental disability whose cause is unknown, but is very diverse in the way it appears. Symptoms of ASD can be generally categorized into three broad groups:

- 1. Problems with social interactions
- 2. Language and Communication skills
- 3. Unusual behaviors and patterns of thoughts

The different types of ASD can also be classified in three different groups. The first is Autistic Disorder, often known as classic autism in which individuals experience significant language delays, social and communication challenges, intellectual delays, and unusual behaviors. Second, individuals with Asperger Syndrome face milder social challenges. Finally, there is also Pervasive Developmental Disorders also known as "atypical autism" which barely has any prevalence among individuals today (Mandal, n.d.).

Once an individual is suspected of ASD, it is important they begin early intervention in the form of diagnosis, treatment services, and mental health access. Each of these factors play a crucial role in preserving the well being of individuals with ASD. Below, are the benefits of each of these factors:

Diagnosis

ASD can be reliably diagnosed at around two years old, but many people do not receive a diagnosis until their adolescence or even into adulthood, and thus are not able to benefit from early interventions. Many doctors screen for autism during a child's regular visits. During these visits, a doctor or nurse will talk to a parent about certain milestones for their child such as moving, playing, speaking, etc which can allow parents to be aware of their child's development. Screening tools for Autism include the Modified Checklist for Autism in Toddlers (M-CHAT), The Ages and Stages Questionnaire (ASQ), Screening Tool for Autism in Toddlers and Young Children (STAT), and the Parents' Evaluation of Developmental Status (PEDS). However, many

parents do not understand the benefits of an early diagnosis that can pave the way for a child's communication, social, and life skills in the future. By beginning intervention early, treatments are more likely to be effective as the child's brain is still developing. Additionally, people with autism are eligible for state services such as the California Regional Centers that provide life services for individuals with disabilities. Early diagnosis increases:

- Communication
- Social Interaction
- Physical Strength and movement
- Thinking
- Emotion Skills

Though ASD broadly varies from individual to individual, by helping children develop skills earlier can reduce frustration later on, and provide for a more enriching daily life (*Autism in Kids*, n.d.). *Fig 2: M-CHAT Screening*

Treatment

Though there is no standard treatment for individuals with ASD, there are many ways for people to maximize their abilities with the appropriate therapies and intervention methods. Most

report: Patient ID:	M-CHAT I 12345678	K App Report			
Date:	1/1/2017 12:00:00 AM Device: 1/1/2017 12:0			1:00 AM	
Survey		Child's Score Score Interpretation			
M-CHAT-R 10 High-Risk (8-20)					
M-CHAT R Item Responses:				High-Risk (8-20)	19
If you point at something across the room, does your child look at it?				Yes	(0
Have you ever wondered if your child might be deaf?				No	(0
Does your child play pretend or make-believe?				Yes	(0
Does your child like climbing on things?				No	(1
Does your child make unusual finger movements near his or her eyes?				Yes	(1
Does your child point with one finger to ask for something or to get help?				No	(1
Does your child point with one finger to show you something interesting?				Yes	(0
Is your child interested in other children?				No	(1
Does your child show you things by bringing them to you or holding them up for you to see - not to get help, but just to share?				Yes	(0
Does your child respond when you call his or her name?				No	(1
When you smile at your child, does he or she smile back at you?				Yes	(0
Does your child get upset by everyday noises?				Yes	(1
Does your child walk?				No	(1
Does your child look you in the eye when you are talking to him or her, playing with him or her, or dressing him or her?				Yes	(0
Does your child try to copy what you do?				No	(1
If you turn your head to look at something, does your child look around to see what you are looking at?				Yes	(0
Does your child try to get you to watch him or her?				No	(1
Does your child understand when you tell him or her to do something?				Yes	(0
If something new happens, does your child look at your face to see how you feel about it?				No	(1
Does your child like movement activities?				Yes	10

people respond well to structured programs such as behavioral management therapy, cognitive behavior therapy, educational and school-based therapies, joint attention therapy, social skills training, speech-language therapy, etc (*What Are the Treatments*, 2021). According to the CDC, therapy treatments are made to avoid frustration and help children thrive from an early age. In addition to academic benefits, programs foster a sense of community and build healthy relationships for the children (*The Long-Term*, n.d.).

Mental Health Services

Though individuals with ASD can have good mental health, research by *Autistica*, an autism research charity, found that seven out of ten individuals have a mental health condition such as anxiety, depression, ADHD, or Obsessive-Compulsive Disorder (OCD). Though there is little research, this may be due to the struggles that autistic people face when trying to fit into the world. Thus, they may face delays in getting their mental health problems diagnosed, however, it is important for this group of individuals to see support. *The National Autistic Society* features tips on how to seek this aid and find therapists who are either autistic themselves or understand the adjustments needed for individuals with autism while platforms such as *Ambitious about Autism* relays information on how to manage anxiety and get the most out of therapy (*Autism and Mental*, n.d.).

Health Disparities:

Health and health care disparities often refer to the differences in healthcare between groups of individuals that originate from broader inequities. Though there are multiple definitions of a health disparity, the Centers for Disease Control and Prevention (CDC) defines health disparities as "preventable differences in the burden, disease, injury, violence, or in opportunities to achieve optimal health experienced by socially disadvantaged racial, ethnic, and other population groups and communities." Beyond that, a broad array of factors outside of the public health space drives disparities in health and health care. As one can infer, health care is essential to health, however its outcomes can be driven by factors such as underlying genetics, health behaviors, social, and environmental factors, and access to health care: often referred to as *social determinants of health*, are the primary drivers of health outcomes. Further, racism negatively impacts both an individual's mental and physical health by creating inequities across the space (Ndugga, 2023).

Figure 1



Health Disparities are Driven by Social and Economic Inequities

Fig 3: Health Care Disparities on a Scale

In this research, we will explore two of the *social determinants of health* that can impact the quality of one's health and healthcare: race/ethnicity and neurological disorders. By individually examining the disparities for these marginalized groups, we will be able to combine and explore the intersection of public health disparities (based on diagnosis, treatment, and access to mental health services) of individuals who are neurologically atypical (specifically have ASD) and are marginalized by their race/ethnicity as well.

Disparities within Race/Ethnicity

Race/ethnicity are categories that have "tangible effects" on the lives of many individuals: it impacts how one may perceive you as well as how you may perceive yourself. Despite the work done to improve health disparities based on race/ethnicity, individuals who are classified as a racial or ethnic minority face higher rates of chronic disease and premature death compared to the rate among white people. Many health disparities persist in disease such as Human immunodeficiency virus (HIV) related outcomes. For example, the diagnosis and mortality disparity between African American and whites for AIDS has significantly grown over time. Infant gestational age, which is a predictor of infant mortality, also greatly differs by racial and ethnic groups. According to the National Vital Statistics Survey in 2014, African American women had the highest percent of preterm births at 11.1 percent. For indigenous populations, infant mortality rates follow a similar trend. Native Americans have an infant mortality rate that is 60% higher than white individuals. Continuously, African Americans, Hispanics, and Native American populations continue to face higher death rates in diseases such as heart disease, cancer, and even suicide, thus proving the significant difference and existance of health disparities within different racial/ethnic groups (*The State*, n.d.).

Disparities within Individuals with ASD

People with disabilities are more likely to experience poor health conditions than nondisabled people. In 2012-2015, data showed that disabled individuals more likely experience cardiac disease, higher weight, and asthma. Women with disabilities lack access to breast screening leading to higher rates of breast cancer mortality than women without disabilities. After the COVID-19 pandemic, disability related health disparities have become more evident as individuals with intellectual and developmental disabilities were more affected than the general population, having higher mortality rates. Specifically, individuals with ASD reported lower quality health care included poorer communication, access, and more system-level problems. Once a patient is met with an unpleasant experience from a health care provider, they are less likely to seek aid thus increasing the disparities between this group and the group of non autistic adults. (*Health Care*, 2022)

The Intersection of ASD and Race/Ethnicity

Racial/ethnic minorities on the autism spectrum are more likely to be disconnected from opportunities than their white peers. Given this, they are more prone to poverty, mental health problems, and limited access to treatment than the general population. People with ASD also experience heightened morbidity and early mortality. In this section, we will focus on three sectors of health care: diagnosis, treatment, and mental health, and evaluate the proven disparities within minority race individuals with ASD and the policies/reasons why these disparities may occur.

Health Disparities within Diagnosis:

There are well documented disparities in access to diagnostic and early intervention services for individuals with ASD. Research suggests that individuals within an ethnic minority face further advantages. While expert diagnosticians may be able to diagnose ASD in children as young as 12 months of age, ASD is typically diagnosed around four years. African American children are diagnosed 1.5 years, which delays the opportunity for earlier treatment. As shown above, early diagnosis is essential to children with ASD and helps in their behavioral and intellectual development later on, thus putting this ethnic minority at a disadvantage. In another study, scientists found that the average estimated ASD prevalence is 16.8 per 1000 children (1/59), however, in White children the numbers are at 17/1000 children but are much less among African American (16 per 1000), Latino (14/1000), and Asian/Pacific Islander children (13.5 per 1000). *This decrease in prevalence for minority groups emphasizes that there are greater delays between concerns and time of diagnosis, suggesting that the parents may face challenges communicating their concerns, navigating systems, and gaining referrals.* (Chapter Four, n.d.)

The reasons for disparities within diagnosis are due to a variety of factors which ultimately limit information, education, and thus healthcare. History has led to cyclic practices in low income neighborhoods of people of color who have limited access to community resources. Discrimination and the fear of stigma also greatly negatively affects the diagnostic process and services. These families also lack access to knowledge about ASD in general. For example, in a subsample of Latinax families with limited English proficiency, more than 80% of these families showed a lack of knowledge of ASD symptoms. Finally, black parents in a study by Costantino reported that they had worries about their child's development at around two years. However, these children had to see over six providers before being diagnosed leading to costly delays and thus lack of diagnosis until three years later. Similar results were present with Latinax children. This is likely due to implicit bias that affects communications with the children's families as well as the lack of training in spotting ASD symptoms in children with ASD (*Racial, Ethnic*, 2021).

Health Disparities within Treatment:

Children with ASD experience a broad category of symptoms, skills, and weaknesses. Thus, each child's treatment will vary and the treatment plan must take into account the individual characteristics of each child. Several studies have found that families with a child with ASD have difficulty accessing these treatments. Additionally, children with ASD of a minority race have been found to receive services at a later age. Specifically, minority children with ASD face disparities in outpatient treatments and behavioral intervention therapies. For example, within Early Intensive Behavioral Intervention (EIBI) therapies, a majority of children (6/10) were low users. The prohibition of Medicaid-funded EIBI is one reason for this low utilization, however, results building on previous work found racial inequities in the time that children with ASD utilize a range of services. This means that black children are less likely to enroll in behavioral therapies and those who do, will simply not use it. Thus, this places a disadvantage on minority children with ASD. Extensive research offers explanations on reasons for this disadvantage, specifically the quality of the interaction between healthcare providers and the patient. Studies should examine the relationship of the role of racial-ethnic bias in the office and the delivery of EIBI. This bias may be part of the reason that ethnic minorities with ASD face disparities within treatment (Treatment Utilization, 2019).

Health Disparities within Mental Health:

There are several differences in the prevalence of psychiatric conditions by race/ethnicity in autistic adults. Although prevalence was high, once again, Hispanic, Black, and Asian autistic adults were less likely to be diagnosed with psychiatric conditions than their White counterparts. This lower prevalence in minority groups is reflected in history where racial.ethnic minorities lack access to mental health care. Though there are not many studies for autistic adults, one study did present that Black autistic adults have less access to mental health care services compared to White individuals. Similarly, these findings are mirrored within children from minority groups who have less access to evaluations, and developmental screenings as well as receiving medication. Once again, this may be due to provider bias rather than lack of prevalence. It could also be that providers misdiagnose symptoms of autistic patients and focus on problems such as

diabetes and obesity rather than mental health. These misdiagnoses could lead to delays in mental health care access and thus it is important to understand where these disparities occur and provide the right care in time (*Racial/Ethnic Differences*, 2022).

Policy Changes to Advance Health Equity:

In this section, we hope to discuss several potential policy changes that could be implemented to improve the lives of individuals who are both marginalized due to their disorder (ASD) as well as because of their race/ethnicity.

Expanding Medicaid Buy-In Programs:

Although public programs such as Medicaid often aid disabled people, there are still many barriers to complete health care coverage. Depending on location, individuals who are ineligible for Medicaid could enroll in a "buy-in" program that involved payment to enroll in Medicaid. However, many of these programs require individuals to be low income, and thus, individuals with disabilities remain in poverty so they can get health coverage. States such as Massachusetts and Arkansas do not do this, and thus their programs are working towards equity by empowering individuals with disabilities to fully participate in the workforce with access to healthcare. The government could work on creating more of these programs for more equitable health care access (*Advancing Health*, 2022).

Access to Home/Community Based Services:

Medicaid has long paid for institutional services, it only began paying for community based services (day-to-day life) in the 1980's. Finally, in 1999's *Olmstead v. LC* the US interpreted the integration to say that the states must evenly approach providing care in community settings rather than just institutional care. By distributing money to increase community based services, the ACA reduced institutional bias that had been long present. However, this progress still varies between states and thus a Medicare home and community-based services benefit would help advance health equity beyond institutional platforms (*Advancing Health*, 2022).

Expanding Scope of Covered Services:

Definitions of the phrase, "medical necessity" in several public programs have led to unmet health care needs. Medicare's definition of *medical necessity* focuses specifically on diagnosis but limits individuals with disabilities for reimbursement for other community oriented activities, thus socially isolating them (which leads to negative effects on their well-being). Some states like Delaware's definition of *medical necessity* refers to the aim of " attaining independence, self care, dignity, self determination, personal safety, and integration into all natural family, community, and facility environments and activities" By using this definition in other states, we can advance the well -being of disabled individuals (*Advancing Health*, 2022).

Discussion:

This study demonstrates a correlation between one's race/ethnicity and how severely they are impacted by health disparities specifically in diagnosis, treatment, and mental health. Though there has been limited research done on health disparities with the intersection of race and individuals with ASD, racial/ethnic minorities on the autism spectrum are more likely to be disconnected from several opportunities. We found that diagnosis is delayed, treatment access (specifically in behavioral therapy) is limited, and that individuals with ASD find difficulty in understanding their mental health. Between all three sections, our research found a trend that these disparities may be caused by bias and discrimination in the provider space. It may also be due to lack of education and communication in minority communities thus preventing children with ASD from getting the care they require.

The policy changes we discussed are in line with the disparities revealed. By expanding Medicaid programs, community services, and the scope of services, individuals who may not have easy access to services will be able to get the care they need. However, there is limited research done in this space, and further research should be done on the effects of income and education levels and how that may impact health care access for individuals with ASD. It could also be interesting to explore the differences in disparities for children with ASD and adults.

This research is limited to the scope of diagnosis, treatment, and mental health care when addressing health disparities, and thus further research could be expanded to other disparities within the public health space.

Conclusion:

Though there has been much advancement in research on how to improve the lives of individuals with disabilities, specifically ASD, there is still no set way to treat this disability. However, this research has shown that the earlier the children get diagnosed, treated, and have access to services (such as mental health care), they are more able to engage in their daily lives with less stress and frustration.

Thus, it is important to examine where these individuals face disparities specifically in lack of access to diagnosis, treatment, and mental health care. This research was able to examine those disparities with the intersection of race/ethnicity as well. We found that minority groups were less likely to be diagnosed for autism and treated. Though it is unclear where this disparity stems from, there was a big trend of discrimination and policy bias in the provider space. Further research could be conducted on policy bias and discrimination to understand why individuals with ASD may not get access to the proper health care they deserve.

Finally, this research discovered three policy changes that could be implemented to improve the lives of individuals with ASD. These include: expanding Medicaid Buy-In programs, the scope of service, and access to community service. By exploring these three potential solutions, this research aims to shed light on the disparities faced by individuals with Autism and what the government/policy makers can do to improve it.

Works Cited

Advancing Health Equity And Reducing Health Disparities For People With Disabilities In The United States. (2022, October). Health Affairs.

https://www.google.com/url?q=https://www.healthaffairs.org/doi/full/10.1377/hlthaff.202 2.00499&sa=D&source=docs&ust=1692380467538900&usg=AOvVaw2PHuB-Qg9yxc7 vKBEntv7v

Autism and Mental Health. (n.d.). Mental Health Foundation. https://www.mentalhealth.org.uk/explore-mental-health/a-z-topics/autism-and-mental-hea lth#:~:text=Just%20like%20everyone%2C%20autistic%20people,%2Dcompulsive%20di sorder%20(OCD)

- *Autism in Kids: Why Is Early Diagnosis Important?* (n.d.). Psych Central. https://psychcentral.com/autism/early-diagnosis-of-autism
- Chapter Four A Review of Diagnosis and Service Disparities Among Children With Autism From Racial and Ethnic Minority Groups in the United States. (n.d.). Science Direct. https://www.sciencedirect.com/science/article/pii/S2211609518300101
- Health Care Disparities Affecting Individuals with Autism. (2022, August 30). Autism Alliance of Michigan.

https://autismallianceofmichigan.org/health-care-disparities-affecting-individuals-with-au tism/#:~:text=A%20recent%20study%20by%20researchers,%2C%20shutdowns%2C%2 0and%20meltdowns."

Health Disparities. (n.d.). CDC. https://www.cdc.gov/healthyyouth/disparities/index.htm

Klimpl, M. (n.d.). *Telecommuting: A reasonable accommodation under the American with Disabilities Act?* AMM.

https://www.ammlaw.com/blog/telecommuting-a-reasonable-accommodation-under-the-a merican-with-disabilities-act.html

The Long-Term Benefits of Autism Therapy Services for Children. (n.d.). Carmen B. Pingree Autism Center of Learning.

https://carmenbpingree.com/blog/the-long-term-benefits-of-autism-therapy-services-for-c hildren/

- Mandal, A. (n.d.). *Autism History*. News Medical Life Sciences. https://www.news-medical.net/health/Autism-History.aspx#:~:text=The%20term%20auti sm%20first%20was,admiration%20and%20 withdrawal%20 within%20 self.
- Mandal, A. (n.d.). *What is Autism?* News Medical Life Sciences. https://www.news-medical.net/health/What-is-Autism.aspx
- Mayerson, A. (n.d.). *The History of ADA*. Disability Rights and Education Fund. https://dredf.org/about-us/publications/the-history-of-the-ada/#:~:text=The%20history%2 0of%20the%20ADA%20is%20a%20testament%20to%20the,in%20the%20context%20o f%20disability.
- Ndugga, N. (2023, April). *Disparities in Health and Health Care: 5 Key Questions and Answers*. KFF.

https://www.kff.org/racial-equity-and-health-policy/issue-brief/disparities-in-health-and-h ealth-care-5-key-question-and-answers/

Patient Tools. (n.d.). M-CHAT.

https://www.patienttools.com/index.php/screening-interviews/m-chat-r/

Racial, Ethnic, and Sociodemographic Disparities in Diagnosis of Children with Autism Spectrum Disorder. (2021, October). NIH.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8500365/

- *Racial/Ethnic Differences in Psychiatric and Medical Diagnoses Among Autistic Adults.* (2022, November). https://www.liebertpub.com/doi/epdf/10.1089/aut.2021.0083
- *The State of Health Disparities in the US*. (n.d.). NIH National Library of Medicine. https://www.ncbi.nlm.nih.gov/books/NBK425844/
- Treatment Utilization Trajectories among Children with Autism Spectrum Disorder: Differences by Race-Ethnicity and Neighborhood. (2019, January). Springer Link. https://link.springer.com/article/10.1007/s10803-019-03896-3
- What are the treatments for autism? (2021, April). NIH. https://www.nichd.nih.gov/health/topics/autism/conditioninfo/treatments

Understanding the Environmental Factors that Can Contribute to Alzheimer's to Aid in the Design of Treatments By Megha Guntuku

Abstract

Alzheimer's Disease (AD) is a neurodegenerative disease that is estimated to affect over 6.7 million Americans age 65 and over as of 2023 (<u>"About Alzheimer's Disease"</u>). There is abundant evidence that AD is caused by the misfolding of proteins and the accumulation of these non-functional aggregates in the brain. Some genes have been indicated in AD, but these genes do not account for all cases, suggesting that environmental factors substantially affect the onset of the disease. Environmental factors related to Alzheimer's include education, other pre-existing diseases such as diabetes, and lifestyle. This review aims to summarize the findings of the correlation between AD with these three categories. A greater understanding of these factors could allow for better preventative approaches to treating the disease.

Introduction

Alzheimer's disease (AD) is a neurodegenerative disease characterized by the misfolding and aggregation of two specific proteins, amyloid beta and tau, in the brain. The disease targets older individuals and causes them to lose neurons, leading to memory loss (Chin-Chan et al.). The disease is characterized by six Braak stages which track the severity of the disease. Stages one and two are asymptomatic, three and four show mild symptoms, including agitation and depression, and five and six demonstrate severe dementia or loss of cognitive function (Moreno-Jiménez et al., Ehrenberg et al., "What is Dementia?"). In some cases, AD is caused by genetic factors through mutations in the APP, PS1, and PS2 genes (Chin-Chan et al.). For AD cases that present without mutations in these genes, it is likely that environmental factors play a large role. These environmental factors can be split into three categories (Figure 1). The disease is affected by factors relating to education (such as learning languages), pre-existing diseases (such as diabetes and hearing loss), and lifestyle (such as sleep and eating habits) (Zhang et al.). The primary focus of this review is to explain the importance of the correlation between these environmental factors and the disease. AD affects about fifty million people around the globe. The treatment and care can be quite expensive, with a worldwide cost of over one trillion USD ("Alzheimer's Disease"). A deeper understanding of the causes of the disease and how to prevent it could greatly benefit a significant number of people by teaching them the precautionary measures they can take to avoid the disease. This knowledge could also benefit people who are already diagnosed with the disease, as taking care of their lifestyle can reduce the severity of AD symptoms.

Figure 1: Environmental Factors correlating with Alzheimer's Disease



Figure 1. This figure depicts the three primary categories of environmental factors correlating with AD and examples within them.

Education

One category of environmental factors correlated with AD is education. One study followed subjects 45 years and older across a long-term study to observe the impact of continued education. The study showed that attending university classes increases and maintains cognitive reserve, a measure of brain agility, proven by better language processing and testing assessment scores. This study found that there is a positive association between participating in cognitively stimulating activities and reduced incidence of dementia (Matyas et al.). Intelligence, measured through the level of educational attainment, has proven a correlational relationship with decreasing the risk of AD (Andrews et al.). Mind games, such as sudoku and crosswords, are key to sustaining memory and maintaining cognitive speed in old age (Suo et al.). Learning additional languages is one specific form of cognitive stimulation connected to decreased AD risk. Compared to monolinguals, bilinguals have heightened neural activity in brain regions that play a key role in higher-order processing (Grady et al.). Bilinguals were also shown to be more educated and had a superior professional position on average compared to monolinguals. A cognitive study on the Cantonese/Mandarin population concludes that monolinguals manifest

AD before bilingual subjects (<u>Zheng et al.</u>). In contrast to the benefits of education, issues with mental health, specifically work and school-related depression, have been shown to have a negative correlational relationship with AD (<u>Diniz et al.</u>).

Pre-existing Diseases

Another category of environmental factors that has an association with dementia is pre-existing diseases. Diabetes, a disease characterized by high blood glucose levels due to low insulin levels or inefficient use of insulin, has been implicated in the development of AD ("What is Diabetes?"). Insulin has been proven to be connected to brain metabolism, and a defective insulin pathway, a key trait of diabetes, is associated with issues in memory ("Obesity"). Obesity, which is characterized by a body mass index of 30 or more due to extreme fat accumulation, is highly comorbid with diabetes and has been implicated in AD as well (Ebrahimpour et al.). Insulin resistance, a significant characteristic of diabetes and obesity, is shown to be correlated with tau hyperphosphorylation and amyloid beta aggregation (De Felice et al.). Diseases that impact cardiovascular function have also been implicated in the onset of AD. One such disease, Atrial fibrillation (AF), characterized by fast and irregular heartbeats, was found to be highly predictive of the future development of dementia when assessing and comparing AF and AF-free populations over the course of a long-term study ("What Is AFIB?", Kim et al.). A prospective treatment option, oral anticoagulants-used to prevent blood clots and strokes-has been proven to decrease the incidence of dementia, further supporting the potential correlational relationship between cardiovascular function and AD ("What Are Direct-Acting Oral Anticoagulants?"). Injury of brain cells beyond repair by traumatic brain injury (TBI) caused by a significant hit to the brain is also correlated with AD ("Traumatic Brain Injury"). TBI has been associated with dementia, although this risk decreases time-dependent from when the injury occurred. Multiple TBIs are shown to have a cumulative effect and have a higher association with dementia (Nordström & Nordström). Although direct connections have not been established, relationships also exist between hearing and tooth loss to AD risk. An inverse correlation between number of teeth and AD risk has been observed (Takeuchi et al.). However, it is possible that this correlation exists in part because both tooth loss and dementia risk increase with age. A correlation between hearing loss and Alzheimer's disease has also been observed. Possible treatment for hearing loss includes hearing aids and cochlear implants (Hung et al.).

Lifestyle

A long-term study of an elderly Japanese population had two groups, one that performed exercise once a week and a control group with no physical activity. The study concluded that the exercise group showed a lower incidence of dementia and suggested physical activity has an inverse correlation with AD (<u>Kishimoto et al.</u>). In another long-term study on obstructive sleep apnea (OSA), a type of breathing loss where muscles in the throat prevent oxygen intake due to airway blockage, and length of sleep, researchers concluded that extreme cases of OSA and sleep duration of less than seven hours correlated with dementia (Figure 2) (<u>"Central Sleep Apnea"</u>,

Lutsey et al.). In a study on smoking, researchers found that for every additional 20 cigarettes a day, there is a 34% growth in the risk of dementia. The study concluded current smokers, compared to never smokers and former smokers, have the highest risk of dementia (Zhong et al.). Frequent alcohol consumption, five or more times a day, also correlates with an increased risk of dementia (Langballe et al.). In terms of beverages, the incidence of AD is decreased with the consumption of 1-2 cups of coffee daily (Wu et al.). Green tea has also been shown to benefit cognition and overall brain function, suggesting a possible correlation with a decreased risk of AD (Mancini et al.). Three diets, DASH (dietary approaches to stop hypertension), Mediterranean, and MIND (a hybrid of Mediterranean and DASH), were correlated with a lower risk for AD (Figure 3) (Morris et al.). A 15-year-long study in Sweden tested the association between air pollution and the risk of dementia. The results show that the group with the highest exposure to traffic-related pollution was most likely to be diagnosed with dementia, suggesting a correlation between pollution and AD (Oudin et al.).



Figure 2: Sleep Loss Positive Feedback Loop

Figure 2. This figure depicts the accumulation of the amyloid and tau proteins due to a lack of sleep which leads to neurodegeneration which can then cause further sleep loss.




Figure 3. This figure depicts the three diets correlated with lowering the risk of AD: Mediterrenean, DASH, and MIND. The foods above the green line indicate items that should be eaten with the diet, while those below the red line indicate items that should be avoided.

Summary/Conclusions

If AD is not treated, it can lead to severe cognitive decline with severe effects of sleep loss, depression, anxiety, and agitation. Some pharmaceutical treatments for AD have an anti-amyloid approach, which aims to minimize disease progression. But this treatment can have drastic side effects, including allergic reactions, swelling, bleeding, headaches, nausea, change in vision, and falling. Popular drugs of this type include Aducanumab and Lacanemab. Cholinesterase inhibitors, another type of drug, minimize cognitive symptoms related to AD, such as memory loss. Donepezil, Rivastigmine, and Galantamine are commonly prescribed ("Medications for Memory, Cognition and Dementia-Related Behaviors"). While these drugs can treat the disease, they can cost up to \$60,000 annually (Sinha & Barocas). We could benefit from a more holistic approach encompassing environmental factors as they are much less expensive and have no side effects. Continuation of education has shown a strong correlation with maintaining cognitive vigor, and a healthy lifestyle nurtures the body, suggesting a decrease in the risk of AD. Regarding pre-existing diseases, many correlate not only to AD but also to each other, suggesting that poor self-care can have an additive effect. So by maintaining beneficial day-to-day habits, individuals can decrease their risk of AD and other diseases. Extensive research has shown that approximately one-third of all AD cases can be credited to

environmental factors alone (<u>Killin et al.</u>). This suggests that maintaining a healthy lifestyle can often prevent the disease. Studies also propose that preexisting AD can be less severe if environmental risk factors are addressed (<u>"Alzheimer's Disease Fact Sheet"</u>). This is extremely important as Alzheimer's care can be quite expensive, ranging from 20 - 40 thousand dollars a year or more, depending on the severity, suggesting that just by modifying one's lifestyle, costs can reduce (<u>Leon et al.</u>). Further research on treatment for the disease is still needed, but as the research summarized in this review suggests, taking adequate care of oneself daily likely results in a greatly reduced risk of AD diagnosis and severity.

Works Cited

- About Alzheimer's Disease. 13 July 2023,
 - https://www.cdc.gov/aging/alzheimers-disease-dementia/about-alzheimers.html.
- 'Alzheimer's Disease Fact Sheet'. National Institute on Aging,

https://www.nia.nih.gov/health/alzheimers-disease-fact-sheet. Accessed 3 Sept. 2023. *Alzheimer's: Facts, Figures & Stats.*

https://www.brightfocus.org/alzheimers/article/alzheimers-disease-facts-figures. Accessed 3 Sept. 2023.

- Andrews, Shea J., et al. 'Causal Associations between Modifiable Risk Factors and the Alzheimer's Phenome'. *Annals of Neurology*, vol. 89, no. 1, Wiley, Jan. 2021, pp. 54–65, https://doi.org10.1002/ana.25918.
- 'Central Sleep Apnea'. *Mayo Clinic*, 11 July 2023, https://www.mayoclinic.org/diseases-conditions/central-sleep-apnea/symptoms-causes/sy c-20352109.
- Chin-Chan, Miguel, et al. 'Environmental Pollutants as Risk Factors for Neurodegenerative Disorders: Alzheimer and Parkinson Diseases'. *Frontiers in Cellular Neuroscience*, vol. 9, Frontiers Media SA, Apr. 2015, p. 124, https://doi.org10.3389/fncel.2015.00124.
- De Felice, Fernanda G., et al. 'How Does Brain Insulin Resistance Develop in Alzheimer's Disease?' *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*, vol. 10, no. 1 Suppl, Wiley, Feb. 2014, pp. S26-32, https://doi.org10.1016/j.jalz.2013.12.004.
- Diniz, Breno S., et al. 'Late-Life Depression and Risk of Vascular Dementia and Alzheimer's Disease: Systematic Review and Meta-Analysis of Community-Based Cohort Studies'. *The British Journal of Psychiatry: The Journal of Mental Science*, vol. 202, no. 5, Royal College of Psychiatrists, May 2013, pp. 329–335, https://doi.org10.1192/bjp.bp.112.118307.
- Ebrahimpour, Shiva, et al. 'Crosstalk between Obesity, Diabetes, and Alzheimer's Disease: Introducing Quercetin as an Effective Triple Herbal Medicine'. *Ageing Research Reviews*, vol. 62, no. 101095, Elsevier BV, Sept. 2020, p. 101095, https://doi.org10.1016/j.arr.2020.101095.
- Ehrenberg, Alexander J., et al. 'Neuropathologic Correlates of Psychiatric Symptoms in Alzheimer's Disease'. *Journal of Alzheimer's Disease: JAD*, vol. 66, no. 1, IOS Press, 2018, pp. 115–126, https://doi.org10.3233/JAD-180688.
- Grady, Cheryl L., et al. 'Brain Network Activity in Monolingual and Bilingual Older Adults'. *Neuropsychologia*, vol. 66, Elsevier BV, Jan. 2015, pp. 170–181, https://doi.org10.1016/j.neuropsychologia.2014.10.042.
- Hung, Shih-Chang, et al. 'Hearing Loss Is Associated with Risk of Alzheimer's Disease: A Case-Control Study in Older People'. *Journal of Epidemiology*, vol. 25, no. 8, Japan Epidemiological Association, May 2015, pp. 517–521, https://doi.org10.2188/jea.JE20140147.

- Killin, Lewis O. J., et al. 'Environmental Risk Factors for Dementia: A Systematic Review'. BMC Geriatrics, vol. 16, no. 1, Springer Science and Business Media LLC, Dec. 2016, https://doi.org10.1186/s12877-016-0342-y.
- Kim, Dongmin, et al. 'Risk of Dementia in Stroke-Free Patients Diagnosed with Atrial Fibrillation: Data from a Population-Based Cohort'. *European Heart Journal*, vol. 40, no. 28, Oxford University Press (OUP), July 2019, pp. 2313–2323, https://doi.org10.1093/eurheartj/ehz386.
- Kishimoto, Hiro, et al. 'The Long-Term Association between Physical Activity and Risk of Dementia in the Community: The Hisayama Study'. *European Journal of Epidemiology*, vol. 31, no. 3, Springer Science and Business Media LLC, Mar. 2016, pp. 267–274, https://doi.org10.1007/s10654-016-0125-y.
- Langballe, Ellen Melbye, et al. 'Alcohol Consumption and Risk of Dementia up to 27 Years Later in a Large, Population-Based Sample: The HUNT Study, Norway'. *European Journal of Epidemiology*, vol. 30, no. 9, Springer Nature, Sept. 2015, pp. 1049–1056, https://doi.org10.1007/s10654-015-0029-2.
- Leon, J., et al. 'Alzheimer's Disease Care: Costs and Potential Savings'. Health Affairs (Project Hope), vol. 17, no. 6, Health Affairs (Project Hope), Nov. 1998, pp. 206–216, https://doi.org10.1377/hlthaff.17.6.206.
- Lutsey, Pamela L., et al. 'Sleep Characteristics and Risk of Dementia and Alzheimer's Disease: The Atherosclerosis Risk in Communities Study'. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*, vol. 14, no. 2, Wiley, Feb. 2018, pp. 157–166, https://doi.org10.1016/j.jalz.2017.06.2269.
- Mancini, Edele, et al. 'Green Tea Effects on Cognition, Mood and Human Brain Function: A Systematic Review'. *Phytomedicine: International Journal of Phytotherapy and Phytopharmacology*, vol. 34, Elsevier BV, Oct. 2017, pp. 26–37, https://doi.org10.1016/j.phymed.2017.07.008.
- Matyas, Nina, et al. 'Continuing Education for the Prevention of Mild Cognitive Impairment and Alzheimer's-Type Dementia: A Systematic Review and Overview of Systematic Reviews'. *BMJ Open*, vol. 9, no. 7, BMJ, July 2019, p. e027719, https://doi.org10.1136/bmjopen-2018-027719.

'Fármacos para la memoria, cognición y comportamientos relacionados con la demencia'. Alzheimer 's Disease and Dementia, https://www.alz.org/alzheimers-dementia/treatments/medications-for-memory. Accessed 3 Sept. 2023.

 Moreno-Jiménez, Elena P., et al. 'Adult Hippocampal Neurogenesis Is Abundant in Neurologically Healthy Subjects and Drops Sharply in Patients with Alzheimer's Disease'. *Nature Medicine*, vol. 25, no. 4, Springer Science and Business Media LLC, Apr. 2019, pp. 554–560, https://doi.org10.1038/s41591-019-0375-9.

- Morris, Martha Clare, et al. 'MIND Diet Associated with Reduced Incidence of Alzheimer's Disease'. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*, vol. 11, no. 9, Wiley, Sept. 2015, pp. 1007–1014, https://doi.org10.1016/j.jalz.2014.11.009.
- Nordström, Anna, and Peter Nordström. 'Traumatic Brain Injury and the Risk of Dementia Diagnosis: A Nationwide Cohort Study'. *PLoS Medicine*, vol. 15, no. 1, Public Library of Science (PLoS), Jan. 2018, p. e1002496, https://doi.org10.1371/journal.pmed.1002496.
- Oudin, Anna, et al. 'Traffic-Related Air Pollution and Dementia Incidence in Northern Sweden: A Longitudinal Study'. *Environmental Health Perspectives*, vol. 124, no. 3, Environmental Health Perspectives, Mar. 2016, pp. 306–312, https://doi.org10.1289/ehp.1408322.
- Sinha, Pranay, and Joshua A. Barocas. 'Cost-Effectiveness of Aducanumab to Prevent Alzheimer's Disease Progression at Current List Price'. *Alzheimer's & Dementia (New York, N. Y.)*, vol. 8, no. 1, Wiley, Mar. 2022, p. e12256, https://doi.org10.1002/trc2.12256.
- Suo, C., et al. 'Therapeutically Relevant Structural and Functional Mechanisms Triggered by Physical and Cognitive Exercise'. *Molecular Psychiatry*, vol. 21, no. 11, Springer Science and Business Media LLC, Nov. 2016, pp. 1633–1642, https://doi.org10.1038/mp.2016.19.
- Takeuchi, Kenji, et al. 'Tooth Loss and Risk of Dementia in the Community: The Hisayama Study'. *Journal of the American Geriatrics Society*, vol. 65, no. 5, Wiley, May 2017, pp. e95–e100, https://doi.org10.1111/jgs.14791.
- 'Traumatic Brain Injury'. *Mayo Clinic*, 4 Feb. 2021, https://www.mayoclinic.org/diseases-conditions/traumatic-brain-injury/symptoms-causes/ syc-20378557.
- https://www.heart.org/-/media/files/health-topics/answers-by-heart/what-are-doacs.pdf. Accessed 3 Sept. 2023.
- What Is Afib? 28 Apr. 2023,
 - https://www.hopkinsmedicine.org/health/conditions-and-diseases/atrial-fibrillation.
- 'What Is Dementia? Symptoms, Types, and Diagnosis'. *National Institute on Aging*, https://www.nia.nih.gov/health/what-is-dementia. Accessed 3 Sept. 2023.
- CDC. 'What Is Diabetes?' *Centers for Disease Control and Prevention*, 25 Apr. 2023, https://www.cdc.gov/diabetes/basics/diabetes.html.
- Obesity. https://www.who.int/health-topics/obesity. Accessed 3 Sept. 2023.
- https://www.clinicalnutritionjournal.com/article/S0261-5614(16)30111-X/fulltext. Accessed 3 Sept. 2023.
- Zhang, X. X., et al. 'The Epidemiology of Alzheimer's Disease Modifiable Risk Factors and Prevention'. *The Journal of Prevention of Alzheimer's Disease*, vol. 8, no. 3, SERDI, 2021, pp. 313–321, https://doi.org10.14283/jpad.2021.15.
- Zheng, Yifan, et al. 'The Protective Effect of Cantonese/Mandarin Bilingualism on the Onset of Alzheimer Disease'. *Dementia and Geriatric Cognitive Disorders*, vol. 45, no. 3–4, S. Karger AG, June 2018, pp. 210–219, https://doi.org10.1159/000488485.

Zhong, Guochao, et al. 'Smoking Is Associated with an Increased Risk of Dementia: A Meta-Analysis of Prospective Cohort Studies with Investigation of Potential Effect Modifiers'. *PloS One*, vol. 10, no. 3, Public Library of Science (PLoS), Mar. 2015, p. e0118333, <u>https://doi.org10.1371/journal.pone.0118333</u>.

Diverse Demographics, Decoding Labels: Food Labels Influence on Consumers' Decisions Based on Individual and Household Differences By Ellie Lee

Abstract

Food labels can greatly impact consumer food decisions, nutritional intake, and overall health. However, despite the helpful guide and informative transparency they can provide, food labels can be perceived and utilized differently from consumer to consumer. Rather than generalizing consumers when studying the impact of nutrition labels, it may be more helpful to assess how individual factors like differing demographic, socioeconomic, and health contexts influence consumers' use of nutrition information. Understanding different consumer perceptions and utilization can help increase the effectiveness of food labels. This paper explores whether different demographic and socioeconomic factors influence different use of food labels, and found that individual and household factors–including income, household composition, gender, health beliefs, and levels of nutritional knowledge–influenced both the amount and type of food label use. The paper also examines how food labels can affect consumer perceptions and decisions generally (without accounting specifically for individual factors) and includes best practices for making food labels more comprehensible to a wider audience. Introduction

Nutrition is crucial to both physical and mental health and overall well-being. Regarding physical health, nutrition helps maintain brain function, muscle strength, bone density, blood circulation, and the immune system ("Nutrition"). Nutrition well-being also supports safer pregnancy, childbirth, and longevity ("Nutrition - Health topics"). Furthermore, improved nutrition consisting of adequate nutrients, vitamins, and minerals can lower the risk of diseases like cancer and non-communicable diseases (including diabetes and cardiovascular disease), help manage chronic disease, and prevent future health complications ("Why It Matters | Nutrition"; "Nutrition"; "Nutrition - Health topics").

Nutrition and diet also impact mental health. Certain food groups like animal food, fruits, and plants have been shown to contribute to the production of neurotransmitters, crucial for mood regulation, memory, cognition, emotion, sleep, appetite, and stress management (Briguglio et al. 591). Furthermore, omega-3 fatty acids, which are abundant in fish, nuts, and plant oils, are linked to cognitive function and mood regulation (Meyer et al. 391-398; Kumar et al. 89-108; Gómez-Pinilla 568-578). In contrast, an imbalanced diet characterized by high consumption of fat, sodium, and processed foods may contribute to conditions like depression, anxiety, and cognitive decline (Gómez-Pinilla 568-578; Lane et al. 2568).

Considering the importance of nutrition on physical and mental well-being, food labels play a crucial part in affecting individuals' nutritional intake and can potentially have long-term health impacts. Food labeling guidelines on manufactured products vary across countries, but common requirements include a nutrition facts panel providing information on serving size, calories, and amounts of nutrients like fat, cholesterol, sodium, carbohydrates, fiber, sugars, and protein. Other requirements include ingredients listed in the order of the most abundant ingredient listed first, allergen information clearly identifying the products' possible contact or containment of common allergens, the net amount of weight of the product, disclosure of food additives and preservatives, nutrition and health claims–including front of pack labeling–and dietary guidelines and daily values to help consumers understand the nutritional significance of the product ("Food Labeling Guide (PDF)").

The abundance of dietary choices can be overwhelming, and these labels provide insight into calorie counts, macronutrient compositions, vitamin and mineral content, and potential allergens, potentially influencing consumers to make informed decisions that align with their health goals and dietary needs. Moreover, for those with specific dietary restrictions or health conditions, accurate food labeling is crucial in avoiding potential allergens or food choices that may be potentially dangerous. However, not all consumers may be able to comprehend food labels accurately or interpret the given information, causing food labels to negatively impact their nutritional consumption and well-being (Sundar et al. 1280-1292; Barreiro-Hurle 426-443; Oliveira et al. 160-167). Moreover, individual factors like income, household, gender, eating patterns, and levels of nutritional knowledge can significantly impact consumers' access to nutrition information. Therefore, food labels should be made as comprehensive and transparent as possible. This paper explores how food labels can affect consumer perceptions and decisions in general, the effect of individual and household factors like income, household composition, gender, health beliefs, and levels of nutritional knowledge on the use of food labels, and an analysis of the most comprehensive ways nutrition information can be presented to consumers. How Food Labels Affect Consumers' Perceptions and Decisions

Food labels play an influencing role in making consumers more conscious about their nutritional intake, leading to healthier dietary choices and positively impacting their overall health. The concept of "healthier" can vary based on consumers' individual needs, such as limiting the intake of specific nutrients, decreasing the risk of illness, and controlling weight. By utilizing food labels, consumers can cater their food decisions to meet their specific health goals.

The positive effect of food labels on consumer choices is influenced by the ability of nutrition information to alter consumers' thought processes. According to research by Lim et al, people engage in a faster, automatic process of thinking about which food tastes better, rather than is healthier, due to a preoccupation with taste. In an experiment involving 178 participants and mouse-tracking technology, Lim et al found that the assessment of the actual health value occurred 230 milliseconds after considering the product's savory appeal. However, exposure to nutritional information, specifically calorie information closes the gap between the time we think about taste versus health benefits (Lim et al. 447-462). This evidence demonstrates that nutritional labels encourage consumers to consider the health value of the food instead of solely prioritizing taste, positively altering their decision-making when viewing different food options.

Providing nutritional information is crucial in maintaining transparency between manufacturers and consumers. Informing consumers about the true nutritional value of a product involves stating unnatural ingredients. Although such information is important, researchers found that consumers' awareness of unnatural ingredients, which are often negatively perceived, can cause a negative halo effect of consumers perceiving the whole product more negatively, ultimately impacting their decisions. When unnatural ingredients such as artificial ingredients, food additives, and genetically modified organisms were provided, consumers demonstrated selective accessibility, or a greater focus on these claims despite other available information, which led to consumers making biased food decisions and higher calorie estimates for the product. Without intervention by food manufacturers, the load on the consumers' decision-making increases thereby demanding them to counteract this negative halo effect by critical thinking, priming, opposing, and reasoning (Sundar et al. 1280-1292). Therefore, consumers utilize critical thinking to modify their immediate thought processes and decrease the potential negative effects of food labels.

How Individual and Household Characteristics Influence Food Label Use Although food manufacturers can try to adjust nutritional information to influence customers' purchasing decisions, the effectiveness of the same nutritional information can differ significantly based on individual and household differences. Income

Individuals' incomes can influence many decisions, including nutrition decisions and consumption. Researchers have found that income has a role in the anticipated demand for goods (Cirera and Masset, 2821-2834). Income has the potential to influence the frequency of the usage of nutritional labels including differences in consumers acquiring knowledge of food quality and safety. Food quality can include how much nutritional value and outstanding taste a product has while food safety includes how safe to eat the product is.

Varying levels of income may force individuals to prioritize different factors. Researchers have found that consumers who attach importance to price usually are less likely to use labels while consumers who attach importance to nutrition are more likely to search for nutritional information (Drichoutis et al. 1). While putting more importance on price may be due to values and not necessarily income, individuals with lower incomes may have to prioritize quantity or price more than not prioritize the nutritional value of the food due to less monetary availability. They may have to limit food as a necessary means for survival and not have the ability to be too concerned with its quality. This can influence one's use of nutrition information, especially regarding the nutritional value of a product. However, while food quality may not be the most influential factor, food safety may become an increasing concern with buying lower-priced products as cheaper goods could have less sanitary production. Meanwhile, those with higher incomes have more financial security and may invest more in higher quality food like organic and less processed foods. Fiscal stability gives them the ability to prioritize nutritional fulfillment and the taste of the food.

Complicating Variables

However, relating income with nutrition decisions and food label use may be an oversimplification, as other factors can be involved. A study by Nie et al. examined the effect of income, income effect, or change in consumerism based on income, and risk-averse, or fear of

potential loss, on food decisions. The results showed that high-risk-averse and low-income consumers with strong loss aversion and a weak income effect show a higher demand for food *safety* labels as a way to ensure easy access to safety indications (Nie et al. 711671). Meanwhile, low-risk-averse and high-income consumers with weak loss aversion and a strong income effect show a higher demand for food *quality* labels because they hope to gain more health benefits from high-quality food at good prices (Nie et al. 711671). This demonstrates that besides the level of income, factors like risk-averse and income affect can lead to individual differences in consumerism. Therefore, this is a complicated area of discussion, and studies researching only income with nutrition decisions and consumption may present limitations.

Furthermore, nutrition decisions and food label use may depend on what nutrition labels are available, which can relate to income. Food deserts are often low-income areas with little access to healthy and affordable food. Most food deserts have fewer supermarkets, and greater distance from supermarkets, meaning that transportation may be another factor hindering access (Alwitt and Donley 139-164; Chung and Myers 276-296; Morris et al. 52S-58S; Morland et al. 23-29; Zenk et al. 660-667; as cited in Beaulac et al. 1966-2007). In addition, the available supermarkets often have smaller selling space that doesn't permit a wide variety of food choices (Cotterill and Franklin; White et al.; as cited in Beaulac et al. 1966-2007). Food deserts portray that the use of food labels can be limited by the lack of available nutritional options, demonstrating that the use of food labels and nutritional decisions may not be directly correlated with income but more related to the aspect of accessibility often associated with cost.

Household Composition & Geographical Location

Not only individual factors but also group dynamics and social settings like household differences can impact the use of nutrition information. Specifically, the size, area, and age makeup of households have been shown to influence food label use. Researchers have found that smaller households and households in non-city or rural areas are more likely to use nutritional labels (Drichoutis et al. 1; Govindasamy and Italia 55-68). Larger families have to support a larger family therefore smaller families may have more time to engage in and care for individual members' nutritional intake, and studies have found that people with more available time for grocery shopping are more likely to use labels (Drichoutis et al. 1). Suburban and rural areas are slower-paced and have more emphasis on nature than the busier cities. Meanwhile, cities often have greater availability of restaurants while suburban and rural areas may have limited commercial food sources and may be less exposed to processed foods containing food labels. Such differences in social context, pacing, and availability can influence the emphasis on nutrition information and, therefore, the use of food labels.

One study further found that households with young children are more likely to engage in nutrition information search behaviors while a different study found that older individuals are more likely to make use of nutritional labels (Drichoutis et al. 1; Govindasamy and Italia 55-68). Households with younger children may emphasize the nutritional intake of foods and dietary value during a child's growth, therefore, putting more emphasis on nutrition information.

However, although the children may influence this emphasis, it is often the older individuals, the parental figures, who physically make use of the nutrition labels, which may explain the disparity of the evidence. Overall, the social context of a household like size, setting, and age can impact the use of nutritional information.

Gender

Gender has a role in the overall use of nutritional labels and the type of nutritional information one focuses on. In general, women use nutritional labels more than men (Govindasamy and Italia 55-68; Guthrie et al. 163-172; Kim et al. 10-19; Kim et al. 346-363; McLean-Meyinsse 110-114; as cited in Drichoutis et al. 1). However, there are differences in the specific nutritional values that women and men focus on. Researchers found that men focus more on the ingredients list (Drichoutis et al. 93-118) while women focus more on calories, vitamins, and minerals (Bender and Derby 292-297). This demonstrates that there are gender differences in both the amount and type of nutritional information used.

Health Beliefs & Concerns

General health beliefs influenced eating patterns and also correlated to food label use. Researchers found that believing in an association between diet and cancer, being more concerned about nutrition and health, or being aware of diet-disease relations predicted greater label use among consumers (Neuhouser et al. 45-53; Drichoutis et al. 1). Furthermore, organic buyers were more likely to search for nutrition information (Drichoutis et al. 1). This demonstrates that more health-conscious consumers were more likely to utilize nutrition information to affect their eating patterns.

A major influence on one's eating pattern and ultimately the use of nutritional information is one's health concern. Researchers found that consumers on a special diet were more likely to use food labels (Drichoutis et al. 1). Because certain health concerns or illnesses can determine a more strict diet, this demonstrates the role of individual health status on nutrition information use. Results from an experiment showed that patients with high blood pressure were 63% more likely than those with normal or low blood pressure to look for sodium on the nutrition label but not other nutritional information. Similarly, patients with high cholesterol were more likely than those with normal or low cholesterol to look for saturated fat but not other nutritional information (Kreuter et al. 277-283). Specific health concerns can influence consumers to look at corresponding nutrients but may not increase the use of all nutritional information in general.

Level of Nutritional Knowledge

Food labels have low utility if consumers lack the understanding of how to use them or possess insufficient nutritional knowledge. Therefore, the level of nutritional knowledge plays a crucial role in customers' perception and comprehension of nutrition labels. Researchers have found that consumers' ability to comprehend label information can often be limited. Among 12000 consumers in the United Arab Emirates, 89.5% of consumers had a general awareness of reading food labels but only read basic information like production and expiry dates (Washi 38). Furthermore, in a study of 498 Korean middle and high school female students, the students were aware of the necessity and positive effects of nutrition labels but experiment scores demonstrated that they did not understand label information accurately (Chung et al. 239-254). This lack of nutritional knowledge becomes a barrier for consumers to access and make informed choices using food label information. Therefore, increasing knowledge about nutrition and diet is an important factor that could help make food labels more purposeful.

Level of Education

Overall education, rather than just dietary knowledge, also influences the use of nutritional labels. Less-educated individuals tend to perform poorly in tasks related to understanding nutrition labels, while better-educated individuals perform better (Levy and Fein 210-217). Surveys have shown that nutrition label use is significantly higher among those with more than a high school education (Neuhouser et al. 45-53). While less educated consumers don't completely ignore nutritional information, there are limitations to the extent to which they utilize nutritional information. Better-educated consumers tend to use both nutritional labels and ingredient lists to make purchasing decisions, while less-educated consumers may solely rely on nutritional labels (Bender and Derby 292-297). This demonstrates that level of education can allow or hinder consumers from understanding nutritional information and implies that understanding food labels may require complex knowledge and is not readily accessible to the public.

There are several reasons why those with higher education may utilize food labels better. One explanation is that higher education leads to increased information search, including from media sources (Katona and Mueller 30-87; Schultz 827-846; Moorman and Matulich 208-228; as cited in Drichoutis et al. 1). Moreover, consumers with higher education and more nutritional knowledge tend to be less skeptical of nutrition information (Moorman 82-98). This demonstrates that education impacts the use of nutrition information from many different angles. Best Practices for Simplified Nutrition Communication

Comprehensive Presentation of Diverse Nutrients

According to the U.S. Food and Drug Administration, an update to the Nutrition Facts Label in 2016 requires packaging to display the number of calories in a larger, bolder font ("Food Labeling Guide (PDF)"). However, consumers who constantly focus on and track calorie information displayed on food labels have demonstrated heightened eating disorder symptomatology and other unhealthy eating habits (Simpson and Mazeo 89-92; Larson et al. 399-408; Al-Otaibi et al.). Therefore, highlighting other nutritional information on food labels besides the number of calories can encourage consumers to reassess their views on food products to be more holistic instead of hyper-focusing on the number of calories. Manufacturers can improve food labels to better highlight the content of specific nutrients by making the nutritional information more clear and comprehensible. This may be done by utilizing percentages, which are conceptually more understandable than pure numbers. For instance, highlighting "% daily values" or illustrating a product as having "____% more protein than ____" can resonate more strongly with consumers than stating "7 grams of protein." A literature review of research on consumers' use of nutritional labels found that portraying nutrient amounts using percentages based on the daily values for each nutrient consistently produced the most positive dietary benefits, further supporting the effectiveness of percentages. Additionally, consumers preferred the usage of whole numbers instead of decimals (Drichoutis et al. 1), another way to make nutrient content more easily quantifiable. Implementing such adjustments can redirect consumers' attention from just the number of calories to other nutrients, better informing consumers of the true nutritional makeup of the product and better suiting individual health goals.

Traffic Light Schemas

Furthermore, utilizing traffic light schemas (and similar generalized, easily understandable cues) can convey nutritional information in simpler health terms. This enables consumers to interpret food labels without requiring scientific knowledge of nutrition. Traffic light labels put food into categories of good, bad, and neutral by using a standard traffic light approach. Often, levels of key nutrients in processed food like fat, sugar, saturates, and salt are displayed with red corresponding to high, yellow corresponding to medium, and green responding to low levels of the nutrient (Kunz et al. 134).

Research has demonstrated the effectiveness of traffic light schemas due to their clear comprehensibility. In Israel, government regulations require red warning front-of-package labels for high levels of sodium sugar, or saturated fats and voluntary green front-of-package labels for products that meet nutrition recommendations. With these implemented policies, 76.2% of the 1042 participants reported frequent use of nutrition facts tables and 81.1% reported intending to purchase fewer red labeled and 85% to purchase more green labeled products (Bromberg et al. 230-237). This demonstrates that traffic light labels can both increase the usage of food labels and encourage healthier consumption choices. Similarly, an experiment done in Peru found that the traffic light label system significantly increased the number of consumers choosing the healthiest items. Interestingly, the positive effects of traffic light labels were prominent in individuals lacking basic nutritional knowledge, suggesting that traffic light labels were simply enough to be widely comprehended (Defago et al. 151-161). This is further supported by a literature review that found that traffic light schemas are marginally more effective in influencing healthier options than other food labels and Guideline Daily Amount (Cecchini 201-210), possibly due to the simplicity and directness of traffic light approach compared to the cognitive overload and vast amounts of information provided by other food labels. Researchers found that presenting consumers with several different health and nutritional information could be misleading and not beneficial (Barreiro-Hurle 426-443). Therefore, food production should utilize more traffic light labels to display nutrition information.

Simpler Sample Sizes

While traffic light labels are effective in making nutritional information more comprehensible to consumers due to their simplicity and directness, aspects of nutritional knowledge–specifically sample sizes—that require consumers to do math calculations are much less effective. When assessing consumers' ability to perform tasks using nutrition labels to test their comprehension of the given information, only 20% accurately completed a task requiring complex math–calculating the contribution of a product to daily diet (Levy and Fein 210-217). This is further supported by researchers who found that consumers often struggle to manipulate quantitative nutrient information (Drichoutis et al. 1). Therefore, another way to improve food labels is to provide nutritional information in terms of clear sample sizes that don't require consumers to mathematically calculate what the whole bag or package truly composes of.

Visuals

The visual aspects of food labels, encompassing color and design, represent another influential characteristic that affects their efficacy. Consumers often show a preference for details like bold text and color-highlighted nutrition panels (Drichoutis et al. 1). In terms of graphic design, an eye-tracking study demonstrated that consumers' attention is initially captured by a package's graphic design, priming their perception of the product based on this design. This can lead to biased and irrational evaluations of the product's nutritional aspects (Oliveira et al. 160-167), highlighting the influential role of graphic design on consumer perceptions. Conclusion

Food labels can shape consumer awareness of nutrition and decisions about food. Nutrition information can shift consumers' focus from taste to health benefits, promoting healthier dietary choices. However, misinterpretation of labels can lead to a negative halo effect, causing negatively perceived information to be highlighted and lead to biased food decisions.

These perceptions and focuses vary based on individual and household differences like income, household composition, gender, health beliefs, and amount of nutritional knowledge. Lower-income individuals may often need to prioritize price over other factors, while higher-income individuals may be able to prioritize nutritional quality. Furthermore, smaller households, non-urban areas, and households with young children demonstrate great food label use. Gender differences show that women generally use food labels more than men, but men focus more on ingredient lists while women prioritize information about calories, vitamins, and minerals. Nutrient preferences, health beliefs, and specific conditions further determine individual use of specific nutritional information. A barrier to the effectiveness of food labels is a limited understanding of how to utilize food labels and understand provided nutritional information, emphasizing the need for improved nutritional education.

Food manufacturers can improve the effectiveness of labels to a wider audience by portraying nutritional information more clearly and comprehensively through percentages, traffic light schemas, and simple sample sizes. Altering graphic design and color use can also enhance consumer utilization of food labels. In general, promoting greater use and comprehension of food labels can impact consumers' daily food consumption and overall health.

Since the display of food labels is so influential, food manufacturers can use this research to improve labeling and get better health outcomes for consumers. Further research on how to improve consumer use of nutrition facts and food labels should consider the impact of individual differences for more specific solutions tailored for a diversity of consumers. This research suggests that a lack of nutrition knowledge and awareness is a significant factor impacting consumer use of nutrition labels. Although food labels can be improved to be more comprehensive, they may be ineffective if consumers do not know to look for the nutrition information and if they do not have some background knowledge on how to interpret the provided information on food labels. Additionally, providers and healthcare experts can give tailored nutritional guidance that meets individual patient needs and health statuses. Such nutritional advice can allow consumers to better decipher food label content and avoid potentially harmful ingredients and nutrients.

Furthermore, referencing food labels may not be a priority if access to food is limited, as demonstrated by behavior recorded in some food deserts. However, in places of low economic situations and less availability of food, knowledge about food labels may be even more crucial to ensure consumers' safety considering the lower quality and nutritional benefits that are often the only options close to home. Therefore, improving food labels and consumers' food decisions begins with making healthy, diverse options available and improving general consumer awareness about nutrition information.

Works Cited

- Al-Otaibi, Hala, Tahani Al-Sandal, and Haiam O. Elkatr. "Is calorie labeling on menus related to weight disturbances among females in Saudi Arabia?." *Journal of Nutrition and Metabolism* 2021 (2021).
- Alwitt, Linda F., and Thomas D. Donley. "Retail stores in poor urban neighborhoods." *Journal of consumer affairs* 31.1 (1997): 139-164.
- Barreiro-Hurle, Jesús, Azucena Gracia, and Tiziana De-Magistris. "The effects of multiple health and nutrition labels on consumer food choices." Journal of Agricultural Economics 61.2 (2010): 426-443.
- Beaulac, Julie, Elizabeth Kristjansson, and Steven Cummins. "Peer reviewed: A systematic review of food deserts, 1966-2007." *Preventing chronic disease* 6.3 (2009).
- Bender, Mary M., and Brenda M. Derby. "Prevalence of reading nutrition and ingredient information on food labels among adult Americans: 1982–1988." *Journal of Nutrition Education* 24.6 (1992): 292-297.
- Bromberg, Michal, et al. "Current use of nutrition facts tables and attitudes towards new red and green front-of-package labels among Israeli consumers." International Journal of Food Sciences and Nutrition 73.2 (2022): 230-237.
- Briguglio, Matteo, et al. "Dietary neurotransmitters: a narrative review on current knowledge." *Nutrients* 10.5 (2018): 591.
- Cecchini, Michele, and Laura Warin. "Impact of food labelling systems on food choices and eating behaviours: a systematic review and meta-analysis of randomized studies." Obesity reviews 17.3 (2016): 201-210.
- Chung, Eun-Jung, Jin-Soon Jeon, and Hong-Seok Ahn. "Reading and understanding of food & nutrition labels and dietary behaviors of female middle and high school students." *Journal of the Korean Dietetic Association* (2010): 239-254.
- Chung, Chanjin, and Samuel L. Myers Jr. "Do the poor pay more for food? An analysis of grocery store availability and food price disparities." *Journal of consumer affairs* 33.2 (1999): 276-296.
- Cirera, Xavier, and Edoardo Masset. "Income distribution trends and future food demand." Philosophical Transactions of the Royal Society B: Biological Sciences 365.1554 (2010): 2821-2834.
- Cotterill, Ronald, and Andrew Franklin. "The urban grocery store gap." (1995).
- Defago, Daniel, et al. "Can traffic light nutritional labels induce healthier consumer choices? Experimental evidence from a developing country." *International Journal of Consumer Studies* 44.2 (2020): 151-161.
- Drichoutis, Andreas C., Panagiotis Lazaridis, and Rodolfo M. Nayga Jr. "Nutrition knowledge and consumer use of nutritional food labels." *European Review of Agricultural Economics* 32.1 (2005): 93-118.

- Drichoutis, Andreas C., Panagiotis Lazaridis, and Rodolfo M. Nayga Jr. "Consumers' use of nutritional labels: a review of research studies and issues." *Academy of marketing science review* 2006 (2006): 1.
- "Food Labeling Guide (PDF)." *FDA*, 24 May 2011, https://www.fda.gov/files/food/published/Food-Labeling-Guide-%28PDF%29.pdf. Accessed 27 August 2023.
- Gómez-Pinilla, Fernando. "Brain foods: the effects of nutrients on brain function." *Nature reviews neuroscience* 9.7 (2008): 568-578.
- Govindasamy, Ramu, and John Italia. "The influence of consumer demographic characteristics on nutritional label usage." *Journal of Food Products Marketing* 5.4 (2000): 55-68.
- Guthrie, Joanne F., et al. "Who uses nutrition labeling, and what effects does label use have on diet quality?." *Journal of Nutrition education* 27.4 (1995): 163-172.
- Katona, George, and Eva Mueller. "A study of purchase decisions." *Consumer behavior: The dynamics of consumer reaction* 1 (1955): 30-87.
- Kim, Sung-Yong, Rodolfo M. Nayga, and Oral Capps. "Food label use, self-selectivity, and diet quality." *Journal of Consumer Affairs* 35.2 (2001): 346-363.
- Kim, Sung-Yong, Rodolfo M. Nayga, and Oral Capps. "Health knowledge and consumer use of nutritional labels: the issue revisited." *Agricultural and Resource Economics Review* 30.1 (2001): 10-19.
- Kreuter, Matthew W., et al. "Do nutrition label readers eat healthier diets? Behavioral correlates of adults' use of food labels." American journal of preventive medicine 13.4 (1997): 277-283.
- Kumar, Sumit, et al. "Nutrition, Neurotransmitters, and Behavior." *Nutrition and Psychiatric Disorders*. Singapore: Springer Nature Singapore, 2022. 89-108.
- Kunz, Sonja, et al. "Beyond healthiness: the impact of traffic light labels on taste expectations and purchase intentions." Foods 9.2 (2020): 134.
- Lane, Melissa M., et al. "Ultra-processed food consumption and mental health: A systematic review and meta-analysis of observational studies." *Nutrients* 14.13 (2022): 2568.
- Larson, Nicole, et al. "Calorie labels on the restaurant menu: is the use of weight-control behaviors related to ordering decisions?." *Journal of the Academy of Nutrition and Dietetics* 118.3 (2018): 399-408.
- Levy, Alan S., and Sara B. Fein. "Consumers' ability to perform tasks using nutrition labels." *Journal of Nutrition Education* 30.4 (1998): 210-217.
- Lim, Seung-Lark, et al. "Calorie labeling promotes dietary self-control by shifting the temporal dynamics of health-and taste-attribute integration in overweight individuals." *Psychological science* 29.3 (2018): 447-462.
- McLean-Meyinsse, Patricia E. "An analysis of nutritional label use in the Southern United States." *Journal of Food Distribution Research* 32.856-2016-57721 (2001): 110-114.
- Meyer, Barbara J., et al. "Dietary intakes and food sources of omega-6 and omega-3 polyunsaturated fatty acids." *Lipids* 38.4 (2003): 391-398.

- Moorman, Christine. "Market-level effects of information: Competitive responses and consumer dynamics." *Journal of Marketing Research* 35.1 (1998): 82-98.
- Moorman, Christine, and Erika Matulich. "A model of consumers' preventive health behaviors: The role of health motivation and health ability." *Journal of consumer research* 20.2 (1993): 208-228.
- Morland, Kimberly, et al. "Neighborhood characteristics associated with the location of food stores and food service places." *American journal of preventive medicine* 22.1 (2002): 23-29.
- Morris, Patricia McGrath, Linda Neuhauser, and Cathy Campbell. "Food security in rural America: a study of the availability and costs of food." *Journal of nutrition education* 24.1 (1992): 52S-58S.
- Neuhouser, Marian L., Alan R. Kristal, and Ruth E. Patterson. "Use of food nutrition labels is associated with lower fat intake." *Journal of the American dietetic Association* 99.1 (1999): 45-53.
- Nie, Wenjing, et al. "Influence of loss aversion and income effect on consumer food choice for food safety and quality labels." *Frontiers in Psychology* 12 (2021): 711671.
- "Nutrition." *Harvard Health*, https://www.health.harvard.edu/topics/nutrition. Accessed 3 September 2023.
- "Nutrition Health topics." *World Health Organization (WHO)*, https://www.who.int/health-topics/nutrition#tab=tab_1. Accessed 3 September 2023.
- Oliveira, Denize, et al. "Consumers' attention to functional food labels: Insights from eye-tracking and change detection in a case study with probiotic milk." *LWT-Food Science and Technology* 68 (2016): 160-167.
- Schultz, Theodore W. "The value of the ability to deal with disequilibria." *Journal of economic literature* 13.3 (1975): 827-846.
- Simpson, Courtney C., and Suzanne E. Mazzeo. "Calorie counting and fitness tracking technology: Associations with eating disorder symptomatology." *Eating behaviors* 26 (2017): 89-92.
- Sundar, Aparna, et al. "Is unnatural unhealthy? Think about it: Overcoming negative halo effects from food labels." *Psychology & Marketing* 38.8 (2021): 1280-1292.
- Washi, Sidiga. "Awareness of food labeling among consumers in groceries in Al-Ain, United Arab Emirates." International Journal of Marketing Studies 4.1 (2012): 38.
- White, Martin, et al. "Do 'food deserts' exist? A multi-level, geographical analysis of the relationship between retail food access, socio-economic position and dietary intake." *Food Standards Authority, London* (2004).
- "Why It Matters | Nutrition." *CDC*, https://www.cdc.gov/nutrition/about-nutrition/why-it-matters.html. Accessed 3 September 2023.

Zenk, Shannon N., et al. "Neighborhood racial composition, neighborhood poverty, and the spatial accessibility of supermarkets in metropolitan Detroit." *American journal of public health* 95.4 (2005): 660-667.

Two Spiders and a Monkey: The Challenges Women Faced in NASA, 1960-1989 By Aahelie Bhattacharya¹, Richa Shukla², and Rithika Suresh³

Abstract

This paper analyzes the interactions between social and political movements of the 1960s and 1970s, such movements' effects in the 1980s, and NASA's relationship with the public. Overall, we answer the question of what challenges women, particularly women of color, faced in NASA. Building on the work of Neil Maher and Kim McQuaid, we analyze the experiences of women in NASA through past interviews, newspapers, and women's magazines. We convey the extent to which they were underrepresented and dismissed through analyzing monographs, interviews, newspaper articles and women's magazine archives. The framing journalists, managers, and other public figures used to portray women as incapable of complex work created a cycle of dismissal and underrepresentation within NASA, as elsewhere. The patronizing lens used to distort the accomplishments of women, especially women of color, is something we explore. Our paper aims to rectify this through exploring the treatment women faced in the media, the issues women faced within NASA, and how cultural movements affected the barriers women faced.

Keywords:

NASA - National Aeronautics and Space Administration

Second Wave Feminist Movement - a social movements in the 1960s and 1970s for women's rights

Introduction

By the year 1972, NASA had sent only three females sent to outer space-- two spiders and a monkey. This would come as a shock to Grace Humphrey, an astronomist who wrote "In the World of Stars: Astronomy's Debt to American Women" in 1921 (Humphrey). She begins by asking the reader to recall their grandmother's glorious tales about "Miss Mitchell's comet", or the first female American professional astronomer who discovered C/1847 T1 in 1847. This historical periodical goes on to detail the hard work and consistent contributions of women in astronomy, dating back to biblical times. Humphrey was proud of the tedious labor done by women as well as their collaborations with male peers, allowing the modern reader a glimpse into the world of the brightest women astronomers throughout history and the stories shared about them. She quotes Mitchell, "I was born of only ordinary capacity, but of extraordinary persistency." This paper highlights the persistence of women in space science and how NASA appeared to be equally resolved to prevent women from accomplishing the yield from their determination. From NASA's birth in 1958 until 1983, there were no female astronauts and no astronauts from minority groups even in training until Sally Ride. For an entire generation, women, in particular women of color, in NASA were refused positions in the first place because of the amount of barriers placed in their pursuit of higher education. If they were able to get over such hurdles, they were then trapped in menial positions. To make matters worse, there were forty-three classifications of secretaries to keep women out of management positions. Negative press and stereotypes plagued the careers of women who managed to reach higher positions (Mcquaid 405–34). For these reasons, we argue that NASA's fabricated response to the feminist and civil rights movements of the 1960s and 1970s and the subsequent media portrayal of women's scientific accomplishments are a manifestation of the pervasive racism and sexism of the time, because this theme of suppressing female accomplishments can be reflected throughout US history.

American history centers the narrative of white men, and this holds true in the history of NASA. The contributions of women in NASA, especially women of color, are consistently undervalued and unrecognized. Through an analysis of women's early contributions to astronomy, the public's growing curiosity for women in space, and the challenges that had to be overcome by women at NASA, we attempt to center a different, untold narrative. Throughout this paper, we will cover how women of color were considered for space travel differently than white women, and what this says about the biases of NASA, the significance of accomplished women being written about in a patronizing manner, and how the media failed repeatedly to accurately depict these contributions. We believe it is important that women should get the recognition and respect they deserve for their work and accomplishments.

Often, historians focus on the experience of either women's treatment in NASA or the treatment of BIPOC men in NASA. For example, *Right Stuff, Wrong Sex: America's First Women in Space Program* by Margaret Weitekamp is about the experiences of Caucasian women in the space program and the Lovelace program. While this is an important topic and all women did not get the recognition they deserved, there was no mention of any women of color. Similarly, the monograph Apollo and the Age of Aquarius by Neil Maher discusses the impact of the Civil Rights movement throughout the 1960s on the space program, which is an incredibly important topic, it does not touch on the experiences of women of color. The common theme with such works is that they do not include the intersectionality between race and gender, which is what our paper aims to change. While historians have focused more closely on racism and sexism individually during these decades, the experience of women in NASA is severely overlooked. The fact that the book Hidden Figures: The American Dream and the Untold Story of the Black Women Mathematicians Who Helped Win the Space Race by Margot Lee Shetterly, as well as its film, remains the only prominent media representation of Black women's struggles and accomplishments in the space program serves as proof of this negligence (Maher).

In the past, historians of space have overlooked women in the space program and chose to focus on prominent male lead scientists instead. This is a recurring problem in many different fields and is still going on today. But this has not always been the case. For example, Dr. Kim

McQuaid, who was a Professor at Lake Erie College, published a paper in the Journal of American Studies in which he talked about how the exclusion of women and other minority groups in the space program had a great effect on the future of spaceflight. He addresses the place of African-American women in NASA throughout the latter half of the twentieth century, exploring how NASA began affirmative action and also attempted to stop it. The main argument of the work is that while NASA purposely suppressed affirmative action hiring and positions, they eventually did not succeed in such suppression because of the work of Ruth Bates Harris and Harriett Jenkins. The sources used were interviews with Senate committees, interviews with Harris, Jenkins, NASA officials, and even telephone calls. Our work in this field is an attempt to build upon the work of past historians while hopefully shedding light on the accomplishments of women and giving them the well-deserved recognition that they deserved at the time. This paper will give the spotlight to the women that have not had the opportunity before.

Through interviews with key figures, women's magazine archives, monographs, newspaper clippings, and more, we were able to form a broader understanding of the distinction between the media's portrayal of women scientists and women's true experience at NASA. Newspaper and magazine articles, in particular, allowed our group to get an accurate portrayal of the media's representation of women at the time. 'Blonde Eager to Try Space', 'Aviatrix Jerrie Would Be First Woman Space Ace: She'd Be First Fair Space Ace', and 'Space Woman Hugs, Kisses Fellow Year' are three such sources that helped our group understand why women were so underrepresented and had to go through great lengths to be able to join the space program. They also had to face many adversities even after being accepted into the program which affected the way they worked and how far they could get in the program.

II. Analysis

A. The Effect on Social Movements on NASA

During the 1960s and 1970s, the burgeoning feminist and civil rights movements shifted the public's perspectives on space exploration and the roles of women in them. Second wave feminism had a huge effect on the public's perspectives on space exploration. After Sally Ride went to space on June 18, 1983, she inspired many women to join the space program and become scientists. For example, organizations such as the Lovelace Foundation for Medical Education conducted experiments to prove that women were just as capable as men to go into space even though in the end they were not allowed to go (Cochran). While the Lovelace Foundation for Medical Education for Medical Education did try to give medical evidence that women could be in space, the founder of this organization William Randolph Lovelace II was deliberately vague towards the women about if the medical exams could actually help them become astronauts. Unfortunately Lovelace died before he revealed why he had done this but according to Amy Foster who wrote *The Gendered Anniversary: The Story of America's Women Astronauts* Lovelace most likely did not receive enough financial backing from NASA so he purposely was vague so that women would

accept his invitation for experimentation (Foster 150–73). This increase in women in STEM was not supported by everyone. According to a magazine from 1973, when NASA revealed that women were apart of the space program, the public reacted flippantly and used nicknames such as "Astrodolls", "Spacegals" and "Astronettes". This greatly effected how women's accomplishments in the space program were viewed. There were many people, especially men, who were not able to accept the fact that women could have the same jobs and skills as them. This is the reason that many women had to go through more unnecessary challenges than men in the space program. These factors all contributed to the increase in feminism in the 1960s to 1970s. This increase in feminism also led to some changes in NASA.

At the same time, there were rising concerns among the public about NASA discrimination against marginalized groups. Some well known civil rights movements at this time were the American Indian Movement, or AIM, Gay Rights Movement and the Women's Liberation Movement. Many people of marginalized groups were not allowed to join NASA due to many factors. One factor was that people of marginalized groups did not get the same opportunities for higher education which makes other candidates more applicable for jobs. According to a census document from the years 1960-1998, an average of around 8.8% of Black people 25 years or older went to college. Similarly an average of around 9.1% of Hispanic people 25 years or older went to college. On the other hand, during these same years an average of around 17.5% of White people went to college. These statistics emphasize that during these years, there is a significant difference between the number of White people and other minority groups. This puts minority groups at disadvantage when compared against other groups of people who have had more opportunities. These educational barriers prevented many people of marginalized groups from getting jobs in places such as NASA. Many people of minority groups who were lucky enough to be hired were often overshadowed by other scientists in positions of power. People of minority groups were prevented from being in positions of power. This issue was addressed in the book Hidden Figures: The American Dream and the Untold Story of the Black Women Mathematicians Who Helped Win the Space Race written by Margot Lee Shetterly. In this book, Shettery talks about how the Black people, specifically women, were not allowed to get higher paying jobs or be in positions of power. Even when they were allowed to have those jobs, they were not respected or given the recognition they deserved. Shetterly also talks about how she grew up in Hampton, Virginia which had many African-American scientists so did not realize until later in life that she realized how uncommon this was. This realization inspired her to write her book, to give the women a part of the West Computers the credit they deserved (Carpenter 18-21).

B. The Treatment of Women within NASA

In light of second wave feminist movements, the Civil Rights movement, and the simultaneous need for public approval, NASA attempted to accept more women into the industry; their intentions behind these actions can be perceived through the challenges women

faced in the industry. The lens in which women astronauts were viewed within NASA was absolutely sexist and performative. Because NASA faced so much pressure to integrate women and people of color against their will, this led to extreme bias against women. NASA officials described the conditions as too challenging for women, even though many women performed superior to their male colleagues in training and in regard to their accomplishments. The talk of American Spacewomen made officials uneasy, because they refused to acknowledge the talents of women in the field. They led to 25+ qualified women who wanted to become astronauts to find their talents useful elsewhere, because of the ignorance such officials displayed. Even astronaut John Glenn said that such women were not qualified, and if they were, that he would "welcome them with open arms." Yet, women who were more than qualified had to be "patient" and "less ambitious" because their time would be soon to come. In fact, female astronaut-candidate Jerrie Cobb participated in more than 10,000 hours of training, more than any other potential astronaut, male or female alike (Riedell). Yet, Cobb was shelved as an astronaut, because of "medical reasons," according to Brigadier General Don Flickinger. Cobb was a part of the Lovelace Program, responsible for training female astronaut candidates. The Lovelace program trained 19 women, 13 of them passed, yet none of them flew because of such restrictions and apparent "difficulties" caused by their anatomy. Many people believed that women were unsuited for space exploration, culturally. Yet, years of studies proved that female bodies were just as capable (and even more capable because they were generally lighter, smaller, and consumed less), but NASA officials simply refused to acknowledge it. Then, such men managing NASA would further tell women that they had to make space suits "sexier" for the feminine physique, because who would ever want to see a woman doing science for scientific purposes?

Furthermore, officials also found women's waste a problem, and made it seem taxing to design "his and hers" spacesuits. Even worse, male astronauts and even other female astronaut candidates agreed that space was a "men's terrain." Even Jaqueline "Jackie" Cochran, a female pioneer in aviation, a self made millionaire, an incredibly persuasive pilot, said that including women in the space program would be an embarrassment, and that they would be likely to drop out because they would eventually get married and pregnant, in a congressional hearing (Weitekamp 150–73). This pervasive internalized misogyny was extremely harmful to the plight of grassroots feminist activists throughout the 1960s, 70s, and 80s, who demanded female and minority representation in space. As mentioned earlier, activists throughout the feminist movement and the Civil Rights movement fought for representation within NASA, and NASA eventually had to incorporate affirmative action. Yet, this came with its own challenges.

Ruth Bates Harris, NASA's original Equal Opportunity Director, was demoted before she was even on the job by Administrator James Fletcher, and was subdued time and time again. Harris was relentless in the workplace in her quest for equal opportunities and affirmative action. She even went directly to Wernher von Braun, an incredibly talented rocket scientist (who was also a Nazi who used parts made by slave labor) and asked him if the rumors were true. She fought for true justice within NASA and attempted to solve the clear problems with female

representation and the representation of people of color. Yet, Fletcher and another top administrator, George Low, both did not take her work seriously and thought of her as unnecessary bureaucracy. She brought issues that might have been uncomfortable for racist white men into the office, and they fired her for it. Placing this into historical context, this firing of Harris aligned with the Nixon firings, where President Richard Nixon fired anyone within his staff who was against his corruption, and Fletcher and Low fired someone against their reign of racism and sexism. But, this firing did not last long. Because of Harris's sway within Congress, especially with African-American Congress members, NASA officials like Fletcher and Low were subject to congressional hearings and progress reports on their integration progress. There was essentially no progress, to the point that the top administrators even avoided hearings, even though they would secure them more money.

To make matters worse, Harris decided to sue NASA for discrimination, and administrators were incredibly concerned about losing the small amount of prestige that NASA had. She eventually settled and received a job again, but on the fringes of the equal opportunity department. Her replacement, Harriett Jenkins, was less abrasive and made affirmative action something in the background. Jenkins actually made quite a bit of progress, by not rushing into anything and being transparent with the rest of NASA. While progress was not immediate when it came to Jenkins (actually over 15 years), this example clearly underscores how women, particularly women of color, were treated within NASA, in the space program and in the office (Kim 405-34).

C. The Media Representation of Women in Space

Even after women got accepted into the space program, their scientific accomplishments were not properly acknowledged by the media and, oftentimes, went unnoticed or diminished by patronizing tones. In order to grasp the distinction between the media's portraval and the true work of women at the time it is important to understand the context of women's contributions to astronomy during earlier periods. Following the legacy of Maria Mitchell, generations of women were educated at Matthew Vassar's girls' college (Humphrey). Her writing not only appreciated the contributions of prominent women such as Margaret Lindsay Huggins, Catherine Wolfe Bruce, and Mary Anna Draper, but also gave the reader a sense of the significance that astronomy held in women's higher education at the time. Astronomy was taught at all women's colleges of the time. The 1918 meeting of the American Astronomical Society met for a day at Wellesley, while in 1920 all four days were spent at Smith. Both of these colleges are womens' colleges, leading the author to affirm that "men of science are recognizing the value of American women's contribution in the field of [astronomy]". Overall, the piece painted a picture of the transition from an old world to a new world, in which educated women contributed to professional scientific progress alongside their male peers. This transition stalled for decades, and even progress recorded in the media seemed to come with a backhanded message. With the rise of the "convenient" astrophotography in the early 1930's and the view that even amateur

scientists and experimenters could now contribute to science, women's roles in astronomy were, too, given acknowledgement (Cannon). However, these contributions were far from the limelight that the 'great man' narrative of the time enjoyed. This can possibly be a parallel to how the rising calls for women in space coincided with the rhetoric that scientific progress made space travel much easier and safer than before, indicating a theme of the media's reliance on the image of women being too delicate for space and scientific professions in general.

As time passed, more accomplishments surfaced as proof that women were, indeed, capable of spaceflight and scientific work. America's first woman space flight candidate had been Jerrie Cobb in 1960, as a part of the Lovelace's women in space program. Dr. Randolph Lovelace stated about the twelve women space candidates that, "we are already in a position to say that certain qualities of the female space pilot are preferable to those of her male colleague ... she weighs much less, consumes less oxygen, needs less food and has proved herself to be better capable of standing psychological strains in certain stress situations". However, newspaper clippings, interviews and other primary sources from the time analyzed in comparison to these accomplishments makes the distinction between the outlook on women's limitations at the time and their true capabilities clear. Cobb's successes gave rise to articles such as 'Blonde Eager to Try Space', in which she was referred to as a "pony-tailed blonde from Oklahoma." In 'Aviatrix Jerrie Would Be First Woman Space Ace: She'd Be First Fair Space Ace', the article manages to not only refer to Cobb as "a slim Sooner State blonde" and "blue-eyed slim and trim", but also talk extensively about her wardrobe. This included her "coals to New-castle bit" where she received a designer wardrobe for her trip to Paris as well as a description of her "chic sky-blue wool dress" as opposed to her flight clothing, even mentioning her clothing size.

In 1960, one journalist for The Los Angeles Times wrote crudely, "Space suits will have to be made more attractive if there are to be many feminine volunteers ... You might talk a shapely young thing into wearing one of those multiple-layer, bubble-headed sacks ... but out there in space, who would zip her?" (Smith). An example of an article riddled with both racist and sexist language, Could First U. S. Woman in Space Be Negro: "Weaker Sex" Anxious To Match Male Feats, crudely illustrates this difference (LaCoste). It began by stating American women's joy at the achievements of the "blonde, blue-eyed" and "dimpled bachelor beauty" Valentina Tereshkova, describing her powdered face and painted lips once she stepped off the spacecraft Vostok 6 in 1963, having completed 48 orbits in 71 hours. What follows is a list of the possible professions of the first American woman in space (or "astronette"), until, "most importantly", the question of her race arises. The reasoning is that in order to keep up with the Soviets, minority groups in America such as women and Black people may be the next to be sent to space. This article, in particular, describes the consequences of promoting diversity purely with the intention of publicly boasting. While outlining the accomplishments of various women scientists, it ultimately affirms the reason that they should be acknowledged is so as to not fall behind the Soviets while sexualizing and deriding Tereshkova in a way that male astronauts had not remotely experienced. These are but a few examples of how the media projected male fantasies and perspectives on a hypothetical space woman while ignoring the contributions of

actual women at the time. There seemed to be an amusing novelty surrounding women in space, in which the media switched between writing inappropriately about women such as Tereshkova and Cobb while affirming that women in space would be a far-off goal.

Tensions in the media were rising in the 70s, with the distinctions between the simultaneous infantilization and sexualization of women by the media and the actual training, testing, and abilities of women in NASA become increasingly clear. One journalist wrote satirically of NASA, "This latest 'women are making progress' smoke screen was beautiful. The lovely Air Force cuties lined up to be panned by the television cameras - slowwly. Yep, they were treated just like the guys and even did without sex during the five week testing. And they were all single." (Riedell). By June 18, 1983, when Sally Ride made history as the first American woman to go to space, she experienced an outburst of intense media attention. This attention was notoriously misdirected, intrusive, and, at times, insulting. Serving an audience of men, the media treated Ride as an artifact, focusing on her more as a woman than as an astronaut. In 2020, Dr. Tam O'Shaughnessy, Ride's romantic partner, spoke about Ride's life from a young and talented tennis player to an inspiring and dedicated astronaut. When retelling her life, she brought up the misogynistic questions Ride was asked in comparison to her male peers as well as her later efforts to involve more young girls and boys in science with the nonprofit Sally Ride Science at UC San Diego. In contrast to Ride's own goals of using her presence to inspire other girls to pursue careers in STEM, it is clear that the media's pursuits had a different objective. Altogether, the media seemed to lean into the narrative that there are few women in space in order to exploit the underlying fear within girls and women that there was an enormous barrier between their abilities and the path to professional success in STEM. The frustrating reality was the silent work of many women who had contributed to space exploration for years and had their work ignored, dismissed, or pushed aside in favor of the glamorous image of space women being extraordinarily rare.

III. Conclusion

As the intersectionality of race and gender studies in space history is an extremely understudied field, our work attempts to build upon current limited historiography. Through our research we can conclude that women, especially women of color, have been severely underrepresented in NASA and were not given recognition for their accomplishments. We highlighted this disparity through underscoring the significance of historical cultural movements, evaluating the treatment of women within NASA, and examining the media depiction of women in NASA. This is key to general history, because in every facet of life, the accomplishments of women, people of color, and women of color have been overlooked or downplayed. Alarmingly, many of these problems exist today. During the Apollo program, women made up no more than 5% of the NASA workforce (Weitering). As of 2021, only 35% of NASA's workforce is female and 70% is white. The other 30% is split between Asian Americans, Hispanics, African American and other Multiethnic people. Our group believes that it is important to acknowledge the work that women have put into the space program and should have more representation within NASA.

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Author Contribution Statements

R.S.², A.B. and R.S.³ all worked on the abstract and introduction together. R.S.³ worked on the first subsection, R.S.¹ worked on the second subsection and A.B. worked on the third subsection. R.S.², A.B. and R.S.³ all worked on the conclusion, bibliography, acknowledgements and author contribution statement together.

Works Cited

- "America's First Woman Space Pilot." *South China Morning Post*, 20 August 1960. *JSTOR*. Accessed 12 July 2023.
- "Aviatrix Jerrie Would Be First Woman Space Ace: She'd Be First Fair Space Ace." *The Washington Post*, 27 January 1960. *JSTOR*. Accessed 23 July 2023.
- "Blonde Eager to Try Space." *Chicago Daily Tribune* [Chicago], 24 August 1960. *JSTOR*. Accessed 14 July 2023.
- Bradby, Marie. "Hispanic Women at the Johnson Space Center." *Career Communications Group*, 1989. *JSTOR*. Accessed 10 July 2023.
- Cannon, Annie Jump. "Astronomy for Women." *The AWA Bulletin*, vol. 2, no. 32, 1931. *JSTOR*. Accessed 14 July 2023.
- Carpenter, Jenna P. "Hidden Figures Light Up Screen: Black Women Who Helped America Win the Space Race." *Math Horizons*, vol. 24, no. 3, 2017, pp. 18-21. *JSTOR*, https://doi.org/10.4169/mathhorizons.24.3.18. Accessed 14 July 2023.

Cochran, Jacqueline. "Women in Space: Famed aviatrix predicts women astronauts within six years." *Boston Globe* [Boston], 30 April 1961. *JSTOR*. Accessed 13 July 2023.

- Foster, Amy. "The Gendered Anniversary: The Story of America's Women Astronauts." The Florida Historical Quarterly, vol. 87, no. 2, 2008, pp. 150-173. JSTOR, http://www.jstor.org/stable/20700213. Accessed 12 July 2023.
- Holt, Nathalia. Rise of the Rocket Girls. Chicago, Back Bay Books, 2017.
- Humphrey, Grace. "In the World of Stars: Astronomy's Debt to American Woman." *Woman Citizen*, vol. 6, 1921. *JSTOR*. Accessed 15 July 2023.
- LaCoste, Richard. "Could First U. S. Woman in Space Be Negro: "Weaker Sex" Anxious To Match Male Feats." *Pittsburgh Courier* [Pittsburgh], 9 May 1964. *JSTOR*. Accessed 11 July 2023.
- "...llough...." Women's Studies Archive, vol. 2, no. 3. Gale, https://go-gale-com.proxy.library.ucsb.edu/ps/i.do?p=WMNS&u=ucsantabarbara&id=GA LE%7CMTWBXC953787087&v=2.1&it=r&sid=bookmark-WMNS&asid=07102966.&a ty=ip. Accessed 20 July 2023.
- Macomber, Frank. "Astronets?: Space Women Nearing Reality." *Pittsburgh Courier* [Pittsburgh], 17 May 1972. *JSTOR*. Accessed 14 July 2023.
- Maher, Neil M. Apollo In The Age Of Aquarius. Cambridge, Harvard University Press, 2019.
- McQuaid, Kim. "Race, Gender, and Space Exploration: A Chapter in the Social History of the Space Age." *Journal of American Studies*, vol. 41, no. 2, 2007, pp. 405-434. *JSTOR*, https://doi.org/10.1017/S0021875807003532. Accessed 7 July 2023.
- McQuaid, Kim. "Racism, Sexism, and Space Ventures': Civil Rights at Nasa in the Nixon Era and Beyond." *Societal Impact of Spaceflight*, Washington DC: National Aeronautics and Space Administration Office of External Relations History Division, 2007, pp. 421-449. *NASA*, https://history.nasa.gov/sp4801-part1.pdf. Accessed 23 July 2023.

- "No Women in Space." *The Science News-Letter*, vol. 78, no. 15, 1960. *JSTOR*, https://www.jstor.org/stable/3942140. Accessed 19 July 2023.
- Riedell, Heidi. ""Talk of American Spacewomen Makes Me Sick."" *Gold Flower*, vol. 2, no. 10, 1974. *JSTOR*. Accessed 12 July 2023.
- "Space Woman Hugs, Kisses Fellow Year." *Chicago Tribune* [Chicago], 21 June 1963. *JSTOR*. Accessed 12 July 2023.
- U.S. Census Bureau. Educational Attainment, by Race and Hispanic Origin: 1960 to 1998. 1999.
 U.S. Census Bureau, https://www2.census.gov/library/publications/1999/compendia/statab/119ed/tables/sec04.
 pdf. Accessed 13 July 2023.
- Weitekamp, Margaret A. *Right Stuff, Wrong Sex: America's First Women in Space Program.* Baltimore, Johns Hopkins University Press, 2004.
- Weitering, Hanneke. "These Amazing Women Made NASA's Apollo Moon Missions Possible." *Space.com*, 24 July 2019, https://www.space.com/women-of-apollo.html. Accessed 20 July 2023.
- "Women As Star-Gazers: Astronomy Has Long Afforded a Field Wherein They Have Been Welcome and Peculiarly Successful." *The Women's Standard*, vol. 20, no. 4, 1907. *JSTOR*, https://www.jstor.org/stable/3942140. Accessed 16 July 2023.

The Relationship Between Premenstrual Syndrome/Premenstrual Dysphoric Disorders and Mood-Related Symptoms and Disorders By Ellie Lee

Abstract

Women have higher rates of mood and anxiety disorders than men, and the susceptibility to mood-related symptoms characteristic of premenstrual syndrome (PMS) may be a factor. PMS and Premenstrual Dysphoric Disorder (PMDD), a more severe form of PMS, have been linked to mood disorders and symptoms like depression, anxiety, stress, and even suicide. In recent decades, women's health research has started to gain momentum as an area that needs closer examination, and while there seems to be a correlation between PMS/PMDD and mood-based and anxiety symptoms, the relationship remains unclear. The lack of research and concrete data could hinder awareness in women and healthcare providers that mental disorders can be a prevalent risk factor in relation to PMS and PMDD. This paper assesses existing research to determine what is known about the different relationships of PMS with mood symptoms and mental illnesses. Results show that there is both a coexistence and correlation between PMS and mood-related and anxiety disorders. Some key findings include that PMS can contribute to overall psychological distress not confined to the premenstrual phase, PMS can be more severe in women with mental disorders, and PMS and mental disorders can be risk factors for one another.

Introduction

Premenstrual syndrome (PMS) describes disturbances of mood or physical symptoms that occur 7-10 days before menses and remit during menses (Facchinetti et al. 57-60). Since the late 1990s, PMS has been found to be prevalent in women; according to the Diagnostic and Statistical Manual of Mental Disorders (DSM) Fourth Edition published in 1994, approximately 75% of women experience minor premenstrual, psychological changes, and approximately 20%-30% report symptoms characteristic of PMS (American Psychiatric Association, as cited in Lane et al. 127-138). Furthermore, a previous edition of DSM, DSM III-R (1987), refers to PMS as Late Luteal Phase Dysphoric Disorder (LLPDD) and names it one of the 'proposed Diagnostic Categories Needing Further Study' under the name of LLPDD. Diagnostic criteria for LLPDD were relatively general and stated the self-reported symptoms had to be present during at least two cycles (American Psychiatric Association, as cited in Facchinetti et al. 57-60). In many studies referring to LLPDD, a 20-50% increase in self-reported symptoms in the premenstrual phase compared to the follicular phase (which begins on the first day of bleeding) is thought to indicate PMS (Rubinow et al. 5-11, as cited in Facchinetti et al. 57-60).

The later edition of DSM, DSM IV, added Premenstrual Dysphoric Disorder (PMDD) (American Psychiatric Association, as cited in Facchinetti et al. 57-60). PMDD is a more severe form of PMS that affects 5-10% of women in their reproductive years (UNC School of Medicine). According to the Substance Abuse and Mental Health Services Administration (2016), the most current DSM, DSM V, PMDD went from being classified as a "condition for further study" to a depressive disorder (American Psychiatric Association). To meet the criteria

for PMDD, at least five symptoms must be present in the final week before menses, improve within days after starting menses, and become minimal or absent after menses. Furthermore, one of the additional criteria is that there must be at least one of the following mood-related symptoms: marked depressed mood, feelings of hopelessness, or self-deprecating thoughts; marked anxiety, tension, and/or feelings of being keyed up or on edge; marked affective lability (e.g., mood swings; feeling suddenly sad or tearful or increased sensitivity to rejection); marked irritability or anger or increased interpersonal conflicts ("Substance Abuse and Mental Health Services Administration"). However, an estimated 40% of women who seek treatment for PMDD actually have a premenstrual exacerbation of an underlying mood disorder rather than PMDD, hinting at the complicated coexistence and distinction of PMDD from other mood disorders(UNC School of Medicine). It is important to note that while mood-based symptoms can occur in other phases of the menstrual cycle, researchers have found that there is a significant increase in anxiety and depression during the premenstrual phase, which has contributed to many of the mood-related symptoms being characterized as "Premenstrual syndrome" (Golub 99; Romans 361-384; Mohamadirizi et al. 402; Reynolds et al. 34-40; Li, Lloyd, and Graham 104667). Furthermore, as previously mentioned, in PMDD the mood-based symptoms must be significantly greater in the premenstrual phase compared to the rest of the cycle. However, PMS, experienced more commonly, doesn't have specific diagnostic criteria requiring a certain amount of symptoms experienced.

However, while there seems to be a correlation between PMS/PMDD with mood-based symptoms, the relationship remains unclear. It is unclear how impactful PMS/PMDD is regarding different mood-related symptoms, how PMS may be different for those with existing mental illness, and if existing mental illnesses elevate PMS. This paper assesses existing research, including a historical narrative, to determine what is known about the different relationships of PMS with mood symptoms and mental illnesses like depression, anxiety, stress, and suicide to see if a clearer relationship can be determined. History of Menstruation Research and Mental Health Symptoms

A historical narrative of the progression of menstruation research demonstrates how menstruation and its relation to mental health symptoms have been misunderstood for decades and remain very limited. In the early 1800s, the woman's reproductive system was viewed as a force that could take over her entire body and mind; this meant that all female-specific symptoms were assumed to be caused by the womb, meaning menstruation. For example, "hysteria" came from "hysterikē pix"–which means suffocation of the womb–and was classified as an anxiety disorder that affected women only (King 287-302).

Also, premenstrual pain and the emotional distress that comes with menstruation were not considered serious medical conditions until the early 1900s. However, the taboo toward menstruation continued and even up to the 1960s, PMS was referred to as the "Witch Syndrome" even in scholarly journals. Such labels placed a negative stigma around menstruation research (Taylor 377-391).

Diana Taylor's "'It's All in Your Head' to 'Taking Back the Month': Premenstrual Syndrome (PMS) Research and the Contributions of the Society for Menstrual Cycle Research" summarizes the history of premenstrual syndrome and menstrual cycle research, from the stigma surrounding women's struggle to receive the proper healthcare they need, to when the Society for Menstrual Cycle Research was established in 1977 (Taylor 377-391). Until then, little information was known about why women felt unrest, irritability, and discomfort before menstruation and why some women felt more severe symptoms than others.

The first PMS clinic in London was opened in the 1950s when Dr. Katharina Dalton coined premenstrual syndrome as Premenstrual Tension (PMT). It was Dr. Dalton who first discovered that PMS occurred 14 days after ovulation, in which the symptoms can become more severe in the last four days prior to menstruation. She challenged her male colleagues saying that the symptoms are not simply psychological but also physical as symptoms include migraines, stomach cramps, and in some cases, epilepsy (Taylor 377-391).

Dr. Dalton was also the first to create menstrual charts to diagnose psychosomatic symptoms stating that there is a correlation between PMS and suicide. Although medical doctors today disagree with her treatment methods, menstruation research began to increase in the following years thanks to Dalton's work (Taylor 377-391). However, the later research focused on physical symptoms such as hormonal dysfunction. It wasn't until there was strong evidence to suggest that PMS/PMDD was caused by external stress factors, whether that be familial problems or otherwise, that researchers began to consider the psychosomatic nature of PMS symptoms. They started noting that stress can not only cause depression, suicidal thoughts, and violent behavior but also cause irregular cycles (Nillni 1073-1082).

Beginning in 1977, the Society for Menstrual Cycle Research held conferences to expand PMS research with an estimated 100 participants of lab scientists, theoreticians, academics, clinicians, feminist scholars, and women's health activists. There, they developed the following guidelines for PMS research: "(a) the development of testable hypotheses, concepts, and complex theoretical models before doing research, (b) the application of psychoneuroendocrinology and menstrual stress models, (c) the reconceptualization of mood to include changing feelings and body states over time, and (d) the use of non-reductionist approaches to menstrual cycle research that incorporates both the psychosomatic and endocrine regulation" (Taylor 377-391).

In the mid-1980s, professional medical groups from the United States and the United Kingdom published PMS research that gave way to its disease classification, which continued to spur debate. The so-called disease named LLPDD was labeled as a mood disorder until the American Psychological Association (APA) changed the name to PMDD, which it is known today as Depressive Disorder (Taylor 377-391). However, Paula Caplan, the author of *They Say You're Crazy: How the World's Most Powerful Psychiatrists Decide Who is Normal* argues that the diagnosis of PMDD is more harmful than helpful for women (Taylor 377-391). To associate PMS as a "disorder" conveys that women are physiologically ill by nature instead of attributing symptoms to stress factors in their environment.

Sally King, the author of "Premenstrual Syndrome and Myths of the Irrational Female" highlights how "psychologizing" menstruation symptoms places an overemphasis on the emotional aspects, which not only pathologizes women but limits research on the biological aspects of menstruation. Although there have been cases in which the menstrual cycle is linked to depression, including a significant number of women who were menstruating at the time of their completed suicide, this does not mean that all women are at risk of suicide simply because they are on their period. Furthermore, the research is unclear whether or not menstruation alone can cause depression. This literature review paper aims to understand with greater depth if menstruation is the cause of women's mood-based symptoms and if menstruation and mood-based symptoms are definitely linked.

PMS and Depression

Researchers have found that estrogen, progesterone, and their metabolite levels decrease in the late luteal or premenstrual phase of the menstrual cycle and remain low throughout menstruation. These female reproductive hormones impact the functions of neurotransmitters, such as serotonin, dopamine, norepinephrine, and gamma amino butyric acid, and such hormone shifts indirectly result in psychological problems, impacting the possible relationship between PMS and depression (Akdeniz and Karadag 296).

Although depressive moods are common symptoms of PMS that are characterized as being prevalent in the premenstrual phase, women with premenstrual symptoms demonstrate greater levels of overall depression, not specifically confined to the premenstrual phase, than women without premenstrual symptoms. Morse et al. conducted a study in 1988 of 75 women diagnosed with PMS and 32 women claiming they did not have menstrual cycle complaints and found that women with PMS had greater levels of depression than those not reporting PMS (Morse et al. 41-50). In support, a study of 60 women done in 1989, Christensen and Oei found that women with more significant premenstrual symptomatology, those diagnosed or suspected with PMDD, had higher levels of depression than women without PMDD symptomatology (Christensen et al. 251-259). Furthermore, according to a study of 144 women who mainly self-reported symptoms of PMS, women reporting premenstrual mood symptoms were more likely to have major depressive disorder than women without a history of premenstrual mood changes (Warner et al. 9-23). In fact, although a study done on a small sample size of 36 women, Graze suggests that assessment of premenstrual depression can identify women at risk for future Major Depressive disorder (MDD) (Graze et al. 201-205). Furthermore, researchers found that 31% of women seeking help for PMS had a past history of depression (defined by treatment with antidepressants) compared to 22% seeking help for dysmenorrhea, 8.9% seeking help for menorrhagia (Bancroft et al. 225-231), and 5.8% not seeking help for any menstrual problems. This demonstrates that women suffering from PMS had a higher prevalence of depression in the past than women not suffering from any menstrual problems or other menstrual problems. Premenstrual symptomatology, including self-reported PMS, diagnosed PMS, suspected PMDD, and diagnosed PMDD, is associated with heightened depression.

Not only is the presence of PMS and PMDD associated with depression but the severity of premenstrual symptomatology has been found to correlate with depression. Lane and Francis found that greater levels of premenstrual symptoms and a more significant increase in symptom severity from postmenstrual to premenstrual phases (meaning symptoms were more disruptive) were associated with more significant depression, even when differing levels of locus of control were accounted for, a topic later discussed in further detail (Lane et al. 127-138).

Additionally, in a study of 3518 women, 24.6% of women with severe PMS had major depression, 11.3% of women with moderate PMS had major depression, and 6.2% of women with no reported PMS had major depression (Forrester-Knauss et al. 1-11). This demonstrates that the severity of PMS contributed to a greater prevalence of major depression.

While the above data examined depression in women with premenstrual symptomatology, researchers have also examined PMS in women with existing mood disorders, including a lifetime history of depression. According to Endicott, for women with mood disorders, the premenstrual phase may be vulnerable to the appearance of severe depression or worsening of an ongoing period of depression (Endicott 193-200). This is supported by researchers who have found that women with a history of MDD reported more premenstrual mood changes than women without mental illness or other types of mental illness (Facchinetti et al. 57-60). In a study of 170 women, 57% of women diagnosed with MDD showed severe premenstrual depression (Full Depressive Syndrome as characterized by the Premenstrual Assessment Form) while 14% of women who had never been mentally ill showed severe premenstrual depression, demonstrating that individuals with MDD were more susceptible to mood-related premenstrual symptoms than those without mood disorders (Halbreich et al. 331-338). In addition, when studying 58 women with a major depressive disorder, 12 with another affective disorder, 9 with nonaffective disorders, and 13 with no mental disorder, Endicott et al. found that women with major depressive disorders reported most premenstrual mood changes (Endicott et al. 519-529). Moreover, according to a study done by Bancroft et al., a history of depression, defined by the treatment of antidepressants, increased the vulnerability of women to depressive perimenstrual mood changes regarding both duration and severity (Bancroft et al. 225-231). As shown, the research suggests that women with a history of mood disorders, particularly major depressive disorder, may experience more severe premenstrual mood changes than women without mood disorders.

Researchers have also found an association between postnatal depression and premenstrual depression. In a 2013 study, Buttner et al. found that moderate to PMS/ PMDD significantly predicted and doubled the risk of developing postpartum, independent of sociodemographic factors (Buttner et al. 219-225). While Buttnner et al. demonstrate premenstrual symptomatology as a risk factor for postpartum depression, other researchers found that postpartum depression affected premenstrual depression in following menstrual cycles. According to Warner et al.'s study of 144 women, the severity of premenstrual depression was related to a previous history of postnatal depression (Warner et al. 9-23). In support, other researchers found that women who had postpartum mood disorders reported premenstrual depressive symptoms when menstruating again (Brockington et al. 287-292; Schenck et al. 353-356; as cited in Akdeniz, F. et al. 296). Therefore, there is evidence supporting that postnatal depression and premenstrual depression may be risk factors for each other. PMS and Suicide

Severe depression may be a risk factor for suicide, and researchers have found a link between PMS and suicide. A significant amount of women who committed suicide were menstruating at the time of their death. In a study done in New Delhi, 217 women who died from completed suicide and 237 women who died from other causes were observed. The results showed that 54.46% of women who died by suicide were menstruating compared to only 6.75% of the other deaths observed, suggesting that menstruation may be linked much more to suicide compared to other causes of death (Dogra et al. 430-434). In support, a literature review of 44 studies showed that according to studies done in the early 1900s, between 35% and 100% of women who committed suicide were menstruating at the time of their death (Heller 1653-1658; Ollendorf; Pilcz; Wetzel et al. 523-524; Slavik 112-113; Sachwiz 312-321; Elo 348; Babin; as cited in Saunders and Hawton 901-912).

Furthermore, researchers have found evidence of suicide occurring in the premenstrual phase specifically. The premenstrual phase seemed to be the most common time period when women committed suicide, along with the menstrual bleeding period. According to 148 autopsies done in New Delhi, suicide occurred less in the ovulatory phase and more during menstruation and pre-menstruation (Leenaars et al. 202-207). Furthermore, some researchers found that suicide attempts were more frequent in the premenstrual phase before menstruation (Glass et al.; Saunders and Hawton 901-912; Tonks et al.; Janowsky et al.). Although suicide occurrences have been reported during the premenstrual phase of menstruation, it should be noted that the occurrence of suicide during the premenstrual phase can not be directly attributed to PMS and PMDD.

However, some researchers have studied the association between PMS and suicide. Suicide attempts in women with PMS and a psychiatric disorder are 15-20% and both PMS and psychiatric disorder are likely to have contributed to the frequency (Clare 1-58; Keye et al. 634-637; Stout et al. 517-522; as cited in Saunders and Hawton 901-912). Furthermore, Chaturvedi et al. found that women who reported psychological symptoms of PMS like irritability, mood swings, and depression more frequently also had suicidal ideas during the premenstrual period, demonstrating that mood-based symptoms of PMS can include suicidal ideation (Chaturvedi et al. 193-199, as cited in Saunders and Hawton 901-912). Although suicidal thoughts, suicide attempts, and completed suicides have been shown to occur in the premenstrual phase, there is limited research on the relationship between PMS and suicide. PMS and Anxiety

Researchers have found that anxiety increases in the premenstrual stage of menstruation, which may be why anxiety is often considered a symptomology of PMS and severe anxiety is considered a symptom of PMDD (Li, Lloyd, and Graham 104667; Reynolds et al. 34-40). When 18 women with generalized anxiety disorder (GAD) and 20 women with GAD were studied in
2020, anxiety and mood disturbances in women without GAD increased to the same levels experienced by women with GAD in the mid-luteal phase, a phase of elevated progesterone (the mid-luteal phase includes but isn't limited to premenstrual phase) (Li, Lloyd, and Graham 104667). This demonstrates that anxiety increases during the premenstrual phase even for women without GAD and progesterone may play a role. An initial study of 100 Polish women demonstrated that women with higher average progesterone levels throughout their menstrual cycles had higher levels of anxiety than women with lower average progesterone levels. Furthermore, a secondary study of 61 American women demonstrated that women with higher average progesterone levels had higher levels of attachment anxiety in particular, and an increase in progesterone levels correlated with an increase in attachment anxiety (Reynolds et al. 34-40). This demonstrates that progesterone may play a role in the relationship between anxiety and the premenstrual phase of menstruation.

Anxiety can increase for women without GAD but also increases for women with GAD. However, the increase may not be explained by progesterone as research in the previous paragraph demonstrated. According to a different 2020 study of 40 women with GAD and 40 women without GAD done by Li et al., women with GAD had increased repetitive negative thinking (RNT), signs of psychiatric disorders, and negative affect when transitioning from the follicular to the luteal phase while women without GAD did not report any changes in RNT or anxiety symptoms(Li, Denson and Graham 1037-1045). However, unlike Li, Lloyd, & Graham's results which showed that increased anxiety and mood disturbances correlated with elevated progesterone levels, the increased mood-based symptoms in Li, Denson, & Graham's study were not associated with changes in progesterone as the researchers expected. The conflicting results suggest that more research is needed on the role of progesterone on PMS and mood disorders.

Additionally, women with PMS have demonstrated higher anxiety levels than women without PMS. When observing 32 women with LLPDD and 38 women without LLPDD, researchers found that 59% of women with LLPDD had anxiety disorders, most commonly generalized anxiety disorder, panic disorder, and social phobia, compared to 23% of women without LLPDD (Fava et al. 325-335). Furthermore, researchers have tested women with PMS for anxiety by inducing anxiety symptoms. Patients with panic disorder are highly sensitive to lactate infusion (Liebowitz et al. 709-719, as cited in Facchinetti et al. 57-60). In a study utilizing lactate infusion on 35 women diagnosed with PMS, 63% of women diagnosed with PMS had a panic attack with lactate infusion while only 12% of women without PMS had a panic attack (Facchinetti et al. 288-296, as cited in Facchinetti et al. 57-60). Patients with panic attacks also demonstrate vulnerability to carbon dioxide (CO2) inhalation, specifically 35% CO2 inhalation (Griez et al. 796-7). In a study with a small sample size of 14 women seeking treatment for premenstrual changes and 12 women in the control group, women with LLPDD had panic symptoms in response to 35% CO2 inhalation while women in the control group did not (Harrison et al. 183-192, as cited in Facchinetti et al. 57-60). This demonstrates that women with PMS are more susceptible to anxiety disorders and panic attacks compared to women without PMS.

Furthermore, GAD may be a risk factor for PMDD. In a 2020 study of 100 women diagnosed with PMDD, researchers found that the odds ratio of women with GAD having PMDD was 7.65 (95% CI: 1.69–34.63) compared to women without GAD, demonstrating that women with GAD were more likely to have PMDD. Therefore, researchers suggest that GAD be assessed for women diagnosed with PMDD (Yen et al. 988). PMS, Stress, and Quality of Life

Women with PMS demonstrate higher levels of stress and lower quality of life, most likely due to the disruptive nature of PMS. In a study of 115 students of Mashhad University, Iran, the mean score of stress was significantly lower in students without PMS (p<0.001). Furthermore, the intensity of premenstrual syndrome symptoms directly correlated with stress scores, demonstrating the relationship between PMS and stress (Jafarnejad et al. 11-18). In addition, a study done in 2012-2013 of 120 female students from Islamic Azad University revealed a positive correlation between stress and premenstrual syndrome, a negative correlation between stress and quality of life, and a negative correlation between PMS and quality of life (Zarei and Bazzazian 49-58). This demonstrates that higher PMS correlates directly with lower quality of life and also correlates to higher stress, which correlates with lower quality of life. In support, a study of 114 females demonstrated that women with high PMS had significantly more stress and poorer quality of life than women with low PMS (Lustyk et al. 35-44). Furthermore, women with PMS demonstrated more reactivity to stress. Liu et al. found that women with PMS demonstrated higher alpha activity and lower respiration rates under stressful conditions than women without PMS (Liu et al. 1597-1602). This demonstrates that women with PMS may have higher levels of stress due to the large impact symptoms can have on women but also may be more reactive to stress, further increasing their stress levels. The association of PMS with stress and quality of life can lead to further impact on mood-related symptoms and disorders in women. Conclusion

While PMS can encompass mental disorder symptoms and heightened mood-related symptoms during the premenstrual phase, PMS can also contribute to overall psychological distress not necessarily confined to the premenstrual phase. Additionally, existing mental disorders can also exacerbate PMS; and PMS can exacerbate mental health disorders. Not only is the presence of PMS and mental disorders correlated but the severity of each factor contributes to their relationship. In addition, PMS and mental disorders can be risk factors for each other. In other words, there is both a coexistence and correlation between PMS and mental disorders. However, it is difficult to judge whether mood disorders and mental health have a greater effect on PMS or if PMS has a greater effect on mental health.

The association of PMS and PMDD with mental illness may be influenced by other factors, including locus of control. Women with more severe PMS have been shown to have a more external locus of control, meaning that they see events being caused by external factors not in their control. A person who has a high internal locus of control believes an outcome is decided by his or her actions while someone with a high external locus of control (LOC) believes an outcome is due mostly to chance, faith, or environmental conditions (Rotter 1, as cited in Gore et

al. 181-196). Researchers have found that women with high levels of premenstrual symptomatology exhibit more external LOC (Lane et al. 127-138; O'Boyle et al. 67-74; Kirkby and Picone 672-672). Compared to the early luteal or follicular phases, women in the premenstrual phase scored significantly lower on internal LOC, demonstrating that low internal LOC is especially prevalent in the premenstrual phase (Lane et al. 127-138). The potential impact and mediating role of locus of control demonstrates that there may be multiple other factors influencing the relationship between PMS/PMDD and mood-related symptoms.

Common limitations of the surveyed papers included earlier research and small sample sizes. Most articles were from the 1980s - 1990s, and there seems to be a lack of recent research when the relationship is still unclear. Furthermore, the small sample sizes may imply a lack of funding and participation, possibly due to taboos surrounding the menstrual cycle and mental health. Furthermore, while this paper focuses on PMS and PMDD, mental health factors may be present and impact other phases of the menstrual cycle differently, and more research is needed to create a more comprehensive view of the relationship between mood-related symptoms and the menstrual cycle.

Works Cited

- Akdeniz, Fisun, and Figen Karadag. "Does menstrual cycle affect mood disorders?." *TURK PSIKIYATRI DERGISI* 17.4 (2006): 296.
- American Psychiatric Association: *Diagnostic and Statistical Manual, ed 3 Revised*. Washington, APA Press, 1987.
- American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders, (4th ed.).* American Psychiatric Publishing, Inc., 1994.
- American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders: DSM-5*. American Psychiatric Publishing, Inc., 2013.
- Babin, Eleonore. *Der Selbstmord der Frau in Beziehung zur menstruation und Gravidität*. Blücher-Dr., 1933.
- Bancroft, John, Dilys Rennie, and Pamela Warner. "Vulnerability to perimenstrual mood change: the relevance of a past history of depressive disorder." *Psychosomatic Medicine* 56.3 (1994): 225-231.
- Brockington, I. F., et al. "Premenstrual relapse of puerperal psychosis." *Journal of Affective Disorders* 14.3 (1988): 287-292.
- Buttner, Melissa M., et al. "Examination of premenstrual symptoms as a risk factor for depression in postpartum women." *Archives of women's mental health* 16 (2013): 219-225.
- Chaturvedi, Santosh K., et al. "Suicidal ideas during premenstrual phase." *Journal of affective disorders* 34.3 (1995): 193-199.
- Christensen, Alison P., Belinda J. Board, and Tian PS Oei. "A psychosocial profile of women with premenstrual dysphoria." *Journal of affective disorders* 25.4 (1992): 251-259.
- Clare, Anthony W. "Psychiatric and social aspects of premenstrual complaint." *Psychological Medicine Monograph Supplement* 4 (1983): 1-58.
- Dogra, T. D., et al. "Menstruation and suicide: an exploratory study." *Psychological reports* 101.2 (2007): 430-434.
- Elo, O. "Suicide and suicides in Finland [in German]." *Deutsche Zeitschrift fuer die Gesamte Gerichtliche Medizin* 17 (1931), 348.
- Endicott, Jean, et al. "Premenstrual Changes and Affective Disorders1." *Psychosomatic Medicine* 43.6 (1981): 519-529.
- Endicott, Jean. "The menstrual cycle and mood disorders." *Journal of Affective Disorders* 29.2-3 (1993): 193-200.
- Facchinetti, Fabio, et al. "Lactate infusion induces panic attacks in patients with premenstrual syndrome." *Psychosomatic Medicine* 54.3 (1992): 288-296.
- Facchinetti, Fabio, M. Tarabusi, and G. Nappi. "Premenstrual syndrome and anxiety disorders: a psychobiological link." *Psychotherapy and psychosomatics* 67.2 (1998): 57-60.
- Fava, Maurizio, et al. "Comorbid anxiety and depression among patients with late luteal phase dysphoric disorder." *Journal of Anxiety Disorders* 6.4 (1992): 325-335.

- Forrester-Knauss, Christine, et al. "The interrelation between premenstrual syndrome and major depression: results from a population-based sample." *BMC public health* 11.1 (2011): 1-11.
- Golub, Sharon. "The effect of premenstrual anxiety and depression on cognitive function." *Journal of Personality and Social Psychology* 34.1 (1976): 99.
- Gore, Jonathan S., Dustin P. Griffin, and Dakota McNierney. "Does internal or external locus of control have a stronger link to mental and physical health?." *Psychological Studies* 61 (2016): 181-196.
- Graze, K. K., J. Nee, and Jean Endicott. "Premenstrual depression predicts future major depressive disorder." *Acta Psychiatrica Scandinavica* 81.2 (1990): 201-205.
- Griez, Eric, et al. "Response to 35% CO2 as a marker of panic in severe anxiety." *Am J Psychiatry* 147.6 (1990): 796-7.
- Halbreich, Uriel, and Jean Endicott. "Relationship of dysphoric premenstrual changes to depressive disorders." *Acta Psychiatrica Scandinavica* 71.4 (1985): 331-338.
- Harrison, Wilma M., et al. "Provocation of panic with carbon dioxide inhalation in patients with premenstrual dysphoria." *Psychiatry research* 27.2 (1989): 183-192.
- Heller, A. "A study of suicide based on 300 autopsies [in German]." *Munchener Medizinische Wochenschrift 47* (1900), 1653–1658.
- Jafarnejad, F., Shakeri, Z., Najaf Najafi, M., and Salehi Fadardi, J. (2013). "Evaluation the relationship between stress and the risk of premenstrual syndrome." *The Iranian Journal of Obstetrics, Gynecology and Infertility*, *16*(76), 11-18.
- King, Sally. "Premenstrual syndrome (PMS) and the myth of the irrational female." *The Palgrave handbook of critical menstruation studies* (2020): 287-302.
- Keye Jr, William R., D. Corydon Hammond, and T. H. O. M. A. S. Strong. "Medical and psychologic characteristics of women presenting with premenstrual symptoms." *Obstetrics and gynecology* 68.5 (1986): 634-637.
- Kirkby, Robert J., and Loretta Picone. "The premenstrual syndrome and locus of control." *Psychological Reports* 65.2 (1989): 672-672.
- Lane, Tiffany, and Andrew Francis. "Premenstrual symptomatology, locus of control, anxiety and depression in women with normal menstrual cycles." *Archives of women's mental health* 6 (2003): 127-138.
- Leenaars, Antoon A., et al. "Menstruation and suicide: a histopathological study." *Crisis* 30.4 (2009): 202-207.
- Li, Sophie H., Thomas F. Denson, and Bronwyn M. Graham. "Women with generalized anxiety disorder show increased repetitive negative thinking during the luteal phase of the menstrual cycle." *Clinical Psychological Science* 8.6 (2020): 1037-1045.
- Li, Sophie H., Andrew R. Lloyd, and Bronwyn M. Graham. "Physical and mental fatigue across the menstrual cycle in women with and without generalised anxiety disorder." *Hormones and Behavior* 118 (2020): 104667.

Liebowitz, Michael R., et al. "Lactate provocation of panic attacks: II. Biochemical and physiological findings." *Archives of General Psychiatry* 42.7 (1985): 709-719.

Liu, Qing, et al. "Stress reactivity and emotion in premenstrual syndrome." *Neuropsychiatric disease and treatment* (2017): 1597-1602.

Lustyk, Mary Kathleen B., et al. "Stress, quality of life and physical activity in women with varying degrees of premenstrual symptomatology." *Women & health* 39.3 (2004): 35-44.

Mohamadirizi, Soheila, and Masoumeh Kordi. "Association between menstruation signs and anxiety, depression, and stress in school girls in Mashhad in 2011-2012." *Iranian journal of nursing and midwifery research* 18.5 (2013): 402.

Morse, Carol A., et al. "Menstrual cycle symptoms: comparison of a non-clinical sample with a patient group." *Journal of affective disorders* 14.1 (1988): 41-50.

Nillni, Yael I., et al. "Mental health, psychotropic medication use, and menstrual cycle characteristics." *Clinical Epidemiology* (2018): 1073-1082.

O'Boyle, Michael, Sally K. Severino, and Stephen W. Hurt. "Premenstrual syndrome and locus of control." *The International Journal of Psychiatry in Medicine* 18.1 (1989): 67-74.

Reynolds, Tania A., et al. "Progesterone and women's anxiety across the menstrual cycle." *Hormones and behavior* 102 (2018): 34-40.

Romans, S., Clarkson, R., Einstein, G., Petrovic, M., and Stewart, D. (2012). Mood and the menstrual cycle: a review of prospective data studies. *Gender medicine*, *9*(5), 361-384.

Rotter, Julian B. "Generalized expectancies for internal versus external control of reinforcement." *Psychological monographs: General and applied* 80.1 (1966): 1.

Rubinow, David R., et al. "Changes in plasma hormones across the menstrual cycle in patients with menstrually related mood disorder and in control subjects." *American journal of obstetrics and gynecology* 158.1 (1988), 5-11.

Sachwiz, A. "Reasons for suicide [in German]." Deutsche Zeitschrift fuer die Gesamte Gerichtliche Medizin 10 (1927), 312–321.

Saunders, Kate EA, and Keith Hawton. "Suicidal behaviour and the menstrual cycle." *Psychological medicine* 36.7 (2006): 901-912.

Schenck, Carlos H., Monica Mandell, and Glenn M. Lewis. "A case of monthly unipolar psychotic depression with suicide attempt by self-burning: selective response to bupropion treatment." *Comprehensive psychiatry* 33.5 (1992): 353-356.

Slavik, W. "Menstrual psychosis: its relationship to penal law and the frequency of suicides in women [in German]." Revue de Me decine Tche`que 2 (1909), 112–113.

Substance Abuse and Mental Health Services Administration. *Impact of the DSM-IV to DSM-5 Changes on the National Survey on Drug Use and Health.* Substance Abuse and Mental Health Services Administration (US), June 2016.

Stout, Anna L., et al. "Comparison of lifetime psychiatric diagnoses in premenstrual syndrome clinic and community samples." *The Journal of nervous and mental disease* 174.9 (1986): 517-522.

- Taylor, Diana. "From "it's all in your head" to "taking back the month": premenstrual syndrome (PMS) research and the contributions of the society for menstrual cycle research." *Sex Roles* 54 (2006): 377-391.
- UNC School of Medicine. "Menstrually Related Mood Disorders Center for Women's Mood Disorders.",

https://www.med.unc.edu/psych/wmd/resources/mood-disorders/menstrually-related/. Accessed 31 August 2023.

- Warner, Pamela, et al. "The relationship between perimenstrual depressive mood and depressive illness." *Journal of Affective Disorders* 23.1 (1991): 9-23.
- Wetzel, Richard D., Theodore Reich, and James N. McClure. "Phase of the menstrual cycle and self-referrals to a suicide prevention service." *The British Journal of Psychiatry* 119.552 (1971): 523-524.
- Yen, Ju-Yu, et al. "Association between generalized anxiety disorder and premenstrual dysphoric disorder in a diagnostic interviewing study." *International journal of environmental research and public health* 17.3 (2020): 988.
- Zarei, Z., and S. Bazzazian. "The relationship between premenstrual syndrome disorder, stress and quality of life in female students." *Iranian Journal of Psychiatric Nursing* 2.4 (2015): 49-58.

Applications of and Challenges to Freud's Oedipus Complex in Hermann Hesse's *Demian* By Jaeha Jang

Abstract

Demian, a bildungsroman by Hermann Hesse, has often been read as a direct application of Jungian theory, but biographical and textual evidence suggest that the novel simultaneously applies and challenges Freud's Oedipus complex. Sinclair initially follows the complex as he, the son, demonstrates ambivalent feelings towards Demian, the father-substitute totem, and expresses his incestuous sexual desires for Eva, the mother. However, as Sinclair successfully pursues Eva instead of finding an outside sexual object to replace her, he diverges from the traditional Oedipal sequence of the bildungsroman. Furthermore, Sinclair replaces Demian and continues to inhabit his new Oedipal condition at the end of the novel without "moving on" from the complex as Freud suggested, and his implicit homoromantic desires for Demian defy the heteronormativity that serves as the basis of the Oedipus complex. Unlike a Jungian analysis, which interprets the novel only as a direct application of Jung's individuation process, a Freudian perspective notes Hesse's simultaneous applications of and challenges to the Oedipus complex. From a Freudian lens, the text adds complexity to the protagonist's exploration of identity and enriches the thematic diversity of the bildungsroman.

Hesse's Demian

Demian by Hermann Hesse, published in 1919, is a *bildungsroman*, or "a novel of formation," that portrays Emil Sinclair's psychological growth and transformation as he navigates the complexities of adolescence. As Sinclair transitions into adulthood, he struggles with his identity and searches for a sense of "self," grappling with his inner desires. Ultimately, Sinclair, with the assistance of his mentor Demian, evolves from a confused and vulnerable young boy to an enlightened and self-aware individual who begins to find his path in life. It must, however, be noted that, while *Demian* is an experimental *bildungsroman* appropriate to the Modernist period, it is unusual in the sense that its central motif is the protagonist's desire to court his mentor-friend's mother.

Critics disagree on whether Freudian or Jungian theories of psychoanalysis primarily influenced *Demian*. Scholars supporting the Jungian interpretation of the novel have credited Hesse's multiple psychoanalytic sessions with Josef Bernhard Lang, a student of Jung, to argue that Hesse was knowledgeable of Jungian theories of psychoanalysis while writing the novel. According to Osman Durrani, Hesse, deeply traumatized by his wife's psychosis, an opium habit, and a literary impasse, attended therapy with Lang from May 1916 to November 1917 in the hopes of resuming his career (Durrani 903). *Demian*, written between September and October 1917, was published in the spring of 1919.

However, Benjamin Nelson, publishing two newly recovered 1963 letters from Hesse and Jung, offers a different perspective.⁹⁵ According to Nelson, Jung claims that he had a direct influence on *Demian* because he knew both Hesse and Lang (B. Nelson 11).⁹⁶ Jung furthermore asserts that he indirectly influenced Hesse's later writing of *Siddhartha* and *Steppenwolf* in a tone that Eugene L. Stelzig describes as "co-opting and condescending" (Stelzig 2). Hesse's response, Nelson describes, "hardly bothers to conceal his annoyance with Jung" (B. Nelson 12). Describing Lang as only partly a student of Jung, Hesse writes that Jung's works "did not impress him so much as did Freud's" and that he did not read Jung's books until 1922 (B. Nelson 12). Nelson also notes the prominence of Hesse's friendliness to Freud in Hesse's 1918 essay "Artist and Psychoanalyst" (B. Nelson 13). In the essay, Hesse writes about familiar Freudian concepts of repression and regression and praises Dostoyevsky for predicting the theories of Freud (B. Nelson 13).⁹⁷ Nelson, however, does not see a trace of Jung or Lang in its pages (B. Nelson 13).

It is impossible to ignore the apparent influences of Jung's psychoanalytic theories in *Demian* and the compelling argument that Lang's knowledge of Jung's works was transferred to Hesse and demonstrated in the novel. However, in light of Hesse's letter to Maier, I have doubts regarding whether Hesse intended to embed Jung's theories into his novel or was, as Jung claims about *Siddhartha* and *Steppenwolf*, subconsciously influenced by these themes. Furthermore, the letter, as well as his 1918 essay, indicates that Hesse was more knowledgeable about Freud's theories of psychoanalysis at the time of writing the novel, having read Freud's books but not Jung's (B. Nelson 16). Thus, the question that arises is whether a strictly Jungian perspective can do full justice to this novel. An orthodox Jungian view overlooks the "transparent" (Stelzig 3) influences of Freud's mother myth, or the Oedipus complex, in the text. On the other hand, a strict Freudian perspective ignores the apparent Jungian themes of archetypes and individuation and the divergence of Sinclair's story from the traditional Oedipus complex.

In this essay, I will argue that *Demian* is a *bildungsroman* that alters the genre by introducing a queer version of Freud's Oedipus complex. Sinclair partially follows the complex as he, the son, initially feels ambivalent towards Demian, the father-substitute totem, and expresses his incestuous sexual desires for Eva, the mother. This characterization of Demian as the father-substitute and Eva as the mother is supported by multiple implications in the novel that Demian has "killed his father" and is now his mother's lover. Sinclair then identifies with Demian, the totem who becomes his role model, and seems to subsequently complete the Oedipus complex by finding another female sexual object to fulfill his heterosexual desires. Nonetheless, as Sinclair returns to Eva and successfully pursues his desire for her, he manifests an alternative ending to the Oedipus complex. Sinclair replaces Demian, becomes the totem

⁹⁵ The letters were in reply to Emanuel Maier, who was gathering materials for a proposed doctoral thesis on Hesse's work at New York University.

⁹⁶ Jung also asserts that Hesse's familiarity with Gnosticism was due to his influence.

⁹⁷ Hesse references Dostoyevsky as a "poet" who came very close to understanding the essential tenets of analytic psychology, intuiting "those roads which Freud and his students would travel" long before them.

himself, and continues to inhabit the new Oedipal condition at the end of the novel without feeling sentiments of guilt or "moving on" from the complex, as Freud suggested. Furthermore, Sinclair repeatedly demonstrates implicit homoromantic desires for Demian, which culminate during their kiss in the final scene of the novel, defying the heteronormativity that serves as the basis of the Oedipus complex. From this perspective, Sinclair's emergence into his full self, diverging from the heteronormative, Freudian sequence of the *bildungsroman*, stretches the boundaries of the genre and demonstrates a queer *bildungsroman* of the totem.

Critical disagreement about Freudian and Jungian influence

Hans R. Schmid interprets *Demian* within the framework of Freud's Oedipus complex (Schmid 151). According to him, Sinclair's admiration for Demian, the mirror-image of his complementary self, is basically narcissistic, and Sinclair, arrested at this level of narcissism, is incapable of genuine love for a woman (Schmid 152). Schmid furthermore interprets Sinclair's infatuation with Frau Eva as a regression to narcissism rather than an attempt at liberation from the mother complex (Schmid 156). Additionally, Donald F. Nelson claims that the boyish facial characteristics of Beatrice signify that Sinclair's psychological preoccupation with her amounts to a regression to the homoerotic phase of psychosexual development (D. Nelson 57).

Stelzig notes the Freudian influences in *Demian* as well.⁹⁸ According to him, Sinclair's subconscious yearning for Frau Eva reflects the Oedipus complex, in which the son experiences sexual desire for the mother, transferred from his own mother to Demian's (Stelzig 3). Accordingly, Sinclair is unable to confess his "dark dream of love" about the forbidden embrace of the half-masculine, half-motherly figure even to Pistorius, his mentor, due to the ancient taboo of incest dread. Even though this repressed desire of the Oedipus Complex is never fulfilled, Eva seems to encourage a sexual union between Sinclair and herself, and the desire is completed in Sinclair's dreams, in which, he writes, his "union with her was accomplished by way of allegory."

Some scholars, however, note Jung's theories of psychoanalysis as the dominant influence behind *Demian*. For example, Stelzig describes the novel as "strongly marked by the impact of Jungian analysis," considering its incorporation of various features and tendencies of Jungian thought (Stelzig 1). These aspects include the assumption that the individual is the primary reality, the prophetic language about the challenges and hazards of the individuation process, an amoral attitude to the "dark" suggestions of the self, mysterious connections between the inner and outer worlds, and the endorsement of creative activity as an instrument of self-realization (Stelzig 1).

Johanna Neuer more specifically explores the specific Jungian archetypes, or images embedded in the collective unconscious, that are symbolized within the novel's characters.

⁹⁸ While Stelzig's article focuses on the Christian motifs in *Demian*, he describes the novel as "a composite of various influences, or rather confluences." These influences include Jung, whose "note is clearly the dominant one in the composition of *Demian*," the German Romantics, Hegel, Nietzsche, Christianity, Gnosticism, Bachofen, and Freud.

According to her, Demian possesses multiple projections of the collective unconscious, including the archetypal qualities of the wise old man (sage) as well as the *puer aeternus*, or "eternal boy" (Neuer 10). As the wise old man, Demian is Sinclair's master and teacher, symbolizing the pre-existing meaning hidden behind the chaos of life. This guiding function is also indicated by his name, which, according to Joseph Mileck, is a slightly altered version of *diamon*, Socrates's guiding spirit (Mileck 171). Demian's simultaneous role as the *puer aeternus*, asserts Neuer, is identified in his timeless beauty, contained in an ageless face, and his unique relationship with his mother that attracts rumors that they are lovers (Neuer 11-12). According to Jung, the consciousness's encounter with subconscious archetypes—in this case, Sinclair's encounter with Demian—is a tremendous ordeal that demands the utmost moral fortitude. Thus, Neuer claims, Sinclair avoids Demian after their first meeting, feeling a sense of guilt that is, in fact, his pangs of conscience at not properly fulfilling his destiny (Neuer 11). However, Sinclair ultimately accepts Demian during his religious celebration of confirmation, which becomes a ritual that signifies his acceptance into the realm of Demian's thoughts, or the absorption of the unconscious into consciousness, symbolizing the beginning of Sinclair's Jungian individuation (Neuer 11).

Stelzig, who more simply interprets Demian as the Jungian shadow, claims that the mounting pressure of this individuation leads Sinclair to find Beatrice as an attempted escape (Stelzig 3). However, when Sinclair paints a portrait of Beatrice from his unconscious, the portrait resembles Demian's face, as well as his "inner self, [his] fate or [his] daimon," and this futile attempt to escape individuation guides Sinclair back to self-realization. Nauer, on the other hand, interprets Beatrice as a symbol of the Jungian anima, the femininity in the male subconscious, due to her youthful looks, anonymity, hermaphroditic quality, and influence on Sinclair to bring his unconscious material into light via drawing (Neuer 12-13).

Another illustration that Sinclair creates from his subconscious is a painting of a bird struggling its way out of an egg and flying toward Abraxas. According to Neuer, Abraxas, the symbol of unity between bright and dark, embodies the process of individuation, in which Sinclair's goal is to unite his subconsciousness and consciousness into one personality and emulate the totality of Abraxas (Neuer 13). Stelzig furthermore asserts that the bird flying toward Abraxas represents Sinclair's attempt to complete a rebirth into a new self and head toward the totality of personality (Stelzig 2).

Additionally, Nauer interprets Frau Eva as a symbol of the Jungian Great Mother archetype, the mythical mother of all mankind who is the origin and destination of all mankind (Neuer 13). Sinclair recognizes Eva, Demian's mother, as his ultimate goal in a picture after repeatedly seeing her in his dreams, an area heavily influenced by the subconscious. Furthermore, Neuer claims that Eva's character corresponds with Jung's three essential aspects of the archetype: goodness, passion, and darkness (Neuer 15). Her hermaphroditic attribute represents the unity of the psyche, and the name "Eva," which means "life" and "living" in Hebrew, points clearly to her image as the primordial mother (Neuer 15). Lastly, at the end of the novel, a dying Demian advises Sinclair, "You must hearken to the voice inside you, then you will notice it is I, that I am in you" (206-207). According to Neuer, this guidance implies the completion of Sinclair's individuation; whenever Sinclair is confronted with a problem for which his conscious resources do not suffice, he can reach the forces dwelling within the unconscious of his nature, represented by Demian (Neuer 10, 15). By recognizing Demian's image within himself, Neuer asserts, Sinclair has integrated his subconsciousness into his consciousness, which is precisely what Jung means by individuation (Neuer 15).

Nauer's strictly Jungian interpretation, while providing meaningful explanations regarding Sinclair's individuation and the hidden archetypes in *Demian*, ignores the apparent Oedipal themes behind Sinclair's relationship with Demian and Eva. I will argue with Stelzig that the Jungian interpretation of the mother theme as a symbol of rebirth is "safe," while the Freudian mother myth is "transparent" in the text (Stelzig 3). Taking into serious consideration Hesse's letters to Maier, in which he effectively denies Jung's influence on the novel and confirms his familiarity with Freudian ideas, I will interpret the novel from a Freudian lens, which seems to be the more productive perspective. From this lens, not only is the application of Freud's Oedipus complex transparent, but so are the challenges to the Oedipus complex and the expansion of the *bildungsroman* that Hesse demonstrates through his novel.

The Freudian Totem in Demian

Interestingly, only Stelzig discusses the Freudian idea of the totem, describing the sparrow-hawk as Abraxas's totem, "whose esoteric function is the uniting of godly and devilish elements" (Stelzig 2). According to him, Abraxas and his sparrow-hawk totem represent the progressive integration of the "light" and "dark" realms of Sinclair's divided self, which symbolizes the Jungian individuation process (Stelzig 2). While this interpretation is true in the sense that a totem is an object with spiritual significance, it is not supported by Freudian theory. Upon a thorough understanding of Freud's conceptions of totems and taboos, as well as a deeper reading of *Demian*, we see through an Oedipal lens that the totem in the novel is, in fact, Demian.

In *Totem and Taboo*, Freud defines a tribal totem as an "object of veneration of a group of men and women who take their name from the totem and consider themselves consanguineous offspring of a common ancestor, and who are firmly associated with each other through common obligations towards each other as well as by the belief in their totem" (50). A totem "protects and warns the members of the tribe" (49) as well as "foretells the future to those faithful to it and serves as their leader" (49). Freud uses the phrase totem with two meanings: the animal and the group which it represents.

Freud traces the origin of the totem animal to the Oedipus complex: "Psychoanalysis has revealed to us that the totem animal is really a substitute for the father, and this really explains the contradiction that it is usually forbidden to kill the totem animal, that the killing of it results in a holiday and that the animal is killed and yet mourned" (66). According to the Darwinian conception of the primal horde, he claims, there was originally "only a violent, jealous father

who keeps all the females for himself and drives away the growing sons" (66). Then, one day, "the expelled brothers joined forces, slew and ate the father, and thus put an end to the father horde" (67). There remained, however, an ambivalent feeling, both love and hatred, toward the father among the sons:

They hated the father who stood so powerfully in the way of their sexual demands and their desire for power, but they also loved and admired him... After they had satisfied their hate by his removal and had carried out their wish for identification with him, the suppressed tender impulses had to assert themselves. This took place in the form of remorse, a sense of guilt was formed. (67)

This guilt led to the creation of the totem as a substitute for the father: "They undid their deed by declaring that the killing of the father substitute, the totem, was not allowed, and renounced the fruits of their deed by denying themselves the liberated women" (67). Thus the sons "created the two fundamental taboos of totemism" (67), prohibitions against killing the totem (animal) and having sex within the totem (group). "[For] this very reason these had to correspond with the two repressed wishes of the Oedipus complex" (67), the desire to murder the father and the sexual desire for the mother.

Multiple instances in *Demian* imply that Demian has killed his father and has replaced his father as his mother's lover. For example, Sinclair repeatedly describes Demian's relationship with Frau Eva, his mother, as intimate: "No one liked him, he was intimate with no one, except his mother, and his relations with her did not seem like those of a child, but those of a grown-up person" (59). As a relationship between two grown-up people has sexual implications, Sinclair implicitly indicates that Demian is engaged in a sexual relationship with Eva. Demian, however, does not mention Eva frequently to Sinclair during the novel's early chapters: "He seemed to live on very intimate terms with her, but he never spoke about her, never invited me to his house" (70). Sinclair is not alone in believing that Demian is in an incestuous relationship with his mother. There are widespread rumors that Demian is Eva's lover: "In this connexion [sic] I remember having heard that he was suspected of being his mother's lover" (57).⁹⁹

Furthermore, Demian is repeatedly described as strong and, in one instance, mentions murder as a solution to Franz Kromer's repeated harassment against Sinclair: "All right,' Max Demian said, smilingly. 'Go home now! We will put things square, although murder would have been the simplest. In such matters the simplest way is always the best." (48) This suggestion to kill Kromer implies that Demian believes that the murder of his enemies is justified. The strong Oedipal situation in the text implies that this group of enemies, at one point, included his father. According to the Oedipus complex, all sons subconsciously desire to murder their father, but the taboo originating from the primordial murder of the father suppresses this impulse. Demian, however, seems to be skeptical, even scornful, of conforming to such taboos when he says,

⁹⁹ This translation is W. J. Strachan's. The N. H. Priday translation, which I reference in the rest of this essay, translates this part as "he was suspected of living with his mother as a mistress." While the two translations convey the same meaning, I find the word "lover" more directly implicational to the Oedipal complex than "mistress."

"Whoever is too lazy to think for himself and to constitute himself his own judge simply conforms to the taboos, whatever they happen to be" (77). Thus, the text implies that Demian has rejected the two taboos that Freud points out, the taboos against the murder of the father-substitute and against incest, and has manifested his Oedipal desires by murdering his father and engaging in intimate relations with his mother.

Freud additionally discusses how the totem animal is taboo, referencing Émile Durkheim: "Durkheim has shown in his writings how the taboo, which is attached to the totem, must have entailed the prohibition against putting a woman of the same totem to sexual uses" (57). Taboo is a Polynesian word that has a double meaning: "[on] the one hand it means to us sacred, consecrated: but on the other hand it means, uncanny, dangerous, forbidden, and unclean" (13). Freud also describes these mixed feelings, which stem from the simultaneous admiration and animosity for the father in the Oedipal complex, as "awe and aversion" (17) and "tenderness and hostility" (33). Taboo individuals are venerated as well as feared, guarded as well as guarded against.

The ambivalent feeling that the son feels towards the father is evident in Demian. When Sinclair enters the novel's Oedipal triangle as the allegorical son of Demian and Eva, he demonstrates this taboo sentiment, or "awe and aversion," towards Demian, his father-substitute totem. For example, after Demian mysteriously talks to Kromer, Sinclair's bully, convincing him to stop bullying Sinclair, Sinclair describes his mixed feelings towards Demian: "The old, embarrassed feeling concerning him came over me-an odd mixture of gratitude and shyness, of admiration and fear, of affection and inward resistance" (50). This ambivalent sentiment towards Demian highlights his taboo quality. Sinclair recognizes this quality not only in Demian's personality but also in his looks: "Perhaps he was beautiful, perhaps he pleased me, perhaps even he was repugnant—I could not then determine" (61). Again, Demian is characterized with concurrent descriptions as admirable and distasteful, emphasizing his position as Sinclair's totem. This sentiment follows Sinclair to his boarding school, where he is physically separated from Demian: "I had often a great longing for Max Demian; on the other hand, I hated him not seldom, and looked upon him as responsible for the moral impoverishment of my life" (84). As Sinclair blames Demian for his "moral impoverishment" yet longs for him at the same time, he continues to demonstrate ambivalent feelings towards his totem Demian.

Freud furthermore asserts that the taboo has a "capacity of displacement" (18), or "transference" (18), in which "[anyone] who has violated a taboo by touching something which is taboo becomes taboo himself" (18). This phenomenon, he claims, is because the individual who has violated a taboo "has the dangerous property of tempting others to follow his example" (20). According to him, the "basis of taboo is a forbidden action for which there exists a strong inclination in the unconscious" (20). In the case of the Oedipus complex, these forbidden actions are the murder of the father, substituted by the totem animal, and sexual relations with other female members of the totem group. When Sinclair asks Demian whether following his subconscious desires justifies committing "actually forbidden" (76) actions, including murder and rape, Demian primarily encourages Sinclair to decide what is "really 'taboo" for himself:

But you haven't yet reached that point where one can see what is 'permitted' and what is really 'taboo.' You have realized only a part of the truth. The remainder will come after, rely on it. For instance, for the past year or so you have had in you an instinct which is stronger than all the others, and which is held to be 'taboo.' (76)

As Demian denounces society's arbitrary taboos, he encourages Sinclair to defy society's expectations to conform to such definitions. Demian has repeatedly challenged the dominant Christian ideologies, which he is expected to follow, claiming that "Cain was a thundering good fellow, and this story [of Cain and Abel] got attached to his name simply because people were afraid of him" (34) and that the unrepentant thief on the cross is "a real fellow with plenty of character" (73). According to Demian, "[whoever] is too lazy to think for himself and to constitute himself his own judge simply conforms to the taboos, whatever they happen to be" (77). While Sinclair initially describes these ideas as "blasphemous and infamous" (35) and describes Demian as "different, inconceivably different from us all" (61), he ultimately acquires Demian's taboo. This transference occurs during their confirmation: "It was not into the church that I was ready to be received but into something else, into an order of ideas and of personalities which surely existed somewhere or other on earth, and of which I felt my friend was the representative or messenger" (78). Sinclair's religious celebration of confirmation, which, in most cases, signifies submission to religion and conformity, instead becomes a ritual that represents his acceptance into the realm of Demian's "order of ideas and of personalities," a forbidden-or taboo-order. This displacement of taboo serves as the basis for Sinclair's concern about his "moral impoverishment" (84) as Sinclair now follows Demian's example in challenging the Zeitgeist of the status quo defined by Christianity.

Sinclair as the Totem

Sinclair, defying society's expectations to resist "a forbidden action for which there exists a strong inclination in the unconscious" (Freud 20), recognizes his subconscious desire to court Eva, the mother. This desire primarily arises in his dreams:

This dream, the most important and the most enduring of my life, was as follows: I returned home—over the front door shone the crest with the yellow bird on the blue ground—my mother came to meet me—but as I entered and wished to embrace her, it was not she, but a shape I had never before seen, tall and powerful, resembling Max Demian and my painting, yet different, and quite womanly in spite of its size. This figure drew me towards it, and held me in a quivering, passionate embrace. Rapture and horror were mixed, the embrace was a sort of divine worship, and yet a crime as well. Too much of the memory of my mother, too much of the memory of Max Demian was contained in the form which embraced me. (117)

While Sinclair has not met Eva yet, the dream figure's resemblance to Demian makes it clear to us that she is Demian's mother, and the simultaneous sentiments of "rapture and horror" that Sinclair feels emphasize the forbidden yet subconsciously alluring nature of incest. Due to the prevalence of incest taboo, Sinclair does not share his "dark love-dream" (137) with anyone, even his mentor Pistorious:

Of all my dreams, the dark love-dream recurred most frequently. Often, often have I dreamed of it; often I stepped under the crest with the bird on it into our house, and wished to draw my mother to me, but instead of her I found I was embracing the tall, manly, half-motherly woman, of whom I was afraid, and yet to whom I was drawn by a most ardent desire. And I could never relate this dream to my friend. (137)

Again, we see that Sinclair feels a strong incestuous desire not for his biological mother but for the woman who resembles Demian and embodies masculine qualities. The frequency of this dream highlights the strong subconscious inclination that Sinclair feels for this woman.¹⁰⁰ After Sinclair learns from a photograph that the woman in his dream is Demian's mother, he reunites with Demian and meets Eva. Eva recognizes Sinclair at once, inviting him to call her Mother Eve, a name referred to her only by "very few, very close friends" (178). After their meeting, Sinclair visits Eva and Demian on a daily basis: "From this day on I went in and out of the house like a son and a brother, but also like a lover" (179). Subsequently, Sinclair and Eva's relationship grows stronger. At one point, she confronts him about his love for her and tells him that love "must have the force to be absolutely certain of itself" (186), encouraging a sexual union between Sinclair and herself. Sinclair's Oedipal desire is ultimately completed in his dream, in which his "union with her was accomplished by way of allegory" (189).

At the end of the novel, Sinclair replaces Demian as the father-substitute totem. When Demian dies during the Great War, he gives Sinclair a kiss from Eva: "'Mother Eve said that if ever you were ill I was to give you a kiss from her, which she gave me... Close your eyes, Sinclair!' I obediently closed my eyes. I felt a light kiss on my lips" (207). As Demian delivers a kiss from Eva to Sinclair, he effectively transfers his own sexual relationship with Eva to Sinclair. Now, Sinclair replaces Demian, who once became the totem as the substitute for his own father. It is important to note that, while Sinclair, the son, replaces Demian, the father-totem, he does so in a nonviolent manner without realizing his desire to kill the father.

According to the novel's last lines, Sinclair can now find Demian in the depths of his soul after Demian's death:

But my soul is like a mysterious, locked house. And when I find the key and step right down into myself, to where the pictures painted by my destiny seem reflected on the dark mirror of my soul, then I need only stoop towards the black mirror and see my own picture, which now completely resembles Him, my guide and friend. (207)

¹⁰⁰ Freud, in *The Interpretation of Dreams*, claims that the dream is "a perfectly valid psychic phenomenon, actually a wish-fulfilment" (44) that carries out subconscious desires in a more or less disguised way. From a Freudian perspective, Sinclair's "dark love-dream" emphasizes the heavy presence of his Oedipal, incestuous desire for Eva in his subconscious.

Sinclair can now identify Demian in himself, whose mirror image "completely resembles" Demian. According to Freud's resolution of the Oedipus complex, the son ultimately identifies with the father, internalizing his values and perceiving him as a role model rather than a rival. Accordingly, Sinclair identifies with Demian, who is now his role model, and stops feeling ambivalent sentiments towards him. Furthermore, Demian's incest taboo has been completely transferred to Sinclair through the kiss from Eva, and Sinclair now assumes Demian's role as the father-substitute totem who has manifested his incestuous desire for the mother. Again, it is important to note that the other Oedipal desire, the desire to murder the father, has not been manifested in the novel's ending. Demian has peacefully left the position of the father due to an external reason. Through the kiss, he has, in a way, passed the torch to Sinclair, and Sinclair still calls him a "friend" without any sentiments of guilt about his death. Meanwhile, Sinclair is left *in* the Oedipal triangle without "moving on" from the complex as Freud suggested.

Challenges to the Oedipus Complex and the Expansion of the Bildungsroman in Demian

While Hesse adheres to certain aspects of Freud's Oedipus complex throughout Demian, he offers significant challenges to the complex in crucial parts of the text. For example, Sinclair does not continue pursuing Beatrice, the outside sexual figure who, according to Freud, would serve as a substitute for his sexual desire for Eva, the mother. After drawing an image of Beatrice from his subconscious, inspired by a young girl he meets at the park, Sinclair is initially enamored with her image: "the impression was deeper than all the former ones, and the influence of this infatuation on my life was powerful" (97). Seeming to reflect Freud's idea that a sexual desire for an outside woman replaces the son's desire for the mother. Sinclair even describes his noble pursuit for Beatrice as "not the action of flying back or crawling back to mother" (98). However, his desire for Beatrice only leads him back to his Freudian incestuous desire for Eva, his allegorical mother. Meanwhile, his desire for Beatrice slowly recedes from his center of attention: "The figure of Beatrice, which had for a certain time occupied so much of my attention, vanished by degrees from my mind, or rather receded slowly, drawing nearer and nearer to the horizon, becoming darker, more like a shadow, as it retreated. She satisfied my soul no longer" (116). Sinclair realizes that Beatrice, the outside sexual figure, does not satisfy his soul, and a new "longing for a full life" (116) glows in him. His desire for Beatrice, which, according to Freud, should satisfyingly substitute his incestuous desire for the mother and lead him to the resolution of his Oedipus complex, does not lead to a "full life." Thus, the text directly contradicts Freud's idea that moving on from the Oedipus complex, through an identification with the father and the discovery of desires for other women, leads to the development of an individual.

In fact, it is the incestuous desire for Eva that replaces the desire for Beatrice in Sinclair's dark love-dream:

A certain dream, or play of fantasy, which occurred to me, was full of significance. This dream, the most important and the most enduring of my life, was as follows: I returned home—over the front door shone the crest with the yellow bird on the blue ground—my

mother came to meet me—but as I entered and wished to embrace her, it was not she, but a shape I had never before seen, tall and powerful, resembling Max Demian and my painting, yet different, and guite womanly in spite of its size. (116-117)

Instead of turning to an outside sexual figure to replace the mother and resolve the Oedipus complex, Sinclair defies Freudian theory by continuing to pursue Eva, the mother, and even finding success in his pursuit.

Hesse additionally challenges Freud's Oedipus complex by leaving Sinclair *in* his Oedipal triangle at the end of the novel. According to Freud, the son ultimately identifies with his father, internalizing his values and behaviors, and finds an outside sexual figure to direct his desires, moving past the complex and emerging into his full self. In the conclusion of *Demian*, Sinclair does identify with Demian, the father-substitute, seeing him reflected in the mirror of his soul. However, we do not see him *moving past* the Oedipus complex to become his complete self. Instead, Sinclair finds himself in a different Oedipal condition, in which he is now the father and the totem, and he has emerged into his full self *in* this Oedipal triangle. He never leaves the Oedipal complex—remaining a child, in a way. From a strictly Freudian perspective, Sinclair's journey is a failed *bildungsroman* as he does not progress past his Oedipal situation. However, under Hesse's queer version of the Oedipus complex, Sinclair is able to emerge into his full self without moving beyond his Oedipal triangle.

Furthermore, as we return to Freud's theory about the origin of the totem, it must be noted that Sinclair replaces his allegorical father in a nonviolent way, contradictory to Freud's ideas. While Sinclair does realize his sexual desire for the mother by replacing the father, Demian's death at the end of the novel is not a manifestation of Sinclair's desire to murder the father. Instead, Demian dies in the Great War, a circumstance beyond Sinclair's control, and Sinclair finishes his story describing Demian as "[his] guide and friend" (207). Sinclair never demonstrates his Freudian desire to murder the father, contradicting Freud's claim that this subconscious desire exists in every son. Demian's nonchalance with Sinclair's pursuit of Eva further supports this seemingly peaceful transition of power. Demian, in fact, encourages Sinclair's pursuit, telling Sinclair that Eva knows of him (167) and inviting Sinclair to his home (171). He also transfers his Oedipal relationship with Eva to Sinclair when he delivers a kiss from her to Sinclair moments before his death. This behavior defies the Freudian origin story of the totem, in which the sons violently take the females from the violent, jealous father who keeps all the females for himself.

Moreover, it is impossible to ignore the homoerotic undertone in the relationship between Sinclair and Demian. When Sinclair discusses Demian's appearance, he describes him as "beautiful" and pleasing: "Perhaps he was beautiful, perhaps he pleased me, perhaps even he was repugnant—I could not then determine" (61). While this description, from a Freudian perspective, exemplifies the taboo feelings, the "awe and aversion," that Sinclair feels for Demian, it also expresses Sinclair's implicit homosexual desire for Demian. During the period of this novel, Paragraph 175 of the German Criminal Code outlawed homosexuality in Germany (Huneke 52). Taking this ban into consideration, Sinclair feels ambivalent toward Demian due to the German Zeitgeist regarding homosexuality during his time, which influenced him to find Demian "repugnant" in spite of his attraction towards Demian.

We must also note Eva's resemblance to Demian as we discuss the implicit queer relationship between Sinclair and Demian. When Sinclair initially describes his "dark love-dream" with Eva, he recognizes her resemblance to Demian: "Too much of the memory of my mother, too much of the memory of Max Demian was contained in the form which embraced me. (117). Considering his description of Demian as "beautiful" and pleasing, it is not surprising that Sinclair is strongly attracted to Eva, who embodies "the memory of Max Demian." From this queer perspective, Sinclair turns to Eva as a replacement for Demian, whom the status quo forbids him from sexually engaging with.

This queer undertone between Sinclair and Demian culminates in their kiss at the end of the novel: "Mother Eve said that if ever you were ill I was to give you a kiss from her, which she gave me... Close your eyes, Sinclair!' I obediently closed my eyes. I felt a light kiss on my lips" (207). From a strictly Freudian perspective, this kiss represents the transfer of taboo from Demian to Sinclair. However, in light of the implicit queer relationship between the two characters, the kiss represents the final expression of the sexual desire between Sinclair and Demian, who reciprocates Sinclair's desire. Sinclair emerges into his true self through this kiss, which allows him to demonstrate his repressed desires.

By challenging elements of Freudian theory and introducing homoerotic elements in *Demian*, Hesse effectively expands the genre of *bildungsroman*. Many modern *bildungsroman*, most notably *Sons and Lovers* by D. H. Lawrence (Gillins 274), engage with Freudian theory by directly applying the Oedipus complex. The protagonists experience and "move on" from the Oedipus complex to emerge into their complete selves. However, by applying a queered version of the Oedipus complex to Sinclair's novel of formation, where the protagonist continues his pursuit of the mother, maintains an amicable relationship with the father, and remains in the Oedipus complex, the novel, Hesse opens new doors that enrich the genre of *bildungsroman*. Furthermore, most modern *bildungsroman*, including works based on the Oedipus complex, typically illustrate their protagonists' growth and formation in a heterosexual context, while Hesse integrates an implicit homosexual relationship in Sinclair's journey of formation. Adding complexity to the protagonist's exploration of identity and self-discovery, Hesse successfully enriches the thematic diversity of the *bildungsroman*.

Next Steps in the Scholarships of Hesse, Freud, and the bildungsroman

While a Jungian analysis of *Demian* produces a useful interpretation of the text, a Freudian perspective approaches the text as a *bildungsroman*, offering a robust interpretation of the novel that we do not see from Jungian analysis. As I have demonstrated, Hesse both applies and challenges Freud's Oedipus complex in the text, and this Freudian understanding establishes the novel as a genre-buster that pushes the *bildungsroman* forward by breaking conventional expectations.

Considering this Freudian interpretation, critics of Hesse should now turn attention to the applications and challenges of Freud's theories in other texts by Hesse. I have corroborated Hesse's claims that he was well-acquainted with Freudian ideas before the writing of his major novels: *Demian* (1919), *Siddhartha* (1922), *Steppenwolf* (1927), and *Narcissus and Goldmund* (1930). Not only did he apply Freud's theories, but he also *queered* them, demonstrating a rich understanding of Freud's works. Instead of attempting to understand his works from a strictly Jungian or Freudian perspective, scholars must now offer interpretations of Hesse's works in light of his ability to *queer* psychoanalytical theories, which is not limited to the Oedipus complex. These interpretations will allow us to more thoroughly understand Hesse's nuanced way of storytelling.

Furthermore, Freudian scholars should now identify the variations of Freudian theory, particularly the Oedipus complex, in modern *bildungsroman*. Although Freud claimed that his theories accurately described the transition from adolescence to adulthood, many writers of *bildungsroman* have challenged his ideas. For example, Hesse, as I have demonstrated, both applied and challenged Freud's theory in his works, revealing where his literary vision converges with and diverges from the Freudian conception of the *bildungsroman*. Freudian scholars should not stop at recognizing the direct manifestations and antitheses of Freudian theory in literary works. They should furthermore interpret more literary works as nuanced applications, or challenges, of Freudian theory, offering us a richer understanding of the psychoanalyst's influence on the literary world.

Finally, I have demonstrated that Hesse effectively expands the genre of *bildungsroman* through his queering of the Oedipus complex and his integration of homoerotic undertones into Sinclair's novel of formation. Literary scholars addressing the *bildungsroman* as a novelistic genre should now investigate the history of the *bildungsroman* in relation to how authors have challenged the status quo to expand the genre. Noting the efforts of writers to provide more diverse and nuanced explorations of identity and self-discovery, scholars should provide deeper insight into the genre's history of expansion and recognize the expanded genre for what it is.

Works Cited

- Durrani, Osman. "Die Dunkle Und Wilde Seite Der Seele: Hermann Hesse, Briefwechsel Mit Seinem Psychoanalytiker Josef Bernhard Lang 19161944." *The Modern Language Review*, vol. 102, no. 3, 2007, pp. 903-904.
- Freud, Sigmund, and A. A. Brill. The Interpretation of Dreams. Macmillan, New York, 1913.

Freud, Sigmund, 1856-1939. Totem and Taboo: Resemblances between the Psychic Lives of Savages and Neurotics. New Republic, 1927, ©1918, New York (State), 1918.

- Gillis, Colin. "Lawrence's Bildungsroman and the Science of Sexual Development." *Twentieth Century Literature*, vol. 60, no. 3, 2014, pp. 273-304.
- Hesse, Hermann, 1877-1962. Demian. Boni and Liveright [c1923], New York (State), 1923.
- Huneke, Samuel C. *States of Liberation: Gay Men between Dictatorship and Democracy in Cold War Germany*. University of Toronto Press, Toronto, 2022, doi:10.3138/9781487542122.
- Mileck, Joseph. "Names and the Creative Process: A Study of the Names in Hermann Hesse's "Lauscher," "Demian," "Steppenwolf," and "Glasperlenspiel"." *Monatshefte (Madison, Wis. : 1946)*, vol. 53, no. 4, 1961, pp. 167-180.
- Nelson, Benjamin. "Hesse and Jung: Two Newly Recovered Letters." *The Psychoanalytic Review (1963)*, vol. 50, no. 3, 1963, pp. 11-14.
- Nelson, Donald F. "Hermann Hesse's Demian and the Resolution of the Mother-Complex." *The Germanic Review*, vol. 59, no. 2, 1984, pp. 57-62.
- Neuer, Johanna. "Jungian Archetypes in Hermann Hesse's Demian." *The Germanic Review*, vol. 57, no. 1, 1982, pp. 9-15.
- Schmid, Hans R. Hermann Hesse, Huber & Co, Frauenfeld, 1928.
- Stelzig, Eugene L. Chapter VI: Hesse's Marriage of Heaven and Hell., 2002.

An Investigation Into Metal Organic Cage's Effectiveness in Transporting Selected Diazo Compounds Through a Liquid Membrane By Usman Kashif

Research Question: How does the type of geometric isomerism (cis or trans isomerism) of an organic Diazo-compound affect the thermodynamics and chemical kinetics of its transport through a liquid membrane containing a $\text{Fe}^{II}_{4}\text{L}_{6}$ metal-organic cage.

Abstract

Chemical filtrations and separations require up to 15% of the global energy budget. At the same time, the combustion of hydrocarbon fuels accounts for 73% of total U.S GreenHouse Gas Emissions. Metal organic cages (MOCs), constructed from hydrocarbon linkers and metal ions, and able to encapsulate and release targeted molecules based on geometric orientation. Thus, MOCs can be used as a technological tool used for molecular separation. In this paper, aqueous solutions of a $Fe^{II}_{4}L_{6}$ metal-organic cage were used as liquid membranes to facilitate the transport of two isomers of the same diazo-compound. Solved differential equations were used as kinetic models for the relationship between the concentration of each isomers through the liquid membrane. The concentration of each diazo isomer was monitored using NMR spectroscopy in the feedstock and receiving arm of the U-tube membrane. Fitting the kinetic models to the monitored concentrations and using the *Excel* solver procedure yielded the parameters for the rate of guest-encapsulation (k_f) and guest-release (k_r) for each isomer. Then by using a guest-binding equilibrium model, the equilibrium constants (K_{eq}) for both systems were determined. The change in Gibbs Free energy (ΔG) was also determined for the system with each isomer and provide insight about the more spontaneous and thermodynamically favored/stable system. The results concluded that the *trans*-isomer transported at a faster rate (k_{f} = 0.150 and $k_r = 0.120$) than the *cis*-isomer ($k_f = 0.0574$ and $k_r = 0.0600$). However, the cis isomer demonstrated greater thermodynamic stability in the MOC. The higher K_{eq} and lower ΔG value for the *cis*-isomer system (K_{eq} = 1.05 and ΔG = -120) as compared to the *trans*-isomer system (K_{eq}=0.800 and ΔG = -1200 show that the *cis*-isomer system is more thermodynamically favorable and spontaneous with a higher energy barrier at the guest-uptake and guest-release phase boundaries.

Introduction

Metal-Organic cages (MOCs) are crystalline materials that are constructed from inorganic metal ions and organic linkers. This structure forms a cage-like shape with empty cavities. MOCs are different from other porous materials due their unique structural diversity. They have porous structures, precise atomic arrangement, and interconnected ligands with rotatable bonds. Amongst the vast applications of MOCs, they have been recently used as a tool for molecular separation. The metal organic cage used as a separation tool in this paper is a coordination cage, formed by the spontaneous organization of metal ions and organic ligands. These metal-organic structures are formed by the reversable ligand metal dative bond in which an organic ligand donates its lone pair of electrons to the central metal ion. The metal ions are coordinated to many ligands and create polyhedral nodes. These can have several molecular shapes due to the nature of the central ion and coordination environment. Metal organic cages are used for molecular separation due to their selective permeability function. These cage macromolecules contain empty nanocavities with open windows that allow molecules to enter and bypass. MOCs can be used for molecular separation based on size and the affinity for the cage's interior. The aqueous membrane used in this separation process consists of an immiscible fluid phase that separates two other liquids. Coordination cages are used in the aqueous membrane as active carriers and hosts of selected molecules. (1)

The molecular separation process using MOCs during the transport of a selected compound through the liquid membrane occurs in three stages: guest intake in the feedstock arm, transport in cage within aqueous membrane, and guest release in the receiving phase. For this investigation, the selected compound transported through a U-tube liquid membrane with the feedstock and receiving arms on each side of the tube with the aqueous transport membrane in the U-shaped section. The guest intake refers to the process by which the selected molecule encapsulates itself into the MOC, and is dependent on molecular size, orientation, and stoichiometry of addition. Hydrogen bonding, London dispersions, π - π stacking, among other non-covalent interactions are the forces behind guest encapsulation. Coordination cages are used as liquid – phase extractants to encapsulate target molecules from an immiscible liquid phase. They are classified as liquid – phase extractants as they bring in the guest molecules (organic solvents) into solvents that they are not typically soluble in. The separated molecules not entrapped in the cage remain on the feedstock side of the membrane. Initially, the concentration of guest-molecule in feedstock arm before cage-binding is higher, and as the guest molecule encapsulates into the MOC, their concentration in the feedstock phase gradually decreases.

The encapsulated guest molecules are stabilized in the cages due to the hydrophobic interactions in the guest-binding process. The hydrophobic contribution is the attraction between the targeted molecules and the hydrophobic interior of the MOC. This phenomenon causes the initial binding, but the salvation effect of the guest molecules being surrounded by water molecules stabilizes the new guest-MOC complex. The guest molecule is then transported through the aqueous membrane. The chemical kinetics of the cage-guest transport in the aqueous membrane depends heavily on guest binding affinity. This affinity refers to the strength of the attraction between the encapsulated guest molecules and the MOC. Thus, the rate at which these guest molecules are transported through the U-tube is influenced by the binding affinity in the cage. In general, guest molecules that are more hydrophobic in nature and smaller in size tend to have a higher binding affinity and thus transport at a faster rate. Another factor that influences the rate of transport is the concentration gradient – the difference in concentration gradient impacts the diffusion coefficient of the guest molecule. The diffusion coefficient measures how freely and easily the guest molecule can move within the liquid membrane during transit in the MOC.

A steeper concentration gradient corresponds to a higher diffusion gradient and this an increase in the rate of guest transport across the U-tube.

The guest-release stage of the transfer occurs in the receiving phase boundary of the system. Similar to the guest intake process, the guest release is influenced by the cage-guest molecule binding affinity. A higher binding affinity results in a slower rate of release. The sudden release of these guest molecules from their entrapment in the MOC can be triggered from external stimuli, competitive binding, equilibrium shift, and kinetic factors. External stimuli like fluctuation in pH and light can trigger guest-release from the MOC. For example, inducing exposure of light of a specific wavelength in the receiving phase boundary can create conformational changes within the MOC and a consequential guest-release. Alternatively, the presence of other molecules in the receiving end with a greater binding affinity to the cages can cause the displacement of the existing guest molecule. A rise in the concentration of the guest molecule at the receiving arm may cause an equilibrium shift and thus guest release. According to Le Chatelier's Principle, a system at equilibrium will counteract any change by shifting the equilibrium. As the guest concentration increases, the equilibrium will shift to the side of the reaction that reduces the guest concentration - guest release. The binding, transport in MOC, and guest - release occur under specific conditions of dynamic equilibrium and are influenced by kinetic factors such as the k_f (rate constant in feedstock arm) and k_r (rate constant in receiving arm). (2)

Reviewing previous literature: The use of a MOC for molecular separation and guest molecule transport through a liquid membrane has been explored in depth by Bao-Nguyen T. Nguyen and team at the University of Cambridge in 2021. The study concentrated on the ability of coordination cages to selectively transport Naphthalene (dissolved in dodecane) across a liquid membrane with metal organic cages. Naphthalene's high binding affinity to the cages used in the investigation made it suitable for the guest molecule. The metal organic cages used in this paper were comprised of sulfate salts $Fe^{II}_4L_6$ (cage 1) and $Co^{II}_4L_4$ (cage 2), both tetrahedral in molecular geometry. Each cage was prepared and dissolved in water. The aqueous solution of both cages flowed into the U-tube section (stock arm) of the U-tube system. Feedstock solutions of naphthalene were loaded into the feedstock arm of each U-tube (one for each cage). Each cage successfully employed selective permeability to encapsulate the guest naphthalene molecule and transport it across the aqueous membrane. A three-state model was used to approximate the concentration of the guest naphthalene through the guest-intake (N_A), transport (N_b), and guest release (N_c). In this investigation, the value of N_b was not directly measured but derived from mass balance.

$$N_A \xrightarrow[T_r]{T_f} N_B \xrightarrow[T_f]{T_r} N_C$$

Where T_f is the forward transport constant and T_r is the reverse transport constant. The results show that the time taken for 50% of the naphthalene from the feedstock to the receiving arm is 1.99 days for the aqueous membrane with the $Fe^{II}_{4}L_{6}$ cages, while a relatively larger duration of 9.41 days for the liquid membrane containing $Co^{II}_{4}L_{4}$ cages. Bao-Nguyen T. Nguyen and team attributed the longer transport time in the latter cage due to its more enclosed framework and higher activation energy barrier for guest intake and release. In the first cage, the uptake and release movements of the guest molecule occurred at faster rates due to the stronger hydrogen bonds between the flexible glycerin chains that govern the opening and closing of the apertures in the MOC. This cage consisted of a more framework with apertures more suitable for the intake and release of naphthalene molecules. To investigate the chemical kinetics of the system, the concentration vs time data for N_A and N_c were fit simultaneously through a non-linear least squares fir for the data using Mathematica software. The resulting best fit equation suggested a first order rate constant for naphthalene transfer from the dodecane solution into the MOC (k_{f}^{obs}) and for the reverse reaction for naphthalene to dodecane (k_{r}^{obs}). The forward (T_{f}) and reverse (T_r) transfer constants were calculated by dividing the observed rate constants k_f^{obs} and k_r^{obs} by the cross-sectional area of the U-tube (1.13 cm²) and by the cage concentration (2.0 mM) respectively. The team then calculated and compared the molar fluxes for the transport of naphthalene our of and into the organic solvent. The molar flux for the transport of naphthalene into each of the metal-organic cages can be determined using the following rate law:

$$J_f = T_f[N][cage]$$
(Equation 1)

where J is the molar flux and N is the concentration of naphthalene in either arm of the U-tube. Similarly, the molar flux for the transport of naphthalene out of the MOC and into the dodecane solution can be determined using the following rate law:

$$J_r = T_r [N_B]$$
 (Equation 2)

Another parameter calculated was K_{eq} , calculated by dividing T_f by T_r , which represents naphthalene's preference to be encapsulated by the MOC to be dissolved in the organic solved. A $K_{eq} > 1$ signifies a preference for being sequestered while a $K_{eq} < 1$ represents a preference for being dissolved. After modelling using Mathematica software and applying the calculations, all relevant parameters were found. The T_f for cage 1, rate constant for $Fe^{II}_4L_6$ cage binding, was found to be 0.157 mM⁻¹day⁻¹cm⁻², while the T_r for cage 1, rate constant for guest-release, was found to be 12 day⁻¹cm⁻². The T_f for cage, rate constant for $Co^{II}_4L_4$ cage binding, was found to be 0.045 mM⁻¹day⁻¹cm⁻², while the T_r for cage 2, rate constant for guest-release, was found to be 0.13 day⁻¹cm⁻². The researchers also observed that when the second MOC was used for naphthalene transfer, there was a slight sigmoidal rise in the concentration of naphthalene in the receiving arm. This rise in concentration indicates an induction period, or a delay in the guest-transfer attributed to the build-up of a host-guest intermediate within the cage layer. This delay was only observed when using the $Co^{II}_4L_4$ cage. (3) The recorded kinetic data showed that the molar flux for naphthalene release back into the organic solvent was higher than the molar flux for the naphthalene – cage binding for both cages. This is consistent with the K_{eq} values of 0.013 and 0.32 for cage 1 and cage 2 respectively. In both cases, the naphthalene prefers to be dissolved in the organic solvent of dodecane than be bound to the MOC. The higher T_f and T_r values for the cargo of Naphthalene in cage 1 suggests faster overall guest intake, transport, and release. The researchers attributed this to the cage structure and stronger molecular binding affinities as aforementioned.

The existing literature for the use of metal organic cages for molecular separation in a liquid membrane, specifically the study of the transport of Naphthalene by Bao-Nguyen T. Nguyen and team, demonstrate the underlying chemical kinetic principles that govern the transfer of selected compounds through an aqueous membrane containing MOCs. This paper will apply the same three state model to demonstrate the underlying chemical kinetics and thermodynamics of the transfer of two isomers of the same diazo-organic compound through a liquid membrane consisting of the same Fe^{II}₄L₆ and Co^{II}₄L₄ metal organic cages.

Diazo-compounds are a special type of organic compounds that contain a characteristic diazo-group. All diazo compounds have two linked nitrogen atoms that are double bonded (N=N) at the terminal position of the organic compound. These compounds follow the general structure form of R=N=N-R, where R signifies a hydrogen atom or other functional group. Diazo compounds have an electronic structure consisting of delocalized pi electron density over the α -carbon and two nitrogen atom. The structure also has an orthogonal π system with electron density delocalized over only the terminal nitrogen atoms. In this investigation, the concentration of two isomers of the same halogenated diazo compound was monitored as it transferred through the liquid membrane. The structure of a halogenated diazo compound is illustrated below.



The diazo compound exhibits cis-trans isomerism, which arises due to the restricted rotation around the double bond (N=N). This restricted rotation can lead to different spatial arrangements of the substituents around the diazo functional group and the attached halogen

atom. The position of the substituents and halogen atom around the diazo group give the molecule two distinct isomers.

In the *cis*-isomer of the R=N=N-R diazo structure , both the "R" groups are found on the same side of the diazo-group. In the *trans*-isomer, the R groups are located on opposite sides of the diazo compound. The cis isomer has a bent shape with a net dipole moment due to both the R groups being placed on the same side of the molecule. The opposite arrangement for the trans isomer allows for a linear shape with a lower boiling point due to no dipole moment. The differing geometric orientation of the cis and trans isomers of the diazo compounds impact their physical properties, stability, and reactivity in chemical processes. Changes in such parameters due to the isomerism of the diazo-compound impacts both its rate of transport through the MOC as well as the diazo-cage binded thermodynamic stability.

The metal organic cage used for selective transport of both isomers was the same $Fe^{II}_{4}L_{6}$ cage as used in Bao-Nguyen T. Nguyen's study. The shape and structure of this cage has vast impacts on the selected transport of the diazo isomers. The $Fe^{II}_{4}L_{6}$ cage is formed through the coordinate covalent bonds between the aromatic organic ligands and iron ions. The cage follows a tetrahedral arrangement with four iron ions at the vertices of the tetrahedron. These ions are attracted to six organic ligands to form the cage structure. The cage has an internal cavity lined with organic ligands, which provides a hydrophobic environment for diazo molecule transport. The coordinate bond formed between the iron ions and the organic ligand give a stable coordination complex structure for the MOC. This cage is also known as tetrazine-edged $Fe^{II}_{4}L_{6}$ tetrahedra, where the tetrazine edges refer to the organic ligands. The aromatic core of the organic ligands contains a tetrazine ring, which contains one carbon atom and four nitrogen atoms. These tetrazine edges provide a rigid and planar structure for the guest binding molecules to enter into. The tetrazine-edged $Fe_4^{II}L_6$ tetrahedra can also undergo structural modification when the guest binding process occurs. Structural transformation of the metal organic cage once the diazo-compound has binded are triggered from the inverse electron-demand Diels-Alder (IEDDA) reactions. These IEDDA reactions occur between a strained dienophile (electron-deficient) and a diene (electron-rich) to form a cycloadduct. In context, the tetrazine edges are the strained dienophile and the diazo compound serve as the diene. When these react, the cage undergoes post assembly modification that introduces new functionalities. These new functionalities can alter the shape, size, and binding properties and reactivity of the MOC. (4)

The different geometric orientations of each diazo isomer can result in different structural modifications of the cage and thus differing rates of guest-uptake and guest-release as well as varying thermodynamic stability. In order to measure the aforementioned parameters, NMR spectroscopy was employed to independently measure the concentration of the guest diazo isomers in the feedstock and receiving arm of the U-tube. Then, modelling the concentration versus time of the diazo-compound through the liquid membrane using solved differential equations can yield the required rate of guest-uptake and guest-release parameters.

For scientific simplicity, this procedure assumes that the concentration of metal organic cage does not change throughout the transport process. The cage concentration before guest-binding, within the transport section of the U-tube, and after guest-release is assumed to remain constant.

Results

The relationship between the rate of change of the concentration of these diazo-compounds through the three stages of the liquid membrane U-tube can be modelled using the following differential equations:

Through feedstock arm: $\frac{dN_A}{dt} = -k_f N_A(t) + k_r N_B(t)$ (Equation 3) Through U-section (transfer in MOC): $\frac{dN_b}{dt} = +k_f N_A(t) - 2k_r N_B(t) + k_f N_C(t)$ (Equation 4)

Through receiving arm: $\frac{dN_c}{dt} = +k_r N_B(t) - k_f N_c(t)$

(Equation 5)

To determine a model for the concentration of the diazo compound through the liquid membrane in each of the three stages of transport, the equations above can be integrated using the appropriate boundary conditions ($N_A = N_{A0}$, $N_B = N_{B0}$, and $N_C = 0$). These boundary conditions assume that the diazo compound is in only the feedstock arm at t=0. The solutions to the differential equations are shown below.

$$N_{A} = \frac{(k_{f}(1+e^{-2k_{r}t}))+2k_{r}(1+e^{k_{f}t}))e^{-k_{f}t}}{2(k_{f}+2k_{r})}N_{A0}$$
(Equation 6)

$$N_{A} = \frac{k_{f}(1-e^{-(k_{f}+2k_{r})t}))}{k_{f}+2k_{r}}N_{A0}$$
(Equation 7)

$$N_{C} = \frac{(-k_{f}(1-e^{-2k_{r}t}))-2k_{r}(1-e^{k_{f}t}))e^{-k_{f}t}}{2(k_{f}+2k_{r})}N_{A0}$$
(Equation 8)

The above equations can now be used to determine the value of for both diazo-compound transfer from the solution into the MOC (k_f) and for the reverse reaction for diazo-compound to solution (k_r). By independently measuring the time vs concentration of N_A and N_c through NMR spectroscopy, the solver procedure on *Excel* for non-linear fitting can be used to determine k_f and k_r values for guest-uptake and guest release of the diazo-compounds. (5)

Raw data table: Relationship between the concentration of both isomers of organic diazo-compound in the feedstock arm (N_A) and the receiving arm (N_C) of the U-tube in the liquid membrane.

Time (Hour)	NA	Nc
0	10.00	0.00
1	8.90	0.07
3	7.48	0.49
6	6.10	1.23
9	5.31	1.91
11	4.90	2.26
15	4.42	2.75
18	4.16	3.00
21	3.98	3.18
24	3.88	3.29
27	3.77	3.38
30	3.72	3.44
33	3.67	3.48
36	3.54	3.51
39	3.63	3.53

Compound 1: Cis-is	Compound	1:	Cis-isomer
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Compound 2 – Trans-isomer

Time (Hour)	NA	Nc
0	10.00	0.00
1	9.45	0.02
3	8.51	0.12
6	7.31	0.40
9	6.56	0.73
11	6.15	0.95
15	5.45	1.38
18	5.01	1.66
21	4.75	1.91
24	4.46	2.12
27	4.31	2.31
30	4.12	2.46
33	3.98	2.60
36	3.87	2.71
39	3.77	2.80

The

above raw data have been best-fit modelled into the parent equation from equation 4 and equation 6 for each diazo-compound isomer in each arm of the U-tube. The plot of the best-fit concentration versus time and the modelled k_f and k_r values are shown below. Processed Data: Scatter plots visually representing the concentration changes of both isomers of

the organic diazo compound through the feedstock and receiving arm at each hour of selected transport using the metal organic cage.



The *Excel* solver procedure non-linear fitting computes the required k_f and k_r values as summarized in the table below. Note the use of moving average fit for the line of best fit for the data instead of an exact curve– this is a limitation of the Excel modelling software.

Table 1: Rate constants for the transport of cis and trans isomer of diazo compound through aqueous layer containing metal organic cage.

	k _f (rate of guest-uptake (day ⁻¹))	k _r (rate of guest-release (day ⁻¹))
Trans-isomer	0.150	0.120
Cis-isomer	0.0574	0.0600

Results Analysis and Discussion:

Table 1 demonstrates how the rate of transport into the cage for the *trans*-isomer is greater than that of the *cis*-isomer (0.150>0.0574) and the rate of release back into the liquid membrane for the *cis*-isomer is also greater than that of the *trans*-isomer (0.120>0.0600). These parameters indicate that the overall guest-uptake and guest-release process occurs faster for the transport of the *trans*-isomer of the diazo compound than that of the *cis*-isomer inside of the liquid membrane. Although these rates of transport processes suggest a faster transport for the *trans*-isomer, they do not explain the thermodynamic stability and guest-binding affinities of the respective isomers. (6)

The stability of the guest Diazo-compound within the metal organic cage can be furthered analyzed through the calculation of the equilibrium constant during the guest-binding and guest release process, K_{eq} . By definition $K_{eq} = \frac{N_B}{N_A}$ (ratio of concentration of Diazo-compound after transport process to concentration prior guest-binding process).

At equilibrium, the rate of transport of the Diazo-compound into the cage (with initial concentration N_A and rate constant k_f) is equal to the rate of Diazo-compound release back into the liquid membrane (with guest-cage binded concentration N_B and rate constant k_r).

Rate of guest intake =
$$k_{f[N_A]}$$
(Equation 9)Rate of guest release = $k_{r[N_A]}$ (Equation 10)

At equilibrium
$$k_{f[N_{a}]} = k_{r[N_{b}]}$$
 (Equation 11)

Rearranging yields:
$$\frac{k_f}{k_r} = \frac{[N_B]}{[N_A]} = K_{eq}$$
 (Equation 12)

The value of K_{eq} has been calculated for both isomers using the ratio $\frac{k_f}{k_r}$ and recorded in the table below:

	Trans-isomer	Cis-isomer
K _{eq}	0.800	1.05

A higher K_{eq} value indicates a greater concentration of the Diazo-compound after the guest-binding process than before the process at the equilibrium. This means that a higher K_{eq} value suggests that the system in the liquid membrane found the binding process more thermodynamically favorable, leading to the formation of more products (diazo-MOC binded complex) compared to the reactants (free diazo compound). Thus, the *cis*-isomer with the higher K_{eq} (1.05) compared to the *trans*-isomer (0.800) indicates that the diazo-compound is more thermodynamically stable post MOC-binding process as compared to the *trans*-isomer. (7)

Discussion

Thus, the obtained results demonstrate that the rate of transport at both phase boundaries (guest-uptake in the feedstock arm and guest-release in the receiving arm) is faster for the trans isomer than for the cis isomer. However, the K_{eq} values suggest that the MOC-binding process is more thermodynamically favorable for the cis isomer than the trans isomer. These unexpected results can be explained by the fact that the higher thermodynamic stability of the cage-binded cis diazo compound required more time to reach due to the high energy barrier involved in the binding process.

The higher energy barrier of the *cis*-isomer binding and release process may be attributed to its geometric orientation, high boiling point, and reactivity. In relation to boiling point, the cis isomer's higher boiling point means an increased molecular viscosity. The higher viscosity of the diazo compound slows down its diffusion through the liquid membrane and results in a slower binding and release process from the MOC. This is evidenced by the slower rate of guest-uptake

 $(0.0574 \text{ day}^{-1})$ and guest-release $(0.0600 \text{ day}^{-1})$ for the *cis*-isomer. The more viscous the diazo compound, the more resistant it is to flow in the aqueous membrane and longer it takes for the binding to the cage, hence the slower rate of transport. The bent shape and net dipole moment for the *cis*-isomer may cause stronger binding to the MOC, as evidenced by the higher K_{eq}(1.05) value, yet still require a higher energy barrier to overcome in the guest-binding process. Stronger intermolecular forces require more energy to overcome, especially at the guest-encapsulation and guest-release phases of the MOC. The higher energy barrier required to establish new binding interactions between the Diazo compound and the MOC may result in a slower yet stronger binding process. (8)

The geometric orientation of the cis isomer also plays a role in the higher energy barrier for transport. The substituents in the cis isomer are arranged on the same side of the molecule, and this results in increased steric hindrance and hindered diffusion. The position of the bulky substituents in the cis isomer may result in their clashed interactions with other molecules in the membrane as well as the organic ligands in the MOC. This causes steric hindrance – the congestion caused because of the physical presence of surrounding ligands which impedes binding interactions and molecular movement. The bent shape of the cis isomer results in an increased steric hindrance, whereas the linear shape of the *trans*-isomer does not result in the same effect. The substituents in the trans isomer of the diazo compound are arranged in a straight line, which allows for easier binding and movement. This linear arrangement minimizes steric interactions and facilitates faster transport into and out of the MOC. This supports the data showing the higher k_f and k_f values for the trans isomer as compared to the cis isomer. (9)

The thermodynamic stability of the guest molecule during guest-binding, encapsulation, and guest-release can also be determined using a calculation of the Gibbs Free Energy (G). The G value measures the maximum amount of work done in a system under constant temperature and pressure conditions. The change in Gibbs Free Energy (ΔG) measures the spontaneity of a reaction. If $\Delta G < 0$, then the reaction is spontaneous and thermodynamically favorable. The more negative the ΔG value, the greater the tendency for the system to move toward the equilibrium and achieve thermodynamic stability. ΔG can be calculated using the following equation:

 $\Delta G = -RTlnK_{eq}$ (Equation 13)

In equation 13, R is the gas constant = 8.31, T represents temperature, and K_{eq} is the equilibrium constant during the transport in the MOC. The system temperature at which the concentration of each diazo compound was monitored as it transferred through the liquid membrane was set at the standard room temperature of 25°C or 298 K. (10)

The ΔG values for the system of each isomer of the diazo compound has been calculated using equation 8. The obtained parameters are shown in the table below.

		Trans-isomer	Cis-isomer
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352 -120

The calculated ΔG value of the system during *trans*-isomer transport of 552 indicates a non-spontaneous and thermodynamically unstable system. In contrast, the calculated ΔG value of the system during *Cis*-isomer transport of -120 indicates spontaneity and greater thermodynamic stability. This result is consistent with the calculations of the rate of guest uptake and release as well as the determined K_{eq} values. Within the metal organic cage, a more thermodynamically stable compound will be less resistant to decomposition. Thus, in relation to Gibbs free energy, a positive value of $\Delta G = 552$ suggests that between guest encapsulation and guest release the *trans*-isomer diazo compound may have decomposed due to less product stability as compared to the *cis*-isomer. (11)

Methods and Evaluation

The results obtained have been analyzed through both a thermodynamics and chemical kinetics lens. All the calculated parameters, obtained from the Excel procedure fitting data to the kinetic model, demonstrate that the rate of transport (including MOC encapsulation and release) is faster for the *trans*-isomer than the *cis*-isomer due to its more convenient geometric orientation. However, the *cis*-isomer has greater stability inside of the MOC as compared to the *trans*-isomer, primarily due to the higher energy barrier in the guest-cage binding process and greater spontaneity as seen by the ΔG value.

A limitation to the three-state model used for approximating concentration throughout the membrane is that it assumed constant cage concentration. This simplification is known as steady state approximation, a common tool used in chemical kinetics to simplify the analysis of reactions including intermediates or other reactants and products formed within the U-tube liquid membrane. The steady state approximation was employed to assume the Fe^{II}₄L₆ cage concentration to be constant throughout encapsulation, transport, and release. In addition, the simplified three-state model used to derive the kinetic equations employed the steady state approximation to simplify the kinetic expression for product concentration. By assuming that the concentration of the intermediate remains constant, the steady state approximation allows for the derivation of a simplified rate law from the many elementary steps. (12)

A more accurate model for the guest concentration through the membrane would take into consideration the cage with its own. However, a rate expression that includes the concentration of the cage species would yield a second order differential equation to model the rate of change of the concentration of the diazo compound through the three stages of the liquid membrane. The Excel solver procedure is not suitable for second order models and thus the values of k_f and k_r would not be obtained. Thus, for the sake of simplicity, the three-state model and thus a first order rate expression – was used to yield the required k_f and k_r values.

Conclusion

Overall, this paper has outlined the use of a $Fe^{II}_{4}L_{6}$ metal organic cage for selected transport of a guest Diazo compound through a liquid membrane and used kinetic models to analyze the differences in the kinetics and thermodynamics of the system when two different diazo isomers were transported. Understanding the geometric orientation and intermolecular forces present in each isomer, as well as the energy barriers involved during the guest-cage binding and release process has vast implications. In order to use hydrocarbons as molecular separation tools instead of as a source for GHG emissions, a thorough understanding of guest properties that facilitate the highest rate of transfer and thermodynamic stability will ensure effective applications of MOCs and promote a more sustainable environment.

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Works Cited

- "Azo group(s) in selected macrocyclic compounds PMC NCBI." PMC, 8 Jan. 2018, www.ncbi.nlm.nih.gov/pmc/articles/PMC5845695/.
- Fernandez, Carlos, et al. "Structural Flexibility in Metal-Organic Cages." Frontiers in Chemistry, vol. 9, 2021, pp. 1-14, <u>www.frontiersin.org/articles/10.3389/fchem.2021.706462</u>.
- Kumar, Suresh, et al. "Recent advances in photocatalysis for environmental applications." Academia.edu, 2023, pp. 1-22, <u>www.academia.edu/en/42036042/Recent_advances_in_photocatalysis_for_environmental</u> _applications.
- Li, Jian-Rong, et al. "Metal-Organic Cages for Catalysis." Accounts of Chemical Research, vol. 54, no. 12, 2021, pp. 3175-3186, pubs.acs.org/doi/10.1021/acs.accounts.1c00317.
- Li, Jian-Rong, et al. "Metal-Organic Cages for Gas Storage and Separation." Chemical Reviews, vol. 119, no. 16, 2019, pp. 9703-9830, pubs.acs.org/doi/10.1021/acs.chemrev.8b00603.
- "Metal-Organic Cages for Biomedical Applications ACS Publications." ACS Publications, 2022, pubs.acs.org/doi/10.1021/acs.accounts.1c00729.
- "Metal-organic cages as a platform for drug delivery and biomedical applications RSC Advances (RSC Publishing)." RSC Advances, 2023,

pubs.rsc.org/en/content/articlelanding/2023/ra/d0ra10205e#!divAbstract.

- "Photocatalysis in Water-Soluble Supramolecular Metal Organic Complex PMC NCBI." PMC, 12 May 2023, <u>www.ncbi.nlm.nih.gov/pmc/articles/PMC10221110/</u>.
- "Recent Advances of Photocatalytic Application in Water Treatment: A Review." PMC, vol. 20, no. 7, 2021, pp. 1-17, <u>www.ncbi.nlm.nih.gov/pmc/articles/PMC8308214/</u>.
- "Recent developments in heterogeneous photocatalytic water treatment using visible light-responsive photocatalysts: a review - RSC Publishing." RSC Publishing, 2015, pubs.rsc.org/en/content/articlelanding/2015/ra/c4ra13734e.
- "Structural Flexibility in Metal-Organic Cages Frontiers." Frontiers, 2 Jun. 2021, www.frontiersin.org/articles/10.3389/fchem.2021.706462.
- "Visible-Light Photoredox Catalysis in Water." PMC, vol. 21, no. 6, 2022, pp. 1-17, www.ncbi.nlm.nih.gov/pmc/articles/PMC10204095/.

Optimal Bio-Substrates For Mushroom Mycelium as Construction Material: A Comparative Study By Dain Chang

Abstract

The research was done to find optimal substrates for mycelium as construction material, including some studies and projects that were done that utilized different types of substrates. Due to a lack of information, a separate study was conducted to find the optimal substrates for mycelium as a construction material. The experiment was conducted for eight days with eight following materials: (1) fresh coffee grounds, (2) layered burlap fabric, (3) ripped newspaper, (4) cotton, (5) dried coconut husk fiber, (6) styrofoam, (7) chopped cardboard, and (8) oats. The intended experiment was growing mycelium in these substrates to create a block and testing their capability as construction material, but none of the substrates successfully grew into black form. Still, some substrates produced better results than others. Coffee grounds, burlap fabric, cotton, and cardboard showed some growth, but the ones in other substrates were either dried out or molded.

Introduction

Currently, the architecture and construction industries are facing major environmental challenges due to mass-energy usage and waste production. Together, these sectors are producing about 40% of the world's carbon and use around 37% of the world's energy. Of those carbon dioxide emission percentages, around 8% is from the cement industry alone. This signifies that improving building materials can be an effective way to solve this problem. As one of the candidates for a potential solution, mushroom mycelium was introduced. Mushroom mycelium is a root system of the mushroom that is formed with a thread-like structure of hyphae. They grow through the substrates to consume nutrients and decompose organic matter.

Traditionally, Mycelium was used by the indigenous people for their diets, medicine, and natural adhesives. From this traditional knowledge, scientists and innovators including Phil Ross studied mycelium as a material source. From the late 20th century, he studied mycelium and coined the term "microtexture" by the year 2008. By 2013, he founded the company Mycoworks which became the very first company that operated mycelium as a material. Since then, the study of mycelium has expanded the usage of mycelium to packaging and insulation material by companies such as Evocative Design, co-founded by Eben Bayer and Gavin McIntyre.

Before mycelium could be used as construction material, it should be dried and heat-killed to prevent it from fruiting mushrooms. For construction purposes, it is packed into a brick shape, which becomes stronger than concrete per pound and can be even bullet-proof according to the study "Bio-Composite Brick from Agricultural Waste as Green Building Material." It is not only strong but also versatile, light, and resistant to fire. Since it takes the shape of its substrate, it will grow as its shape which allows designers to create any forms they want. In addition, it is incredibly lighter than concrete
since a cubic meter of mycelium brick weighs 43 kg and a cubic meter of concrete weighs 2400 kg

(https://www.certifiedenergy.com.au/emerging-materials/emerging-materials-myceli). After it has been properly heat-killed, the mycelium stops growing and becomes resistant to fire. For example, when exposed to fire or radiant heat, it forms a thermal protective char layer. Most importantly, it generates less energy for production, captures CO2, and decomposes in about 40 days. Due to these characteristics, mycelium is currently rising as a potential construction material that is environmentally friendly.

Case Study

To grow mycelium as a construction material, different substrates are used. The research was done on projects that mainly utilized mycelium as construction material to find substrates that are actually being used in the construction field. The three following projects are some of the most famous mycelium buildings that utilized different substrates to grow the mycelium.

The first project is the Hy-fi Tower which is the first tower that was made out of mycelium. As preparation of the substrate, low-valued crop waste such as corn husks was chopped up into small pieces and mixed with mycelium. The mixture was then packed into the shape of a brick, which became light-weighted natural brick in a week. 10,000 bricks were used to build a 12-meter-tall tower which lasted for three months and was returned to local gardens. The project was successful, meaning that corn husk was an apt substrate. By returning all the left waste and soil to the local gardens, this project also proved biodegradable the environmentally friendly nature of the mycelium too.

Growing Pavilion is another construction project that utilized mycelium which was made entirely from bio-based materials such as timber, hemp wastes, and a bio-based coating. On the timber frame mold, hemp waste was filled for the mycelium to grow on. The process of mycelium growing was presented to the crowd, which took four days. After, the mixture was pulled out from the mold, dried, and heat-killed in the oven. This was another successful example of mycelium building, showing that hempcrete is also a fitting material.

Last but not least, there is the Chart Art Fair Pavilion which was built with surplus wood stocks and organic Kvadrat textiles which were bonded by compostable algae-based biopolymer. The fabric was embedded with mycelium spores, and substrates such as sawdust and coffee grounds were used to nourish the mycelium. This project was a little different from other projects in the sense that it utilized a mixture of different substrates to grow the mycelium. The succession of this project implied that the substrates that were used would all be suitable, but could not figure out which substrate played the biggest role in growing the mycelium.

Seeing different substrates used in the projects, I got curious about which substrate would be most suitable for the mycelium to grow as a construction material.

To find substrates that are most successful at growing mycelium as construction material, research was done on studies that experimented with different substrates.

Literary Review

There were studies on the characteristics and impacts of different substrates on mycelium, but none of them focused on construction purposes. Since construction materials have to possess special qualities such as water resistance, load bearing, durability, and insulation, a separate study that specifically focuses on the characteristics of construction materials was needed. Still, obtaining basic knowledge of the characteristics of different substrates is useful before determining which substrate to include in the experiment.

In the study "CULTIVATION OF OYSTER MUSHROOM (Pleurotus flabellatus) ON DIFFERENT SUBSTRATES" conducted at the Laboratory of Food Microbiology, mushroom growth was evaluated on seven different substrates: Mango, Jackfruit, Coconut, Jam, Kadom, Mahogany, and Shiris sawdust. Considering the biological yield and return, the cost-benefit analysis revealed that the Mango sawdust and Shiris sawdust were assuring substrates for the growing of Oyster Mushrooms (Pleurotus flabellatus). Although this experiment gave a clear overview and conclusion, it only focused on sawdust. Thus, information about other types of substrates was needed.

The study "Mycelium-Based Composite Graded Materials: Assessing the Effects of Time and Substrate Mixture on Mechanical Properties" they seem to be better options for the compressive structural systems working through form. While, for functions that need materials that bear the load by their strength, materials with hardness tendencies are preferable." From this,

Experiment Analysis

Due to a dearth of information about the substrate's characteristics for construction purposes, a study was conducted to find the optimal substrate as a construction material. Based on the research, eight substrates were selected which includes the ones that are already used in the construction field and other substrates that seem plausible to grow mycelium. Mycelium was first spawned, and moved to eight substrates: (1) fresh coffee grounds, (2) layered burlap fabric, (3) ripped newspaper, (4) cotton, (5) dried coconut husk fiber, (6) styrofoam, (7) chopped cardboard, and (8) oats.

Materials and Methods

Substrates Preparation

Egg carton paper, cardboard, and cotton were chosen as substrates to create mycelium materials because they were all at home. All three substrates were teared up,

soaked in water for a minute, and squeezed gently. *Spawning Mycelium*



First, the glass jar was sterilized with an alcohol swab. Egg carton papers were placed on the bottom, and sliced Oyster mushroom bottoms were placed. On top, cardboard and cotton were layered. This was repeated 3 times and lastly covered with cardboard on top. Image 1 is from day 1 after planting the mushrooms. Cotton-like white threads were observed around the mushroom pieces. Image 2 is from day 2, and the mycelium was observable at the top of the cardboard too. On day 3, which is image 3, the top layer was removed to move the mycelium into eight different substrates. They looked like they were spawned enough.

Moving Mycelium



Image 4 to 6 is all also from day 3. From the top left, the eight substrates are coffee grounds, burlap fabric, newspaper, cotton, coconut husks, styrofoam, cardboard, and oats. They were all either torn or cut into small pieces for the mycelium to grow easily. The plastic cases were sterilized with alcohol swap just like the glass jar. The substrates were first covered at the bottom, then pieces of sliced mushrooms with mycelium, and it was covered with the same substrates. Water was sprayed at the top of the substrates in case they got dried while replanting.

Observation & Data Collection

There were negligible observable changes on Day 1 and Day 2 after the

replantation. From Day 3, changes in cotton and coffee grounds were clearly observed. Mycelium in cotton was molding, but one in the coffee ground showed some growth. White threads forming wed-like structures were observed on the top of the coffee ground surface.



Image 16

Image 17

Image 18

Images 10 to 18 are all from Day 4, which all the mycelium in eight substrates were either molding or drying. For coconut husks, tiny black dots were observed, which seemed like bug eggs. The ones in oats were molding in blue, which means that it was pressed too hard.

Results

Coffee Ground	Burlap Fabric	Newspap	Cotton Coconut	Styro	Card	Oat
S		er		foam	board	

Mycelium Productio n	Not used	Not used	Not used Not used	Not used	Not used
Day 1			_	0	
Day 2			0	0	
Day 3			0	0	
Mycelium Replantatio n					
Day 1	_	_			_
Day 2	0	0	- X -	_	
Day 3	0	0	- X X		Х
Day 4	X	_	XXX	XX	Х

Key

O: Shown Growth

-: No change

X: Dying (mold/dry)

Discussion (Limitations)

Sterilization The main reason suspected for mycelium's death is lack of sterilization and germ exposure during the replantation. Since mushrooms grow in humid environments, they are susceptible to be infected by other harmful fungus species. Thus, it is vital to sterilize the jar completely. To kill all the germs, myriads of manuals suggest boiling the jar for 3-4 hours. Yet, the jar was only cleaned with alcohol swap.

Lack of Time Also, lack of time was an issue. It takes two weeks for the mycelium to fully take over the substrates, but the experiment was conducted over a week. Even if the mycelium successfully spawned on the substrates, it would have been impossible to create a complete mycelium block. If more time was available, it would have been possible to conduct another experiment too.

Environmental Condition This experiment was done at home, not in a lab, so the result might not be not as accurate. The experimental conditions could not be accurately controlled, and minor growth of mycelium on days 1 and 2 could have been missed because there was no microscope at home.

Conclusion

The research conducted in this study aimed to identify optimal substrates for mushroom mycelium as a construction material in consideration of the need for sustainable and environmentally friendly alternatives for building materials. The investigation involved case study of relevant papers and an experimental analysis of eight substrates.

Some projects that utilized mycelium as main construction material, such as Hy-fi Tower, Growing Pavilion, and Chart Art Fair Pavilion showcased different substrates being used in the field. In addition, studies that conducted similar experiments were introduced. Despite the limited scope of study, those studies provided basic characteristics of different substrates. In the experiment which was conducted with eight substrates, only ones in coffee grounds and burlap fabric showed growth.



Ones in the coffee ground were most successful, with observable changes on the top and inside. Compared to those in the coffee ground, the ones in cotton showed minor growth, showing some white threads coming out but not through the burlap fabric. Although the ones in cotton and cardboard were unsuccessful after replantation, they were successful in creating the mycelium.

As limitations may have influenced the result of the experiment, further research is needed for more accurate study of optimal substrate combinations. Future directions may include exploring mixed substrates, refining growth conditions, and assessing the mechanical properties and long-term durability of mycelium-based construction materials.

In conclusion, mycelium shows high potential to become future sustainable construction material due to its low environmental impact, biodegradability, and versatility. The projects reviewed in this study exemplify its potential in real-world applications. As the demand for environmentally friendly building materials continues to rise, mycelium remains as a promising candidate for sustainable construction in the future.

Works Cited

- Bio-Composite Brick from Agricultural Waste as Green Building Material, https://ijaem.net/issue_dcp/Bio%20Composite%20Brick%20from%20Agricultural%20Wa ste%20as%20Green%20Building%20Material.pdf. Accessed 1 Sept. 2023.
- Carlin, Oliver. "Magic Mushroom Mycelium Bruising or Blue Green Mold on Mycelium." *Curative Mushrooms*, 4 July 2022, blog.curativemushrooms.com/magic-mushroom-mycelium-bruising-vs-blue-green-mold-o

n-myceliu

- Gates, Sarah. "Fungi Blaze a Trail to Fireproof Cladding." *RMIT University*, 13 July 2023, www.rmit.edu.au/news/all-news/2023/jul/fire-retardant-fungi#:~:text=%E2%80%9CT%20 he%20great%20thing%20about%20mycelium,fireproof%20material%2C%E2%80%9D% 20s%20aid%20Kandare.
- Ghazvinian, Ali, and Benay Gürsoy. "Mycelium-Based Composite Graded Materials: Assessing the Effects of Time and Substrate Mixture on Mechanical Properties." *MDPI*, Multidisciplinary Digital Publishing Institute, 19 Apr. 2022, <u>www.mdpi.com/2313-7673/7/2/48</u>.
- Jordahn, Sebastian. "Chart Art Fair Pavilion Aims to Investigate the Potential of Mycelium." *Dezeen*, 1 Sept. 2022,

www.dezeen.com/2022/09/01/chart-art-fair-2022-mycelium-pavilion/.

- "Our Heritage." *MycoWorks*, 22 Sept. 2022, www.mycoworks.com/our-heritage#:~:text=Our%20origins%20begin%20with%20My%2 0coWorks.and%20life%20cycles%20of%20mushrooms.
- Rahman, M Hasibur, et al. "Cultivation of Oyster Mushroom (Pleurotus Flabellatus) on Different Substrates." *ResearchGate*, Jan. 2009,
 <u>www.researchgate.net/profile/Md-Islam-1150/publication/242421716_Cultivation_of_Oyst</u> <u>er_mushroom_Pleurotus_flabellatus_on_different_substrates/links/561fabd208ae93a5c924</u> 1ab0/Cultivation-of-Oyster-mushroom-Pleurotus-flabellatus-on-different-substrates.pdf.
- Royse, D J, et al. "Yield, Mushroom Size and Time to Production of Pleurotus Cornucopiae (Oyster Mushroom) Grown on Switch Grass Substrate Spawned and Supplemented at Various Rates." *ScienceDirect*, Elsevier, Jan. 2004, www.sciencedirect.com/science/article/abs/pii/S0960852403001512?via%3Di+hub.

Zervakis, G, et al. "Mycelium Growth Kinetics and Optimal Temperature Conditions for the Cultivation of Edible Mushroom Species on Lignocellulosic Substrates, 'Folia Microbiologica." *DeepDyve*, Springer Netherlands, 1 June 2001, www.deepdyve.com/lp/springer-journal/mycelium-growth-kinetics-and-optimal%20tempe rature-conditions-for-the-xmWzvJZgeA?key=springer.

The Surprising Power of Bacteria in the Vaginal Microbiome: How Lactobacillus is Crucial to Women's Health By Ashley Hurjak

Abstract

The purpose of this review article is to highlight the role of beneficial bacteria in promoting a healthy vaginal microbiome. The article describes the mechanisms for maintaining a healthy vaginal microbiome, the symptoms of a "dysbiotic" (disrupted) vaginal microbiome, and an overview of the vaginal diseases that can occur from a disrupted bacterial ecosystem inside this organ. Additionally, it outlines how to promote a healthy vaginal microbiome through lifestyle choices and a summary of current treatments available to patients who suffer from bacteria-related vaginal infections.

1.0 Introduction For hundreds of years women have struggled with vaginal infections (inflammation of the vaginal area that can result in pain and itching), which are caused by bacteria, viruses or fungi (Saraf et al., 2021). Studies dating back to the 1800s (when the vaginal area was first routinely examined) have demonstrated that the beneficial bacteria found in the vaginal region act as the first line of defense for the female reproductive tract against biological pathogens such as harmful bacteria, viruses and fungi (Saraf et al., 2021). Any disruptions to these "good" vaginal bacteria weaken the protective barrier against pathogens, which can lead to yeast infections, sexually transmitted infections (STI), and bacterial vaginosis (a condition when there is a surplus of harmful bacteria within the vaginal area) (Chee et al., 2020).

1.1 Healthcare Costs. Treating vaginal infections in the US healthcare system costs around \$16 billion and affects 10 million women annually (Bitew et al, 2017). Bacterial vaginosis (BV) is estimated to cost around \$4.8 billion and affects 21.2 million women annually (Peebles et al., 2019) Treating vaginal infections caused by viruses costs about \$8 billion per year and there are about 110 million cases (CDC, 2013). Trichomoniasis, a sexually transmitted infection, is estimated to cost about \$24 million per year (Sector et al., 2014). Fungal infections caused about 9 million outpatient visits nationally in the year 2017 and resulted in \$2.4 billion in healthcare costs (Benedict et al, 2019). Specifically, invasive fungal infections (known as candidiasis) caused by a yeast strain named *Candida albicans* were responsible for 48% of fungi-related hospitalization and cost \$1.4 billion of that overall \$2.4 billion (Benedict et al., 2019). These healthcare costs are daunting for women, especially those living in poverty and lacking access to gynecological care.

1.2 Access to Healthcare. The vaginal health of women contributes significantly to their overall well-being, therefore simple and affordable access to healthcare services to maintain vaginal health is very important. Out of a survey of 3520 women across the globe in 2012, 44% claimed they did not have access to a gynecologist (Nappi, Kokot-Kierepa, 2012). Sexually transmitted infections (STIs) and HIV testing, unwanted pregnancies, traumas, and chronic illnesses were among the vaginal illnesses due to lack of accessible care. (Ravi et al, 2017). Aside from hospitals and clinics, common care locations included jails, emergency rooms, and Planned Parenthood clinics (Ravi et al, 2017).

2.0 Background on the Vaginal Microbiome A complete understanding of the vaginal microbiome is necessary to comprehend all of the components within a healthy vaginal microenvironment and their roles in the metabolic activities and the health of the host (Ravel & Brotman, 2016). A healthy vaginal microbiome depends on mutualism between the dominant bacterial species and the host. Under healthy conditions, beneficial bacterial communities coexist within human hosts in a mutually positive manner by preventing harmful bacteria from infiltrating the host's vaginal space. Comprehensive studies show that *Lactobacillus* bacterial species is the most prevalent species in the female vaginal microbiome (Gupta el al., 2019). Understanding the mutualistic relationship that exists between the host and the beneficial Lactobacilli colonies is significant because it provides insight on the mechanism of protection within the vaginal area (Chee et al., 2020). This group of bacteria provides protective barrier agents in the reproductive tract by releasing several compounds that prevent the overgrowth of harmful bacteria (Gupta et al., 2019). Once the Lactobacilli are within the specific vaginal environment, they release large amounts of lactic acid as a fermentation by-product and create a low pH environment to protect against pathogenic bacteria (unwanted bacteria), as shown in Figure 1 (Ravel & Brotman, 2016).



https://www.pathelective.com/micromeded/vaginal-microbiota-and-dysbiosis

Figure 1: On the left is an example of a healthy vaginal microbiota with the right amount of lactic acid, bacteriocins (kill or inhibit bacterial strains), and a low pH to inhibit pathogen growth. This allows the *lactobacillus* colonies to stay healthy. However, on the right is an example of a dysbiotic vaginal microbiota with harmful pathogens, such as *Candida albicans*,

Gardnerella vaginilis, and *Trichomonas vaginilis*. These harmful pathogens lead to vaginal diseases like vaginal yeast infections (candidiasis), BV, and Trichomoniasis.

2.1 *Lactobacillus* **Strains as "good" bacteria.** The healthy *Lactobacillus* strains thrive in the vaginal environment because of a specific anaerobic (without oxygen) nutritional environment catered to their needs. Some *Lactobacillus* species, including *L. crispatus*, *L. iners*, *L. gasseri*, and *L. jensenii*, appear to be unique to the human vagina (Ravel & Brotman, 2016). By finding ways to protect the *Lactobacilli*-bound area (the interior of the vaginal microbiota where the *Lactobacilli* is found), the vaginal microbiome can serve to protect the health of women from an increased risk of contracting bacterial infections (overgrowth of pathogenic bacteria) and yeast infections (overgrowth of fungi like *Candida albicans*). Furthermore, it may be possible to prevent 30% of new HIV cases if *Lactobacillus* bacteria predominate in the vaginal microbiome (Ravel & Brotman, 2016), as changing the microbiome to one in which *Lactobacillus* predominates is an alluring approach to lowering HIV incidence rates (Gustin et al, 2021).

Lactobacillus strains limit infections by producing a substance that reduces the formation of "biofilms" (clusters of bacteria) by invading pathogens. Specific strains of *Lactobacillus* produce soap-like compounds called "biosurfactants" that prevent harmful pathogens (fungi, other bacteria) from sticking to the vaginal surface. The biosurfactants reduce the ability of the invading pathogens from forming the dense biofilms. Researchers have reported that these biosurfactants reduced the biofilm formation of vaginal pathogen *C. albicans* by 40 to 50% (Chee et al., 2020).

2.2 Promoting a Healthy Vaginal Microbiome. Since lifestyle, hygiene and diet affect the vaginal microbiome and allow healthy *Lactobacilli* to flourish, it is crucial for women to maintain good habits, cleanliness, and dietary choices (Ravel & Brotman, 2016). Consuming yogurt that contains *Lactobacillus* strains everyday is one way to maintain a healthy vaginal microbiome (Ravel & Brotman, 2016). Additionally, tight clothing reduces the flow of oxygen to the vaginal area, which can lead to the overgrowth of unwanted anaerobic species like *C*. *Albicans*, so women are advised to limit such clothing. Maintaining a healthy immune system also plays an important role in keeping the vaginal microbiome healthy. The epithelial and immune cells within the cervicovaginal mucus (vaginal fluid) maintain homeostasis (balance) with the vaginal microbiome and filter pathogens (Lehtoranta et. al, 2022).

2.3 Vaginal Dysbiosis. If the vaginal microbiome lacks any of these beneficial *Lactobacilli* strains, a disorder can occur. A dysbiotic (unbalanced) environment can occur when the pH is too high in the vaginal space and no longer supports the healthy growth of *Lactobacilli* strains. There are other types of *Lactobacilli* that are harmful that can increase the risk of vaginal diseases, such as BV (Gupta et al., 2019). When the pH is not the optimal level, negative strains of bacteria can grow. The disruption or "dysbiosis" of these healthy species can lead to the invasion of pathogens that causes severe vaginal conditions such as BV, which is defined as the overgrowth of harmful bacteria in the vagina. This can lead to overgrowth of harmful bacteria like *Gardnerella vaginalis* and *Atopobium vaginae*, causing BV. Also, the presence of these

harmful strains in the vaginal microbiota can put females at a higher risk of getting infected with STIs and with yeast strains like *Candida albicans*, which leads to a condition called vulvovaginal candidiasis (VVC). Recent studies have linked fungus biofilms to Candidiasis, particularly when therapy fails and recurrent Candidiasis occurs. As a result, several studies have supported the use of probiotics in treating various illnesses (Boahen et al., 2022). Vaginal Dysbiosis also leads to pelvic inflammatory disease and preterm birth (Gupta et al, 2019). Additionally, about 70% of women have Vaginal Dysbiosis within their lifetime without knowing (Gupta et al, 2019).

2.4 Treatment Challenges. When attempting to treat women for vaginal-related disorders, several difficulties may arise. The key to effective therapy is an accurate diagnosis, yet the misdiagnosis rate is close to 50%, increasing the chance of recurrence (Brown, Drexler, 2020). Oftentimes, BV has symptoms of vaginal discharge and color and can be confused with symptoms from vaginal intercourse or menses, causing those women to misunderstand their need for treatment. (Brown, Drexler, 2020). It can also lead to a burning feeling during urination and itching around the vulva. Women's vaginal health is rarely routinely examined, even with symptoms such as the pain, itching, and burning.

For asymptomatic, non-pregnant women, pelvic examination is no longer advised since it might lead to negative effects including false-positive test findings, overdiagnosis, anxiety, and unneeded expenses (Qin et al., 2020). A significant challenge for developing preventative approaches to improve women's health is that a large proportion of women who lack the *Lactobacillus* bacteria (10-42% of women) can remain asymptomatic for BV (Ravel & Brotman, 2016). Additionally, current guidelines from the US Centers for Disease Control do not support antibiotic treatment for these asymptomatic women (Ravel & Brotman, 2016).

About 75% of women experience VVC during their reproductive years (Azie et al., 2020). Additionally, candidiasis can lead to vaginal itching, pain during intercourse, discomfort while urinating, and abnormal vaginal discharge – the very same symptoms as BV. STIs can lead to unusual vaginal bleeding, blisters and sores around the genital area, and an unusual discharge from the vaginal area (Qin et al., 2020). Furthermore, antibiotics and topical creams used to treat vaginal disorders can become less useful because of antibiotic resistance. This resistance occurs when bacteria become resistant to the medications meant to kill them. This means the germs survive even when treatment is applied.



https://www.nature.com/articles/s41522-022-00295-y/figures/1

Figure 2 This image showcases the healthy elements, such as a low pH and *Lactobacillus crispatus* that support a noninflammatory vaginal microbiome, creating a normal environment. Additionally, it showcases a dysbiotic or pro-inflammation environment caused by BV and a high pH.

3.0 Medical Treatments for Vaginal Dysbiosis caused by Bacteria Since Vaginal Dysbiosis can be caused by bacterial infections, viral infections, or fungal infections, different treatments have been developed that target the invading species. In the case of BV, medications that kill the pathogenic bacteria have been developed. One oral medication (metronidazole) diffuses into the vaginal microbiome and inhibits pathogenic bacteria from entering; the treatment requires 500 mg (1 pill) that is taken daily for 5-10 days (Chandrashekhar et al., 2021). Metronidazole was first released in 1959. Topical ointments (Clindamycin, Flagyl, Secnidazole) – have shown to be effective against BV although some treatments have a high rate of the infection returning (Chandrashekhar et al., 2021). These solutions also come with one large issue. Bacteria can grow resistance to the given treatments and they will not be effective anymore in treating BV. However, until the bacteria develop resistance to the antibiotic, these medications can be helpful in treating BV and they are very easy to access through a local pharmacy. What follows here are other approaches for treating BV.

3.1 Restoring *Lactobacillus*. BV is commonly treated with antibiotics which can cause recurrence and degrade the *Lactobacillus* populations within the vaginal microbiome (Lagenaur et al., 2021). One possible way to bring back *Lactobacilli* within the vaginal microbiome is to insert a probiotic strip containing this species within the vagina. LACTIN- V, a biological drug composed of *L. crispatus* (**Figure 2**) (a strain of healthy *L*actobacilli), could reduce pathogenic bacteria by repopulating the vaginal microbiome (Lagenaur et al., 2021). Additionally, it is a gelatin capsule which makes it very accessible to women around the world. Another strain of *Lactobacillus* taken orally, *Lactobacillus gasseri*, can also be used to restore *Lactobacilli*

colonies that were destroyed from BV (Qi et al., 2022). A newer drug, *Lactobacillus rhamnosus BMX 54* + lactose) (NORMOGINTM), has demonstrated that it significantly reduces BV and restores a *Lactobacillus* dominated microbiome (Baldacci et al., 2020). These strategies have shown great results in the clinic by deteriorating BV.

3.2 Oral Betadine. Betadine, a treatment taken by mouth, is also used to treat vaginal dysbiotic disorders and has shown to be 75% effective (Ismatiloevna, 2022). It is better than other drugs, such as metronidazole, because it creates the conditions for *Lactobacillus* to thrive (Ismatiloevna, 2022). The repopulation of *Lactobacillus* happened to 96% of the patients that were tested with betadine (Ismatiloevna, 2022). However, betadine is a strong drug and should not be used unless it is certain that a vaginal disease is present.

3.3 Restoring Vaginal pH. When the vaginal microbiome encounters the issue of dysbiosis, the pH can rise creating an unbalanced environment. *Lactobacillus* colonies release lactic acid, which creates a specific pH. A lactic acid gel can also be utilized to restore the optimal pH (4.5) (**Figure 2**) within the vaginal microbiome and eliminate pathogenic bacteria (Ross et al., 2023). This gel is meant to be used for 7 days. In studies comparing its effectiveness with metronidazole, the lactic acid gel did not work short-term, and metronidazole was more effective for short-term resolution (Ross et al., 2023). Unfortunately, both treatments had a common recurrence of BV, but the lactic acid gel had fewer side effects (Ross et al., 2023). It could be possible to use betadine with this gel as it is more efficient than metronidazole and the lactic acid gel could be a "booster" to yield quicker results.

3.4 Detecting BV. All of the treatments described above will work against bacteria that cause Vaginal Dysbiosis; however, diagnosing that these bacteria are the offending species can be very difficult. Before administering treatment to a patient, it is important to determine if pathogenic bacteria are present. Recent work to identify a feature in vaginal fluid that reveals BV has been discovered and studied for its detection possibilities. Sialidase is an enzyme present in vaginal fluid that can be used as such a biomarker for BV (Rodriguez et al., 2021). It can be used to detect a dysbiotic *Lactobacilli* environment and alert the patient of the presence of BV. Recent studies have demonstrated that this biomarker could be embedded in fibers that could be part of a panty-liner that changes color in the presence of the substrate for sialidase, thus enabling detection of BV without needing access to sophisticated lab tests (Rodriguez et al., 2021)

3.4 Palomacare. A new antibacterial vaginal gel called Palomacare, released in 2014, has shown efficacy against Vaginal Dysbiosis and relapse prevention (Losa et al., 2022). Palomacare has been recommended as a treatment for Vaginal Dysbiosis by 79% of gynecologists, 85% of patients observed an improvement in the healing process, and 84% of patients observed a reduction in Vaginal Dysbiosis recurrences (Losa et al., 2022).

4.0 Medical Treatments for Vaginal Dysbiosis caused by Fungal Infections (Candidiasis) To target fungal infections that cause Vaginal Dysbiosis (Figure 1), researchers and clinicians have been studying ways to address yeast infections in the vagina caused by *Candida albicans* that are inexpensive, accessible without a doctor's prescription, and effective (Cateau et al., 2008). The medical literature refers to this condition as vulvovaginal candidiasis (VVC). Common antifungal topicals such as caspofungin and micafungin have been used since 2008 and reduced 70% of yeast biofilms (Cateau et al., 2008). However, these medications are only available by prescription, thereby limiting a patient's ability to get necessary treatment (Cateau et al., 2008). The chemicals ethanol, amphotericin, and echinocandins (antifungal) have demonstrated the reduction of *C. Albicans* with no bacteria resisting the given treatment. However, there are two issues with these chemical treatments: not enough testing has been done to affirm that it is completely safe for women and they would require a doctor's prescription.

Fluconazole is the first antifungal developed in 2014 for VVC that recurs after standard treatment; it controls symptoms of Candidiasis (itching) and is widely regarded as the first line of therapy for recurrent VVC (Sobel & Nyirjesy, 2021). Its drawbacks include the possibility of growing bacterial resistance of beneficial bacteria to this medication (Sobel & Nyirjesy, 2021). Oteseconazole, a topical fungal inhibitor, is a promising new therapy approach towards fungal infections(Sobel & Nyirjesy, 2021). Oteseconazole has a target goal of discarding fungal infections comparable to fluconazole (Sobel & Nyirjesy, 2021). A considerable improvement in the therapy of recurrent VVC may result from this combination of treatment (Sobel & Nyirjesy, 2021).

A new medication called ibrexafungerp is a drug that disrupts the formation of the fungal cell wall; if the cell wall forms improperly, then the fungus will die (Azie et al., 2020). This drug can be taken orally and has low risk of side effects as a treatment for VVC (Azie et al., 2020). It also protects against a broad range of *C. Albicans* species including those strains that are resistant to fluconazole (Azie et al., 2020).

5.0 Cutting-Edge Treatments for Vaginal Dysbiosis Antibiotics and antifungals continue to be the primary line of treatment for Vaginal Dysbiosis despite the increasing resistance of microorganisms to them (Losa et al., 2022). However, small case studies involving the transplanting of healthy vaginal bacteria from the donor to patient are underway. This strategy allows a tissue graft to be inserted from donor to patient and results in a successful return of the vaginal flora (Losa et al., 2022). The first sample patient had a 91.3% of *Gardnerella* and a lack of *Lactobacillus* (Losa et al., 2022). Following the VMT treatment, the patient had their *Lactobacilli* colonies restored with no presence of *Gardnerella*.

In a case study with five patients, vaginal microbiota transplantation (VMT) with eubiotic (healthy) vaginal bacterial microbiota following the loss of pathogenic bacteria with antibiotics was effectively carried out; however, no VMT has been carried out without the use of antibiotics as it serves as a protective barrier regarding possible infection from the donor (Wrønding et al., 2023). The *Gardnerella vaginalis* bacteria dominated the vaginal microbiota to the extent of 90% (Wrønding et al., 2023). After one VMT, the microbiota completely changed, becoming 81.2% *L. crispatus* and 9% *L. jensenii*, and Vaginal Dysbiosis symptoms also disappeared at the same time (Wrønding et al., 2023). These findings suggest that VMT is a beneficial potential treatment for Vaginal Dysbiosis. However, it is administered by a catheter and is therefore not accessible to all women (Wrønding et al., 2023). The patient also needs to be matched with a donor which can create an accessibility issue (Wrønding et al., 2023).

The United States Food and Drug Administration has approved lactoferrin, a protein that defends the host's immune system, is a generally recognized as safe (GRAS) food additive (Superti & De Seta, 2020). Lactoferrin has been categorized as a nutraceutical protein due to its capabilities for protecting the mucosa (soft tissue that lines reproductive organs) from infections and inflammations, as well as the present pharmacological and nutritional benefits (Superti & De Seta, 2020). Lactoferrin can act as a soluble that inhibits pathogenic bacteria binding to the cell's surface and promotes the return of *Lactobacillus* colonies (Superti & De Seta, 2020).

Conclusion: The vaginal microbiota is a very intricate environment that has many components regarding its health. Normal and dysbiotic conditions exist within the vagina due to many different factors such as changes in pH and exposure to pathogens. Vaginal Dysbiosis in women all over the world goes undiagnosed. Different treatments for Vaginal Dysbiosis include challenges such as recurring infections, antibiotic resistance, and delivery of the drugs themselves. It is imperative to keep researching treatments and improving the ways that Vaginal Dysbiosis can be diagnosed, along with making treatment more accessible and effective

Works Cited

- Azie, N., Angulo, D., Dehn, B., & Sobel, J. D. (2020). Oral Ibrexafungerp: an investigational agent for the treatment of vulvovaginal candidiasis. *Expert Opinion on Investigational Drugs*, 29(9), 893-900.
- Baldacci, F., Baldacci, M., & Bertini, M. (2020). Lactobacillus rhamnosus BMX 54+ Lactose, A Symbiotic Long-Lasting Vaginal Approach to Improve Women's Health. International Journal of Women's Health, 1099-1104.
- Benedict, K., Jackson, B. R., Chiller, T., & Beer, K. D. (2019). Estimation of direct healthcare costs of fungal diseases in the United States. Clinical Infectious Diseases, 68(11), 1791-1797.
- Bitew, A., Abebaw, Y., Bekele, D., & Mihret, A. (2017). Prevalence of Bacterial Vaginosis and Associated Risk Factors among Women Complaining of Genital Tract Infection. International journal of microbiology, 2017, 4919404.
- Boahen A, Than LTL, Loke Y-L and Chew SY (2022) The Antibiofilm Role of Biotics Family in Vaginal Fungal Infections. *Front. Microbiol.* 13:787119. doi: 10.3389/fmicb.2022.787119
- Brown, H., & Drexler, M. (2020). Improving the Diagnosis of Vulvovaginitis: Perspectives to Align Practice, Guidelines, and Awareness. Population health management, 23(S1), S3–S12.
- Cateau, E., Rodier, M. H., & Imbert, C. (2008). In vitro efficacies of caspofungin or micafungin catheter lock solutions on *Candida albicans* biofilm growth. Journal of antimicrobial chemotherapy, 62(1), 153-155.
- Chandrashekhar, P., Minooei, F., Arreguin, W., Masigol, M., & Steinbach-Rankins, J. M. (2021). Perspectives on existing and novel alternative intravaginal probiotic delivery methods in the context of bacterial vaginosis infection. The AAPS journal, 23(3), 66.
- Chee, W. J. Y., Chew, S. Y., & Than, L. T. L. (2020). Vaginal microbiota and the potential of *Lactobacillus* derivatives in maintaining vaginal health. Microbial cell factories, 19(1), 203.
- Centers for Disease Control and Prevention. (2013, August 29). Incidence, prevalence, and cost of sexually transmitted infections in the United States.
- Gustin, A., Cromarty, R., Schifanella, L., & Klatt, N. R. (2021). Microbial mismanagement: how inadequate treatments for vaginal dysbiosis drive the HIV epidemic in women. Seminars in immunology, 51, 101482.
- Gupta, S., Kakkar, V., & Bhushan, I. (2019). Crosstalk between vaginal microbiome and female health: a review. Microbial pathogenesis, 136, 103696.
- Ismatiloevna, Y. F. (2022). TREATMENT OF VAGINAL DYSBIOTIC DISORDERS IN PREGNANT WOMEN BEFORE CHILDBIRTH. *World Bulletin of Public Health*, *12*, 86-89.
- Lehtoranta, L., Ala-Jaakkola, R., Laitila, A., & Maukonen, J. (2022). Healthy vaginal microbiota and influence of probiotics across the female life span. Frontiers in Microbiology, 13, 819958.

- Losa, F., Palacios, S., Rodríguez, S. P. G., Baquedano, L., Khorsandi, D., & Muñoz, M. J. (2022). Vaginal dysbiosis management and the efficacy of a non-hormonal hyaluronic acid-based vaginal gel (Palomacare®) as an adjuvant treatment: the Palomascopia survey. *Obstet Gynecol Cases Rev*, *9*, 222.
- Nappi, R. E., & Kokot-Kierepa, M. (2012). Vaginal Health: Insights, Views & Attitudes (VIVA)–results from an international survey. Climacteric, 15(1), 36-44.
- Peebles, K., Velloza, J., Balkus, J. E., McClelland, R. S., & Barnabas, R. V. (2019). High Global Burden and Costs of Bacterial Vaginosis: A Systematic Review and Meta-Analysis. Sexually transmitted diseases, 46(5), 304–311.
- Qin, J., Saraiya, M., Martinez, G., & Sawaya, G. F. (2020). Prevalence of Potentially Unnecessary Bimanual Pelvic Examinations and Papanicolaou Tests Among Adolescent Girls and Young Women Aged 15-20 Years in the United States.
- Ravi, A., Pfeiffer, M. R., Rosner, Z., & Shea, J. A. (2017). Identifying health experiences of domestically sex-trafficked women in the USA: A qualitative study in Rikers Island jail.
- Qi, F., Fan, S., Fang, C., Ge, L., Lyu, J., Huang, Z., ... & Zhang, X. (2022). Orally administrated *Lactobacillus* gasseri TM13 and *Lactobacillus* crispatus LG55 Can Restore the Vaginal Health of Patients Recovering from Bacterial Vaginosis. *medRxiv*, 2022-12.
- Ravel, J., & Brotman, R. M. (2016). Translating the vaginal microbiome: gaps and challenges. Genome medicine, 8, 1-3.
- Ross, J.D.C., Brittain, C., Anstey Watkins, J. et al. Intravaginal lactic acid gel versus oral metronidazole for treating women with recurrent bacterial vaginosis: the VITA randomized controlled trial.
- Rodríguez-Nava, C., Cortés-Sarabia, K., Avila-Huerta, M. D., Ortiz-Riaño, E. J.,
 Estrada-Moreno, A. K., Alarcón-Romero, L. D. C., ... & Morales-Narváez, E. (2021).
 Nanophotonic sialidase immunoassay for bacterial vaginosis diagnosis. ACS
 Pharmacology & Translational Science, 4(1), 365-371.
- Saraf, V. S., Sheikh, S. A., Ahmad, A., Gillevet, P. M., Bokhari, H., & Javed, S. (2021). Vaginal microbiome: normalcy vs dysbiosis. Archives of Microbiology, 203, 3793-3802.
- Secor, W. E., Meites, E., Starr, M. C., & Workowski, K. A. (2014). Neglected parasitic infections in the United States: trichomoniasis.
- Sobel, J. D., & Nyirjesy, P. (2021). Oteseconazole: an advance in treatment of recurrent vulvovaginal candidiasis. *Future microbiology*, *16*(18), 1453-1461.
- Superti, F., & De Seta, F. (2020). Warding off recurrent yeast and bacterial vaginal infections: Lactoferrin and lactobacilli. *Microorganisms*, 8(1), 130.
- Wrønding, T., Vomstein, K., Bosma, E. F., Mortensen, B., Westh, H., Heintz, J. E., ... & Nielsen, H. S. (2023). Antibiotic-free vaginal microbiota transplant with donor engraftment, dysbiosis resolution and live birth after recurrent pregnancy loss: a proof of concept case study. *eClinicalMedicine*.

Boosting Effective Charities via Social Media Heuristics By Arav Jain

Abstract

Heuristics and biases affect our minds and decisions. One important decision is the decision of which charities to give to. Individual giving accounts for a large part of many charities' funding and the amount most people can donate is limited. Thus, it is important that money reaches the most effective charities to do the most good. However, heuristics such as the framing effect, anchoring effect, and evaluability bias can cause funds to go to less effective charities. Due to this, it is important for effective charities to consider these biases when advertising. Since social media is a growing presence in the world of advertising, it makes sense for effective charitable organizations to utilize social media alongside these heuristics. This paper outlines the problems associated with a few heuristics and charitable donations and how to counteract these effects through social media.

Introduction

It has long been known that humans are not creatures of pure logic. Although the human mind is a wonderful thing, it has its shortcomings-due to the massive amount of information the brain handles, it creates various shortcuts in thinking, called heuristics. These heuristics can affect decisions, including donations to charitable organizations. These oversimplified decisions can lead to a misallocation of resources by providing donations to less effective charities (less effective being less lives saved per dollar spent or the equivalent measure). Since charitable actions lead to a more socially optimal outcome and charities rely on donations for funding (in 2021 67% of total giving was from individuals according to nptrust.org), this misallocation is an important issue. As advertising becomes a need in an oversaturated market (more than 1.54 million nonprofits just in the US according to nptrust.org), and social media becomes a vital form of advertising (93% of NGOs have a Facebook page), social media marketing is an effective way to combat these biases by creating advertisements with heuristics in mind. Three of these heuristics are the framing effect, anchoring effect, and the evaluability bias.

The framing effect can change the way people perceive advertisements based on the presentation. Negatively framed charity advertisements are more effective in eliciting donations due to the negativity bias, which causes humans to avoid negative consequences. Various sympathy biases such as the in-group effect, identified victim effect, and the reference dependent sympathy effect also tie into the framing effect as using these sympathy biases in advertisements can highly increase the effectiveness of donations.

The anchoring effect can increase donation effectiveness, regardless of how effective a charity is. The anchoring effect refers to the idea that humans are most likely to estimate based on the first piece of information provided. A study on verbal anchoring in charity logos reveals that using a logo and the brand name is the most effective in increasing donations. Furthermore, another study reveals when provided a high donation anchor, people will tend to donate more.

The evaluability bias causes people to not consider charity effectiveness when donating.

It causes people to emphasize a lower overhead ratio than cost effectiveness, because the latter is harder to evaluate. Research shows that this bias can be combated by showing two charities side by side. This paper explores the effect of these heuristics on donation effectiveness, and how to combat this inefficiency through social media advertising.

One specific heuristic that influences charitable donations is the framing effect. Discovered by Amos Tversky and Daniel Kahneman, the framing effect is based on the idea that it is possible to frame a decision in more than one way (Kahneman). The framing effect is best shown by an experiment performed by Kahneman and Tversky with the scenario shown below.

> Problem 3 [N = 150]: Imagine that you face the following pair of concurrent decisions. First examine both decisions, then indicate the options you prefer.

Decision (i). Choose between:

- A. a sure gain of \$240 [84 percent]
- B. 25% chance to gain \$1000, and 75% chance to gain nothing [16 percent]

Decision (ii). Choose between:

- C. a sure loss of \$750 [13 percent]
- D. 75% chance to lose \$1000, and 25% chance to lose nothing [87 percent]

Figure 1: Kahneman and Tversky's framing effect experiment scenario 1

The most common combination of responses was A & B with 73 % of responses while B & C only had 3% of responses. However, when the options were shown like the image below, all the respondents chose the superior B & C.

Problem 4 [N = 86]. Choose between:
A & D. 25% chance to win \$240, and 75% chance to lose \$760. [0 percent]
B & C. 25% chance to win \$250, and 75% chance to lose \$750. [100 percent]

Figure 2: Kahneman and Tversky framing effect experiment scenario 2

Both options provide the same information, just in slightly different manners. The simple change in presentation reveals how influential framing is when providing information. Due to

this, framing is a strategy frequently used by marketers (Chang). The reliance on individual donations has led charities to advertise themselves through various components such as vivid images and moving words (Chang). However, the effectiveness of framing can aid less effective charities by providing more funds to them than would be socially optimal. Thus, it is important to study the framing effect in various charity advertisements, in order to make sure effective charities get the money they need.

One well known example of framing in charity advertising is choosing to portray the donation in a negative or positive manner, known as message framing. Advertisements may be framed positively ("A child will be saved with your donation") or negatively ("A child will live in poverty without your donation) (Chang). The same message framing can be done with positive or negative imagery, known as image framing. Another instance of framing is whether statistics are provided in the short-term (A child dies every day without your donation) or long-term (365 children die every year without your donation), known as temporal framing. An online study done by Chang, Chun-Tuan, and Yu-Kang Lee studied the effects of message framing, image framing, and temporal framing in charity advertisements. 186 participants were shown various advertisements with each of the variables manipulated and were asked to rate their behavioral intention (their intention to donate or tell others to donate).



Figure 3: Results of positive message framing, variable image framing, and variable temporal framing



Figure 4: Results of negative message framing, variable image framing, and variable temporal framing

One trend to be noticed from the data is that the combination of positive photo and positive message is less effective at both temporal variations than the combination of negative photo and negative message. This can be explained by the negativity bias, which states that humans place more emphasis on loss than gain (Rozin). This emphasis can lead to avoidance of loss, and thus, cause people to be more willing to donate to the cause. The negative framing could also induce feelings of sympathy if no action is taken (Chang). This effect of framing is known as the sympathy bias, which can generate greater sympathy relative to the actual needs of the victim (Sudhir).

Three such instances of the sympathy bias were studied by K. Sudhir et all: the identified victim effect, the in-group effect, and the reference dependent sympathy effect. The identified victim effect refers to the effect of increasing sympathy by making the social distance between the victim and the donor less. As Joseph Stalin said, "The death of one Russian soldier is a tragedy; the death of millions is a statistic" (Sudhir). The feeling of knowing a victim evokes the emotional part of the brain and creates greater sympathy for the victim than a statistic (Sudhir). The in-group effect is the increase in sympathy by portraying the victim as part of the same group as the donor. By portraying the victim as part of the same group as the donor, the donor feels closer to the victim and is more likely to donate more. The reference dependent sympathy effect refers to the increase in sympathy when the victim's situation is a decline rather than the

actual situation. For example, sympathy is greater for someone who becomes homeless rather than the chronically homeless.

The researchers used a large charity called HelpAge India to test out the effects of these sympathy biases by modifying various flyers sent to a cold list of 200,000 high net worth individuals. To test the identified victim effect, the researchers sent out two flyers, pictured below.

Individual Condition				
Photo of	Sushila worked as a school teacher and retired comfortably. But she became			
Sushila	destitute when her husband passed away and other family members refused to support			
	her.			
	Support a Gran has helped Sushila_meet her basic needs of food, clothing and shelter in			
	her time of need. Today in her seventies, she leads a dignified life.			
	Your tax deductible donation of $₹9000$ a year (that is just $₹750$ a month) helps Sushila			
	and people like her live a life of dignity in their golden years.			
Group Cond	ition			
Photo	These ladies share a common story. They worked as school teachers and			
Collage of	retired comfortably. But then they became destitute when their husbands passed away			
four	and other family members refused to support them.			
unnamed	Support a Gran has helped them all meet their basic needs of food, clothing and shelter in			
ladies	their time of need. Today in their seventies, they lead a dignified life.			
	Your tax deductible donation of ₹9000 a year (that is just ₹750 a month) helps these			
	and other people like them a life of dignity in their golden years.			

Figure 5: Two flyers used in the sympathy bias experiment

One flyer focused on a single person who needed help, while the other focused on multiple victims. The flyer with the individually identified victim had a donation rate of 0.235% and an average of 8.83 rupees per mailing, while the group flyer had a donation rate of 0.092% and an average of 4.20 rupees per mailing. The donation rate and average donation were over double for the individually identified victim. Thus, the identified victim effect is significant when framing charity advertising. The absence of the identified victim effect in a charity advertisement could lower the donations to it, even if the charity is more effective in saving lives.

Furthermore, the researchers tested the in-group effect by using the same victim in the above image (Sushila), who is a Hindu woman, and another victim who was a Christian woman (Shirley Barrett). Since the donor list was 90% Hindu, the Hindu Woman was "in-group" for most of the recipients, while the Christian woman was "out-group". The donation rate was much higher for Sushila (0.277%) compared to Shirley (0.194%) and so was the average donation amount: 11.29 rupees for Sushila and 6.38 for Shirley.

The next experiment tested the reference dependent sympathy effect by using the same Sushila flyer as above, but by having one treatment drop the first line "Sushila worked as a school teacher and retired comfortably." Under lab conditions the line would be replaced with "Sushila lived a life of deprivation", but since the experiment was a field experiment, this would be unethical. By removing the first line, the flyer does not provide any information as to whether Sushila has always lived a desolate life. The results yielded that the reference condition (flyer with the first line) had a 0.225% response rate and an 8.29 rupees average donation, while the uncertain condition (flyer without the first line) had a 0.149 % response rate and a 6.28 rupees average donation. Both the in-group effect and reference dependent sympathy effect show big increases in donation effectiveness, and thus, are important to incorporate in effective charity advertisements.

In order to maximize donations, an effective charity should make use of all of the framing biases. In social media form, a charity should use the negativity bias in conjunction with the reference dependent sympathy effect and the identified victim effect in all of its posts and fundraisers. For example, "James used to have a happy and successful life until hard luck fell on him. Now, without your donations James may live his life out on the street." By identifying James, the identified victim bias is induced, and by showing that James fell to his current state, the reference dependent sympathy effect is used. To further promote the negativity bias (shown by the threat of him living on the street), a picture of James on the street would be a good addition to the social media post. Furthermore, charities could use viewer demographics, provided on most social media sites such as Facebook or Instagram, to find the majority of a certain demographic (race, income, class, etc.) in their followers/donors. Presenting a victim of that majority demographic in a social media post would further increase donations by utilizing the in-group effect.

The Anchoring Effect

Another heuristic that influences donations is the anchoring effect. The anchoring effect is the tendency to start with an initial value (the anchor) and estimate to the final result. A good demonstration of the anchoring effect was an experiment done by Kahneman and Tversky, in which participants were asked to estimate the percentage of African countries in the UN (Kahneman). They were first asked to spin a wheel of fortune that gave a number between 0 and 100 and then asked to estimate up or down from that number. Although this number was unrelated to the actual value, it still affected responses: the median response for the people who received 10 on the spinner was 25 and the median response for the people who received 65 was 45. It is clear that people will anchor to any piece of information they are given, which is something important when asking for donations.

Charities often provide a suggested donation amount in their advertisements, which can act as an anchor, but it is possible that compliance to the anchor may decrease if the amount is perceived as too high or unfair (Hysenbelli). A study by Dorina Hysenbelli, Enrico Rubaltelli, and Rino Rumiati studied this by assigning participants to three groups: no anchor, low anchor, and high anchor. All groups were read the same story about a girl with brain damage who needed help. The low anchor group had the statement "On average, Italians donate $\in 10$ to support this project", the high anchor had the same statement but with $\in 90$, and the no anchor had no such statement. Every group was asked how much they would hypothetically donate to the cause. The no anchor group had an average of 19.46 euros, the low anchor had an average of 22.13, and the high anchor had an average of 32.23. The results show that people tend to base donation amounts off the anchor provided and that higher anchors are better for larger donations.

Another common form of anchoring is called verbal anchoring, which involves adding a phrase or slogan to a logo in order to guide the viewer to the message of the logo. To test the effectiveness of verbal anchoring in charity organizations, a study divided 203 participants into three groups where they were shown well known charities—one shown just a logo (no anchor), one shown a logo and brand name (some anchoring), one shown a logo, brand name, and slogan (significant anchoring) (Plomp). The participants were then asked to rate various aspects on a 1-7 scale such as their attitude towards the organization. The results showed that no anchoring and complete verbal anchoring had similar average "attitude towards organization" values of 6.07 and 6.08 respectively, while some verbal anchoring had a slightly higher value of 6.20. Participants' willingness to donate was 4.67 for no anchor, 4.78 for some anchoring, and 4.75 for significant anchoring.

The results display that some verbal anchoring can be beneficial in conveying a better attitude towards the organization and increasing willingness to donate. This is most likely because the extra anchoring may have been too direct in its intention to influence people's perception of the logo. This is similar to how an unrealistic donation anchor can lower the number of people who are willing to donate close to that amount. Based on the two studies, it is possible for charities to take advantage of anchoring to increase willingness to donate and donation amount. The problem is that this anchoring effect could lead to donations to a less effective charity that would optimally deserve less donations.

Consequently, it is important effective charities adopt these anchoring effects to ensure they receive the funds they deserve. Effective charities should have a distinct logo and name that they can use as their profile picture on social media, and make sure to use high, but realistic anchoring amounts in social media fundraisers.

The Evaluability Bias

Although the anchoring and framing effects increase donations when used in social media advertising, they can be used by less effective charities as well, furthering the misallocation of funds. It is important that effective charities have an edge over less effective charities by showcasing their effectiveness in advertising. However, people tend to focus on the overhead costs of a charity rather than the cost effectiveness.

This phenomenon was studied in an online experiment by Lucius Caviola, Nadira Faulmüller, Jim. A. C. Everett, Julian Savulescu, and Guy Kahane. 94 participants were divided into three groups: one group that was shown Charity A and Charity B, one shown only Charity A, and one shown only Charity B. The participants were presented with a singular line describing the charity-for example, Charity A was presented as "Per \$1,000 donated, \$600 go into administration. With the remaining \$400, 5 lives are saved.". Charity A was more than twice as effective as Charity B, and Charity B had lower overhead costs. After seeing the charity/charities in their group, participants were asked how much they would hypothetically donate from \$100 to \$500. The results showed that the group with Charity A had a far lower average donation (156.37) than Charity B (254.31).

This showed that when shown separately, people put more emphasis on overhead costs

than cost effectiveness. This is due to the evaluability bias, which states that people tend to evaluate an attribute based on how easy it is to evaluate. Overhead costs are easier to evaluate as they are a ratio of dollars to dollars, while cost effectiveness is in terms of human lives per dollar. The difference in units makes it harder to evaluate cost effectiveness, and people end up considering it less important.

However, when the charities were presented side by side, Charity A had a significantly higher average donation (309.68) than charity B (101.87). Thus, when compared side by side, the evaluability bias disappears. This is most likely because showing the charities side to side makes the cost effectiveness easier to evaluate because there is a reference. This means that people do value cost effectiveness more, but due to the evaluability bias, they end up valuing overhead costs.

The presence of the evaluability bias means that funds are not donated to effective charities, which probably means thousands more lives could have been saved (Caviola). So why is it so hard to evaluate cost effectiveness? In the experiment, it was most likely the units being harder to evaluate (dollars per life vs dollars per dollar), but in reality, few organizations even bother to calculate how many lives are saved for how many dollars (Baron). However, there are many resources to find charities with high operating expenses, such as Charitynavigator.org which publishes lists like "10 inefficient fundraisers" (Baron). Thus, people end up focusing on overhead costs, even when it is almost irrelevant to the goals of charitable organizations. Due to this expectation of low overhead costs, charities are forced to keep costs low, and to even use low costs as an appeal to donate (Baron). For example, CARE, a prominent nonprofit advertises: "More than 90 percent of our expended resources – among the highest of all philanthropic organizations – support our poverty-fighting projects around the world. Less than 10 percent of expended resources go toward administrative and fundraising costs (CARE).

To counteract the evaluability bias, effective charities should put up some posts that compare the charity's effectiveness to another charity, since research shows the evaluability bias disappears with side-by-side comparison. Furthermore, charities should post their rankings on websites that rank charities by cost effectiveness like *GiveWell*. By giving a frame of reference, cost effectiveness becomes easier to evaluate and causes the evaluability bias to disappear, which allows donors to focus on cost effectiveness.

Conclusion

In conclusion, heuristics have a large impact on our decisions and affect donations to charities. The framing effect has a powerful effect on how many donations a flyer or advertisement for a charity receives. The anchoring effect can change the perception of a charity and the amount someone is willing to donate. The evaluability bias can cause people to focus on overhead cost—completely the wrong attribute. It is important for the effective charities of the world to apply framing and anchoring to their advertisements and to take the correct steps to counter the evaluability bias. By doing these steps on social media platforms of effective charities, the same strategies that worked on standard advertising can be applied to a modern age of charity.

Works Cited

Baron, Jonathan, and Ewa Szymanska. "Heuristics and Biases in Charity." 2011.

- "CARE USA Financial Reports and Information." Care USA. 14 Jan. 2022, https://www.care.org/financial-reports/.
- Caviola, Lucius, et al. "The Evaluability Bias in Charitable Giving: Saving Administration Costs or Saving Lives?" Judgment and Decision Making, vol. 9, no. 4, 2014, p. 303.
- Chang, Chun-Tuan, and Yu-Kang Lee. "Framing Charity Advertising: Influences of Message Framing, Image Valence, and Temporal Framing on a Charitable Appeal." Journal of Applied Social Psychology, vol. 39, no. 12, 2009, pp. 2910-2935.
- Hysenbelli, Dorina, Enrico Rubaltelli, and Rino Rumiati. "Others' Opinions Count, but Not All of Them: Anchoring to Ingroup versus Outgroup Members' Behavior in Charitable Giving." Judgment & Decision Making, vol. 8, no. 6, 2013.
- Jenni, Karen, and George Loewenstein. "Explaining the Identifiable Victim Effect." Journal of Risk and Uncertainty, vol. 14, no. 3, 1997, pp. 235-257.
- Kahneman, Daniel, et al., eds. Judgment under Uncertainty: Heuristics and Biases. Cambridge University Press, 1982.
- Plomp, A. C. H. J. "The Influence of Verbal Anchoring and Nationality on Consumer Response Regarding Charity Logos: The Netherlands vs Russia." 2021.Kahneman, Daniel, et al., eds. Judgment under Uncertainty: Heuristics and Biases. Cambridge University Press, 1982.
- Rozin, Paul, and Edward B. Royzman. "Negativity Bias, Negativity Dominance, and Contagion." Personality and Social Psychology Review, vol. 5, no. 4, 2001, pp. 296-320.
- Sudhir, K., Subroto Roy, and Mathew Cherian. "Do Sympathy Biases Induce Charitable Giving? The Effects of Advertising Content." Marketing Science, vol. 35, no. 6, 2016, pp. 849-869.
- Tversky, Amos, and Daniel Kahneman. "The Framing of Decisions and the Psychology of Choice." Behavioral Decision Making, Springer, Boston, MA, 1985, pp. 25-41.

Stress and Its Effect on Sport Performance By Joseph Zongen Shen

Abstract

This research aimed to explore the effects of stress on the performance of individual athletes and how stress may be connected to athletic identity, performance injuries, and recovery. This paper's thesis is that mastery of individual sports must come from conditioning, i.e., how the athlete trains in preparation for a competition, their comprehension of the stress induced by participation in sports, and how an athlete can overcome said stress. In addition, the research examined possible applications for regulating harmful athletic stress. The findings conclude that the detrimental effects of stress weakened athletic performance and were exacerbated further by an athlete's negative mental attitude when approaching competition. Furthermore, stress affects athletic identity adversely, especially among athletes in individualized sports, which are significantly more demanding on the athlete. Finally, stress also significantly affected injury and recovery rates among individual and team athletes. Athletes can monitor their stress through heart rate regulation and self–surveys to relieve stress through communication with coaches, hydration, and good sleep habits.

The Mind's Obstructions

Individual sports are both physically and mentally demanding. In a typical competitive two-set junior tennis match lasting two hours, the ball is in play for approximately seven minutes. Interestingly, even after undergoing only those few minutes of physical exertion, both players are usually exhausted at the conclusion due to the stress of the contest. Simply put, due to their absence of teammates and limited mid-match coaching and support, individual sports are mostly played in the mind against mental barriers such as self-doubt, anxiety, and distraction. Sports such as tennis, golf, and track and field demand that athletes concentrate all their mental faculties, including habitual thought patterns that may inhibit optimal performance. Players in individual sports have only a limited time to overcome mental challenges, whereas players in team sports can rely on their teammates in certain scenarios. Extrapolating this, understanding and overcoming the mental side of athletics can also significantly contribute to success in sports and life. Upon examining an athlete's mid-competition performance, identity, and injury incidence/recovery, it can be concluded that mental inhibitions, many of which stem from associated stress, are extremely detrimental to many aspects of an individual sport athlete's lifestyle, contrary to popular belief.

A Framework for Stress and Terms

The term "stress" can be broadly classified into four types: physical, psychosocial, psychological, and psychospiritual stress. This paper will focus mainly on psychological stress, particularly routine stress, which refers to "mundane hassles, strains, or annoyances associated with routine daily activities and transactions of everyday life." (Upchurch Sweeney et al., 2013)

It is important to note that daily stress can be anticipated or unanticipated. Anticipated stressors may include driving in rush hour traffic, paying bills, working long hours, job performance evaluations, or taking children to after-school activities, while unanticipated stressors may include arguments with a spouse, car trouble, getting stuck in long lines at the grocery store, getting sick, losing one's keys, or weather-related inconveniences. (Upchurch Sweeney et al.). This paper examines the effects of athletic stress, with routine stress falling under the category of anticipated stress.

Furthermore, any mentions of "anxiety" should be understood as "an emotion characterized by apprehension and somatic symptoms of tension in which an individual anticipates impending danger." (American Psychological Association).

Finally, for the purpose of this paper, "organized sports" is defined as "[t]he totality of those institutionalized games whose outcomes are dependent upon physical prowess." (Kenyon). It is worth noting that while routine stress is often considered a part of daily life, it can have significant effects on individuals' psychological well-being, particularly in the context of organized sports. The added pressure of competition can exacerbate routine stress and lead to negative outcomes such as burnout, reduced performance, and psychological distress. As such, it is important to understand the various types of stress and their effects on athletes in order to promote their well-being and maximize their potential.

Part 1: An Analysis of the Impact of Stress on the Mind and Body

In the 1930s, endocrinologist Hans Selye conducted an experiment in which animals were exposed to noxious stimuli, and he observed that almost all of them responded similarly to the threat. Selye named this phenomenon the General Adaptive Syndrome (GAS) (Selye), and he identified three main stages of the GAS. First, the animal would detect the threat and enter the "alarm phase," leading to a "resistance phase" during which the animal would attempt to cope with or adapt to the threat. Finally, the experimental subject would become depleted of energy and resources and collapse, entering the "exhaustion phase." This level of exhaustion could result in lasting damage to the adrenal glands and immune system, leading to cardiovascular problems and mental illnesses. While the "exhaustion phase" has been critical to understanding the effects of chronic stress, this paper will primarily focus on the "alarm phase" and the "resistance phase." The objective of this paper is to examine athletic performance under critical duress.

Stressors that are associated with physiological, psychological, or social dimensions are believed to be critical to athletic performance. However, a closer examination suggests that pre-competition stress may be the most significant element in achieving sport excellence (James Santomier Jr). It is widely accepted that the primary motivation behind organized sports is victory. Therefore, the effect of losing on individual athletes can lead to manifestations of "maladaptive schema," such as mental instability, shame, failure, and even vulnerability to harm and illness (Reyhan). While individual sports can instill higher levels of self-confidence, self-reliance, and discipline in children, they can also, more likely, cause athletes to develop an unhealthy relationship with failure due to a lack of support and accountability found in being part of a team.

As a result, individual sport athletes may exhibit greater anxiety and depression levels, not only because of how they internalize failure but also because of their tendency to set unattainable goals for themselves (Nixdorf et al.). These greater anxiety and depression levels are well-documented in an experiment conducted by Pluhar et al., which found that while both individual sports and team sports generally decreased anxiety and depression rates in athletes compared to the general public, there was a significant difference between the rate of depression or anxiety in individual sport athletes (13%) and team sport athletes (7%) (Pluhar et al.). Individual sports in which judges determine success in contests correlate with the highest levels of anxiety in sports, where athletes feel the pressure to "differentiate themselves from their competition in pursuit of perfection and a judge's approval" (Schaal et al.), not to mention the ever-present threat of the judge's personal preferences.

In light of these findings, this paper argues that understanding and managing pre-competition stress is essential for achieving athletic excellence, especially in individual sports. Furthermore, it suggests that sports organizations, coaches, and athletes must actively address the negative effects of pre-competition stress, such as anxiety and depression, on athletic performance.

1.1 Stress and Mid-Competition Performance

Numerous studies have established the impact of stress on athletic performance. Regardless of the source of stress, the human mind exhibits a "fight or flight" response (Jones), with the body experiencing heightened attentiveness, visual and auditory acuity, and physical strength when choosing the "fight" option (Von Rosenberg). However, when the body's perception of the threat surpasses the perceived ability to handle the situation, the body will opt to flee, resulting in decreased fine motor skills and cognitive abilities (von Rosenberg). Woodman and Hardy's (2003) experiments, which explored the link between cognitive anxiety and performance, support this conclusion. Of the 43 studies on the connection between cognitive anxiety and performance, approximately 60% reported a negative relationship, 16% reported insignificant results, and 23% reported a positive correlation (Woodman & Hardy). In an independent study focused on swimmers participating in individual events, cognitive anxiety explained 46% of the variance in swimming performance (Burton). However, while these experiments clearly establish the connection between cognitive anxiety and athletic performance, they do not explain the causes behind this relationship.

In a subsequent experiment, Von Rosenberg explains that the task itself is not inherently stressful; rather, stress is engendered by how the mind perceives the task. Performance is enhanced by challenges that require individuals to use all of their abilities to complete the task. In contrast, tasks perceived as threats, which even the use of all an individual's abilities may not guarantee success, elicit stress, fear, and anxiety, decreasing performance and overall self-confidence (Von Rosenberg). Therefore, how an individual perceives a task is the primary

determinant of the amount of stress experienced and, subsequently, the quality of the ensuing athletic performance.

Alternatively, Vicki Leblanc offers a physiological explanation. In her paper, Leblanc suggests that elevated stress levels can impair the human mind's decision-making ability and ability to divide attention (LeBlanc). When stressed, an individual's decision-making process may become disorganized and suboptimal. Rather than calmly analyzing information and considering all options, the decision-making process of a stressed mind may rapidly assess data and consider only a limited set of alternatives. This type of decision-making, or "hypervigilant decision-making," has long been associated with poor performance (Keinan). In another study, researchers found that stress can directly affect the central nervous system function and general motor patterns (Anderson, Di Nota, Metz, & Andersen). Stress can alter the emotional state, affecting the parts of the mind that dictate general motor patterns such as walking, finer motor patterns such as grabbing and bending, and balance (Maki and McIlroy,). This relationship between stress-associated anxiety and motor skill deterioration is further supported by the experiment in which mice bred with higher anxiety traits exhibited less motor control than those bred with average genetics (Lepicard et al., 2000, 2003). In another study, Nieuwenhuys and Oudejans examined the performance of law enforcement officers reacting under stress and found that performance stress was detrimental to firearms skills. This included decreased targeting ability, reaction times, and shot accuracy, which could result in the inadvertent injury of innocent bystanders (Nieuwenhuys and Oudejans).

1.2 Stress and Athletic Identity

In essence, sports do not cause stress; instead, stress arises as a response to the perceived inability to achieve personal objectives. Ironically, this stress can further impede an athlete's ability. This frequently unbreakable negative cycle may lead to more damage by eroding the athlete's athletic identity or self-esteem. Success, often defined by winning or losing, is highly regarded by society. Losing can cause distress and impact an athlete's psyche (James Santomier Jr). This can cause individuals, especially impressionable children, to question the value of a losing performance. Athletes often perform exceptionally well in individual sporting events but lose simply because their opponent is more talented, older, or skilled. In these cases, young individuals often cannot process their performance and conclude that winning is the only measure of success. This belief can quickly snowball into the incorrect assumption that children who often win are "winners" and everyone else is a "loser." Athletes can fairly gauge their performance through statistics and data in team sports. By contrast, athletes participating in individual sports cannot rely on the notion that "winning is a team effort." As a result, victory and defeat may be perceived from an unhealthy perspective: instead of believing that "I can win," they latch onto the idea that "I must not lose." Competitions and tournaments emerge as threats to self-esteem rather than rewarding challenges. Success or failure becomes embraced not just as part of the athletic identity but the entirety of who the athlete is.

Parents and coaches can also accentuate this uncertainty. According to an experiment conducted by Hellssted, many Australian children point to their parents as a source of pressure to become athletically exceptional. Even at the collegiate level, studies have found statistically significant associations between performance anxiety, parental post-game conversations, and parental pressure to play a particular sport (Lane). These findings highlight the need for a supportive and nurturing environment for young athletes. Instead of placing undue emphasis on winning, parents and coaches can focus on the importance of effort, teamwork, and personal growth. By doing so, they can help athletes develop a positive athletic identity that is not solely defined by success on the field or court.

1.3 Stress and Injuries

Injury is an inherent and unavoidable risk in sports. According to a study conducted in the United States, there are approximately 600,000 injuries annually nationwide among five million high school students (Andersen & Williams). Assuming each student experienced only one injury, the injury rate in recreational sports would be roughly 12%. However, the injury rate among elite athletes is significantly higher. For instance, over a two-year period, 83% of elite gymnasts experienced at least one injury (Mohd & Nor).

While athletes often attribute injuries to physiological causes, research has shown a significant correlation between stress and sports-related injuries. Anderson and Williams proposed a stress-centered model for understanding the psychological causes of athletic injuries. The model identifies cognitive and physiological/attentional components of stress responses, which have reciprocal effects on each other. Under conditions of perceived threat, cognitive appraisal may inhibit physical coordination or ignore critical environmental cues, resulting in a higher risk of severe injuries. The model also highlights the effect of psychological factors, such as anxiety, depression, irritation, and competition anxiety, on the frequency and severity of injuries. These factors were categorized into three groups: personality factors, such as anxiety or attention span, history of stressors, such as prior injury history, and coping resources, such as the various behavioral and social mechanisms an athlete uses to cope with everyday events.

In an experiment designed to test the relationship between illness or injury and competitive anxiety and life stress, M. Marthinus and J.R. Potgieter found a significant correlation between competitive anxiety, daily hassles, and the combined number of injuries in the athletes included in the experiment. Similarly, Lavallée and Flint revealed that competitive anxiety positively correlated with injury frequency. They found that tension/anxiety, anger/hostility, and total negative mood states correlated to the severity of injuries.

Research conducted at the University of Missouri showed that academic stress significantly affects injury rates among football players (Mann, Bryant, Johnstone, Ivey, & Sayers, 2016). Injuries occurred more frequently during periods of high physical stress, such as training camp. Still, interestingly, the injury rate during weeks of high academic stress doubled the injury rate in weeks of low academic stress. When applied to active players, the injury rate tripled during weeks of high academic stress. Additionally, male athletes with higher preseason

levels of anxiety and depression had a 2.1 times higher injury rate compared to male athletes who did not report symptoms of anxiety and depression (Li et al.).

Studies have also suggested that stress may be the single most important factor in recovery and neuroplasticity after motor system injury. Exposure to persistently stressful situations has been reported to be a significant detriment to recovery in stroke victims (Walker, Jones, Patience, Zhao, & Nilsson).

The physiological explanation for the negative impact of stress on athletes is due to the body's natural response to stress, which causes the musculoskeletal system to tense up to guard against impact or pain. Chronic stress leads to constant muscle tension, which hinders coordination, particularly in sports requiring quick movements like tennis and swimming, thereby increasing athletes' risk of injury (Coppel et al.). Moreover, individuals who stress over the possibility of reinjury tend to have a slower recovery than those who participate in relaxation techniques and other stress-relieving activities as part of their recovery ("Stress").

Part 2: A Response to the Negative Impacts of Stress on Athletes

One of the most common counterarguments against the idea that stress negatively impacts athletes is that there are studies that demonstrate the positive effects of stress on athletic performance. Specifically, it has been shown that moderate amounts of stress can increase the secretion of adrenaline in the body, leading to greater alertness and excitement and ultimately contributing to success (Duffek). However, several flaws in this argument need to be addressed. Firstly, this argument assumes that all types of stress are equal and only differ in intensity and duration. This is not true, as different types of stress vary in their nature and effects on the body. For instance, the acute stress that produces the sensation of "butterflies" is distinct from chronic stress associated with the "fight or flight" response. The former is short-term and manageable, while the latter can be long-lasting and negatively impact cognition (Taylor). Thus, it is important to distinguish between different types of stress to avoid confusion and better understand their impacts on athletic performance.

Moreover, even if one assumes that different types of stress can be interchangeable, this argument fails to consider the specific circumstances of athletic competition. It is often difficult for athletes to control their stress levels effectively and ensure that the stress they experience is entirely beneficial (Taylor). By ignoring the potential negative impacts of stress, one risks leaving this "wound" untreated, which can lead to further complications and potentially disastrous consequences. Therefore, it is crucial to acknowledge the potential negative impacts of stress of stress on athletes and develop effective strategies to manage and mitigate them.

Part 3: Monitoring and Coping with Stress

Professional and collegiate athletes, and, to a lesser extent, high school and amateur athletes, experience significant amounts of change in their daily lives due to the demands of their sport. Attending training and practices, competitions, and travelling all affect one's daily stress levels. For these athletes, mental health is a large concern. In a 2019 survey from the American

College Health Association (ACHA), of the 67,972 participants, 18,896 participants (27.8%) reported anxiety and 13,730 participants (20.2%) reported experiencing depression that negatively affected their academic performance. 44,657 participants (50.7% males and 71.8% females) reported feeling, at some point in the past 12 months, "overwhelming anxiety", and 45.1% (37.1% males and 47.6% females) reported experiencing depression that hindered their ability to function normally (Lopes Dos Santos et al.). This decline in mental wellness doesn't only apply to college athletes; it holds true for professional and high school athletes as well (Szczypińska et al.). Therefore, monitoring the mental health of athletes and teaching them appropriate coping strategies is just as important as sculpting them physically.

3.1 Monitoring Mental Health

Internal load, referring to the "individual physiological and psychological response to the external stress or load imposed" (Wallace et al.), is influenced by many factors, which include common everyday occurrences, the environment surrounding the athlete, and the athlete's ability to cope with stress and anxiety (Soligard et al.). Measuring internal load can give a good insight into the mental stability of athletes under pressure and the factors that cause pressure to build in athletes. Unfortunately, unlike external load monitoring, researchers and coaches can measure internal load only indirectly, through heart rate, and sometimes subjectively, through self-ratings of perceived exertion. However, subjective measures have been proven more consistent and accurate than indirect methods (Saw et al.). Two reliable subjective modes of reporting training stress, sessional ratings of perceived exertion (sRPE) (Robson-Ansley et al.) and ratings of psychological mood states (POMS) (Saw et al.) have both been found to be reliable indicators of internal load.

Heart rate is a common tool for measuring physical exertion. Generally, the accepted way of accurately recording heart rate is to monitor an athlete's average heart rate immediately after intensive exercise, recording the time it takes for the athlete's heart rate to drop back down to the resting rate which was recorded before the exercise began (Daanen et al.). This system comes with many flaws. It was found that among college athletes, dehydration is a factor in heart rate recovery. Athletes who followed a prescription hydration plan (PHP) recorded a faster heart rate recovery than those who used their normal "ad libitum" hydration plan (NHP) when subjected to the same exercises instead of long, consistent tasks (Bosquet et al.). Therefore, while heart rate is a useful supplement in determining the internal load of athletes, it is ineffectual and meaningless unless paired with other instruments that measure athletic stress.

Alternatively, sources have reported the validity and reliability of subjective athlete questionnaires such as sRPE and POMS (Foster; Sweet et al.). Unlike heart rate, a rigid system doesn't restrain self-report surveys and so can be used to calculate internal load through different interchangeable metrics depending on the situation. These metrics include session load (sRPE x session duration in minutes), daily load (sum of all session loads in a day), weekly load (sum of

all daily loads in a period of seven days), and strain (weekly training load x standard deviation of weekly training load) (Foster).

3.2 Managing Stress and Coping Strategies

Upon identifying the need for stress reduction, an athlete should evaluate their options for managing stress.

Coaches can play a significant role. Now, many coaches maintain a welcoming, open-door policy, encouraging athletes to seek guidance on stress-related challenges. Furthermore, coaches can teach basic life skills within the scope of their practice. Coaches can encourage positive self-talk, practice deep-breathing techniques and mindfulness, and develop good sleep habits (i.e., being in bed by 10 o'clock, putting mobile phones in a separate room, and aiming for eight hours of sleep every night).

Athletes themselves can experiment with a variety of coping mechanisms then conclude as to which one fits their personal needs the best. Jean Taché and Hans Selye suggest four different stress-coping approaches. First, an athlete can change their environment and modify conditions in their environment, such as moving out of a high-stress environment and surrounding oneself with a competent and supportive team. Second, stress often arises from one's interpretation of a situation rather than the situation itself. Stress and struggle will never go away; it is just that as one evolves and adapts, this struggle takes less lethal — but equally stressful — forms. Thus, a shift in perspective can help mitigate stress. Athletes can learn not to immediately associate criticism with personal inadequacy, defeat with failure, and success with the goal of sports. Third, athletes can regulate stress by finding adequate responses to stressors. By engaging continuously in high-stress situations, such as athletic competitions, an athlete will become proficient in dealing with certain types of stressors, and consequently, the stress it induces lessens. Finally, athletes can engage in diversionary activities to alleviate stress and tension. Ways to do so include meditation, yoga, and breathing exercises, all of which can help an athlete decompress before or after a stressful event.

The Long Road Ahead

The evidence strongly suggests that the impact of stress on the body before, during, and after athletic competitions is not well understood or adequately considered. Stress can lead to self-defeating decisions during competitions, inappropriate framing of successes and failures, and decreased efficacy of recovery methods. Thus, the next logical step is to develop strategies to manage athletic stress and accurately measure stress in athletes.

Athletes can adopt healthier lifestyle habits, such as a balanced diet, adequate hydration, and a regular sleep schedule, to manage stress. However, parents and coaches play a crucial role in supporting athletes. As key figures in an athlete's development, they should strive to assist athletes in any way possible, such as integrating healthy habits, providing verbal support and affirmation, or amplifying unheard struggles. In addition to these measures, further research is

necessary to identify additional strategies for managing stress and develop more accurate methods of measuring stress in athletes.

Moreover, it is essential to acknowledge that stress is a normal part of competition and that athletes can use stress to their advantage. The key is finding the optimal stress level that promotes peak performance. This can be achieved through techniques such as mindfulness, visualization, and goal-setting, which have been shown to enhance athletic performance under stress (Gould, Dieffenbach, & Moffett).

In conclusion, the effects of stress on athletic performance are complex and multifaceted. While stress can be detrimental to athletic performance, it can also be harnessed to enhance performance. Thus, it is critical for athletes, parents, coaches, and researchers to work together better to understand the role of stress in athletic performance and to develop effective strategies to manage stress and optimize athletic performance.

Works Cited

- American Psychological Association. (2022). APA Dictionary of Psychology. Dictionary.apa.org. https://dictionary.apa.org/anxiety
- American Psychological association. (2018, November 1). Stress Effects on the Body. American Psychological Association. https://www.apa.org/topics/stress/body
- Andersen, M. B., & Williams, J. M. (1988). A Model of Stress and Athletic Injury: Prediction and Prevention. Journal of Sport and Exercise Psychology, 10(3), 294–306. https://doi.org/10.1123/jsep.10.3.294
- Anderson, G. S., Di Nota, P. M., Metz, G. A. S., & Andersen, J. P. (2019). The Impact of Acute Stress Physiology on Skilled Motor Performance: Implications for Policing. Frontiers in Psychology, 10. https://doi.org/10.3389/fpsyg.2019.02501
- Bosquet, L., Merkari, S., Arvisais, D., & Aubert, A. E. (2008). Is heart rate a convenient tool to monitor over-reaching? A systematic review of the literature. British Journal of Sports Medicine, 42(9), 709–714. https://doi.org/10.1136/bjsm.2007.042200
- Burton, D. (1988). Do Anxious Swimmers Swim Slower? Reexamining the Elusive Anxiety-Performance Relationship. Journal of Sport and Exercise Psychology, 10(1), 45–61. https://doi.org/10.1123/jsep.10.1.45
- Daanen, H. A. M., Racinais, S., & Périard, J. D. (2017). Heat Acclimation Decay and Re-Induction: A Systematic Review and Meta-Analysis. Sports Medicine, 48(2), 409–430. https://doi.org/10.1007/s40279-017-0808-x
- Dieter Hackfort, & Charles Donald Spielberger. (1989). Anxiety in sports : an international perspective. Hemisphere Pub. Corp.
- Duffek, J. (2017, November 15). When stress is good for student-athletes and when it's not. USA TODAY High School Sports; USA TODAY High School Sports. https://usatodayhss.com/2017/when-stress-is-good-for-student-athletes-and-when-its-not
- Foster, C. (1998). Monitoring training in athletes with reference to overtraining syndrome. Medicine & Science in Sports & Exercise, 30(7), 1164–1168. https://journals.lww.com/acsm-msse/Fulltext/1998/07000/Monitoring_training_in_athlete s with reference to.23.aspx
- Gould, D., Dieffenbach, K., & Moffett, A. (2002). Psychological Characteristics and Their Development in Olympic Champions. Journal of Applied Sport Psychology, 14(3), 172–204. https://doi.org/10.1080/10413200290103482
- Hellstedt, J. C. (1990, September 1). Early adolescent perceptions of parental pressure in the sport environment. Https://Psycnet.apa.org/Record/1991-07019-001.
- Jones, G. (1995). More than just a game: Research developments and issues in competitive anxiety in sport. British Journal of Psychology, 86(4), 449–478. https://doi.org/10.1111/j.2044-8295.1995.tb02565.x
- Keinan, G. (1987, July 14). APA PsycNet. Psycnet.apa.org. https://psycnet.apa.org/record/1987-20953-001
- Kenyon, G. S. (1972). Sport and society: At odds or in concert? Athletics in America. Oregon State University Press.
- Lane, B. (2020). Associations between Sport Performance Anxiety and Parental Pressure among NCAA Division III Athletes. Www.academia.edu. https://www.academia.edu/73730822/Associations_between_Sport_Performance_Anxiet y and Parental Pressure among NCAA Division III Athletes
- Lavallée, L., & Flint, F. (1996). The Relationship of Stress, Competitive Anxiety, Mood State, and Social Support to Athletic Injury. Journal of Athletic Training, 31(4), 296–299. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1318911/
- LeBlanc, V. R. (2009). The Effects of Acute Stress on Performance: Implications for Health Professions Education. Academic Medicine, 84(Supplement), S25–S33. https://doi.org/10.1097/acm.0b013e3181b37b8f
- Lepicard, E. M., Joubert, C., Hagneau, I., Perez-Diaz, F., & Chapouthier, G. (2000). Differences in anxiety-related behavior and response to diazepam in BALB/cByJ and C57BL/6J strains of mice. Pharmacology Biochemistry and Behavior, 67(4), 739–748. https://doi.org/10.1016/s0091-3057(00)00419-6
- Lepicard, E. M., Venault, P., Negroni, J., Perez-Diaz, F., Joubert, C., Nosten-Bertrand, M., Berthoz, A., & Chapouthier, G. (2003). Posture and balance responses to a sensory challenge are related to anxiety in mice. Psychiatry Research, 118(3), 273–284. https://doi.org/10.1016/S0165-1781(03)00069-6
- Li, H., Moreland, J. J., Peek-Asa, C., & Yang, J. (2017). Preseason Anxiety and Depressive Symptoms and Prospective Injury Risk in Collegiate Athletes. The American Journal of Sports Medicine, 45(9), 2148–2155. https://doi.org/10.1177/0363546517702847
- Lopes Dos Santos, M., Uftring, M., Stahl, C. A., Lockie, R. G., Alvar, B., Mann, J. B., & Dawes, J. J. (2020). Stress in Academic and Athletic Performance in Collegiate Athletes: A Narrative Review of Sources and Monitoring Strategies. Frontiers in Sports and Active Living, 2. https://doi.org/10.3389/fspor.2020.00042
- Maki, B. E., & McIlroy, W. E. (1996). Influence of arousal and attention on the control of postural sway. Journal of Vestibular Research: Equilibrium & Orientation, 6(1), 53–59. https://pubmed.ncbi.nlm.nih.gov/8719510/
- Mann, J. B., Bryant, K. R., Johnstone, B., Ivey, P. A., & Sayers, S. P. (2016). Effect of Physical and Academic Stress on Illness and Injury in Division 1 College Football Players. Journal of Strength and Conditioning Research, 30(1), 20–25. https://doi.org/10.1519/jsc.00000000001055
- Mohd Nor, M. A., & Nor, M. A. M. (2001). The Psychological Aspects of Injury in Sport. Jurnal Teknologi, 34(1).

https://www.academia.edu/961266/The_Psychological_Aspects_Of_Injury_In_Sport

Nieuwenhuys, A., & Oudejans, R. (2011). Anxiety and perceptual-motor performance: toward an integrated modelof concepts, mechanisms, and processes. Psychological Research an International Journal of Perception, Attention, Memory, and Action, 76(6).

https://www.researchgate.net/publication/51753075_Anxiety_and_perceptual-motor_perf ormance_Toward_an_integrated_model_of_concepts_mechanisms_and_processes

- Nixdorf, I., Frank, R., & Beckmann, J. (2016). Comparison of Athletes' Proneness to Depressive Symptoms in Individual and Team Sports: Research on Psychological Mediators in Junior Elite Athletes. Frontiers in Psychology, 7(12). https://doi.org/10.3389/fpsyg.2016.00893
- Pluhar, E., McCracken, C., Griffith, K. L., Christino, M. A., Sugimoto, D., & Meehan, W. P. (2019). Team Sport Athletes May Be Less Likely To Suffer Anxiety or Depression than Individual Sport Athletes. Journal of Sports Science & Medicine, 18(3), 490–496. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6683619/
- Reyhan, S., & Department of Physical Education and Sport Sciences, S. U. (2020). Effect of losing on early maladaptive schemata of individual male athletes. African Educational Research Journal, 8(1), 78. https://www.academia.edu/66045235/Effect.of_losing_on_early_maladaptive_schemat

https://www.academia.edu/66045235/Effect_of_losing_on_early_maladaptive_schemata_ of_individual_male_athletes

- Robson-Ansley, P. J., Gleeson, M., & Ansley, L. (2009). Fatigue management in the preparation of Olympic athletes. Journal of Sports Sciences, 27(13), 1409–1420. https://doi.org/10.1080/02640410802702186
- Rollo, I., Impellizzeri, F. M., Zago, M., & Iaia, F. M. (2014). Effects of 1 Versus 2 Games a Week on Physical and Subjective Scores of Subelite Soccer Players. International Journal of Sports Physiology and Performance, 9(3), 425–431. https://doi.org/10.1123/ijspp.2013-0288
- Santomier, J. (1983). The Sport-Stress Connection. Theory into Practice, 22(1), 57–63. https://www.jstor.org/stable/1476241?seq=1#metadata_info_tab_contents
- Saw, A. E., Main, L. C., & Gastin, P. B. (2015). Monitoring the athlete training response: subjective self-reported measures trump commonly used objective measures: a systematic review. British Journal of Sports Medicine, 50(5), 281–291. https://doi.org/10.1136/bjsports-2015-094758
- Schaal, K., Tafflet, M., Nassif, H., Thibault, V., Pichard, C., Alcotte, M., Guillet, T., El Helou, N., Berthelot, G., Simon, S., & Toussaint, J.-F. (2011). Psychological Balance in High Level Athletes: Gender-Based Differences and Sport-Specific Patterns. PLoS ONE, 6(5), e19007. https://doi.org/10.1371/journal.pone.0019007
- Selye, H. (1950). Stress and the General Adaptation Syndrome. British Medical Journal, 1(4667), 1383–1392. https://doi.org/10.1136/bmj.1.4667.1383
- Soligard, T., Schwellnus, M., Alonso, J.-M., Bahr, R., Clarsen, B., Dijkstra, H. P., Gabbett, T., Gleeson, M., Hägglund, M., Hutchinson, M. R., Janse van Rensburg, C., Khan, K. M., Meeusen, R., Orchard, J. W., Pluim, B. M., Raftery, M., Budgett, R., & Engebretsen, L. (2016). How much is too much? (Part 1) International Olympic Committee consensus statement on load in sport and risk of injury. British Journal of Sports Medicine, 50(17), 1030–1041. https://doi.org/10.1136/bjsports-2016-096581

- Sweet, T. W., Foster, C., Mcguigan, M. R., & Brice, G. (2004). QUANTITATION OF RESISTANCE TRAINING USING THE SESSION RATING OF PERCEIVED EXERTION METHOD. The Journal of Strength & Conditioning Research, 18(4), 796. https://journals.lww.com/nsca-jscr/abstract/2004/11000/quantitation_of_resistance_traini ng_using_the.20.aspx
- Szczypińska, M., Samełko, A., & Guszkowska, M. (2021). Strategies for Coping With Stress in Athletes During the COVID-19 Pandemic and Their Predictors. Frontiers in Psychology, 12. https://doi.org/10.3389/fpsyg.2021.624949
- Taylor, A. (2021, January 20). The effects of stress on athletic performance | Sidekick Blog. Blog.sidekicktool.com.

https://blog.sidekicktool.com/the-effects-of-stress-on-athletic-performance/

- Upchurch Sweeney, C. R., Turner, J. R., Turner, J. R., Barrett, C., Soto, A. V., Whang, W.,
 Korbel, C., Matwin, S., Gorrin, D., Schroeder, B., Turner, J. R., Dekker, J., Levin, B.,
 Turner, J. R., Pishori, A. Z., Grabowski, J., Yard, S., Nelson, K., Denton, E., & Akechi, T.
 (2013). Daily Stress. Encyclopedia of Behavioral Medicine, 537–538.
 https://doi.org/10.1007/978-1-4419-1005-9 942
- vonRosenberg, J. (2019). Cognitive Appraisal and Stress Performance: The Threat/Challenge Matrix and Its Implications on Performance. Air Medical Journal, 38(5), 331–333. https://doi.org/10.1016/j.amj.2019.05.010
- Walker, F. R., Jones, K. A., Patience, M. J., Zhao, Z., & Nilsson, M. (2014). Stress as necessary component of realistic recovery in animal models of experimental stroke. Journal of Cerebral Blood Flow & Metabolism, 34(2), 208–214. https://doi.org/10.1038/jcbfm.2013.211
- Wallace, L. K., Slattery, K. M., & Coutts, A. J. (2009). The ecological validity and application of the session-RPE method for quantifying training loads in swimming. Journal of Strength and Conditioning Research, 23(1), 33–38. https://doi.org/10.1519/JSC.0b013e3181874512
- Williams, A. M., & Reilley, T. (2003). Science and soccer : developing elite performers. Routledge.
- Williams, J. M., & Andersen, M. B. (1998). Psychosocial antecedents of sport injury: Review and critique of the stress and injury model'. Journal of Applied Sport Psychology, 10(1), 5–25. https://doi.org/10.1080/10413209808406375
- Woodman, T., & Hardy, L. (2003). The relative impact of cognitive anxiety and self-confidence upon sport performance: a meta-analysis. Journal of Sports Sciences, 21(6), 443.
 https://www.academia.edu/66617390/The_relative_impact_of_cognitive_anxiety_and_self_confidence_upon_sport_performance_a_meta_analysis

Epileptic Seizure Detection using Decision Forest Machine Learning Algorithms By Pavan Chaganti

Abstract

Epileptic seizures are sudden and uncontrollable electrical activity in the brain, which affect around 50 million people worldwide. Undetected seizures can result in the worsening of epilepsy and delayed treatment. Electroencephalogram (EEG) signals can capture electrical seizure activity and are monitored and analyzed in real-time by doctors to detect epileptic seizures. This is a manual and time-consuming process, which can be replaced with automated seizure detection via machine learning algorithms. This study explores the use of Decision Forest algorithms for epileptic seizure detection and compares the performance between two different models. These two models, Random Forest and Extra Trees, both performed at a high level with Extra trees marginally outperforming Random Forest in several metrics. The results of this study demonstrate that Decision Forest models can achieve a high level of performance for epileptic seizure detection.

Introduction

Epilepsy is one of the most common neurological conditions worldwide, with approximately 50 million people having this disease (World Health Organization, 2023). The most common process followed to diagnose epilepsy is an electroencephalogram (EEG) wave test (Mayo Clinic, 2023). Electrodes are placed on top of the patient's brain and record the brain's electrical activity for up to a few days. Once the recording has finished, healthcare professionals analyze the entire recording, looking for occurrences of epileptic seizures. As this is a very time-consuming process for healthcare workers, and can delay diagnosis, attempts are being made to automate epileptic seizure detection through machine learning. There has been a sizable amount of research done in this area. Up to this point, the machine learning algorithms that have been prevalently used include Support Vector Machine (SVM), Artificial Neural Network (ANN), and K-Nearest Neighbors (KNN) (Malekzadeh et al., 2021). Decision Forest models are a category of very powerful machine learning algorithms and could potentially yield superior results (Rokach, 2016). Within this research, two decision forest algorithms, Random Forest and Extra Trees, were used. The most common machine learning features that are extracted from the raw EEG data and fed into the algorithm include time domain features such as mean, variance, and kurtosis, as well as Hjorth parameters (Malekzadeh et al., 2021). In addition to these features, non-linear features were also employed in this study. This study aims to 1) explore the viability of decision forest algorithms coupled with feature engineering for epileptic seizure detection, and 2) assess the performance of the two decision forest algorithms with respect to each other.

Data Collection

For this study, a dataset of EEG signals from the University of Pennsylvania and Mayo

Clinic was used ("UPenn and Mayo Clinic's Seizure Detection Challenge"). This data consists of samples of one second long EEG signals recorded from the surface of the brain. or interictal (designating it as a signal during which no seizure occurred). Table 1. illustrates the number of signals that were recorded for each patient.

	Number of ictal (seizure) files	Number of interictal (non-seizure) files
Patient 1	70	104
Patient 2	151	2990
Patient 3	327	714
Patient 4	20	190
Patient 5	135	2610
Patient 6	225	2772
Patient 7	282	3239
Patient 8	180	1710

Table 1.

Table 1 : Table showing number of ictal and interictal files captured on each patient.

Each sample contains up to 67 channels of signal data. Each channel corresponds to a distinct electrode placed on the patient's brain (Figure 1)



Figure 1: Example signals from three electrodes, recorded from patient seven.

Feature Extraction

Statistical features and Hjorth parameters (commonly used in seizure detection studies) (Malekzadeh et al., 2021), as well as powerful non-linear features (Shoeibi et al., 2021), were used in this study (Tables 2 - 4). These twelve features were applied to each distinct channel.

e.g. data recorded from 67 electrodes from a given patient will result in a 67 x 12 feature vector.

Name	Formula	Description
Petrosian fractal dimension (PFD)	$\frac{\log_{10}k}{\log_{10}k + \log_{10}(\frac{k}{k + 0.4N\delta})}$	An algorithm to compute the complexity of the EEG signal.
Higuchi fractal dimension (HFD)	Slope of $\{(\log \frac{1}{x}, \log L(k))\}$	Approximate value for the box-counting dimension of the graph of a real-valued function or time series.
Lempel-Ziv complexity (LZC)	$S(h_{i-1} + 1, h_i), i = 1, 2,$	Complexity measure that searches for instances of consecutive binary characters.

Table 2: Description of non-linear machine learning features used in this study.

Name	Formula	Description
Mean	$\frac{1}{n}\sum_{i=1}^{n}x_{i}$	The average of electrode readings across an entire signal
Variance	$\sum_{n=1}^{N} (x_n - AM) \frac{2}{N-1}$	The degree of spread across the signal from the mean electrode reading
Kurtosis	$\sum_{n=1}^{N} (x_n - AM) \frac{4}{(N-1)SD^4}$	The measure of the prominence of the upper and lower ends of the electrode reading distribution
Skewness	$\sum_{n=1}^{N} (x_n - AM) \frac{3}{(N-1)SD^3}$	The measure of the degree of asymmetry in the distribution of electrode readings across the signal

Table 3

Standard Deviation	$\sqrt{\sum_{n=1}^{N} (x_n - AM)^{\frac{2}{n-1}}}$	The typical dispersion of data around the average electrode reading
Max	$Max(x_n)$	The maximum electrode reading in the signal

Table 3 : Description of statistical, time-domain features used in this study

Name	Formula	Description	
Hjorth Activity	var(y(t))	The EEG signal power	
Hjorth Mobility	$\sqrt{\frac{var(\frac{dy(t)}{dt})}{var(y(t))}}$	The mean frequency of the EEG signal	
Hjorth Complexity	$\frac{Mobility(\frac{dy(t)}{dt})}{Mobility(y(t))}$	The change in frequency across the EEG signal	

Table 4

Table 4: Description of Hjorth parameter features used in this study

Application of Machine Learning Models

Machine learning models such as SVM, ANN and KNN have already been heavily used for seizure detection (Malekzadeh et al., 2021). Decision Forest models are a family of very powerful ensemble models that often have lower variance and superior performance to individual models (Rokach, 2016). This study aims to assess the feasibility of two variants of the Decision Forest Model, Random Forest and Extra Trees, as reliable predictors of epileptic seizures.

Firstly, the data set was split into training and testing sets (80% : 20%), using stratified random sampling such that the ictal-interictal ratio within each dataset was maintained (Table 5).

Table 5.		
	Ictal (seizure) files	Interictal (non-seizure) files
Training Set	1112	11463
Testing Set	278	2866
Total	1390	14329

Table 5: Number of ictal and interictal files in training and test sets

Both Random Forest and Extra Trees models were trained and validated using the same training and testing sets, respectively. These models were implemented and trained using the Scikit-learn package.

Results and Discussion

Both models employed an ensemble of 1000 decision trees. The models output a probability (value between 0 and 1) that a given EEG signal contained an epileptic seizure episode. A specific 'threshold' value had to be determined such that probabilities above this value would be considered as predicting a seizure. The optimal threshold can be determined through a precision-recall curve. Precision is the fraction of predictions that are considered seizures under a given threshold, that are truly seizures. In other words, the fraction of positive predictions that are 'true' positives. A low precision would result in too many false alarms and would place a burden on medical resources. Recall is the fraction of true positives that were identified as positive. Within epileptic seizure detection, a high recall (few missed seizures) is needed to avoid adverse effects on the patient's health. There exists a tradeoff between precision and recall, and therefore the two values and their associated implications have to be balanced.

Examining the precision-recall curve (Figure 2) for the Random Forest model, it was observed that as the threshold increased (from left to right), the recall remained high (while the precision increased in value) until a precipitous drop at a precision value of roughly 0.85.



Figure 2 : Precision-Recall curve for Random Forest

The ideal threshold value of 0.7 is at the point right before this steep drop in the curve. This point corresponds to a precision of 0.85 and a recall of 0.92. The perfect values for both of these metrics would be 1, so these values indicate a considerably strong performance. Using the confusion matrix (Figure 3), at this threshold, the True Positive Rate (TPR) is 0.85, the False Positive Rate (FPR) is 0.0065, The True Negative Rate (TNR) is 0.99 and the False Negative Rate (FNR) is 0.15.

Confusion Matrix		
True Positives	False Positives	
221	19	
False Negatives	True Negatives	
39	2889	

Figure 3 : Confusion Matrix for Random Forest

The F1 score $(\frac{2 \times Precision \times Recall}{Precision + Recall})$, which measures a balanced performance between the precision and recall values, is 0.89 (with 1 being the perfect score), again indicating a good model performance. The Receiver Operating Characteristic curve (ROC) produced by the Random Forest model (Figure 4) is very close to an ideal ROC curve which consists of a vertical line starting at (0,0) going up to the upper left corner of the graph, followed by a horizontal line starting at that point on the left corner, extending to the upper right corner. The area under the curve (AUC) of this ROC curve is 0.978, just under a perfect value of 1.

Figure 4 : ROC Curve for Random Forest

The ROC curve's shape and AUC, in addition to the model's precision, recall, and F1 score,



suggest that the Random Forest model is a good, reliable predictor of epileptic seizures based on EEG signals. The same logic was used to determine the threshold and other metrics for the Extra Trees model. To be consistent with the Random Forest model, the ideal threshold for the Extra Trees model was set to 0.74, so as to maintain the same precision value of 0.85 (Figure 6). At this threshold value, the recall for Extra trees is 0.95 and the F1 score is 0.89. Using the

confusion matrix (Figure 5), at this threshold the TPR is 0.98, the FPR is 0.015, the TNF	₹ is
0.98, and the FNR is 0.019.	

Confusion Matrix		
True Positives	False Positives	
255	45	
False Negatives	True Negatives	
5	2863	

Figure 5 : Confusion Matrix for Random Forest



Figure 6 : Precision-Recall curve for Extra Trees The ROC curve produced by the Extra Trees model (Figure 7) is close to an ideal ROC curve. The AUC is 0.983, very close to the ideal value of 1.



Figure 7 : ROC Curve for Extra Trees

At the same precision level, the Extra Trees model had a higher recall and AUC compared to the Random Forest model, while both models had the same F1 score. Both models produced strong results and can be viable in epileptic seizure detection. As the model using the Extra Trees machine learning algorithm performed slightly better in several performance metrics (AUC and recall), tested on a large data set, it is reasonable to assume that the Extra Trees algorithm can provide superior performance to Random Forest in detecting epileptic seizures.

Conclusion

This study aimed to assess whether two Decision Forest models, trained on features derived from EEG signals, could automatically detect epileptic seizures. These models, Random Forest and Extra Trees, both had strong performances, with Extra Trees slightly outperforming Random Forest on most performance metrics. In conclusion, the results indicate that Decision Forest models can achieve a high level of performance for epileptic seizure detection. These machine learning algorithms have the potential to replace manual seizure detection processes and dramatically improve patient outcomes.

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Works Cited

- "Epilepsy." World Health Organization, World Health Organization, 9 Feb. 2023, www.who.int/news-room/fact-sheets/detail/epilepsy.
- "Epilepsy." *Mayo Clinic*, Mayo Foundation for Medical Education and Research, 28 Apr. 2023, www.mayoclinic.org/diseases-conditions/epilepsy/diagnosis-treatment/drc-20350098.
- Malekzadeh, Anis et al. "Epileptic Seizures Detection in EEG Signals Using Fusion Handcrafted and Deep Learning Features." Sensors (Basel, Switzerland) vol. 21,22 7710. 19 Nov. 2021, https://doi.org/10.3390/s21227710.
- Rokach, Lior. "Decision forest: Twenty Years of research." *Information Fusion*, vol. 27, 2016, pp. 111–125, https://doi.org/10.1016/j.inffus.2015.06.005.
- "UPenn and Mayo Clinic's Seizure Detection Challenge." Kaggle, National Institutes of Health, 19 May 2023, www.kaggle.com/competitions/seizure-detection/data.
- Shoeibi, Afshin, et al. A Comprehensive Comparison of Handcrafted Features and Convolutional Autoencoders for Epileptic Seizure Detection in EEG Signals, Jan. 2021, doi.org/10.1016/j.eswa.2020.113788.

Development of a Multi-Package Program for Photovoltaic Analysis of Solar Energy Measurements (Current-Voltage and Power-Time Example) Using Python by Uygar Ege Kocakir, School: Mugla Tobb Science High School

Abstract

This project is an impressive advancement in solar energy research presenting a versatile software package which is cost-free for use in comprehensive photovoltaic data analysis. It counteracts the issues that occur with expensive commercial software, providing scientists and students with invaluable tools. The project began by amalgamating open-source current-voltage and power-time data from different universities, transforming plain text files into a sorted CSV structure by resolution of Python's Pandas library. The data was then assigned into DataFrames for crafting multiple graphical figures utilizing Plotly and dispensing interactivity with offline interactive graphics. An interactive current-voltage chart was spontaneously formulated to promote an improved user experience. Power-time analysis necessitated daily storing of power data, necessitating more data adjustment and conversion to CSV structure, ensuring precision in the ensuing graphs. Both current-voltage and power-time scripts were combined into a simple-to-use package with PySimpleGUI. After assessment, the program showed its usefulness in executing the Fill Factor (FF) examination, obtaining an accurate FF calculation of 0.74, verifying its significance in empirical examination. This Multi-Package Program drastically alters solar energy data processing, getting rid of financial impediments, accelerating analysis, and motivating diversity and access in solar energy research. In the future, a dedicated website is being organized to increase the user base and effects on the domain.

Keywords: Physics, Python software, Photovoltaic Analysis,, Solar energy

Purpose

This project is driven by the following key objectives: The principal objective of this enterprise is to manufacture an economical and straightforward computer application for examining photovoltaic information with great accuracy, thus presenting an economical alternative to costly commercial software programs written in languages unfamiliar to the general public. The project facilitates users to evaluate data and formulate a variety of graphical depictions. This efficacy fortifies the understanding of solar energy data and furthers data-driven decision-making. The project deploys the Plotly library in order to devise interactive graphics, even in a freighted off-site context. This enables a profounder inspection of data, allowing consumers to interact with and derive knowledge from the diagrams. The FF Analysis Facility utilizes Fill Factor (FF) evaluation, an essential parameter for gauging the effectiveness of solar cells. This assessment helps comprehend the proficiency of solar vitality systems, thereby enabling sound scientific and engineering decisions. An intuitive interface, engineered with PySimpleGUI, simplifies data processing for researchers and students. This user-friendly design streamlines scientific research processes, thus providing an accessible and efficient means to analyze data. To summarize, this project endeavors to make solar energy data analysis accessible,

low-priced, and effortless. With these objectives achieved, financial and availability roadblocks researchers and students face are diminished, thereby promoting scientific knowledge in the area of solar energy.

1-The primary goal of this endeavor is to offer scientists and students a cost-efficient and openly available substitute for photovoltaic data investigation. By eliminating economic obstructions and providing open-source tools, the project intends to bring modern solar energy studies to a wider range of people.

2-The secondary goal of this project is to equip users with enhanced data visualization capabilities. With this functionality, customers can craft engaging and interactive graphical representations of solar energy information. This will give them the ability to easily analyze and understand even the most convoluted datasets.

3-An additional goal of the project is to make the job of performing scientific research focused on solar energy more efficient. An user-friendly interface will be created and analytical resources such as Fill Factor (FF) analysis applied in order to expedite data analysis, strengthening the decision-making process. As a result, a major boost will be experienced by knowledge and advancement regarding solar energy technology.

Introduction–Definitions

Photovoltaic Data Interpretation: This endeavor focuses on the exploration and management of solar energy information, specifically voltage-current and power-time data, to enable a more complete understanding of and to enhance solar power production via data interpretation and representation.

Examining Sunlight Statistics: This venture entails exploring and processing data concerning solar energy, especially the current-voltage and power-time information, with the purpose of enhancing and refining solar energy yields by means of inspecting data and generating visualizations.

Free Package Program: This project proposes an economical or complimentary package program for researchers and scholars instead of more expensive paid options, thus facilitating the evaluation of solar energy data.

Interactive Graphics: Utilizing the Plotly library to generate interactive graphics facilitates users to investigate and interact with data more completely, improving the visual portrayal of solar energy data.

The global quest for clean and sustainable sources of energy has reached an extraordinary height, with solar power taking the lead. Photovoltaic (PV) systems have become increasingly popular in recent years, drawing the attention of both researchers and students who want to find new ways of improving their efficiency. The journey, however, is tedious, due to the lack of available, user-friendly software tools for assessing solar energy data that are inexpensive to use. This piece presents an innovative undertaking: a practical, free, and open-source package program for photovoltaic research. This program is created to facilitate users, particularly

analysts and scholars, to investigate solar energy data, inspect voltage-current properties, and evaluate power-time tendencies quickly and accurately. Developed with the implementation of the Python programming language, this package program avails of a medley of data collections and modules to hasten the research process.

The Genesis of the Project

Before investigating the specifics of the package program, it's vital to grasp its origins. The venture started with amassing present-voltage and power-time information from different open-source databases given by universities. This plentiful dataset was in the beginning kept in text (txt) report design. To render this data accessible and suitable to investigation, the venture team utilized Python to transfer it into comma-separated values (CSV) format. Python programming, renowned for its flexibility and voluminous libraries, proved critical to this mission. The Pandas library, a powerful data manipulation tool, was used to alter the CSV data into Pandas DataFrames. By doing so, this enabled the current and voltage data to be organized into assorted columns, granting the capacity to generate varied graphical illustrations, like line graphs, bar graphs, and histograms.

Visualization with Plotly: A Paradigm Shift

Traditionally, creating visualizations of data in Python has largely been accomplished with the use of libraries such as Matplotlib. Nevertheless, the project team decided to take a more innovative and interactive path, taking advantage of the `graph_objects` module of the Plotly library. Plotly provides a strong system for constructing dynamic, interactive figures regardless of an internet connection. Through the Figure component of Plotly, the group created an interactive and versatile current-voltage graph. This advancement boosted the visualization abilities of the software, granting customers the ability to analyze data with enhanced interactivity and exactness.

Evolution to Power-Time Analysis

Having established the current-voltage chart, the following logical step was to construct a power-time graph. This required information to be gathered over periods of five minutes. To accomplish this, a special arrangement was introduced to store the collected data daily as a text file. Nevertheless, a new problem emerged with the power-time chart: how to involve time values as an essential factor. To resolve this, the group converted the txt record to a CSV file and processing the time data as strings using the Pandas library from Python. This alteration made sure that the power-time graph would be accurate and adhere to the required parameters. To come up with the power-time chart, three columns were carefully fashioned. As it was necessary to shift integer data to strings for compatibility, a fresh column was formed to take this transformation. The resultant DataFrame served as the basis for generating diverse two-dimensional diagrams through the Plotly library.

Integration into a Unified Package Program

Upon finishing up the essential steps, the project culminated in the construction of an unified package program. The codes which created the two graphs were blended into a single file, improving the program's convenience and user-friendliness. To give an even better user experience, the Python's PySimpleGUI library was added to the program, allowing users to easily select CSV files from their computers and produce graphs with a few clicks. This interface not only makes the process more straightforward but also gives users flexibility to receive both current-voltage and power-time diagrams from a solitary interface. This all-encompassing approach enhances the usefulness and availability of the package program. The enormity of this multi-package program is beyond dispute. It fills a crucial void in the realm of solar energy exploration, making available to scientists and learners a free, broad, and convenient kit of instruments for examining photovoltaic data. By expediting the handling of trial information and lightening the budget load on researchers and learners alike, this scheme makes data processing and representation much easier. This cutting-edge program stands poised to revolutionize solar energy research, making it far more freely available, efficient, and cost-effectual. Current plans contemplate expansion and the feasibility of access through a website, with the promise of subjecting the program to even wider viewership, accelerating the cause of sustainable energy inquiry. Exploring deeper into the use and consequence of this program, it's perceptible that a major impediment to scientists has been removed, thus blowing open the doors to a new time of solar energy exploration.

Previous Studies

Previous studies have emphasized the lack of free and user-friendly software for solar energy analysis. The high cost and complexity of commercial packages were challenging for researchers and students. In this context, this new Python-based package program represents a significant step in filling this crucial gap in the solar energy sector by simplifying the analysis and visualization of solar energy data. These studies have the potential to accelerate and popularize solar energy research by removing previous barriers. Method

Data Collection

The project initiation involved the extensive collection of solar energy datasets from diverse open-source repositories, with a particular focus on obtaining datasets containing current-voltage and power-time information. These datasets were primarily stored in the less structured text (txt) file format and held crucial data required for comprehensive photovoltaic analysis (Figure 1).

Data Conversion

To facilitate efficient data handling and analysis, the initial step involved the transformation of these raw text files into a more structured and manageable format:

comma-separated values (CSV). Python was employed for this purpose, leveraging its versatile capabilities for file manipulation and conversion.

Data Manipulation with Pandas

Python's Pandas library played a pivotal role in this project. After the successful conversion to CSV format, the next phase involved the creation of Pandas DataFrames. DataFrames are structured data containers that offer powerful data manipulation capabilities. This step allowed for the systematic separation of current and voltage data into distinct columns, setting the foundation for subsequent analysis and visualization.

Current-Voltage Chart Creation

With data now structured within DataFrames, the project proceeded to create a current-voltage chart. This task was accomplished using the Plotly library, specifically the `graph_objects` module. Plotly is renowned for its interactivity and versatility, even in offline environments. Leveraging these capabilities, the team developed dynamic and user-friendly current-voltage charts.

Power-Time Chart Preparation

Following the successful creation of the current-voltage chart, the project shifted its focus towards generating a power-time chart. Creating this chart necessitated the aggregation of data at 5-minute intervals. To facilitate this, a specialized data layout was devised to accumulate data collected at the end of each day in txt file format.

Time Data Transformation

One of the key challenges encountered when dealing with the power-time chart was the inclusion of time data. To address this challenge, the project team undertook the conversion of the txt file into a CSV file. Additionally, Python's Pandas library was employed to process the time data as strings. This transformation was critical to ensure the accuracy and conformity of the power-time graph to the required standards.

Power-Time Chart Generation

To create the power-time chart, three distinct columns were meticulously created within the DataFrame. This process involved the conversion of integer data to strings to ensure compatibility. Subsequently, the Plotly library was harnessed to generate a diverse range of two-dimensional graphics. These graphics allowed for the creation of interactive and informative representations of the power-time data (Figure 2-4).

Integration into a Unified Package Program

Upon successfully generating the two fundamental graphs, the project culminated in the integration of the codes into a unified package program. This consolidation was aimed at enhancing the program's accessibility and user-friendliness. Additionally, Python's PySimpleGUI library was seamlessly integrated into the program's interface, providing users with the convenience of selecting CSV files from their computers effortlessly and generating graphs with utmost ease (Figure 3).

In conclusion, this comprehensive method transforms raw solar energy data into meaningful visualizations. It not only enhances data accessibility and usability for researchers and students in the field but also provides a meticulously structured approach to data manipulation and chart creation. The result is the development of a user-friendly package program with the potential to revolutionize the landscape of solar energy research (Figure 4).

import pandas as pd import plotly.graph_objects as go

Figure 1. Importing Libraries

```
import pandas as pd
        import plotly.graph_objects as go
        import PySimpleGUI as sg
    elif graph_type == 'Voltaj-Zaman':
       df1 = pd.read_csv("/Users/uygaregekocakir/Desktop/MSK0ÇMANALİHOCA/data.csv"
        df1 = df1.drop(index=0)
        fig = go.Figure([go.Scatter(x=df1.iloc[:, 0], y=df1.iloc[:, 1])])
        fig.update_layout(
            xaxis_title="Gerilim, V (V)",
            yaxis_title="Akam, I (A)"
        fig.show()
except pd.errors.EmptyDataError:
    sg.PopupError("Seçilen dosya boş.")
except pd.errors.ParserError:
   sg.PopupError("Seçilen dosya geçersiz CSV formatinda.")
except FileNotFoundError:
    sg.PopupError("Secilen dosya bulunamada.")
```

Figure 2. Voltage-Time Codes in Python



Figure 3. Power-Time Graph Code in Python and beginning of Multi-Package Program

```
from IPython.display import display, Math
Vm = max_x ,Im = max_y ,Voc = max_value0 ,Isc = max_value1
efficiency = (Vm * Im) / (Voc * Isc)
formula = rf"FF=\frac{{V_m \cdot I_m}}{{V_{{oc}} \cdot I_{{sc}}} = {efficiency:.2f}"
display(Math(formula))
```

Figure 4. Codes that shape FF analysis

Results

The development and implementation of a functional, free photovoltaic analysis package program represents a significant milestone in the field of solar energy research. This program, built using the Python programming language and leveraging the power of open-source data from various universities, aims to provide an accessible and cost-effective alternative to commercially available packages in foreign languages. The key outcomes and results of this project are outlined below.

The project began by collecting open-source current-voltage and power-time data from various universities. These data sets, initially in the form of txt files, were converted to CSV files using Python. The Pandas library was instrumental in efficiently organizing the data into DataFrames, with one column dedicated to current data and another to voltage data. This step was essential for creating various types of graphs and visualizations.

To visualize the current-voltage data effectively, the project utilized the Plotly library's `graph_objects` module. This allowed for the creation of interactive, user-friendly graphs, even without an internet connection. By leveraging the `Figure` module, an interactive and versatile Current-Voltage chart was generated, providing users with valuable insights into the data.

The program also enabled users to create power-time charts by utilizing layouts

containing power data at 5-minute intervals. This data was stored in txt files at the end of each day, then converted to CSV files. The time data, initially in string format, was processed using Python's Pandas library filter module, eliminating any errors in the power-time graph. To create this graph, three columns were created, transforming integer data into strings and processing it into a new column (Figure 6-7).

The project combined the code for generating both current-voltage and power-time graphs into a single package program. This program featured a user-friendly interface built with the PySimpleGUI library. Users could effortlessly select a CSV file from their computers and create graphs with a single interface, streamlining the process of data analysis and visualization (Figure 10).

The package program also catered to FF (Fill Factor) analysis using the Current-Voltage chart. It calculated the FF value by identifying the point of maximum current-voltage collision using Python's maximum module. The FF value, calculated as 0.74, demonstrated the accuracy of the operations and measurements performed within the program (Figure 5, Figure 8-9).

This multi-package program represents a significant leap in accessibility and affordability for researchers and students interested in solar energy analysis. It eliminates financial constraints by offering a free alternative to expensive commercial software, making it a valuable resource for the scientific community.



Figure 5. Imagination of FF Analysis



Figure 6. Current-Voltage Graph

0.0.4.0.0.2.4.6





Figure 7. Power-Time Graph

$$FF = rac{V_m \cdot I_m}{V_{oc} \cdot I_{sc}} = 0.75$$

Figure 8. FF Analysis Value

Maximum Voltage Value: 21.1 ; Maximum Current Value: 3.8 Maximum Impact Value : 59.781920496424995 (Index 398 16.904075 , 3.536539)

$$FF = \frac{V_m \cdot I_m}{V_{oc} \cdot I_{sc}} = 0.75$$

Figure 9. FF Analysis Value and Other Values



Figure 10. Multi-Package Program Graphical Users

Conclusions

To sum up, the introduction of the Multi-Package Program for the photovoltaic probe of solar energy data stands as a major success in the realm of renewable energy research and teaching. This advanced technology not only compensates for costly commercial software, but also provides researchers and students with simple access to essential assessment and presentation resources. One of the paramount accomplishments of this campaign is the transformation of open-source current-voltage and power-time statistics from a variety of universities into a user-friendly format. Python, combined with the Pandas library, played a key role in this operation. By converting the information into CSV files and coordinating it into DataFrames, users can conveniently compose line graphs, column diagrams, and histograms, enabling a more intensive comprehension of solar energy idiosyncrasies. The utilization of the Plotly library's graph objects module represents a major milestone in constructing interactive and available visualizations. This functionality permits users to investigate and show their information more efficiently, even in offline mode. The incorporation of temporal information into the power-time chart additionally enhances the program's usefulness, permitting for a thorough examination of solar energy performance across time. The PySimpleGUI interface introduces a new level of convenience to the Multi-Package Program. Its user-friendly feature of loading CSV files and producing both current-voltage and power-time diagrams within the same platform streamlines the investigation significantly. This user-focused approach makes the program available to a broader population, including learners and researchers with different levels of technological knowledge. Furthermore, the program's flexibility goes beyond data visualization. It provides the functionality for FF (Fill Factor) analysis, an essential measure in gauging photovoltaic system effectiveness. The program works out the FF value, which suggests the system's capacity to successfully change daylight into electricity. With an FF value of 0.74, the program shows its exactness in carrying out complicated computations. In regards to broader ramifications, the Multi-Package Program confronts some of the most critical problems in the realm of solar power exploration. It removes financial impediments, allowing scientists and pupils to be involved in high-quality research without the encumberment of costly software packages. This inclusiveness not only ramps up the speed of scientific breakthroughs but also balances the odds for aspiring researchers around the world.

The prospects of this venture portend great things. As the membership rolls increase, this Multi-Package Program could well become a mainstay for solar energy musings and assessments. Ensuring that the program is available on a website will further augment its availability and access, transforming it into an essential resource for the renewable energy world. To sum up, the Multi-Package Program offers considerable progress for the realm of solar power research. Its user-parlance interface, highly potent data investigation functionalities, and competitive value position it as an advantageous resource for veteran researchers and novice investigators alike. By taking away entry constraints and developing a communal research milieu, this initiative establishes the way for a more resplendent and durably-sustainable tomorrow upheld by solar energy.

Suggestions

Creating a functional, free Python package program for photovoltaic analysis of solar energy data is a significant contribution to the field of renewable energy research. This project not only democratizes access to valuable tools for researchers but also empowers students and scientists to work on solar energy projects without the financial burden of purchasing commercial software. In this section, we will discuss some key recommendations and future prospects for your multi-package program.

To enhance the usability of your package program, consider investing time in creating a comprehensive user manual or documentation. A well-structured guide can help users, especially those new to Python or data analysis, navigate the program more effectively. This documentation should include installation instructions, usage guidelines, and examples.

Keep the package program up to date by actively maintaining it. Solar energy research is a dynamic field, and staying current with the latest developments is essential. Regular updates can include bug fixes, performance improvements, and the incorporation of new data sources or analysis methods.

While you've mentioned using open-source data from universities, consider expanding the range of data sources. Collaboration with solar energy research institutions or collecting data from various geographical locations can provide users with a broader dataset for analysis. Incorporate machine learning algorithms into your package program to enable predictive modeling and optimization of solar energy systems. This could help users make data-driven decisions on system design, maintenance, and performance optimization.

Encourage collaboration and engagement within the user community. Create an online platform, forum, or community where users can share their experiences, exchange ideas, and seek assistance when needed. This fosters a sense of belonging and can lead to valuable contributions and improvements from the user community.

In addition to photovoltaic analysis, consider expanding your program to support other renewable energy sources like wind, hydro, or biomass. This can make your package program a comprehensive tool for researchers and engineers working on various renewable energy projects. Explore opportunities for securing funding to support the long-term sustainability and development of your package program. Grants, sponsorships, or partnerships with relevant organizations can ensure that the tool remains accessible and up-to-date.

Works Cited

- Aytekin, Alper, et al. "GELECEĞE YÖN VEREN KODLAMA BİLİMİ VE KODLAMA ÖĞRENMEDE KULLANILABİLECEK BAZI YÖNTEMLER." Avrasya Sosyal ve Ekonomi Araştırmaları Dergisi 5.5 (2018): 24-41. Accessed June 12
- Melda, Ö. Z. E. N. "Albert Einstein. Einstein Seyahatnamesi: Uzakdoğu." 737-742. Accessed June 3
- Şahin, Mehmet, and B. A. T. I. Mehmet. "Fizik Biliminin Ekonomi ve Sosyal Bilimlere Yansıması." *Takvim-i Vekayi* 5.2 (2017): 1-7. Accessed July 13
- Çiçek, Kevser. *BOSE-EİNSTEİN yoğunlaşmasının dinamiği*. Diss. Sakarya Universitesi (Turkey), 2010. Accessed May 24
- Emre, İhsan. *Bilim tarihinde doğa, yasa ve yasalılık: Isaac Newton ve Albert Einstein örneği.* MS thesis. Sosyal Bilimler Enstitüsü. Accessed May 4
- Apatay, Tunc. "Exact solution to elastic behavior of periodic heat generating solid cylinder." *Politeknik Dergisi* 19.4 (2016): 421-426. Accessed August 7
- Şahin, Kemal, and Bülent Onur TURAN. "ÜÇ BOYUTLU YAZICI TEKNOLOJİLERİNİN KARŞILAŞTIRMALI ANALİZİ." Stratejik ve Sosyal Araştırmalar Dergisi 2.2 (2018): 97-116. Accessed August 13

Internet Sources:

https://acikders.tuba.gov.tr/file.php/8/LectureNotes/B12-15.pdf https://www.ibm.com/tr-tr/cloud/learn/monte-carlo-simulation https://aip.scitation.org/doi/10.1063/1.475870 https://depo.pegem.net/9786052419984.pdf

Measuring the Accuracy of Value-At-Risk in Relation to a Stock's Annual Returns By Sanika Shah

Abstract

When considering investment vehicles for long-term growth of wealth, many often choose stock portfolios of diversified equities, so that returns are consistent and stable. Stocks are specifically hand-picked with the utilization of a variety of risk management techniques. While different methods provide varying measures based on a stock's return, all methods eventually seek to quantify the risk associated with an investment. Value-at-risk (VaR) is one such measure that can determine potential loss of a stock portfolio over a given time period with a precise probability. The question in this study is whether VaR is an accurate method for predicting future growth of an individual stock. Data should support the high-risk, high-reward principle in that stocks with high VaRs will have higher returns compared to low-VaR stocks. Analyses of 25 stocks exhibited higher cumulative growth rates for above-average VaR stocks compared to below-average VaR stocks over varying time horizons. Further studies into sector returns highlighted the volatility of technology and manufacturing industry stocks, which was also represented by their high VaRs. The findings in this study can provide insight into the effectiveness of VaR and its capabilities in predicting the future growth of a stock and its risk.

Introduction

The stock market has long been a place of exchange of ownership, or equity, in a corporation through the buying and selling of shares. While countless other forms of investments have arisen (bonds, commodities, currencies, real estate, etc.), holdings of traditional stocks have persisted. With the expectation of growth in mind, most people invest in stock exchanges to later profit from the rise in value of a stock price. Besides the accumulation of wealth from investments, long-term goals retain a focus on maintaining the value of money, also known as purchasing power, during inflationary periods. The U.S. stock market is one of the most highly invested markets in the world and more than half of all households within the nation own U.S. equities (Teweles and Bradley).

Investing in the stock market, however, does not guarantee positive or consistent returns. Stock prices fluctuate frequently, so day-to-day movements can be unpredictable and long-term growth can vary (Schwert). Thus, outperforming the market, represented by Standard and Poor's 500 (S&P 500) index, which holds securities encompassing a wide range of industries to measure the overall U.S. market return, is difficult. Money pooled into mutual funds that are professionally managed has rarely beaten the market. In the past five years, close to 87% of mutual funds underperformed the S&P 500, while in the past 10 years, underperformance rose to 91% (SPIVA). Volatility is hard to navigate, but it exists nonetheless, so investors must account for it by determining their appetite for risk.

Risk and return are closely related, yet their precise relationship is subject to much debate. The risk-return tradeoff is often set as a basic principle, as it fosters the notion that

high-risk assets are more likely to reap high rewards and vice versa (Shefrin). On the other hand, higher risks investments can also lead to greater losses, which encourages people to determine the risk associated with a security before investing. Measuring risk can take a variety of paths. Statistical metrics such as standard deviation and R-squared are utilized to track and explain a stock's movement, while other analyses tools, including the Sharpe ratio and beta, calculate specific risk factors (Lettau and Ludvigson). Risk itself is categorized as systematic or unsystematic risk, the former associated with the overall market, while the latter is based on a certain stock or sector. Managing different forms of risk results in varied investment strategies and complex portfolios.

Value-at-risk (VaR), a technique employed by many financial institutions for risk management, provides the maximum loss an investor may incur in a given time horizon with a certain probability (Abad et al.). This model is centered around the loss of portfolio value, a major reason many focus on risk. VaR has been recognized by the financial community, as evidenced by recognition from the Basel Committee on Banking Supervision, the Bank for International Settlements, and more (Hendricks). VaR is a simple concept, but the methods one may take to achieve an accurate and reliable measure are rather complicated. Most approaches fall within one of the three main methodologies: the historical simulation method, the Monte Carlo method, and the variance-covariance method (Linsmeier and Pearson). Each method has advantages and disadvantages, but fundamental to all methods is their use of historical data. This study focuses on the variance-covariance or parametric method. Within a VaR model, two important considerations must be made: the holding period and the confidence interval. The holding period is the amount of time risk is measured in a portfolio or stock without any changes in investments. In this study, a one year (252 days) holding period is employed. The other significant factor in the model, the confidence interval, defines the degree of probability of the estimate of risk not being exceeded. For instance, a 95 percent confidence interval signifies that a portfolio is expected to exceed the estimated amount of loss only five percent of the time. In other words, the value-at-risk is in the 95th percentile of the distribution of potential losses (Hendricks). If a computed VaR value is \$5,000 in the 95th percentile over a one-day holding period, then the portfolio will exceed \$5,000 in losses with a 5% probability over any one-day time frame (Linsmeier and Pearson). Confidence intervals can usually range from 95th-99th percentiles, but this study focuses solely on the 95th percentile. Based on these metrics, VaR is calculated by the following:

$VaR = (\$100,000*1.645*\sigma)$ (I)

The first numerical value in the equation represents the initial investment into the stock being analyzed, which in this study was \$100,000. The next value, 1.645, is the z-score describing a value's relationship to the mean based on the standard deviation. Since this study was conducted in the 95th percentile, 1.645 directly correlates to the 95th percentile distribution of the data (Parametric Method). The last value in the equation, σ , is the symbol representing standard deviation. Calculated from the data values, standard deviation describes the dispersion of data based on their average proximity to the mean.

This study looks to provide insight into the significance of VaR for an investment. VaR offers a quantifiable measure of risk, but data utilized in the study focuses on VaR's usefulness over different time periods and industries. If high growth is desired by an investor, then VaR could measure potential loss. Likewise, slow but consistent growth may be the goal, so VaR may assist in accurate classification of stocks. Results showed strong support for increased growth among high-VaR stocks and stability in low-VaR stocks. Various sectors are more exposed to volatility than others, but all in all, VaR appears to be an accurate measure of risk and return.

Materials and Methods

This study drew results from 25 stocks that were selected based on their inclusion in one of the five sectors: technology, healthcare, financial services, telecommunications, and manufacturing. Five U.S.-based corporations with the largest market capitalizations within each sector were chosen. Market capitalization is the value of all shares of stock held in a company and it provides a measure of its relative size. Each of the 25 stocks was then analyzed through Yahoo Finance historical data.

Utilizing Microsoft Excel software, a spreadsheet was created with daily stock prices for the 25 stocks in the year 2012. These number values were converted into daily percentage growth and the standard deviation for each stock was found. Inserting the percentage standard deviations into the VaR formula (equation I), each stock's VaR for 2012 was determined.

For further analyses, monthly historical data for each stock and the S&P 500 for the next ten years, 2013-2022, was collected and converted into cumulative percentage and dollar returns on a separate spreadsheet. Each stock's 10-year data was also sorted into two groups based on the stock's VaR. First, the average VaR across all 25 stocks was calculated and then, comparisons were made between each stock's VaR and the average. Those stocks with above-average VaR were separated from those with below-average VaR and the 10-year cumulative returns of the stocks within each of the groupings was averaged per monthly data point.

Excel software provided the means for representing the data visually. Tables and charts demonstrated trends in the data over varying time periods and industries. Analyses of these visuals resulted in the formation of conclusions that drew on the findings of the study in relation to the hypothesis.

Results

Investigating the hypothesis in this study involved analyzing stock returns from 25 companies in five industries. Five U.S. based stocks with the largest market capitalization within each sector was chosen. The first grouping of technology stocks included Apple (AAPL), Microsoft (MSFT), Alphabet (GOOG), Amazon (AMZN), and Nvidia (NVDA). The next sector, healthcare, comprised UnitedHealth (UNH), Elevance Health (ELV), CVS Health (CVS), HCA Healthcare (HCA), and McKesson (MCK). Third is financial services, which covered Visa (V), JPMorgan Chase (JPM), Mastercard (MA), Bank of America (BAC), and Wells Fargo (WFC). Then, the telecommunication sector had Comcast (CMCSA), T-Mobile (TMUS), Verizon (VZ),

AT&T (T), and American Tower (AMT). Lastly, manufacturing stocks included Tesla (TSLA), Intel (INTC), Caterpillar (CAT), Boeing (BA), and Deere & Company (DE). Historical data for each of these stocks from 2012-2022 was collected and results were derived.

The first investigation looked at the VaR for the 25 stocks and compared those values to the stock's cumulative returns over different time periods. The value-at-risk was calculated by utilizing equation I, while the cumulative returns for the stocks was drawn from historical data on stock prices. Within a 1 year period (2013-2014), returns on a \$100,000 investment appear to be consistent across VaRs in the \$1,000 to \$5,000 range. However, after a \$5,000 VaR, the returns vary, and no clear pattern is apparent (Figure 1A). After 5 years (2013-2018), cumulative returns were higher, but still comparable in a VaR range of \$1,000 to \$3,000. After a VaR of \$3,000, returns were scattered (Figure 1B). The last time frame of 10 years (2013-2022) exhibited similar results. Cumulative returns were higher overall, but beyond a \$3,000 VaR, returns demonstrated no trend (Figure 1C).

The second study analyzed the growth of above average and below average VaR stocks over ten years (2013-2022). After the average VaR of all 25 stocks was determined, stocks were divided into groups of above and below average VaR. The average cumulative percentage returns of the two groups, in addition to the S&P 500, were graphed, portraying the increased value of an investment in above-average VaR stocks over time. Moreover, below-average VaR stocks more closely tracked S&P 500 growth. However, it can be recognized that above average VaR stocks had a drastically higher maximum fall in value over the ten years compared to below-average VaR stocks (Figure 2). A two-tailed t-test comparing ten-year above and below average VaR returns showed that the results were statistically significant (p < 0.025).

The third collection of data focused on the average VaR for each of the five industries studied: technology, healthcare, financial services, telecommunication, and manufacturing. The average VaR increased according to the following order of sectors: healthcare, telecommunication, financial services, technology, and manufacturing (Figure 3). Each sector experiences different circumstances that are common to all included stocks, so separating stocks by sector allowed clarity in sector-specific risk.

The fourth and last investigation tracked the average cumulative percentage returns for each sector over ten years (2013-2022). The technology and manufacturing sector showed higher and more volatile returns. However, these sectors displayed higher volatility and especially greater loss in 2022. The healthcare, telecommunications, and financial services sectors demonstrated growth that closely tracked the S&P 500.



B.



C.



Figure 1. Value-at-risk and cumulative stock returns over three time horizons. Scatter plots displaying the value-at-risk based on a \$100,000 initial investment and the cumulative monetary returns for the 25 stocks analyzed over one (A), five (B), and ten (C) years.

A.



Figure 2. 10-Year Cumulative returns for stocks with above and below average value-atrisks. Line graph exhibiting average returns over a ten-year span for 25 stocks categorized into above average and below average value-at-risks. S&P 500 growth is also shown as an overall market measure, p < 0.05.



Figure 3. Average value-at-risk of five stocks within each sector. Bar graph showing the increasing average value-at-risk of five stocks found in each of five different industries.



Figure 4. Ten-year growth of investment in five sectors. Line graph demonstrating cumulative returns in five sectors over ten years.

Discussion

Employing historical data from 25 stocks over ten years to measure the accuracy of the VaR metric has mostly supported the hypothesis in this study. Stocks with relatively high VaRs had greater variability in cumulative returns over one, five, and ten year time spans, whereas low-VaR stocks were more uniform. Moreover, stocks categorized in above-average VaRs showed higher cumulative growth, while below-average VaR stocks more closely followed the S&P 500. Sector-wise, technology and manufacturing had the highest VaRs and the greatest cumulative returns. Thus, particular sectors are more likely to be exposed to risk and reward, but also loss.

The technology sector may have had considerably high cumulative returns because of the explosive growth of the internet, technological devices, and artificial intelligence (AI) in the past decade in almost all industries in the economy. On the other hand, manufacturing demonstrated similar patterns to the technology sector, but is not an industry that is traditionally seen as high risk. However, Tesla, an electric-vehicle pioneer, was within the manufacturing classification and as a result, Tesla's individual stock price over the past ten years may have greatly skewed the overall sector.

Below-average VaR stocks mainly fell within healthcare, financial services, and telecommunications in an expected manner. These industries necessitate stability and consistency. Since they provide essential services to a large population across the U.S., high volatility in their stocks would be unlikely.

Drawing from results across the studies performed, it is clear that high-VaR stocks carry the risk of both high-reward and high-loss. Stock growth is rarely a straight path upwards, so

losses are natural. But, high-VaR stocks appear to face greater losses than the overall market. Since volatility is higher than other stocks, downward trends seem exaggerated in these stocks.

The results in this study could be improved with a deeper study across all industries covering a greater sample of stocks. In this manner, trends would be amplified, as well as the accuracy of results. Furthermore, analysis into specific categorization of stocks into above and below average VaR based on the stock's sector classification can provide insight into sector trends. In addition, more data can be collected from stocks going back further than a decade. Extending the time span would greatly enhance the reliability of VaR as a risk-metric over time.

This study prompts future experiments of other risk assessment techniques and a comparison of their accuracy in relation to each other. Particularly within value-at-risk, different methods exist for calculations, so research could explore the differences between methods, since some are better suited to certain situations and samples of data (Kenton). Another question that arises is whether stock returns breach the limits determined by the potential loss in VaR more often than expected by the probability distribution.

A holistic view on the conclusions of this study points to the risk-return trade-off. While results largely supported the hypothesis in this study, high-VaR stocks experienced similar downfall as upward growth. Low-VaR stocks provided more consistent returns, a safer alternative for those unwilling to take on high risk. Therefore, VaR provides a metric for risk that must be put into the perspective of the investor and their goals.

Works Cited

- Abad, Pilar, Sonia Benito, and Carmen López. "A comprehensive review of Value at Risk methodologies." *The Spanish Review of Financial Economics* 12.1 (2014): 15-32.
- Hendricks, Darryll. "Evaluation of value-at-risk models using historical data." *Economic policy review* 2.1 (1996).
- The Investopedia Team. "What Is the Parametric Method in Value at Risk (VaR)?" *Investopedia*, www.investopedia.com/ask/answers/041715/what-variancecovariance-matrix-or-paramet ric-method-value-risk-var.asp#:~:text=The%20parametric%20method%20looks%20at,of %20an%20investment%20or%20security.
- Kenton, Will. "Understanding Value at Risk (VaR) and How It's Computed." *Investopedia*, www.investopedia.com/terms/v/var.asp.
- Lettau, Martin, and Sydney C. Ludvigson. "Measuring and modeling variation in the risk-return trade-off." *Handbook of financial econometrics: Tools and techniques* (2010): 617-690.
- Linsmeier, Thomas J., and Neil D. Pearson. "Value at risk." *Financial analysts journal* 56.2 (2000): 47-67.
- Schwert, G. William. "Stock market volatility." Financial analysts journal 46.3 (1990): 23-34.
- Shefrin, Hersh. "Do investors expect higher returns from safer stocks than from riskier stocks?." *The Journal of Psychology and Financial Markets* 2.4 (2001): 176-181.
- "SPIVA." S&P Dow Jones Indices,

www.spglobal.com/spdji/en/research-insights/spiva/about-spiva/.

Teweles, Richard J., and Edward S. Bradley. *The stock market*. Vol. 64. John Wiley & Sons, 1998.

Is Safety More Than Fun? By Peichen Dong

Abstract

The human desire for security has deep evolutionary roots, prioritizing safety over enjoyment. Early humans faced various threats and developed vigilance to survive. This tendency to prioritize security is evident in the negativity bias, where negative stimuli receive more attention than positive ones. Understanding this desire for safety helps us appreciate its importance in modern enjoyment. Safety is paramount when seeking pleasure. Neglecting safety protocols can turn enjoyable experiences into tragedies, as seen in drowning statistics. Ensuring safety in recreational activities enhances enjoyment and minimizes risks.

Fear, stemming from the absence of security, hinders enjoyment. Crime rates and neighborhood safety affect individuals' well-being. Addressing safety concerns fosters relaxation and enjoyable experiences. Prioritizing safety fosters trust and security in communities, improving mental health and overall satisfaction. Safe environments enable social connections, fulfilling higher-level needs. Balancing thrill-seeking with safety is essential. While thrill-seekers report higher happiness levels, they engage in riskier behaviors. Finding a balance between excitement and safety is crucial.

In conclusion, prioritizing safety is crucial in fulfilling human needs, as outlined in Maslow's Hierarchy. It allows individuals to engage in enjoyable activities without fear and fosters well-being, trust, and personal growth within communities. Safety enhances the quality of shared experiences and contributes to human evolution.

Keywords: Maslow's Hierarchy of Needs, security, enjoyment, risk, crime rates, mental health, social connections, higher-level needs

Introduction

Safety and fun are two essential components of the universal human experience. According to Maslow's Hierarchy of Needs, both aspects are significant contributors to fulfillment. Security, defined as a state of being free from danger, risk, or injury, is closely tied to the second tier of the hierarchy, representing our need for physical, emotional, and financial stability. Fun, on the other hand, encompasses the enjoyment and amusement we derive from various activities and experiences. As an individual progresses through the levels of Maslow's pyramid, the pursuit of enjoyable experiences can lead to a greater sense of belonging, self-esteem, and even self-actualization. When making decisions in our careers, hobbies, and lifestyle choices, however, it is vital to prioritize security over fun. A secure environment lays the foundation for pleasurable experiences, further enabling us to effectively satisfy our higher-level needs and achieve personal fulfillment.

The Origin of Safety

The desire for a secure environment has been ingrained in human beings long before their desire for enjoyable experiences. Evolutionary psychologists suggest that our ancestors prioritized

security when navigating the dangers of their environment, as it was a crucial factor in our survival as a species (Buss, 2015). According to Maslow's Hierarchy of Needs, safety is a fundamental human need that must be met before anyone can pursue higher-level needs such as social connections or self-actualization, which often involve seeking some form of enjoyment.

Early humans faced numerous threats, such as predators and natural disasters. In response to dangers, they developed a heightened sense of vigilance, allowing them to better detect and avoid risks (Öhman & Mineka, 2001). This tendency to prioritize security over enjoyment is still evident today. Humans are more likely to respond excessively to negative or threatening stimuli than to positive or neutral ones, a tendency called the negativity bias (Rozin & Royzman, 2001). By understanding the evolutionary roots of our innate desire for safety, we can now better appreciate the importance of prioritizing security in humans' modern pursuit of enjoyment.

The Importance of a Secure Environment for Fun

When it comes to seeking pleasure, maintaining a secure environment should always be a priority. Pleasurable experiences can quickly turn into a tragedy when people do not follow basic safety protocols. According to the World Health Organization, drowning accounts for over 320,000 deaths every year, and the majority of these cases could be prevented with the enforcement of proper safety measures (WHO, 2021). Ensuring safety in recreational activities, such as swimming, can greatly reduce the risk of accidents and enhance overall enjoyment for all participants.

Here is another example: during my birthday party last year, I organized a boxing class for my friends and me. The boxing coaches prioritized our group's safety by providing us with adequate safety equipment and giving us clear instructions on how to avoid injuries during the class. Their attention to safety and overall care allowed us to fully enjoy the experience and create lasting memories without worrying about potential risks.

The Absence of Security Brings Fear and Hinders Fun

Fear is a powerful emotion that can prevent us from enjoying life to its fullest. When a secure environment is absent, feelings of fear take over, making it impossible to have pleasurable experiences. The relationship between fear and the absence of safety is seen in crime rates and their impact on individuals' well-being. A study published in the Journal of Health and Social Behavior found that people who perceived their neighborhoods as unsafe, due to social disorder, reported higher levels of subjective alienation and distress (Ross & Mirowsky, 2009). Therefore, it is not an extreme claim to say that addressing safety concerns and creating secure environments would allow individuals to relax and engage in enjoyable experiences without fear.

Consider the following: during a trip with friends last October, we stayed at a camp on a mountain. One night, my friend asked me to venture outside the camp. However, I believed that we should not explore unfamiliar places without parental consent. Recognizing the potential risks associated with wandering off in an unknown area, especially at night, I erred on the side of caution. This decision kept us safe and reinforced the importance of considering safety first when seeking enjoyment or adventure.

Prioritizing Security Can Foster a Sense of Trust and Security

Prioritizing safety can foster a sense of trust and security within a community, contributing to overall well-being and allowing for more meaningful and fulfilling enjoyment. Safe environments provide a strong foundation for individuals to form social connections, which are essential for meeting higher-level needs in Maslow's Hierarchy, such as love and belonging. A study published in the American Journal of Public Health found that communities with higher levels of trust and social cohesion reported better mental health outcomes and overall life satisfaction (Ehsan et al., 2019). By implementing safety precautions and fostering a secure environment, community members can feel at ease participating in different types of events and activities, allowing them to build stronger connections and experience greater enjoyment.

During a family vacation to the Maldives, we went snorkeling. The snorkeling center sent us detailed instructions on how to prevent dangers in the sea, including wearing life jackets, staying within designated areas, and following the buddy system. Their emphasis on safety fostered trust, allowing my family to fully enjoy the breathtaking underwater scenery without any fear or apprehension.

Thrills, Spills, and the Quest for Balance

Some people might argue that one should prioritize enjoyment instead of safety. One reason is that taking risks can be thrilling and exciting. Engaging in risky activities like bungee jumping, skydiving, or fast driving may lead to unnecessary casualties, but thrill-seekers may value the enjoyment above their potential dangers. While a study by the National Center for Biotechnology Information (NCBI) found that thrill-seekers had higher levels of happiness and life satisfaction, it also revealed that they were more likely to engage in risky behaviors that could lead to severe injuries or death (Zuckerman & Kuhlman, 2000). Therefore, it is crucial to find a balance between seeking excitement and ensuring a secure environment.

Conclusion

In conclusion, prioritizing safety over enjoyment is a crucial aspect of fulfilling human needs outlined in Maslow's Hierarchy. By focusing on creating a secure environment, we ensure that individuals can freely engage in enjoyable activities without worrying about potential hazards. Addressing safety protocols as a priority not only eliminates the fear that inhibits our capacity for enjoyment but also emphasizes its foundational role in fostering well-being and personal growth. Moreover, prioritizing safety promotes trust within communities, laying the groundwork for higher levels of the hierarchy, such as love and belonging, esteem, and self-actualization to be satisfied. Ultimately, placing safety at the forefront of decision-making enables us to maximize the pleasure and enrichment that enjoyable activities bring to our daily lives while also contributing to the overall quality of our shared experiences and human evolution.
Works Cited

- Buss, D. M. (2015). Evolutionary psychology: The new science of the mind (5th ed.). Psychology Press.
- Maslow, A. H. (1943). A theory of human motivation. Psychological Review, 50(4), 370-396. doi: 10.1037/h0054346
- Öhman, A., & Mineka, S. (2001). Fears, phobias, and preparedness: Toward an evolved module of fear and fear learning. Psychological Review, 108(3), 483-522. doi: 10.1037/0033-295X.108.3.483
- Rozin, P., & Royzman, E. B. (2001). Negativity bias, negativity dominance, and contagion. Personality and Social Psychology Review, 5(4), 296-320. doi: 10.1207/S15327957PSPR0504_2
- Ball, D.J., & Ball-King, L. (2013). Safety management and public spaces: restoring balance. Risk Analysis, 33(5), 763-771. doi: 10.1111/j.1539-6924.2012.01900.x
- Rosen, M.A., & Lormand, D.K. (2016). The role of safety culture in preventing slips, trips, and falls in the leisure and hospitality industry. Professional Safety, 61(7), 34-40.
- Ross, C. E., & Mirowsky, J. (2009). Neighborhood disorder, subjective alienation, and distress. Journal of Health and Social Behavior, 50(1), 49-64. doi: 10.1177/002214650905000104
- Ehsan, A. M., Klaas, H. S., Bastianen, A., & Spini, D. (2019). Social capital and health: A systematic review of systematic reviews. SSM - Population Health, 8, 100425. doi: 10.1016/j.ssmph.2019.100425
- Mobbs, D., & LeDoux, J. E. (2018). Survival circuits: Mechanisms and significance. Current Opinion in Neurobiology, 49, 14-18. doi: 10.1016/j.conb.2017.10.026
- Zuckerman, M., & Kuhlman, D. M. (2000). PThe AI assistant can't perform formatting tasks as it can only provide text-based responses. However, it can guide you on how to format your research paper.
- Chisholm, D., & Maravic, M. C. (2016). Impact of safety measures on the three most common accidents in the construction industry. Procedia Engineering, 164, 467-473. doi: 10.1016/j.proeng.2016.11.661
- Kozina, A., & Varda, N. M. (2017). The role of trust in creating effective communication as a means of ensuring social and psychological security. European Journal of Contemporary Education, 6(3), 454-460. doi: 10.13187/ejced.2017.3.454
- Furedi, F. (2009). Precautionary culture and the rise of possibilistic risk assessment. Erasmus Law Review, 2(2), 197-220.

The Problem Of Turbulent Flow Fluid Mechanics By Lalith Velamakanni

Abstract

Fluid Mechanics is a branch of physics that describes and explains phenomena related to the energy and motion of fluids. It is a field of great importance in physics and engineering because the majority of physical phenomena include complex interactions with fluids (gases, liquids, plasma, etc.). In applied fields such as aerospace and mechanical engineering, fluid mechanics underpins much of the study that is conducted. However, turbulent flow is a characteristic regarding fluids that continues to puzzle and engage physicists and engineers. An improvement in our understanding of turbulence will result in more efficient designs in systems which rely on fluid mechanics, such as designing of wind power plants. Turbulence is an extremely complicated phenomenon, and the mathematics we use to describe it is quite difficult. The aim of this paper is to give an overview of turbulence as a phenomenon, with a special emphasis on what lends to the difficulty of understanding turbulence and its application in design. Scope for future improvement in our understanding, and development of future applications will also be considered.

Turbulent and Laminar Flow

Fluid Mechanics can be understood as the branch of Physics concerned with the motion and forces regarding fluids. It has continued to engage and perplex the brightest minds till date, and has perhaps contributed more to industrial applications, than any other branch of Science. Fluid mechanics deals with *flow*. The motion of any fluid can be considered "flow"; ranging from the flowing of rivers and streams, to the movement of plasma from the core of the sun . Flow can broadly be categorised into two types - turbulent, and laminar. Laminar flow occurs when fluids flow in predictable, smooth layers, i.e, in *lamellae*. Some places where laminar flow can be observed is the release of water in water fountains, and pipes. A pictorial representation of laminar flow can be seen in Fig. 1.



Fig. 1 : Laminar fluid flow around a spherical object

Turbulent flow is the more common, complicated kind of flow we see everyday, at all scales; from the mixing of our daily coffee, to the giant red-spot on Jupiter, as seen in Fig. 2. Turbulent flow patterns exist everywhere. Some characteristics of turbulence include eddies and vortices, and random, swirl - patterns. As opposed to laminar flow, which is simpler to

understand, turbulent flow is chaotic, and seemingly random, and very hard to predict. A very small change in the initial conditions of a turbulent system can lead to very significant impacts on its development and dynamics; extreme sensitivity to ambient conditions is a key feature of all chaotic physical systems, including turbulent flow.



Fig 2 : Great Red Spot on Jupiter. The swirling patterns caused by the movement of gases on the planet are prime characteristics of turbulent flow.

The Reynolds Number

Osborne Reynolds was an Irish physicist, considered one of the pioneers of early development in fluid mechanics. In 1883, he conducted an experiment, the results of which would provide the basis for today's understanding of turbulent flow, and the conditions which lead to turbulence.

The experiment was a fairly simple one. Reynolds passed water through a long glass tube, at varying velocities. He introduced a coloured dye into the flowing water, to observe the presence of any flow-patterns. Reynolds noticed that at higher velocities and larger radii of the tube used for the experiment, the motion of the dye became chaotic and diffuse, whereas for relatively lower speeds and radii, the dye moved with uniformity. In other words, Reynolds discovered a quantitative criterion which determined whether a fluid flow can be considered turbulent or laminar. This quantitative measure is a dimensionless quantity, and has since been known as the Reynolds number -

$$Re = \frac{\rho u L}{\mu}$$

where ρ is the density of the fluid, *u* is the flow speed, *L* is the characteristic length of the flow (in the case of a fluid moving through a pipe, the diameter of the pipe), and μ is the viscosity (opposition to motion) of the fluid. When the Reynolds number of the fluid flow is greater than 3000, the flow is considered to be turbulent.

The Reynolds number is essentially a ratio between the inertial forces that keep a fluid in motion, and the resistive forces which take the form of viscosity. For substances such as honey which are highly viscous, flow is almost alway laminar. However for fluids such as water, and gases,

turbulent flow is the norm. In Fig. 3, we can see how smoke from a candle transitions from laminar flow, to turbulent flow.

When dealing with the aerodynamics of cars and aircrafts, engineers have to take into account turbulence. This is because when dealing with the air flow around cars and aircraft, the flow is always turbulent. However, the complex nature of turbulence has made it one of the most difficult branches of physics to study.



Fig 3: Slow moving smoke near the wick of the candle exhibits laminar flow, whereas the faster moving smoke higher up transitions to turbulent flow.

The Complex Nature of Turbulence : Navier-Stokes Equations

Fluid Mechanics, as a domain, is known for its computational complexity. Making predictions and generalisations regarding flow can be very difficult, more so for turbulent flow. We can understand this complexity through the lens of the much celebrated Navier–Stokes Equations.

The Navier–Stokes equations are a series of partial differential equations, which relate how velocity, pressure, temperature, density, and viscosity of a moving fluid are related to each other. The Navier-Stokes Equations are derived from the principles of the conservation of mass and momentum, and in theory, give a comprehensive description of the motion of viscous fluids.

Glenn Navier–Stokes Equations Research Center - dimensional - unsteady Time : t Pressure: p Heat Flux: q Coordinates: (x,y,z) Density: p Stress: τ Reynolds Number: Re Velocity Components: (u,v,w) Prandtl Number: Pr Total Energy: Et $+\frac{\partial(\rho u)}{\partial u}+\frac{\partial(\rho v)}{\partial u}+\frac{\partial(\rho w)}{\partial u}=0$ Continuity $\int \partial \tau_{xx}$ $\frac{\partial(\rho u)}{\partial u} + \frac{\partial(\rho u^2)}{\partial u^2} + \frac{\partial(\rho uv)}{\partial u^2} + \frac{\partial(\rho uv)}{\partial u^2} + \frac{\partial(\rho uv)}{\partial u^2}$ $1 \int \partial \tau_{xy}$ <u>dx</u> Re. $\frac{\partial(\rho_w)}{\partial t} + \frac{\partial(\rho_{uw})}{\partial x} + \frac{\partial(\rho_{uw})}{\partial y} + \frac{\partial(\rho_{w}^2)}{\partial z} = -\frac{\partial p}{\partial z} + \frac{1}{Re_r}$ $\left[\frac{\partial \tau_{xx}}{\partial x} +\right]$ $\frac{\partial(uE_T)}{\partial(vE_T)} + \frac{\partial(vE_T)}{\partial(vE_T)}$ $\partial(wE_T)$ $\frac{1}{\Omega_{x}} \left[\frac{\partial}{\partial x} (u \tau_{xx} + v \tau_{xy} + w \tau_{xz}) + \frac{\partial}{\partial v} (u \tau_{xy} + v \tau_{yy} + w \tau_{yz}) + \frac{\partial}{\partial \tau} (u \tau_{xz} + v \tau_{yz} + w \tau_{zz}) \right]$

Fig 4: The Navier-Stokes Equations

The Navier-Stokes equations have been known since the earlier half of the 19th century. This leads us to an important question; why is it that understanding turbulent flow is extremely challenging, even though we have a series of equations explaining all fluid motion? The answer - partial differential equations are extremely complicated, especially the Navier-Stokes equations. The terms in the equations do not have linear relationships with each other, which makes it difficult to obtain solutions. In fact, there is a million dollar prize from the Clay Mathematics Institute, waiting for anyone who can prove that smooth solutions for the equations will always exist. The Navier-Stokes Existence and Smoothness Problem, as it is known, is one of the 7 Millennium Problems; it is considered one among the most complex, and important mathematical mysteries which remain unsolved. Thus, partial differential equations are extremely important domains for mathematicians today as well. Though engineers and physicists use such equations extensively, we lack a comprehensive theoretical understanding.

Analysing laminar flow is easier; as the viscous forces are far larger than the inertial forces; thus they can be neglected. In cases where the Reynolds number of the flow is low, the Navier Stokes equations can be approximated to linear forms, making them easier to solve. However, for cases of turbulent flow, such approximations cannot be made. This is precisely why turbulent flow remains one of the last, unsolved mysteries in classical mechanics. Another key problem is that obtaining solutions for the equations requires a great deal of computing power. Thus, we can appreciate why our knowledge regarding turbulence is still nebulous, given the fact that the fundamental mathematical nature of turbulent flow is still not well understood. Turbulent flow is very hard to predict, due its apparent randomness, which is reflected in the extreme non-linearity of the equations we have to describe it.

Developments and Further Research

We have seen great leaps forward in computing ability, and we have seen the emergence of some advanced modelling techniques to help understand turbulent flow. There has been a great deal of increase in our computer-based models used to examine turbulent flow. For example, Large Eddy Simulation (LES) is a method that is used extensively to model turbulent flow. This method of modelling reduces the complexity of the turbulent flow being analysed, as it focuses on larger length and time scales. This type of modelling ignores the smaller, and more statistically insignificant features of turbulent flow, and focuses on the larger eddies and vortices formed.

Direct Numerical Simulation (DNS) is an extremely effective and sophisticated, albeit expensive, tool used to model turbulent flows. This method resolves the turbulent aspects of some ideal fluid flow within a given time period; this allows researchers to analyse every aspect of some basic flow variations, unlike LES, where the smaller scale turbulence-phenomena are largely ignored. However, such detail comes with heavy costs of computing power, and is therefore only utilised to understand the fundamental aspects of certain basic turbulent systems. DNS can therefore not be used as an all-purpose solution to analyse all turbulent-flow scenarios, which would be an ultimate goal for computational fluid mechanics.

Though computational and statistical methods have been improving, to understand the fundamental mathematics in relation to turbulence will require the proving of the existence of solutions for the Navier-Stokes Equations. Though some strides have been taken in the area by mathematicians such as Jean Leray in the 20th century, and more recently, Terrence Tao, significant progress is yet to be made in this direction.

A more complete understanding of turbulent flow in fluid mechanics will lead to great strides in engineering; for example more efficient aircraft designs, and body designs for race cars, are two immediate applications. More importantly, weather patterns will be understood better, as turbulence plays a massive role in climatic phenomena, as the weather is a consequence of the effects of moving fluids in the Earth's atmosphere. More accurate weather prediction is thus another objective which can be achieved, facilitated by a deeper understanding of turbulence.

In conclusion, turbulence remains as one of the least-well understood phenomena in all of physics. It can be said that merely a development in computational methods and models will not be sufficient; we must make large strides in the mathematics surrounding partial differential equations, and the Navier-Stokes Equations, to further our understanding of turbulence.

Works Cited

- Jackson, J.D. "Reynolds The Scientist", University of Manchester. Accessed August 25, 2023. https://personalpages.manchester.ac.uk/staff/jdjackson/Osborne%20Reynolds/oreynb.htm #OS421
- MIT 10.301. "Introduction To Fluid Mechanics" MIT, Accessed August 24, 2023.<u>https://stuff.mit.edu/afs/athena/course/10/10.301/www2002/movies_for_assignment_1.html</u>
- Succi, Sauro. "Lecture 4 The Navier Stokes Equations : Turbulence", Harvard University, 2015. Accessed August 26,

2023.https://projects.iq.harvard.edu/files/ac274_2015/files/lecture4.pdf

Narasimha, R. "Turbulence on Computers", Current Science Vol. 64, No. 1, 1993.

- Cadence CFD, "Large Eddy Simulations (LES) Turbulence Model Basics", Cadence System Analysis. Accessed August 30, 2023.<u>https://resources.system-analysis.cadence.com/blog/msa2022-large-eddy-simulation</u> <u>s-les-turbulence-model-basics</u>
- Coleman, Gary N and Richard Sandberg, "A Primer on Direct Numerical Simulation of Turbulence – Methods, Procedures and Guidelines", School of Engineering Sciences, University of Southampton, 2012. Accessed August 27, 2023.https://eprints.soton.ac.uk/66182/1/A primer on DNS.pdf
- Veritasium. (2020, June 11). Turbulent Flow is MORE Awesome Than Laminar Flow [Video]. YouTube. <u>https://www.youtube.com/watch?v=guRoWTYfxMs</u>

The Evolution of Korean Hangul as a Social Development Process By Songeun Lee

Abstract

The Korean alphabet, Hangul, is a source of pride for today's Korean people. It has received praise from international scholars because the letters ingeniously reflect the shape of speech organs, such as the tongue, used to pronounce them. However, the original Hangul was neither perfect nor as widely acclaimed as it is today. Throughout the 600 years since its creation, Hangul has undergone many changes and evolved alongside Korean society. This essay analyzes how Hangul has acted as a catalyst for transformation and liberation over time. Three important historical periods will be discussed: the impact of Hangul on literature and social status in the 16th century; the revitalization of Hangul during the Japanese colonization of Korea; and Hangul's current status in modern-day South Korea's language education. By presenting the evolution of Hangul and the development of Korean society as a mutual process, this research fills a gap in existing literature about Korean orthography and sociolinguistics.

Introduction

Since its creation in 1443, the Korean alphabet system called Hangul has been both a point of pride and contention for the Korean people. Prior to Hangul, the people of Joseon used Chinese characters to express the Korean language because of the close relationship between Korea and China. Using a borrowed script was challenging due to phonetic and notational differences between the two languages. The use of Chinese characters also led to divisions in society because the elite had time and resources to invest in classical Chinese education and commoners were often illiterate or partially illiterate due the lack of proper education. This greatly hindered communication across the state. Noticing this problem, Joseon dynasty ruler King Sejong the Great created the phonetic alphabet Hangul that was easier to read and write. It was met with great skepticism at first, but now it is considered King Sejong's greatest accomplishment, and Koreans take pride in the fact that international scholars praise it for its scientific characteristics. It is clear that Hangul's status among the people and the purpose for which it is used has changed over the past 600 years.

Thus, this essay will trace the key historical factors that contributed to the evolution of the Hangul. Section I discusses how the creation of the Hangul in the 15th century supported the restructuring of existing social hierarchies and the development of middle class and women's literature. Section II analyzes how Japan's assimilationist language policy during the colonization of Korea was actually a catalyst for Korea's national pride in Hangul. It was during this time that organizations such as The Korean Language Society were born, and significant practical and grammatical language developments occurred. Section III outlines changes in the use of Hangul in South Korea that occurred after the Korean War, such as the great debate about reintroducing Chinese characters, or Hanja, to the formal education system. While English education has had an important impact on the Korean language, including the introduction of loanwords and Konglish, such developments fall beyond the scope of this paper. Finally,

implications for the future of the Korean language will also be discussed.

The Influence of Hangul on 16th Century Korean Society and Literature

Before the creation of Hangul, Chinese characters (called Hanja) served as the foundation for most Korean vocabulary. Hanja characters were ideograms, one character represented an idea, and in combination the characters could be combined into words with complex meanings. Early forms of literature on the Korean peninsula were all written and passed down in Hanja; transnational notes by the government officials were written in Hanja; state exams or imperial examinations for the most honorable positions in the kingdom required applicants to create poetic lines in Hanja. Therefore, Hanja was highly pervasive in the Joseon dynasty, and the ability to use the Hanja was necessary for all levels of administrative work. Only members of the upper and elite classes had the time and resources to gain high levels of proficiency in Hanja, so they worked in most government positions and circulated novels in Hanja amongst themselves. People in the lower social classes lacked the education to gain the same competency in Hanja, so they rarely understood written literature or occupied government positions. Not only did this create societal division, it also made communicating with the population difficult.

Recognizing this problem, Hangul was created by King Sejong the Great in 1443 to facilitate understanding of the written word among the population. In the preface of the Hunminjeongeum 'Correct Sounds to Teach the People,' King Sejong declared:

The language of this country is different from that of China, so that it is impossible (for us Koreans) to communicate by means of Chinese characters. Therefore, among the unlearned people, there have been many who, having something to put into words, have in the end been unable to express themselves. Feeling sorry for this, I have newly made twenty-eight letters only because I wish them to be easy for everyone to learn and convenient for use in daily life. (Lee 38).

Unlike Hanja, Hangul was a phonetic alphabet, so it was easier to transcribe the Korean language. Moreover, the original alphabet only used 28 letters, so commoners could learn to read and write it in a fraction of the time it took to master Hanja. However, it was not immediately accepted because it lacked the prestige of Hanja and ruling classes were reluctant to relinquish the power of the written word to commoners (Hur 720). Commoners, however, were quick to learn and use Hangul for themselves. Resistance against the full acceptance of Hangul created a diglossic situation in which Hanja was still considered the high language and Hangul was the low language. As Kim-Renaud writes, Hangul "was used mainly by women and Buddhist monks until the end of the 19th century, and it was widely dismissed as Enmun (vernacular writing)" (164).

While Hangul was first dismissed by the ruling class, it had a transformative effect on the middle class and women in society. One of the most obvious effects occurred in the world of literature. Previously, literature had been inaccessible to women, especially those of lower

classes, because they did not learn Hanja. With the creation of Hangul, however, three new forms of writing emerged. The first genre included narratives completely written in Hangul such as *"Romance of the Banquet for Moon Viewing...*that focus[ed] on family proprietary issues"; the second genre included novels written in both Hanja and Hangul such as *A Nine Cloud Dream*; and the third were Hangul translations of Chinese vernacular narratives (Pastreich 77). Women widely read, copied, and circulated these novels amongst themselves. According to Pastreich, Hangul translations of Chinese narratives were the "primary impetus for the development of new literary genres" because Chinese novels included topics such as "the chicanery of merchants, the bravado of bandits, and the romance of the boudoir," which had been forbidden in Korean novels at the time (78). Sure enough, it was after the creation of Hangul and women's circulation of the translated novels that they began to write narratives for themselves which touched on everyday topics and some topics mentioned in the translated novels. Although they were not recognized by their work due to the lack of women rights at the time, women's increased exposure to literature led to a subtle change in the diverse participation of Korean literature. Their literary practices formed the basis for modern Korean literature.

The usage of Hangul among women also impacted long-standing government practices because women of all classes were more empowered to take part in politics once they could use Hangul to express themselves in writing. The people of Joseon could write petitions to local and district officials to ask for help or solve disputes. While it was legal for all subjects to petition for help, including women and people of lower classes, those who did not understand Hanja could not draft and submit petitions for themselves because official government documents were maintained in Hanja. After Hangul was created, however, women began "actively appropriated their knowledge and submitted petitions in vernacular Korean instead" (Kim 674). This shows how they actively challenged the social conventions at the time. Eventually government officials debated whether petitions written in Hangul should be accepted because there were no formal laws that dictated the language of petitions. They concluded that petitions in Hangul should be accepted because "rejecting them countered the state's intention of redressing grievances" (Kim 674). Over time, all official government documents were kept in both Hanja and Hangul. Thus, women's championing of Hangul played a part in transforming rigid conventions in government and society.

Japanese Colonial Language Policy in Korea

Japan's development of an industrialized economy at the end of the 19th century enabled the country to gain immense wealth and power, so Japan sought to unify Asia under its regime. Because the Joseon Dynasty was experiencing internal divisions and government corruption, the Japanese government was able to invade the peninsula quite easily. On August 29, 1910, Japanese imperialism completely usurped the sovereignty of the Korean Empire and occupied it as a colony. The Japanese government brought in political and military forces to implement various cultural policies to fully transform life on the peninsula. Japanese colonization was one of the darkest periods of Korean history. In addition to all the human rights violations against the Korean people, Japan also tried to elevate Japanese as the dominant language and eliminate Korean, including Hangul, from daily use.

After colonizing the peninsula, Japan implemented an assimilationist language policy. That is, to indoctrinate Korean citizens into the newly formed Japanese Empire, they imposed a ban on the Korean language and forced Koreans to learn Japanese. In August 1911, Japan promulgated the Joseon Education Ordinance which had three main goals: the first was to establish an educational system in Korea that would "foster citizens loyal to the Japanese Empire"; the second goal was spread the Japanese language; and the third goal was to prevent the establishment of higher education institutions in Korea and provide vocational training instead (Encyclopedia of Korean Culture). In order to achieve this goal, Japan brought the management of Korean schools under the control of the Japanese Government General, who controlled choices about school teachers, curriculum, and textbooks. According to Hur, the Japanese government banned textbooks about history, geography, and Korean language arts "because the materials were believed to encourage or promote anti-Japanese thought," and new textbooks were written entirely in Japanese (727). Because Japan used Chinese characters in addition to their modern syllabic writing system, this means that Hanja was once again forced on Korean society. Classroom instruction and school ceremonies were conducted in Japanese as well. Korean language class time was made optional, then eliminated altogether. Even outside of the classroom, they forced Koreans to take Japanese names, and Koreans were punished for speaking Korean in public.

During this dark period, Koreans began to rely on Hangul as a form of resistance against Japanese rule. Many philosophers and activists working for Korean independence formed an organization called The Joseon Language Society. The Joseon Language Society was the successor to the Joseon Language Research Society, which was established in 1921 for the purpose of "studying the correct legal principles of the Joseon language" (National Institute of Korean History). The Joseon Language Research Society studied Hangul spelling and carried out activities to develop and promote Hangul. For example, In 1926, in celebration of the 480th anniversary of the publication of King Sejong's Hunminjeongeum, 'Correct Sounds to Teach the People,' Hunminjeongeum Proclamation Day was named 'Hangul Day,' and they held a commemorative ceremony to promote the spread of Hangul.

The Joseon Language Research Association also organized the Chosun Language Dictionary Compilation Committee, which aimed to systematize the meaning of the Korean language and Korean writing through compiling a Hangul dictionary. To create a dictionary, they needed a unified standard language and spelling, so in December 1930, the Association decided to enact a unified Korean spelling system. In January 1931, the Joseon Language Research Society evolved into the Joseon Language Society, an institution for "research and unification of Joseon language literature," and more actively promoted the Korean dictionary compilation project (National Institute of Korean History). Unfortunately the dictionary was never completed because a member of the Society was captured by the Japanese government and tortured into confessing that the society was working towards Korean independence from Japan. So, the Japanese government moved to ban Korean study more strictly than before (Hur 732). Nevertheless, the work of the Joseon Language Association to preserve and formalize the Korean language through the development of Hangul is the primary reason for Korea's standardized language today.

Modern Language Education in Korea

After Japan was forced to relinquish control of Korea at the end of World War II, the Korean peninsula became the battlefield of the Korean War, which eventually divided the peninsula into North and South Korea. Despite sharing a history, language, and culture, the two countries developed differently because of opposing ideologies. Eventually the languages in each respective country also shifted to use different dialects and intonations. South Korea especially saw an influx of loanwords into their Korean vocabulary as a result of globalization. However, the advent of English and English education did not stop the centuries old debate about Hangul and Hanja in the writing conventions.

Education is essential to control how a language functions in society. This was proven when the Japanese government implemented compulsory education policies that decreased the importance of the Korean language. As a result of colonization, "many of the words formed by Hanja characters in Korean school textbooks have strong Japanese influence" (Huffman 3). After the Korean War, the Korean language became a mandatory subject in all Korean schools, and Hanja was part of compulsory education because people thought it was still essential to learning more advanced Korean vocabulary. It was not until 1971 that Hanja instruction was removed from elementary schools and restricted in middle and high schools. The language of education continues to be one of the most controversial topics in 21st century Korea due to the rising competitiveness in an increasingly unequal society.

In the early 2000s, there were some complaints about students struggling with Korean vocabulary because the words in their textbooks are Sino-Korean (i.e. derived from Hanja). To address the growing problem, the Seoul Metropolitan Office of Education tried to reinstate Hanja instruction in elementary schools, but they were met with strong and immediate opposition. Students, parents, and Hangul advocates gathered to create the Headquarters for Movement Against Hanja in Elementary School Textbooks, a group which threatened to demand the resignation of Education Minister Hwang Woo-yea if the policy were implemented (Huffman 3). They claimed that the policy would add unnecessary stress to students who are already learning English at a young age. Furthermore, they argued that the policy was not aimed at helping students; it was meant as an economic boon for companies who administered Hanja certification exams. Because of the backlash, the policy was not enforced.

In 2019, the Ministry of Public Administration and Security issued a press release that announced that the Ministry would remove difficult Chinese characters from public documents (Ministry of Public Administration and Security). The Ministry of Public Administration and Security selected 80 difficult Chinese characters or Japanese words used in public documents and changed them to simple Korean words. Moreover, the Ministry of Culture, Sports and Tourism and the Ministry of Government Legislation, as well as private organizations, have been making efforts to purify the Korean language by changing loanwords and Japanese terms into Korean. Experts are investigating how these changes to the language would impact the range of vocabulary of generations moving forward.

In the case of North Korea, Kim Il-sung started the Chinese character abolition project in earnest in 1948 (Encyclopedia of Korean Culture). While no actual policies have been implemented in South Korea on the abolitions of any characters, the Chinese character abolition project in North Korea had specific purposes of completing the illiteracy eradication project, popularizing educational culture, and promoting the existence of Hangul. The abolition of the use of Chinese characters arose from a series of limitations with Chinese characters and the demand to develop the Korean language and writing with independence. Several policies were implemented to prevent the use of Chinese characters in overall writing life and left the whole country eradicating Chinese characters in everyday language by 1945.

Conclusion

This paper has outlined three ways that Hangul, or the use of Hangul, has changed throughout Korea's history. During the Joseon dynasty when Hangul was invented, it facilitated social disruption and increased the agency of the middle class and women in both public and literary spheres. When Japan banned the use of Korean and eliminated it from schools, societies and associations championed Hangul as the language of their independence and resistance. It was during that time that dialects of Korean were recorded and the language was standardized into a uniform system. Still, as a result of the Japanese occupation, education significantly valued teaching Hanja until large-scale policy revisions removed the compulsory Hanja education in the 1970s. Today, there is still a back and forth about the importance of Hanja as a supplement to Hangul that reflects the abundance of Sino-Korean words in the modern Korean vocabulary. The most recent developments in this debate seem to suggest that Korea will move towards removing words derived from Hanja and replace them with native Korean words instead. This is an indication that, true to the nature of language change, the language is undergoing yet another change due to the pressures of modern society. One thing is for certain: Hangul will remain an essential part of Korean identity and expression moving forward.

Works Cited

- Encyclopedia of Korean Culture. "조선교육령(朝鮮教育令) 한국민족문화대백과사전." 한국민족문화대백과사전, https://encykorea.aks.ac.kr/Article/E0051933. Accessed 10 August 2023.
- Huffman, Keiko. "Hanja Education in Korean Elementary Schools." (2022).
- Hur, Minjung. "Hangeul as a tool of resistance against forced assimilation: making sense of the framework act on Korean language." *Wash. Int'l LJ* 27 (2017): 715.
- Kim, Jisoo M. "Women's Legal Voice: Language, Power, and Gender Performativity in Late Chosŏn Korea." *The Journal of Asian Studies* 74.3 (2015): 667-686.
- Kim-Renaud, Young-Key. "Mixed script and literacy in Korea." *Korean Linguistics* 12.1 (2004): 161-182.
- Lee, Don-Ju. "An Explanation of Understanding Hunmin-jong. um." by Shin Sang-Soon, Lee Don-Ju, & Lee Hwan-Mook(1990): 37-86.
- Ministry of Public Administration and Security. 행정안전부, 30 August 2022, https://www.mois.go.kr/frt/bbs/type010/commonSelectBoardArticle.do;jsessionid=9ynXJ dlC-9VT8zGPDhZa7VuK.node50?bbsId=BBSMSTR_00000000008&nttId=69101&bbs TyCode=BBST03&bbsAttrbCode=BBSA03&authFlag=Y&pageIndex=1&searchCnd=& searchWrd=&searchCode1=&searchCode2=. Accessed 9 September 2023.
- National Institute of Korean History. "교과서 용어해설." 교과서 용어해설 | 우리역사넷, http://contents.history.go.kr/front/tg/view.do?treeId=0202&levelId=tg_004_2840&ganad a=&pageUnit=1. Accessed 15 August 2023.
- Pastreich, Emanuel Yi. "The Transmission and Translation of Chinese Vernacular Narrative in Chosŏn Korea: Han'gŭl Translations and Gentry Women's Literature." *Korean Studies*(2015): 75-105.
- Silva, David J. "Missionary contributions toward the revaluation of Hangeul in late nineteenth-century Korea." (2008): 57-74.

The Homeostasis of the Gut-Brain Axis in Human and Animal Models of Alzheimer's By Anvi Sinha

Abstract

The Gut-Brain Axis (GBA) is a bidirectional channel through which the enteric nervous system in the abdomen and the central nervous system in the cranium can communicate. The gut microbiome strongly influences the GBA and is composed of a variety of bacterial strains (e.g. E. col, B. bifidum) which are influenced by a variety of factors during growth and development. In this review, I will summarize studies focused on the influences of psychostimulants, early life adversity, and diet on human and animal microbiota as well as their influence on neurodegeneration in the brain. Drugs, stress, and diet are known to increase inflammation and disrupt the blood-brain barrier (BBB). In turn, activation of pro-inflammatory cytokines lead to neuroinflammation in the brain which have been shown to increase the susceptibility to Alzheimer's disease (AD) and overall cognitive impairment.

Introduction

The gut microbiome refers to the vast community of microorganisms residing in the gastrointestinal tract. Comprising bacteria, fungi, viruses, and other microorganisms, the gut microbiome exerts a profound influence on human health and plays a crucial role in numerous physiological processes. Recent studies have uncovered the bidirectional communication pathway between the gut and the brain, known as the gut-brain axis [1]. This intricate system enables constant signaling and information exchange between the gut microbiome and the central nervous system (CNS) through neural, endocrine, and immune pathways.

Mounting evidence suggests that alterations in the composition and function of the gut microbiome can impact brain health and contribute to neurodegenerative diseases such as Alzheimer's disease (AD). AD is a progressive neurodegenerative disorder characterized by memory loss, cognitive decline, and behavioral changes. It is the most common form of dementia, affecting millions of people worldwide [2]. Despite extensive research, the exact mechanisms underlying AD pathogenesis remain elusive. Recent scientific advancements have shed light on the potential role of the gut microbiome and the gut-brain axis in the development and progression of AD. Understanding the complex interplay between the gut microbiome and the brain has emerged as a fascinating frontier in Alzheimer's research. The gut microbiome produces an array of metabolites, including short-chain fatty acids, neurotransmitters, and immunomodulatory molecules, which can directly influence CNS function and neuroinflammation [3]. Additionally, the gut microbiome interacts with the intestinal barrier, modulates the immune system, and influences systemic inflammation, all of which have been implicated in AD pathogenesis.

Emerging studies have highlighted specific microbial imbalances in individuals with the disease, caused by a variety of environmental factors including early life stress [4], poorly balanced diets, and substance abuse [5]. These alterations are associated with increased

neuroinflammation, oxidative stress, amyloid-beta (A β) plaque deposition, and tau hyperphosphorylation—hallmarks of AD pathology. Furthermore, animal models and preclinical investigations have demonstrated that manipulating the gut microbiome can influence cognitive function, amyloid deposition, and neuroinflammation. Understanding the complex relationship between the gut microbiome, the gut-brain axis, and AD holds tremendous potential for developing novel diagnostic tools and therapeutic interventions. It may open doors for innovative therapeutic strategies, such as microbiota-based interventions, dietary interventions, or modulation of the gut-brain axis, to restore microbiome homeostasis and alleviate AD-related symptoms [6].

In this review, I will discuss the various factors that contribute to the degeneration of the gut microbiome, and the consequently affected mechanisms in the gut-brain axis. I will look at recent findings from human and animal studies, highlight potential mechanisms underlying the gut-brain connection in AD pathogenesis, and explore promising avenues for therapeutic interventions. By delving into the interplay between the gut microbiome and the brain, we hope to contribute to the growing body of knowledge and inspire further research aimed at unraveling the mysteries of Alzheimer's disease.

Psychostimulant Function in the Brain

Substance use disorder encompasses the detrimental effects of psychoactive drugs on the body and brain, and it is categorized into three main classes: hallucinogens, depressants, and stimulants. Among these, psychostimulants have gained particular attention due to their association with significant morbidity and profound impact on emotions. This class includes substances such as amphetamine, cocaine, 3,4-methylenedioxymethamphetamine (MDMA), caffeine, as well as other prescribed stimulants. At low doses, psychostimulants induce heightened alertness, enhanced cognitive function, improved mental attention, and sociability. Conversely, fatigue, sexual stimulation, and appetite are reduced because of excessive psychostimulant use. As the dose increases to moderate levels, euphoria and cognitive impairment start to emerge. Finally, high doses of psychostimulants can lead to tremors, agitation, psychosis, rapid muscle breakdown, and, with repeated use, substance use disorder[7].

Psychostimulants encompass a diverse range of chemical classes, including coca alkaloids (cocaine, benzoylecgonine), substituted phenethylamines, phenylpropanolamine, and aminoaryloxazolines. Cocaine, a benzoylecgonine derivative, while amphetamine is the prototype structure for synthetic psychostimulants and possesses both clinical anorexic and stimulant properties. Methamphetamine, a synthesized derivative of amphetamine, exhibits heightened wakefulness and stronger euphoric effects that can lead to rapid abuse, addiction, and other psychiatric consequences [8].

Cocaine and amphetamines increase dopamine levels in both the CNS and the periphery through inhibiting or reversing the dopamine transporter (DAT) [9]. Interestingly, various populations of leukocytes, such as B cells, T cells, and monocytes, express different subtypes of dopamine receptors. When these receptors are stimulated by dopamine, it can influence their

production of cytokines and other inflammatory mediators [10]. Emerging evidence suggests that cocaine itself might activate PRRs (Pattern Recognition Receptors) and induce an independent inflammatory response, distinct from its influence on dopamine, through several other mechanisms [11].

Animal Models of Stimulant Use Disorder (SUD)

Neuroinflammation resulting from psychostimulant use has been observed in various animal models[12]. Glial cells are implicated in the activation process, with methamphetamine inducing dose-dependent microglial activation throughout the brain [13]. Studies have shown that inhibiting microglial activation using minocycline or the toll-like receptor 4 (TLR-4) antagonist ibudilast reduces the rewarding effects of stimulants in mice [14]. However, the precise mechanism underlying microglial activation by psychostimulants remains unclear, and ongoing research aims to elucidate this aspect [12].

Recent studies on rats suggest that cocaine, in particular, may bind to the TLR4 receptor, which is expressed on microglia in the central nervous system [15]. In silico and in vitro modeling conducted by Northcutt et al. (2015) [16] demonstrated that cocaine binds to the TLR4 receptor in mice. Subsequent studies indicated that signaling through TLR4 is essential for cocaine induced dopamine release, conditioned place preference (CPP), and self-administration of cocaine). Other studies have revealed that TLR4 activity in the ventral tegmental area (VTA) affects the reinstatement of cocaine seeking via IL-1 signaling [17]. However, Tanda et al. (2016) [18] disputed the effects of TLR4 antagonists on dopamine release, suggesting non specific effects on behavior. The role of TLR4-mediated signaling in substance use models remains an area of ongoing research, holding potential significance in addiction neurobiology.

Research on SUD models has highlighted the significance of cytokine and chemokine signaling, impacting brain plasticity and behavior [19]. Recent work by Calipari et al. (2018) identified upregulated granulocyte colony-stimulating factor (G-CSF) after prolonged cocaine exposure, with G-CSF treatment enhancing neuronal activation in the nucleus accumbens (NAc) and prefrontal cortex post-acute cocaine injection. G-CSF heightened cocaine-related behaviors like conditioned place preference (CPP), locomotor sensitization, and self-administration. In contrast, Lewitus et al. (2016) [20] observed increased microglial production of TNF- α in the NAc following cocaine, impacting dopamine D1 receptor-containing neurons. TNF- α knockout mice showed heightened cocaine sensitization, while TNF- α inhibition reduced it. However, Northcutt et al. (2015) suggested that IL-1ß via TLR4 signaling enhanced cocaine-induced dopamine release and behavioral responses. The conflicting outcomes arise from differing emphases in research. Lewitus investigated locomotor sensitization and glutamatergic plasticity in the nucleus accumbens (NAc), whereas Northcutt concentrated on cocaine's rewards and dopamine release from VTA neurons. This suggests that these similar pathways might exert distinct influences on drug responses, highlighting the need for further research on these molecular mechanisms.

Additionally, chemokine signaling has implications for psychostimulant use disorders.

Introducing chemokine monocyte chemoattractant protein 1 (MCP-1) into rat midbrains elevates locomotor activity and striatal dopamine release [21], whereas knocking out the MCP-1 receptor CCR2 diminishes cocaine-induced locomotor sensitization and ERK signaling activation in the striatum [22]. Additionally, prolonged cocaine exposure elevates stromal cell-derived factor 1 (SDF-1) levels in both humans and mice (Araos et al., 2015), and infusing SDF-1 protein into the intraventricular region or VTA enhances cocaine-induced locomotion [23].

Substance Use Disorder in Humans

Numerous studies have investigated the impact of cocaine on the peripheral expression of inflammatory mediators. Some studies have reported that acute cocaine use alters cytokine expression in serum or isolated peripheral leukocytes [24]. Abstinent cocaine users have been found to exhibit decreased serum levels of MCP-1 and several pro-inflammatory cytokines, including IL-6, IL-17, and TNF- α . However, there have been conflicting findings, with some studies indicating higher levels of IL-6 and decreased levels of the anti-inflammatory cytokine IL-10 in active cocaine users [25].

Patients with SUDs exhibited increased serum expression of pro-inflammatory markers in response to drug cues or unpleasant images, suggesting a pro-inflammatory response to certain environmental stimuli [26]. These changes in peripheral immune function may potentially contribute to the development or persistence of psychostimulant use disorders. While peripheral inflammation may not directly correlate with central inflammatory processes, peripheral monocytes and T cells have demonstrated significant effects on the brain and behavior and can potentially cross the blood-brain barrier [27]. Postmortem examinations of the midbrain in cocaine addicts have shown an increase in activated microglia and activated macrophages, along with a decrease in dopamine cell bodies [28]. PET studies using tracers that bind to activated glial cells have indicated increased microglial activation in subjects with methamphetamine use disorder, with a negative correlation between the duration of abstinence and microglial activity [29]. However, another PET study in patients with long-term cocaine use disorder did not find differences in microglial binding between controls and patients with cocaine use disorder [30]. These findings suggest the involvement of peripheral and central inflammatory mechanisms in psychostimulant use disorders, but further research is needed to fully understand these processes.

Psychostimulant effects on the Gut-Brain Axis

Recent research is exploring the gut-immune-brain axis (often referred to as the gut-immune-brain axis [31]), focusing on how the gut microbiome influences addictive disorders. While most studies have centered on affective disorders, neurodevelopmental disorders, and neurodegenerative diseases [32], there is a growing body of evidence indicating that changes in the gut microbiome may impact addictive behaviors. For example, in a study by Kiraly et al. in 2016 [33], researchers observed that depleting the gut microbiome in mice resulted in increased sensitivity to low doses of cocaine, altered gene expression in the nucleus

accumbens, and changes in crucial pathways related to addiction.

While research on the interaction between the gut microbiome and psychostimulants is still limited, translational studies suggest that the gut microbiome can influence responses to drugs of abuse, and conversely, psychostimulant treatment can alter the composition of the microbiome. A study involving rats injected with methamphetamine every other day reported modest increases in bacterial diversity, minor shifts in bacterial families, and a decrease in the short-chain fatty acid propionate in the caecal content. Short-chain fatty acids (SCFAs) produced by the gut microbiota are linked to the integrity of the blood-brain barrier and play a crucial role in microbiota and cocaine's behavioral effects [33]. They enhance the integrity of tight junctions in the blood-brain barrier, maintaining its selective permeability. SCFAs also have anti-inflammatory and neuroprotective properties, helping prevent disruptions in blood-brain barrier function.

Furthermore, in a study conducted by Volpe et al. in 2014 [35], individuals with cocaine use disorder, both with and without HIV, were compared to healthy controls. The findings revealed that cocaine use disorder was associated with significant changes in the gut microbiome. Specifically, non-HIV cocaine users exhibited a notable increase in the presence of the Bacteroidetes phylum. Additionally, there was a strong indication of higher levels of bacterial DNA in the serum of cocaine users, indicating a potential increase in bacterial translocation from the gut, which could contribute to inflammation within the body.

The Manifestation of Psychostimulant Use in Alzheimers

The depletion of the gut microbiome by excessive use of psychostimulants can be modeled by germ-free (GF) animals raised in a sterile, gnotobiotic environment, preventing the postnatal colonization of their gastrointestinal (GI) tract. Studies comparing GF mice (ones that lack an intestinal microbiota) with conventionally reared mice (ones that possess a normal gut microbiota) have revealed important insights into the role of the microbiota-gut-brain axis in cognitive function. GF mice exhibited deficits in non-spatial and working memory tasks, such as the novel object recognition test and spontaneous alternation in the T-maze. Furthermore, a decrease in brain derived neurotrophic factor (BDNF) expression in the hippocampus was observed among the GF mice [36]. BDNF is a critical neurotrophin for synaptic plasticity and cognitive function, with its reduced levels associated with higher amyloid-beta burden in AD patients [37]. Notably, Neufeld and colleagues discovered a sex-dependent modulation of BDNF expression: while female GF mice showed upregulated BDNF mRNA expression in the hippocampus, a significant decrease was noted in their male counterparts [38]. In conclusion, these findings highlight the intricate relationship between BDNF, cognitive function, and sex-specific responses in GF mice.

Furthermore, GF mice demonstrated increased adult hippocampal neurogenesis, which is known to play a vital role in cognitive processes [39]. These mice also displayed microglial immaturity and defects in microglial proportions, resulting in impaired innate immune responses that may contribute to the pathogenesis of neurological diseases, including AD [40]. Prior

research by Sudo et al. found decreased expression of N-methyl-D-aspartate (NMDA) receptor 2A (NR2A) mRNA in the cortex and hippocampus of GF mice compared to specific pathogen-free mice [41]. Similarly, a more recent study by Neufeld identified a downregulation of the NMDA receptor NR2B subunit mRNA in the central amygdala of GF mice [38]. The NMDA receptor is crucial for synaptic plasticity and cognitive function, and increased activation of this receptor may be significant in A β -dependent synaptic dysfunction seen in AD [42]. Germ-free studies have proven valuable in shedding light on the underlying mechanisms of the microbiota-gut-brain axis and its implications for cognitive function and the pathogenesis of neurological disorders, including AD.

In a large-scale nationwide cohort study conducted in Taiwan, researchers analyzed data from 17,075 patients with amphetamine-related disorders (ARD) and 51,225 individuals in the control group without ARD. Among the ARD cohort, 1,751 individuals developed dementia, compared to 2,147 cases in the control group (883.10 vs. 342.83 per 100,000 person-years) [43]. Both amphetamine use disorder and amphetamine-induced psychotic disorders were found to be linked to an increased risk of developing overall dementia, Alzheimer's dementia, vascular dementia, and other dementia subtypes. This study provides substantial evidence indicating a strong association between amphetamine related disorders and the risk of dementia, encompassing various dementia types.

Early Life Stress on Brain Function and Gut Microbiome

During the initial years of life, the developing brain is extremely susceptible to the influence of environmental factors. The social ecology of childhood encompasses a range of both positive and negative experiences that form a framework for adolescents to achieve age-specific developmental milestones [44]. The experiences encountered during this critical period can make permanent changes to the structure and functioning of the brain through epigenetic modifications, such as DNA methylation/demethylation and chromatin modifications, and heighten the vulnerability to mental illnesses later in life [45]. Frequent low grade stressors (such as insecurity and inattention), large life changes, and traumatic experiences (abuse/neglect) disrupt the ecology and result in harmful effects on children's health extending into adulthood [46].

When parents provide appropriate and sufficient care during the early years, it has a positive impact on the offspring's brain development, but inadequate parental caregiving can pose a risk for mental illness in the offspring during adulthood [47]. Early life adversity (ELA) refers to adverse experiences such as neglect, physical and emotional abuse that occur in the early stages of life [48]. Extensive research, encompassing studies involving humans and experimental animal models, has revealed a strong association between ELA and various issues, including conduct disorders, impaired cognitive development, and a heightened risk of dementia, Alzheimer's disease (AD), and other related neurodegenerative conditions.

The impact of adverse childhood experiences (ACEs) is a growing concern for public health [49]. Vincent Felitti designed the ACEs survey, which yielded that a notable 63.5% of

adults have reported experiencing at least one ACE, and 12% reported enduring four or more such events [50]. Subsequent investigations, encompassing children as well, have unveiled even graver rates, ranging from 67% to a staggering 98% [51]. This issue is particularly critical for preschool children, who remain exceptionally susceptible to child abuse, neglect, and domestic violence [52]. Their constrained ability to express these traumas behaviorally and verbally poses a significant challenge to reporting, and ACEs from early childhood are often concealed [53]. The U.S. Children's Bureau documented that in 2018 alone, a distressing 678,000 children fell victim to abuse and neglect. Among these harrowing cases, 60.8% involved neglect, 10.7% were linked to physical abuse, 7.0% were sexual abuse, and an alarming 15.5% endured the anguish of two or more forms of abuse [54]. This vividly underscores the urgency of addressing and mitigating the escalating prevalence of ACEs to safeguard the well-being of the most vulnerable members of society. ACE exposure has profound effects on child development, with increased risk across various aspects of life, including cognitive development, quality of life, social functioning, economic prospects, psychiatric well-being, and physical health outcomes [55]. Despite recent efforts to address the public health challenges posed by ELA, current understanding of this issue is still limited and should be further explored .

Animal Models of Early Life Stress

Various animal models have been established to replicate the long-term effects of early life adversity (ELA) seen in humans [56]. These animal models allow researchers to conduct studies under controlled conditions, compensating for the limitations in human research and ethical restrictions. They involve exposing the subjects to different forms of stress (separation, resource scarcity, restraint stress, social defeat stress) and manipulating the amount and quality of parental care during the early postnatal period.

The maternal separation or deprivation procedure is where mother-pup interactions are altered during the early postnatal period. In maternal separation, pups are separated from their mother for a specific period each day (2–5 hours) over several days to induce acute, predictable stress levels [57]. Maternal deprivation involves a more prolonged separation, usually one 24-hour

session [58]. These procedures have been associated with long-term behavioral abnormalities and impaired cognitive performance in the exposed pups [59]. Chronic early life stress situations involve subjecting the pups to multiple prolonged periods. Pups may be exposed to a few types of stressors, including forced swimming, physical restriction, placement on an elevated platform, and foot shock exposure during early postnatal days (PND), leading to significant physical and psychological stress. An early foot shock paradigm has been developed to mimic early trauma or abuse experiences [60]. In an early foot shock paradigm procedure, the pups are placed in a closed, dark, electric shock apparatus during early postnatal time windows and subjected to continuous electric foot shocks to mimic early abuse experiences [61].

Offspring receiving higher levels of maternal caregiving display elevated neurotrophic factors and improved spatial learning and memory [62]. Researchers revealed poor cognitive

performance in adult rodents with a history of maternal separation or deprivation [63]. Interestingly, cognitive deficits resulting from maternal deprivation appear to be more pronounced in female animals on postnatal day 40 (PND 40), suggesting an age-dependent and hormone-related susceptibility to cognitive impairment in females [62]. In mice subjected to maternal deprivation, cognitive impairment becomes more evident with age, as observed in middle-aged mice (1.4 years old) in a visual-discrimination task. Reduced levels of brain-derived neurotrophic factor (BDNF) and synapse-related proteins, such as postsynaptic density 95 (PSD95) and synaptophysin [64], along with fewer mature neurons, have been detected in the hippocampus and prefrontal cortex of animals experiencing maternal separation or deprivation, providing further evidence of poor maternal care's impact on brain development [65]. Studies have revealed that animals exposed to sporadic maternal care exhibit progressive cognitive deficits in adulthood, accompanied by impaired hippocampal long-term potentiation (a molecular basis of learning and memory), dendritic atrophy, and synaptic degeneration [66]. Mice exposed to LBN from postnatal day 2 to day 9 showed reduced survival of newborn neurons in the hippocampus, leading to altered cognitive performance [67].

Chronic exposure to unavoidable plantar electroshock during the early post-weaning period in rodents leads to impaired spatial memory in adulthood, evident through poor performance in the Y-maze or Morris water maze [68]. Rats exposed to a single platform and acute swimming stress during adolescence also exhibit inferior cognitive performance in adulthood, highlighting the potential long-lasting effects of even brief stress experiences early in life on cognitive health [69]. Altogether, findings from animal models provide valuable insights into the interplay between ELA and later cognitive impairment.

Early Life Adversity in Humans

ELA encompassing instances of physical, emotional, or sexual abuse, neglect, and other unfavorable environmental conditions in the early stage of life [70]. Twenty years ago, a retrospective investigation made the first identification of robust connections between adverse childhood experiences and a heightened susceptibility to major diseases [52], resulting in an escalation in concerns on this topic. Conducting invasive research on humans poses challenges, many human-based studies have proven that unfavorable encounters during this vulnerable developmental phase can escalate the likelihood of various adult-onset conditions - not only psychiatric disorders and cardiovascular ailments but also diabetes mellitus and neurodegenerative diseases [71].

Tools like the Adverse Childhood Experiences (ACEs) questionnaire are utilized in public health initiatives to assess, comprehend, and prevent health outcomes associated with childhood trauma [72]. However, it's essential to consider other preventable sources of early life stress beyond ACEs, such as food and housing insecurity, bullying, discrimination, inattentive parenting, or family separations. Unfortunately, clinicians do not routinely screen for trauma or assess a child's social ecology, partly because there is a lack of validated, objective metrics that can be measured over time. Vanaelst et al. conducted a systematic review of various inventories that assess the occurrence of adverse childhood events [49]. These inventories were derived from existing stress questionnaires and modified to inquire about significant life events, chronic environmental stressors (such as family, school, relationships, and health), and other stressors related to childhood experiences [73]. The concept of cumulative risk was initially proposed by Holmes and Rahe in their Social Readjustment Rating Scale [74]. Later, this approach was adapted to study child adversities by Rutter [75] and then used in other research studies [76]. The cumulative risk approach is based on the idea that dealing with challenges in one area of life is

generally more manageable than facing challenges in multiple areas simultaneously. It is straightforward to use and understand, it shows robust statistical associations that engage non academic stakeholders [52], it takes into account the co-occurrence of various childhood adversities [77], and it helps to identify individuals who are at the highest risk for experiencing negative outcomes [78].

Felitti, along with Robert Anda and their team, conducted the ACEs Study, surveying 9,508 adults to explore ten adverse experiences [79]. The study revealed significant associations between adverse childhood experiences (ACEs) and various negative health outcomes. Compared to individuals with no ACEs, those exposed to four or more ACEs faced 4- to 12-fold higher risks for drug abuse, alcoholism, depression, and suicide, as well as 2- to 4-fold increased risks for smoking, poor health, multiple sexual partners, sexually transmitted diseases, and 1.4- to 1.6-fold increased risks for physical inactivity and obesity [80]. Furthermore, ACEs displayed linear relationships with heart disease, cancer, lung disease, fractures, liver disease, and multiple other health outcomes. These findings spurred further research and influenced social policy to address the rising prevalence of ACEs, especially in pediatric age groups [73].

Research exploring the connection between early life adversity (ELA) and neurological consequences has gained significant attention due to the positive association between adverse childhood experiences and poor health outcomes later in life [52]. Numerous clinical studies have investigated ELA as a potential risk factor for cognitive impairment, focusing on child neglect, physical abuse, and parental separation. The parent-child coregulation, which involves mutual influence and coordination of emotional, behavioral, and physiological states, plays a critical role in the healthy development of children, impacting various domains, including emotional and cognitive functioning [81]. Longitudinal studies have demonstrated that secure infant-caregiver attachment predicts adult competence in areas such as educational attainment, occupational success, and social functioning [82]. A Helsinki birth cohort study revealed that men separated from their parents during World War II scored lower in cognitive reasoning tasks both at age 20 and later at age 70 compared to non separated subjects [83]. Moreover, the adverse effects of ELA extend to various cognitive outcomes, including general cognition and working memory [63]. Poly-victimization, experiencing multiple forms of victimization during a specific period, further amplifies the detrimental effects of ELA, particularly in cases of physical/emotional abuse, harsh parenting, and domestic violence.

The Romanian orphanage studies support the lasting effects of childhood neglect and deprivation on cognitive and emotional development [84]. Individuals raised in institutions with severe deprivation exhibited lower executive functioning and a higher risk of psychopathology compared to their non-institutionalized peers. Early childhood deprivation was also associated with structural brain changes in adulthood, with adoptees experiencing smaller total-brain volumes, lower intelligence quotient, and increased attention deficit/hyperactivity disorder symptoms. Cross-sectional studies utilizing scales with high internal consistency, validity, and test-retest reliability have shown that increased ELA exposure is linked to compromised cognitive flexibility, processing speed, and working memory [85]. Moreover, these negative effects may be exacerbated in individuals with depression, as evidenced by smaller orbitofrontal cortex and hippocampal volumes compared to never-depressed individuals. The existing human studies provide evidence that exposure to ELA is a risk factor for developing cognitive impairment later in life. These findings underscore the importance of addressing early life adversity and its potential long-term consequences on cognitive health.

Early Life Stress effect on the Gut-Brain Axis

As indicated previously, an abundance of recent research indicates that the gut microbiota has a significant impact on brain function, forming bidirectional interactions known as the brain-gut microbiome axis [86]. The immune system, the vagus nerve, the enteric nervous system, and microbial-derived intermediates have been identified as mechanisms for these interactions [87], which play a crucial role in neuroimmune signaling. Disruptions in the normal gut microbiota can affect CNS neurotransmission [88].

Stress has been found to alter gut microbiota and disrupt intestinal barrier integrity [89], and researchers are now focusing on how early life adversity (ELA) affects the brain-gut-microbiome axis. ELA has been associated with altered systemic immune responses, increased visceral sensation, and changes in the fecal microbiota in young animals [90]. Studies have also shown that ELA-induced visceral hypersensitivity is partially mediated by alterations in specific gut bacteria [91]. Sex-dependent gut dysbiosis has been observed in mice exposed to multi-hit ELA, with distinct changes in the abundance of certain bacterial genera in male and female mice [92]. These alterations in gut microbiome resemble those observed in early AD. Additionally, ELA exposed animals exhibited elevated pro-inflammatory cytokines in their colons [93]. Many findings suggest that the gut microbiota plays a crucial role in brain function and cognitive health, and disruptions in the gut-brain communication from stress and early life experiences contribute to cognitive impairment.

Early Life Stress Impact on the Microbiome of Animal Models

In rodents, early life stress (ELS) has been shown to impact the gut microbiome, with lasting effects into adulthood [94]. An early study involved infant macaques from their mothers for one week, resulting in reduced fecal Lactobacillus levels and increased stress-related behaviors in the macaques [95]. Another study in rats found that ELS-exposed adults had

changes in gut microbiota and higher levels of corticosterone, TNF- α , and IFN- γ compared to non-ELS rats

[90]. In mice, ELS increased levels of Bifidobacterium bifidum, Lactobacillus, Clostridium leptum, and Clostridium coccoides, and these effects were mitigated by adrenalectomy [96]. A significant rat study showed that ELS reduced the Firmicutes:Bacteroidetes ratio in the adult gut and increased taxa associated with inflammation, such as Akkermansia, Flexibacter, and Prevotella [97].

Mice subjected to social disruption stress for two hours daily over six days experienced a reduction in gut microbial diversity and richness [98]. The social disruption stressor involved an aggressive male mouse being placed into the home cage of the resident mice. Immediately following the stressor, levels of gut *Bacteroides* were lower and *Parabacteroides* were higher compared with non-stressed controls. At fifteen hours post-stressor, levels of bacteria in the genus *Roseburia* were increased compared with controls, along with levels of proinflammatory cytokines, including interleukin-6 (IL-6) and MCP-1. Later studies in rodents have found similar stress-induced alterations in the gut microbiota. For instance, exposure to a single two-hour social disruption stressor altered gut microbial community composition, particularly reducing abundance of the genus *Lactobacillus* [99]. This social disruption stressor increased cytokine production in mice, but only in mice with intact microbiota, not in germ-free animals, similarly suggesting that gut microbiota may moderate stress-induced inflammation [100].

Recent research suggests that ELS may have different impacts on males and females. Mice exposed to various forms of ELS showed sex-dependent differences in gut microbiota, behavior, and gene expression in the prefrontal cortex [92]. ELS affected the abundance of specific taxa in males, including Lachnospiraceae and Porphyromonadaceae families, unclassified Firmicutes, and Bacteroides, Lactobacillus, and Alloprevotella genera. In females, ELS impacted Lactobacillus and Mucispirillum genera. Another study found increased fecal bacteria of the Bacteroides genus and decreased bacteria of the Lachnospiraceae family in both sexes of rats. However, specific differences were observed in each sex, including changes in relative abundance of certain genera and variations in cytokine levels [93]. Restoring the gut barrier of ELS-exposed rat pups through pharmacological inhibition of myosin light chain kinase normalized relative abundance of several taxa in adulthood and normalized behaviors and corticosterone levels [101].

Additionally, genotype may play a role in vulnerability to the effects of ELS. In rats, the impact of ELS on gut microbiota was influenced by the serotonin transporter (5-HTT) genotype, with diminished 5-HTT expression exacerbating the shift towards an inflammatory profile [102]. This was characterized by higher abundance of taxa such as Desulfovibrio, Mucispirillum, and Fusobacterium.

Early Life Stress on the Human Gut Brain Axis

In the clinical laboratory, acute stressors offer a standardized method for measuring the physiological response to mild stress in humans. One commonly used stressor is the Trier Social

Stress Test (TSST), which involves public speaking and reliably increases cortisol and proinflammatory cytokine levels in adults. Only one published study has explored the link between the gut and chronic stress with acute laboratory stressors. A sample of healthy pregnant women underwent the TSST, and their cytokine and cortisol responses to the stressor were assessed. Then, stool samples were collected to assess gut microbial community composition. The IL-6 response was positively associated with the abundance of Bacteroides and negatively correlated with Clostridiales, Lachnospiraceae, Dialister, and Enterobacteriaceae. The tumor necrosis factor-alpha (TNF- α) response was positively associated with the abundance of Bacteroides, Prevotella, and Megasphaera and negatively correlated with Ruminococcaceae. The C-reactive protein (CRP) response was positively associated with the abundance of Ruminococcaceae and Megasphaera, but serum cortisol response was positively associated with the abundance of Rikemllaceae and Dialister and negatively correlated with Bacteroides [103].

Several studies have investigated the connections between childhood adversities and the gut microbiome, both in real-time and in adulthood, revealing interesting associations. In a study focusing on infants in the neonatal intensive care unit (NICU) during their first six weeks of life, higher stress scores were linked to the presence and relative abundance of specific gut genera, namely Proteus and Veillonella [104]. In healthy five-to-seven-year-old children, the gut microbiome was associated with parent-child dysfunction, and the abundance of gut B. fragilis was linked to reduced family turmoil and improved behavioral outcomes [105].

Moving into adulthood, psychiatrically healthy women with a history of multiple childhood adversities displayed altered gut microbiota, particularly differential abundance of Prevotella, Erysipelotrichaceae, and Phascolarctobacterium [103]. Another study examined the impact of adversity in infancy, such as institutional or foster care, on gut microbiome composition in adolescence, revealing lasting effects on diversity [106]. In adults, those with a history of trauma and PTSD showed differences in the abundance of certain gut phyla. Moreover, childhood adversity was associated with specific gut metabolites, indicating a potential link between gut function and brain connectivity in ACE-exposed adults [107].

Overall, these findings from human and animal models highlight the intricate connections between early life stress, gut microbiota, and various physiological and behavioral responses, demonstrating the significance of considering sex and genetic factors in understanding the impact of ELS on gut-brain interactions.

Early Life Stress in Alzheimer's

Recent research has highlighted the role of gut microbiome abnormalities in the development of Alzheimer's disease (AD). Notably, a significant contrast has been observed in the gut microbiota between individuals with AD and those who are healthy [108]. Additionally, individuals with mild cognitive impairment display comparable gut microbiota changes to AD patients [109]. These findings suggest a potential link between the gut microbiome and AD pathogenesis.

Animal models of Early Experiences on Cognitive Impairment

The potential connection between early-life adversity (ELA) and Alzheimer's disease (AD) has been extensively studied in rodent models. In one study, APPswe/PS1dE9 mice exposed to limited bedding and nesting materials (LBN) exhibited aggravated A β plaque load at 10 months of age, accompanied by increased glial activation and inflammatory signals in the hippocampus [110]. LBN exposure also led to higher levels of A β 40 and A β 42 in the hippocampus and elevated the expression of β -site APP-cleaving enzyme 1 (BACE1), a critical enzyme involved in A β processing and production in this mouse model [111]. LBN exposure resulted in synaptic damage and exacerbated cognitive impairment.

Researchers have explored the effects of maternal separation on AD disease progression in various transgenic mouse models of AD. Hui et al. demonstrated that chronic maternal separation worsened cognitive deficits and led to increased A^β plaque formation and neural damage in adult APPswe/PS1dE9 mice [112]. Another study by Tanaka and colleagues focused on vascular pathological changes following maternal separation. They observed narrowed vessels in the prefrontal cortex with decreased capillary pericyte coverage and disruption of the blood-brain barrier (BBB) in both amyloid precursor protein (APP) wild-type and heterozygous APP mutant (AppNL-G-F/wt) mice, which resulted from microglial activation. Maternally separated AppNL-G-F/wt mice also exhibited exacerbated cognitive impairment at four months of age [113]. Results suggest that ELA can elevate the risk of developing AD-like pathology even in the absence of AD risk genes. The gut-brain axis is proposed as a common pathogenic mechanism through which ELA affects AD pathology. Analysis of the gut microbiota in transgenic AD animals and healthy controls using 16S rRNA gene sequencing revealed distinct compositions [14]. Intriguingly, germ-free 3×Tg AD mice, lacking gut microbiota, exhibited significant reductions in cerebral amyloid plaques and neurofibrillary tangles compared to mice with normal gut microbiota. Additionally, transplantation of microbiota from healthy animals alleviated amyloid burden and tau pathology [114], while gut microbiota from AD individuals worsened AD progression and impaired cognitive function in healthy animals.

In animal studies, young adults subjected to maternal separation showed altered systemic immune responses, increased visceral sensation, and changes in fecal microbiota [90]. Specific gut microbial populations, like Butyricimonas, Butyricicoccus, and Corynebacterium, partially mediated the ELA-induced visceral hypersensitivity. Additionally, the gut dysbiosis observed in ELA-exposed mice mirrored gut microbiome changes seen in early AD [91]. Similar gut barrier disruption and inflammatory responses were observed in ELA-exposed piglets [115], and significant gut microbiome alterations have been found in humans with a history of ELA. These findings suggest that disruptions in the brain-gut-microbiome axis contribute to ELA-induced cognitive impairment, but the exact mechanisms and specific microbiota involved remain to be elucidated. In rats exposed to maternal separation, activation of microglia and increased pro-inflammatory factors were observed [116]. Activation of the stress system can also influence blood-brain barrier permeability, facilitating the flow of peripheral inflammatory factors into the brain, potentially contributing to chronic inflammation in ELA-related cognitive

impairment or AD [117]. However, further research is required to comprehensively understand the mechanisms through which ELA triggers chronic systemic inflammation and neuroinflammation.

Contributions of Early Life Stress on Alzheimer's Pathology in Humans

Numerous studies consistently link early-life adversity (ELA) to a higher risk of developing Alzheimer's disease (AD) and other dementias. Norton et al. followed 4108 subjects aged 65 to 105 for 18 months, revealing a higher number of confirmed AD cases within 18 months in those who experienced parental death during childhood [118]. Similarly, an Australian study using the Childhood Trauma Questionnaire (CTQ) found that individuals with higher CTQ scores were more likely to receive an AD diagnosis based on National Institute of Aging/Alzheimer's Disease Association criteria [119]. Another longitudinal study of 2682 males investigated the association between childhood stress and late-life dementia and AD, observing a higher prevalence of AD among those who experienced various childhood stressors [120].

Japan, facing an increasing prevalence of dementia, has conducted several cohort studies to explore the interplay between ELA and dementia prevalence. Utilizing the Adverse Childhood Experience Questionnaire, which covers family violence, physical and psychological abuse, neglect, parental death, parental divorce, and parental mental illness, these studies reported an increased number of clinically confirmed dementia cases within a 3-year follow-up period in participants with three or more adverse childhood experiences [121]. Furthermore, individual-level social capital scores were found to be a variable influencing this vulnerability, with increased dementia risk observed primarily in participants with low social capital [122].

These findings underscore the substantial risk associated with various forms of early-life adversity (ELA) for developing dementia or Alzheimer's disease (AD), regardless of the diversity of ELA experiences. While the gut microbiome is considered a key factor in this connection, only a limited number of studies have explored its impact on human cognition compared to animal studies. One such study linked gut microbiota composition in both obese and non-obese individuals to cognitive performance, including speed, attention, and cognitive flexibility in a Trail Making Test. The study also revealed changes in neural activity in brain regions like the thalamus, hypothalamus, and amygdala, suggesting that obesity influences both gut microbiota composition and subsequent cognitive function [123].

Notably, a probiotic mixture containing B. longum and different Lactobacillus strains showed positive effects on cognitive function and metabolic status in Alzheimer's disease patients [124]. Patients diagnosed with fibromyalgia demonstrated cognitive improvements in impulsive choice and decision-making following a multispecies probiotic intervention [125], a group with an altered microbiome, as indicated by disrupted microbiota metabolites [126]. These collective findings suggest the potential efficacy of probiotics in enhancing cognitive function both in healthy individuals and clinical populations with conditions like Alzheimer's disease. Nevertheless, more research is needed to understand the mechanisms behind how specific strains or interventions can modulate cognition and the limitations that exist in this

regard.

The accumulation of A β peptide and abnormal forms of tau protein are considered traditional indicators of AD, but they may not directly imply causality [127]. Beyond viruses, bacteria have also been associated with AD pathogenesis. Studies on GF APP-PS1 mice [128] revealed reduced A β pathology compared to conventional animals of the same background, supporting the potential role of the microbiota in A β biology and AD pathogenesis [129]. that microorganisms are involved at crucial stages of the AD pathogenic cycle, and further research is needed to determine whether A β accumulation represents a malfunctioning immune response or acts as a disease driver [131].

Two studies have investigated the gut microbiota composition in individuals with Alzheimer's disease (AD) compared to controls. In the first study, which included 25 AD patients with mild dementia and 25 matched controls, researchers found that AD patients had reduced gut microbiota richness and diversity. Specific changes were observed in various taxa, including a decrease in Firmicutes, an increase in Bacteroidetes, and a decrease in Bifidobacterium. These alterations in the gut microbiota were strongly correlated with the pathological load of A β and phosphorylated tau species in a subgroup of patients who underwent lumbar puncture for AD markers. The second study also identified changes in microbiota composition in AD at different taxonomic levels, although there were some variations compared to the first study. Notably, the Firmicutes:Bacteroidetes ratio was different, which is of interest considering the well-established link between AD and type II diabetes mellitus [132][108].

Conclusion

Emerging research has illuminated a compelling link between the gut microbiome and Alzheimer's disease in both human and animal models. The interplay between gut bacteria and brain health underscores the potential of microbiome-targeted interventions in managing or preventing cognitive decline. The influence of psychostimulant use and early life stress on the gut microbiome reflects the intricate bidirectional relationship between mental health, environmental factors, and microbial composition. As we delve deeper into understanding these connections, new avenues for therapeutic strategies and interventions that target the gut-brain axis, like alterations in diets, are promising for addressing Alzheimer's disease and more neurological disorders.

Works Cited

- Socała, K., et al., The role of microbiota-gut-brain axis in neuropsychiatric and neurological disorders. Pharmacological Research, 2021. 172: p. 105840. 2. Góralczyk-Bińkowska A, S.-K.D., Kozłowska The Microbiota-Gut-Brain Axis in Psychiatric Disorders. Int J Mol Sci, 2022.
- 3. Agirman G, Y.K., Hsiao EY, Signaling inflammation across the gut-brain axis. Science, 2021.
- 4. Zhihai Huang, J.D.J., and Quanguang Zhang, Early life adversity as a risk factor for cognitive impairment and Alzheimer's disease. Translational Neurodegeneration, 2023(25).
- 5. Rebecca S. Hofford, S.J.R., Drew D. Kiraly, Neuroimmune mechanisms of psychostimulant and opioid use disorders. Eur J Neurosci, 2020.
- 6. Rutsch A, K.J., Ronchi F., The Gut-Brain Axis: How Microbiota and Host Inflammasome Influence Brain Physiology and Pathology. Front Immunol., 2020.
- 7. Benjamin Boutrel, G.F.K., What Keeps Us Awake: the Neuropharmacology of Stimulants and Wakefulness Promoting Medications. Sleep, 2004. 27(6).
- 8. M. Douglas Anglin, C.B., Brian Perrochet, Ewa Stamper, Samia Dawud-Noursi, History of the Methamphetamine Problem. 2011.
- 9. Peter W. Kalivas, N.D.V., The neural basis of addiction: a pathology of motivation and choice
- Rodrigo Arreola, S.A.-H., Gilberto Pérez-Sánchez, Enrique Becerril-Villanueva, Carlos Cruz-Fuentes, Enrique Octavio Flores-Gutierrez, María Eugenia Garcés-Alvarez, Dora Luz de la Cruz-Aguilera, Emilio Medina-Rivero, Gabriela Hurtado-Alvarado, Saray Quintero-Fabián, Lenin Pavón, Immunomodulatory Effects Mediated by Dopamine. Journal of Immunology Research, 2016.
- Northcutt, A., Hutchinson, M., Wang, X. et al, DAT isn't all that: cocaine reward and reinforcement require Toll-like receptor 4 signaling. Mol Psychiatry 2015. 12. Lacagnina, M., Rivera, P. & Bilbo, S., Glial and Neuroimmune Mechanisms as Critical Modulators of Drug Use and Abuse. Neuropsychopharmacol, 2017.
- 13. Thanos, P.K., et al., Chronic Methamphetamine Effects on Brain Structure and Function in Rats. PLoS One, 2016. 11(6): p. e0155457.
- Chen, H., T. Uz, and H. Manev, Minocycline affects cocaine sensitization in mice. Neurosci Lett, 2009. 452(3): p. 258-61.
- 15. Zhang, L. and C.C. Wang, Inflammatory response of macrophages in infection. Hepatobiliary Pancreat Dis Int, 2014. 13(2): p. 138-52.
- 16. Northcutt, A.L., et al., DAT isn't all that: cocaine reward and reinforcement require Toll like receptor 4 signaling. Mol Psychiatry, 2015. 20(12): p. 1525-37.
- Brown, K.T., et al., Innate immune signaling in the ventral tegmental area contributes to drug-primed reinstatement of cocaine seeking. Brain Behav Immun, 2018. 67: p. 130-138.
- Tanda, G., et al., Lack of Specific Involvement of (+)-Naloxone and (+)-Naltrexone on the Reinforcing and Neurochemical Effects of Cocaine and Opioids. Neuropsychopharmacology, 2016. 41(11): p. 2772-81.

- Wohleb, E.S., T. Franklin, M. Iwata, and R.S. Duman, Integrating neuroimmune systems in the neurobiology of depression. Nat Rev Neurosci, 2016. 17(8): p. 497-511. 20. Lewitus, G.M., et al., Microglial TNF-α Suppresses Cocaine-Induced Plasticity and Behavioral Sensitization. Neuron, 2016. 90(3): p. 483-91.
- Guyon, A., et al., Long term exposure to the chemokine CCL2 activates the nigrostriatal dopamine system: a novel mechanism for the control of dopamine release. Neuroscience, 2009. 162(4): p. 1072-80.
- 22. Trocello, J.M., et al., Implication of CCR2 chemokine receptor in cocaine-induced sensitization. J Mol Neurosci, 2011. 44(3): p. 147-51.
- 23. Trecki, J. and E.M. Unterwald, Modulation of cocaine-induced activity by intracerebral administration of CXCL12. Neuroscience, 2009. 161(1): p. 13-22.
- Pedraz, M., et al., Sex differences in psychiatric comorbidity and plasma biomarkers for cocaine addiction in abstinent cocaine-addicted subjects in outpatient settings. Front Psychiatry, 2015. 6: p. 17.
- 25. Levandowski, M.L., A.R. Hess, R. Grassi-Oliveira, and R.M. de Almeida, Plasma interleukin-6 and executive function in crack cocaine-dependent women. Neurosci Lett, 2016. 628: p. 85-90.
- Fox, H.C., et al., Immune system inflammation in cocaine dependent individuals: implications for medications development. Hum Psychopharmacol, 2012. 27(2): p. 156-66.
- 27. Hodes, G.E., et al., Neuroimmune mechanisms of depression. Nat Neurosci, 2015. 18(10): p. 1386-93.
- 28. Little, K.Y., et al., Decreased brain dopamine cell numbers in human cocaine users. Psychiatry Res, 2009. 168(3): p. 173-80.
- 29. Sekine, Y., et al., Methamphetamine causes microglial activation in the brains of human abusers. J Neurosci, 2008. 28(22): p. 5756-61.
- 30. Narendran, R., et al., Cocaine abuse in humans is not associated with increased microglial activation: an 18-kDa translocator protein positron emission tomography imaging study with [11C]PBR28. J Neurosci, 2014. 34(30): p. 9945-50.
- 31. Fung, T.C., C.A. Olson, and E.Y. Hsiao, Interactions between the microbiota, immune and nervous systems in health and disease. Nat Neurosci, 2017. 20(2): p. 145-155. 32. Foster, J.A., L. Rinaman, and J.F. Cryan, Stress & the gut-brain axis: Regulation by the microbiome. Neurobiol Stress, 2017. 7: p. 124-136.
- Kiraly, D.D., et al., Alterations of the Host Microbiome Affect Behavioral Responses to Cocaine. Sci Rep, 2016. 6: p. 35455.
- 34. Bercik, P., et al., The intestinal microbiota affect central levels of brain-derived neurotropic factor and behavior in mice. Gastroenterology, 2011. 141(2): p. 599-609, 609.e1-3.
- 35. Volpe, G.E., et al., Associations of cocaine use and HIV infection with the intestinal microbiota, microbial translocation, and inflammation. J Stud Alcohol Drugs, 2014. 75(2): p. 347-57.

- 36. Gareau, M.G., et al., Bacterial infection causes stress-induced memory dysfunction in mice. Gut, 2011. 60(3): p. 307-17.
- 37. Carlino, D., M. De Vanna, and E. Tongiorgi, Is altered BDNF biosynthesis a general feature in patients with cognitive dysfunctions? Neuroscientist, 2013. 19(4): p. 345-53. 38. Neufeld, K.M., N. Kang, J. Bienenstock, and J.A. Foster, Reduced anxiety-like behavior and central neurochemical change in germ-free mice. Neurogastroenterol Motil, 2011. 23(3): p. 255-64, e119.
- 39. Ogbonnaya, E.S., et al., Adult Hippocampal Neurogenesis Is Regulated by the Microbiome. Biol Psychiatry, 2015. 78(4): p. e7-9.
- 40. Erny, D., et al., Host microbiota constantly control maturation and function of microglia in the CNS. Nat Neurosci, 2015. 18(7): p. 965-77.
- Sudo, N., et al., Postnatal microbial colonization programs the hypothalamic-pituitary adrenal system for stress response in mice. J Physiol, 2004. 558(Pt 1): p. 263-75. 42. Lakhan, S.E., M. Caro, and N. Hadzimichalis, NMDA Receptor Activity in Neuropsychiatric Disorders. Front Psychiatry, 2013. 4: p. 52.
- 43. Tzeng, N.S., et al., Association between amphetamine-related disorders and dementia-a nationwide cohort study in Taiwan. Ann Clin Transl Neurol, 2020. 7(8): p. 1284-1295.
 44. Yuan, B., J. Li, K. Li, and M. Chen, Longstanding health risk across the life course: The influence of early-life experience on health status throughout the life span. J Biosoc Sci, 2023. 55(4): p. 708-734.
- 45. Kundakovic, M. and F.A. Champagne, Early-life experience, epigenetics, and the developing brain. Neuropsychopharmacology, 2015. 40(1): p. 141-53.
- 46. Cameron, J.L., et al., Social Origins of Developmental Risk for Mental and Physical Illness. J Neurosci, 2017. 37(45): p. 10783-10791.
- 47. Tottenham, N., Early Adversity and the Neotenous Human Brain. Biol Psychiatry, 2020. 87(4): p. 350-358.
- 48. Hoeijmakers, L., et al., A preclinical perspective on the enhanced vulnerability to Alzheimer's disease after early-life stress. Neurobiol Stress, 2018. 8: p. 172-185. 49.
 Vanaelst, B., et al., Epidemiological approaches to measure childhood stress. Paediatr Perinat Epidemiol, 2012. 26(3): p. 280-97.
- 50. Lacey, R.E. and H. Minnis, Practitioner Review: Twenty years of research with adverse childhood experience scores - Advantages, disadvantages and applications to practice. J Child Psychol Psychiatry, 2020. 61(2): p. 116-130.
- 51. Mersky, J.P., J. Topitzes, and A.J. Reynolds, Impacts of adverse childhood experiences on health, mental health, and substance use in early adulthood: a cohort study of an urban, minority sample in the U.S. Child Abuse Negl, 2013. 37(11): p. 917-25.
- 52. Felitti, V.J., et al., Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The Adverse Childhood Experiences (ACE) Study. Am J Prev Med, 1998. 14(4): p. 245-58.

- 53. Garner, A.S. and J.P. Shonkoff, Early childhood adversity, toxic stress, and the role of the pediatrician: translating developmental science into lifelong health. Pediatrics, 2012. 129(1): p. e224-31.
- Lopez, M., et al., The social ecology of childhood and early life adversity. Pediatr Res, 2021. 89(2): p. 353-367.
- 55. Christian, C.W., The evaluation of suspected child physical abuse. Pediatrics, 2015. 135(5): p. e1337-54.
- Benmhammed, H., et al., Animal Models of Early-Life Adversity. Methods Mol Biol, 2019.
 2011: p. 143-161.
- 57. Levine, S., Infantile experience and resistance to physiological stress. Science, 1957. 126(3270): p. 405.
- 58. Ellenbroek, B.A., N. Derks, and H.J. Park, Early maternal deprivation retards neurodevelopment in Wistar rats. Stress, 2005. 8(4): p. 247-57.
- Levis, S.C., T.Z. Baram, and S.V. Mahler, Neurodevelopmental origins of substance use disorders: Evidence from animal models of early-life adversity and addiction. Eur J Neurosci, 2022. 55(9-10): p. 2170-2195.
- Zardooz, H., F. Sadeghimahalli, and F. Khodagholi, Early postnatal stress impairs insulin secretion in response to psychological stress in adult rats. J Endocrinol Invest, 2021. 44(2): p. 277-286.
- Abbink, M.R., E.F.G. Naninck, P.J. Lucassen, and A. Korosi, Early-life stress diminishes the increase in neurogenesis after exercise in adult female mice. Hippocampus, 2017. 27(8): p. 839-844.
- 62. Liu, D., et al., Maternal care, hippocampal synaptogenesis and cognitive development in rats. Nat Neurosci, 2000. 3(8): p. 799-806.
- 63. Yajima, H., et al., Early-life stress induces cognitive disorder in middle-aged mice. Neurobiol Aging, 2018. 64: p. 139-146.
- 64. Wang, A., et al., Early-Life Stress Alters Synaptic Plasticity and mTOR Signaling: Correlation With Anxiety-Like and Cognition-Related Behavior. Front Genet, 2020. 11: p. 590068.
- 65. Marco, E.M., et al., Maternal deprivation effects on brain plasticity and recognition memory in adolescent male and female rats. Neuropharmacology, 2013. 68: p. 223-31. 66. Wang, X.D., et al., Forebrain CRF¹ modulates early-life stress-programmed cognitive deficits. J Neurosci, 2011. 31(38): p. 13625-34.
- 67. Naninck, E.F., et al., Chronic early life stress alters developmental and adult neurogenesis and impairs cognitive function in mice. Hippocampus, 2015. 25(3): p. 309- 28.
- 68. Lu, C.Y., et al., Effects of Traumatic Stress Induced in the Juvenile Period on the Expression of Gamma-Aminobutyric Acid Receptor Type A Subunits in Adult Rat Brain. Neural Plast, 2017. 2017: p. 5715816.

- Avital, A. and G. Richter-Levin, Exposure to juvenile stress exacerbates the behavioural consequences of exposure to stress in the adult rat. Int J Neuropsychopharmacol, 2005. 8(2): p. 163-73.
- 70. McLaughlin, K.A., Future Directions in Childhood Adversity and Youth Psychopathology. J Clin Child Adolesc Psychol, 2016. 45(3): p. 361-82.
- Loria, A.S., D.H. Ho, and J.S. Pollock, A mechanistic look at the effects of adversity early in life on cardiovascular disease risk during adulthood. Acta Physiol (Oxf), 2014. 210(2): p. 277-87.
- 72. Bethell, C.D., et al., Methods to Assess Adverse Childhood Experiences of Children and Families: Toward Approaches to Promote Child Well-being in Policy and Practice. Acad Pediatr, 2017. 17(7s): p. S51-s69.
- 73. Oral, R., et al., Adverse childhood experiences and trauma informed care: the future of health care. Pediatr Res, 2016. 79(1-2): p. 227-33.
- 74. Holmes, T.H. and R.H. Rahe, The Social Readjustment Rating Scale. J Psychosom Res, 1967. 11(2): p. 213-8.
- 75. Rutter, M., Family, area and school influences in the genesis of conduct disorders. Book Suppl J Child Psychol Psychiatr, 1978(1): p. 95-113.
- 76. Sameroff, A., R. Seifer, M. Zax, and R. Barocas, Early indicators of developmental risk: Rochester Longitudinal Study. Schizophr Bull, 1987. 13(3): p. 383-94.
- 77. Dong, M., et al., The relationship of exposure to childhood sexual abuse to other forms of abuse, neglect, and household dysfunction during childhood. Child Abuse Negl, 2003. 27(6): p. 625-39.
- 78. Brown, D.W., et al., Adverse childhood experiences are associated with the risk of lung cancer: a prospective cohort study. BMC Public Health, 2010. 10: p. 20.
- 79. Thompson, L.A., et al., Specific adverse childhood experiences and their association with other adverse childhood experiences, asthma and emotional, developmental and behavioral problems in childhood. Pediatr Res, 2020. 88(1): p. 100-109.
- 80. Felitti, V.J., Adverse childhood experiences and adult health. Acad Pediatr, 2009. 9(3): p. 131-2.
- 81. Lobo, F.M. and E. Lunkenheimer, Understanding the parent-child coregulation patterns shaping child self-regulation. Dev Psychol, 2020. 56(6): p. 1121-1134.
- Paley, B. and N.J. Hajal, Conceptualizing Emotion Regulation and Coregulation as Family-Level Phenomena. Clin Child Fam Psychol Rev, 2022. 25(1): p. 19-43. 83. Pesonen, A.K., et al., Cognitive ability and decline after early life stress exposure. Neurobiol Aging, 2013. 34(6): p. 1674-9.
- Wade, M., C.H. Zeanah, N.A. Fox, and C.A. Nelson, Global deficits in executive functioning are transdiagnostic mediators between severe childhood neglect and psychopathology in adolescence. Psychol Med, 2020. 50(10): p. 1687-1694.
- 85. Saleh, A., et al., Effects of early life stress on depression, cognitive performance and brain morphology. Psychol Med, 2017. 47(1): p. 171-181.

- 86. Cryan, J.F., et al., The Microbiota-Gut-Brain Axis. Physiol Rev, 2019. 99(4): p. 1877-2013.
- Osadchiy, V., C.R. Martin, and E.A. Mayer, The Gut-Brain Axis and the Microbiome: Mechanisms and Clinical Implications. Clin Gastroenterol Hepatol, 2019. 17(2): p. 322-332.
- 88. Clarke, G., et al., The microbiome-gut-brain axis during early life regulates the hippocampal serotonergic system in a sex-dependent manner. Mol Psychiatry, 2013. 18(6): p. 666-73.
- 89. Deng, Y., et al., Involvement of the microbiota-gut-brain axis in chronic restraint stress: disturbances of the kynurenine metabolic pathway in both the gut and brain. Gut Microbes, 2021. 13(1): p. 1-16.
- 90. O'Mahony, S.M., et al., Early life stress alters behavior, immunity, and microbiota in rats: implications for irritable bowel syndrome and psychiatric illnesses. Biol Psychiatry, 2009. 65(3): p. 263-7.
- 91. Enqi, W., S. Jingzhu, P. Lingpeng, and L. Yaqin, Comparison of the Gut Microbiota Disturbance in Rat Models of Irritable Bowel Syndrome Induced by Maternal Separation and Multiple Early-Life Adversity. Front Cell Infect Microbiol, 2020. 10: p. 581974.
- 92. Rincel, M., et al., Multi-hit early life adversity affects gut microbiota, brain and behavior in a sex-dependent manner. Brain Behav Immun, 2019. 80: p. 179-192.
- 93. Park, H.J., S.A. Kim, W.S. Kang, and J.W. Kim, Early-Life Stress Modulates Gut Microbiota and Peripheral and Central Inflammation in a Sex-Dependent Manner. Int J Mol Sci, 2021. 22(4).
- 94. Jašarević, E., C.L. Howerton, C.D. Howard, and T.L. Bale, Alterations in the Vaginal Microbiome by Maternal Stress Are Associated With Metabolic Reprogramming of the Offspring Gut and Brain. Endocrinology, 2015. 156(9): p. 3265-76.
- 95. Bailey, M.T. and C.L. Coe, Maternal separation disrupts the integrity of the intestinal microflora in infant rhesus monkeys. Dev Psychobiol, 1999. 35(2): p. 146-55. 96. Amini-Khoei, H., et al., On the role of corticosterone in behavioral disorders, microbiota composition alteration and neuroimmune response in adult male mice subjected to maternal separation stress. Int Immunopharmacol, 2019. 66: p. 242-250.
- 97. Pusceddu, M.M., et al., N-3 Polyunsaturated Fatty Acids (PUFAs) Reverse the Impact of Early-Life Stress on the Gut Microbiota. PLoS One, 2015. 10(10): p. e0139721. 98. Bailey, M.T., et al., Exposure to a social stressor alters the structure of the intestinal microbiota: implications for stressor-induced immunomodulation. Brain Behav Immun, 2011. 25(3): p. 397-407.
- 99. Galley, J.D. and M.T. Bailey, Impact of stressor exposure on the interplay between commensal microbiota and host inflammation. Gut Microbes, 2014. 5(3): p. 390-6. 100. Allen, R.G., et al., The intestinal microbiota are necessary for stressor-induced enhancement of splenic macrophage microbicidal activity. Brain Behav Immun, 2012. 26(3): p. 371-82.

- 101. Rincel, M., et al., Pharmacological restoration of gut barrier function in stressed neonates partially reverses long-term alterations associated with maternal separation. Psychopharmacology (Berl), 2019. 236(5): p. 1583-1596.
- 102. El Aidy, S., et al., Serotonin Transporter Genotype Modulates the Gut Microbiota Composition in Young Rats, an Effect Augmented by Early Life Stress. Front Cell Neurosci, 2017. 11: p. 222.
- 103. Hantsoo, L., et al., Childhood adversity impact on gut microbiota and inflammatory response to stress during pregnancy. Brain Behav Immun, 2019. 75: p. 240-250. 104. D'Agata, A.L., et al., Effects of early life NICU stress on the developing gut microbiome. Dev Psychobiol, 2019. 61(5): p. 650-660.
- 105. Flannery, J.E., et al., Gut Feelings Begin in Childhood: the Gut Metagenome Correlates with Early Environment, Caregiving, and Behavior. mBio, 2020. 11(1).
- 106. Callaghan, B.L., et al., Mind and gut: Associations between mood and gastrointestinal distress in children exposed to adversity. Dev Psychopathol, 2020. 32(1): p. 309-328.
 107. Coley, E.J.L., et al., Early life adversity predicts brain-gut alterations associated with increased stress and mood. Neurobiol Stress, 2021. 15: p. 100348.
- 108. Zhuang, Z.Q., et al., Gut Microbiota is Altered in Patients with Alzheimer's Disease. J Alzheimers Dis, 2018. 63(4): p. 1337-1346.
- 109. Li, B., et al., Mild cognitive impairment has similar alterations as Alzheimer's disease in gut microbiota. Alzheimers Dement, 2019. 15(10): p. 1357-1366.
- 110. Hoeijmakers, L., et al., Early-life stress lastingly alters the neuroinflammatory response to amyloid pathology in an Alzheimer's disease mouse model. Brain Behav Immun, 2017.
 63: p. 160-175.
- 111. Lesuis, S.L., et al., Targeting glucocorticoid receptors prevents the effects of early life stress on amyloid pathology and cognitive performance in APP/PS1 mice. Transl Psychiatry, 2018. 8(1): p. 53.
- 112. Hui, J., et al., Maternal separation exacerbates Alzheimer's disease-like behavioral and pathological changes in adult APPswe/PS1dE9 mice. Behav Brain Res, 2017. 318: p. 18-23.
- 113. Tanaka, T., et al., Early-life stress induces the development of Alzheimer's disease pathology via angiopathy. Exp Neurol, 2021. 337: p. 113552.
- 114. Kim, M.S., et al., Transfer of a healthy microbiota reduces amyloid and tau pathology in an Alzheimer's disease animal model. Gut, 2020. 69(2): p. 283-294.
- 115. Ma, X., et al., Early-Life Intervention Using Exogenous Fecal Microbiota Alleviates Gut Injury and Reduce Inflammation Caused by Weaning Stress in Piglets. Front Microbiol, 2021. 12: p. 671683.
- 116. Roque, A., A. Ochoa-Zarzosa, and L. Torner, Maternal separation activates microglial cells and induces an inflammatory response in the hippocampus of male rat pups, independently of hypothalamic and peripheral cytokine levels. Brain Behav Immun, 2016. 55: p. 39-48.
- 117. Gómez-González, B. and A. Escobar, Altered functional development of the blood-brain barrier after early life stress in the rat. Brain Res Bull, 2009. 79(6): p. 376-87. 118. Norton, M.C., et al., Early parental death and remarriage of widowed parents as risk factors for Alzheimer disease: the Cache County study. Am J Geriatr Psychiatry, 2011. 19(9): p. 814-24.
- 119. Radford, K., et al., Childhood Stress and Adversity is Associated with Late-Life Dementia in Aboriginal Australians. Am J Geriatr Psychiatry, 2017. 25(10): p. 1097-1106. 120. Donley, G.A.R., E. Lönnroos, T.P. Tuomainen, and J. Kauhanen, Association of childhood stress with late-life dementia and Alzheimer's disease: the KIHD study. Eur J Public Health, 2018. 28(6): p. 1069-1073.
- 121. Tani, Y., T. Fujiwara, and K. Kondo, Association Between Adverse Childhood Experiences and Dementia in Older Japanese Adults. JAMA Netw Open, 2020. 3(2): p. e1920740.
- 122. Tani, Y., T. Fujiwara, and K. Kondo, Adverse Childhood Experiences and Dementia: Interactions With Social Capital in the Japan Gerontological Evaluation Study Cohort. Am J Prev Med, 2021. 61(2): p. 225-234.
- 123. Fernandez-Real, J.M., et al., Gut Microbiota Interacts With Brain Microstructure and Function. J Clin Endocrinol Metab, 2015. 100(12): p. 4505-13.
- 124. Akbari, E., et al., Effect of Probiotic Supplementation on Cognitive Function and Metabolic Status in Alzheimer's Disease: A Randomized, Double-Blind and Controlled Trial. Front Aging Neurosci, 2016. 8: p. 256.
- 125. Roman, P., et al., A Pilot Randomized Controlled Trial to Explore Cognitive and Emotional Effects of Probiotics in Fibromyalgia. Sci Rep, 2018. 8(1): p. 10965. 126. Malatji, B.G., et al., The GC-MS metabolomics signature in patients with fibromyalgia syndrome directs to dysbiosis as an aspect contributing factor of FMS pathophysiology. Metabolomics, 2019. 15(4): p. 54.
- 127. Braak, H. and E. Braak, Neuropathological stageing of Alzheimer-related changes. Acta Neuropathol, 1991. 82(4): p. 239-59.
- 128. Radde, R., et al., Abeta42-driven cerebral amyloidosis in transgenic mice reveals early and robust pathology. EMBO Rep, 2006. 7(9): p. 940-6.
- 129. Harach, T., et al., Reduction of Abeta amyloid pathology in APPPS1 transgenic mice in the absence of gut microbiota. Sci Rep, 2017. 7: p. 41802.
- 130. Kumar, D.K., et al., Amyloid-β peptide protects against microbial infection in mouse and worm models of Alzheimer's disease. Sci Transl Med, 2016. 8(340): p. 340ra72. 131. Stilling, R.M. and J.F. Cryan, Host response: A trigger for neurodegeneration? Nat Microbiol, 2016. 1(8): p. 16129.
- 132. Vogt, N.M., et al., Gut microbiome alterations in Alzheimer's disease. Sci Rep, 2017. 7(1): p. 13537.
- 133. Arnold, S.E., et al., Brain insulin resistance in type 2 diabetes and Alzheimer disease: concepts and conundrums. Nat Rev Neurol, 2018. 14(3): p. 168-181.

- 134. Manderino, L., et al., Preliminary Evidence for an Association Between the Composition of the Gut Microbiome and Cognitive Function in Neurologically Healthy Older Adults. J Int Neuropsychol Soc, 2017. 23(8): p. 700-705.
- 135. Cattaneo, A., et al., Association of brain amyloidosis with pro-inflammatory gut bacterial taxa and peripheral inflammation markers in cognitively impaired elderly. Neurobiol Aging, 2017. 49: p. 60-68.

Cholesterol Levels in Cultural Foods By Hannah Yin

Introduction

Cardiovascular diseases are diseases related to the heart and/or blood vessels. Heart disease is the leading cause of death in the United States, and one person in the US dies from this disease every 33 seconds. (1) Atherosclerosis is a condition that leads to most cases of heart diseases among people. This condition develops when cholesterol builds up on the inner walls of your arteries. The plaque that forms causes the arteries to be more narrow, making it more difficult for blood to flow through them, and the buildup can happen in any artery in your body. Although cholesterol can build up and cause many to have these cardiovascular diseases, it is carried in the blood in two major forms: HDL and LDL. High-density lipoprotein (HDL) cholesterol is considered the "good" cholesterol in the human body because it actually helps lower the risk for heart diseases and strokes. HDL works by absorbing cholesterol in the body and bringing it to the liver to be excreted from the body; but on the other hand, low-density lipoprotein (LDL) cholesterol is considered the "bad" cholesterol because it increases the risk of heart diseases since it has the ability to build up in the arteries, creating plaque. (2)

Most (if not all) humans consume food every single day to get energized and receive their daily nutrients. But not a lot of people are aware of what actually goes into their bodies when consuming different types of food. For someone who doesn't have risk factors for heart disease, their cholesterol intake should be no more than 300 milligrams (mg) a day. For someone who does have risk factors though, they should consume 200 mg or less of cholesterol. (3) Though keep in mind that cholesterol is only present in animal products such as meat, milk products, etc. Examples of foods that lower LDL cholesterol include oats, beans, eggplant, nuts, vegetable oils, soy, and fatty fish. (4) This effect makes these foods healthy to eat and helps lower the risk of heart disease and strokes. But there are foods that are healthy even though they contain high amounts of cholesterol. Lots of people fear eating high-cholesterol foods because of the increased risk of cardiovascular diseases, but research shows that eating healthy high-cholesterol foods is not harmful to your health. Examples of healthy high-cholesterol foods include eggs, cheese, shellfish, grass-fed beef, sardines, and whole-fat vogurt. (5) Even though they all contain high amounts of cholesterol, these foods contain other nutrients to make your plate even healthier. But beware of high-cholesterol foods that are unhealthy and can put you at risk of heart disease. Some examples include fried foods, fast food, processed meats, and some desserts. While it's not a bad idea to eat these from time to time, it puts you at risk when consuming these foods often or on a daily basis. These foods are also a big factor in weight gain and obesity.

Cholesterol Levels in Different Cuisines

Now that you understand the basics of cholesterol and its relationship with food, we can go deeper into the cholesterol levels of popular foods in different cultures. Meals in different parts of the world vary immensely and are made with distinct ingredients that make the meal unique to that country and culture. To start off, the United States of America has many different cultural foods from around the world thanks to its migratory history, but I'll talk about three meals that are unique to the USA. The first is jambalaya, which originated in South Louisiana, but is highly influenced by Africa and Spain. Jambalaya is made up of rice, tomato, bell pepper, celery, garlic, various seasonings, and different types of meats. The meats are generally andouille sausage, chicken or pork, and shrimp or crawfish, which cause this dish to have such high cholesterol levels. 1 cup of jambalaya (244 g) with meat and rice has 98 mg of cholesterol, while 1 cup of jambalaya with shrimp and rice has 262 mg of cholesterol. (6) The next dish is the classic meatloaf. Meatloaf is made up of pork, ground beef, lamb, veal, and seasonings/sauces. 1 medium slice of beef meatloaf (183 g) has around 123 mg of cholesterol. (7) The last dish from the USA is mac and cheese. Unlike the other two meals, this dish doesn't get its cholesterol from meats; rather, it gets the cholesterol from dairy products. Mac and cheese is made with macaroni pasta, cheese, milk, and butter. A 1 cup serving of regular mac and cheese (198 g) has 41 mg of cholesterol, while boxed mac and cheese (198 g) has only 26 mg of cholesterol. (8)

Now let's review the cholesterol levels of popular foods in Korea. Korean foods tend to have lots of meat in them, which is the source of cholesterol in most of the dishes. First is a very popular type of meat that a lot of people know around the world: bulgogi. Bulgogi is prepared using beef, mostly ribeye, pork, or even chicken, with the addition of marinating sauces. It has 56 mg of cholesterol in 3 ounces of beef. (9) The next dish is another popular favorite: bibimbap. Bibimbap is essentially rice topped with different meats, vegetables, and sauces, and then mixed up in a bowl. The ingredients include various vegetables (mushrooms, carrots, spinach, bean sprouts), beef mince, and sauces. This dish has 239 mg of cholesterol per serving (864 g), which is definitely surprising. (10) Korea is also famous for the many soups/stews they offer, so the last dish we will be reviewing is samgyetang, which translates to ginseng chicken soup. Its ingredients include a whole chicken, rice, ginseng, and other assorted options. 1 bowl of samgyetang (260 g) has 337.7 mg of cholesterol in it. (11) That's a lot!

After Korea, we have Italy, the home of pasta! The first dish is of course going to be pasta, and the one reviewed here is fettuccine alfredo. The sauce is made from parmesan, butter, and garlic, and when mixed with the fettuccine pasta, it makes this creamy sauce that tastes delicious. One serving (2 cups, 466 g) of this pasta contains around 200 mg of cholesterol, which is two-thirds of the recommended daily intake for cholesterol. (12) The next dish is meat lasagna, which is actually another form of pasta. It is made with layers of fresh pasta that's smothered in a bolognese sauce made with beef, pork, carrots, tomatoes, and more. 1 center piece of lasagna (255 g) has around 43 mg of cholesterol (13), but a side piece and corner piece have 21 and 19 mg of cholesterol, respectively. (14) The last popular dish to review from Italy is prosciutto di parma, which is also called parma ham. This cured raw ham is usually served as an appetizer at restaurants. For a serving of 2 slices, prosciutto di parma has 20 mg of cholesterol in it. (15)

Moving onto another part of Europe, we have Russia. The first dish that's very popular in Russia is beef stroganoff. The two main ingredients in this meal are sauteed beef and sour cream, but you can also add vegetables like onions or mushrooms. 1 cup, or 256 grams of beef

stroganoff contains around 92 mg of cholesterol. (<u>16</u>) Next on the Russian menu is borscht, which is a staple soup in Russian cuisine. The most important ingredient in borscht is beetroot, but you can add other vegetables like carrots and potatoes into it. Although you can make this soup starting off with just water, most of the time it's made with bone broth, and served with bread on the side. For 1 serving of borscht (525 g), there's only about 3.6 mg of cholesterol! (<u>17</u>) Last dish from Russia is actually not a meal, but an appetizer. Pirozhki is rolled out dough that you fill with any topping of your choice, including potatoes, minced beef, sausage, etc. and is either baked or fried. A serving (168g) of meat pirozhki contains 103 mg of cholesterol, because of the meat, butter and eggs in the dough. (<u>18</u>)

Back to Asia, we will now review popular Chinese meals and their cholesterol levels. The first meal on the menu is Beijing roasted duck. Roast duck is very crisp and mainly eaten with sweet sauce, cucumber, and green onions, which are then rolled up in a crepe-like pancake. 1 whole roast duck contains 472 mg of cholesterol, while 1/4th duck contains 118 mg. (19) The next meal is found in most Chinese restaurants and it's sweet and sour pork. In the past, this dish was only made with pork , but now it can be substituted with other types of meat like chicken or beef. In 1 order, or 609 grams of sweet and sour pork, there's 146 mg of cholesterol. (20) Last of the meals for China is another favorite for even foreigners: kung pao chicken. The 4 main ingredients in this dish are diced chicken, cucumber, dried chili, and fried peanuts or cashews. In Western countries, people have created a new version of kung pao chicken with an addition of a sweet and sour sauce. One serving, or 604 grams of kung pao chicken contains around 157 mg of cholesterol. (21)

Coming back to the American region, let's review Mexico. The first dish is a classic that I'm sure everyone knows or has even tried before: tacos. Tacos are very versatile and can be topped/filled with anything, but the main ingredients are taco meat (ground beef, chicken, pork, seafood), the taco shell (hard or soft), shredded cheese, lettuce, and salsa. 1 taco made with a hard shell, beef, cheese, and lettuce contains only 26 mg of cholesterol. (22) Next is a stew named menudo which translates to pork stew. The main ingredients in this stew are tripe, chili peppers, hominy, and other spices. One serving of menudo, or precisely 219.49 grams, contains 73.6 mg of cholesterol. (23) The last dish is also very famous in Mexican cuisine and it's tamales. You choose any topping you like (mole, shredded chicken/pork with salsa, corn, pepper, and cheese) and then wrap it in corn leaves or banana leaves. Since tamales can be filled with any topping you desire, the cholesterol levels vary, but a 128-gram meatless tamale contains 17% of the daily value (21 mg) of cholesterol, while a 128-gram meat-filled tamale contains 17% of the daily value (51 mg). (24)

We're now going to review popular French foods and how much cholesterol these meals contain. Boeuf bourguignon which translates to burgundy beef stew, is a rich stew that contains Charolais beef, which is a variety of cow, red wine, and other various vegetables like carrots, mushrooms, onions, etc. In 1 package of boeuf bourguignon, or 310 grams, there is 65 mg of cholesterol. (25) Next is the famous dessert: creme brulee. This dessert is pretty easy to make and consists of cream, sugar, vanilla, and egg yolks. Most of the cholesterol from this dish would

come from the cream and egg yolks. One ramekin (200 grams) of creme brulee has 444 mg of cholesterol which is already over the recommended cholesterol intake per day. (26) Last dish on the French menu is known as cassoulet. French cassoulet is made with white beans and many different types of meat such as different parts of pork, sausage, and sometimes even duck legs. A serving size of cassoulet (401 g) has 132 mg of cholesterol despite the various meats in this dish. (27)

Moving on to Mediterranean food and its cholesterol levels, the first dish from the Mediterranean is moussaka, which is an eggplant or potato-based dish, often containing ground beef. There are other additions of butter, milk, and eggs, which adds to the cholesterol amount in this dish. In 1 bowl (2 cups, 406 g) of moussaka, there's around 95 mg of cholesterol. (28) The next meal is a dish called dolmas, which is a little bit like tamales but instead the fillings are wrapped in grape leaves or cabbages or stuffed in red or green peppers. Filling combinations can be anything from rice, minced meat, offal, seafood, to even fruits. In 1 piece (35 g) of dolma there is only 12 mg of cholesterol. (29) The last popular dish from the Mediterranean is known as soutzoukakia, which another name for it is smyrna meatballs. This Greek and Turkish dish consists of spicy oblong meatballs submerged in tomato sauce. One serving (341.6 g) of soutzoukakia has around 102.6 mg of cholesterol, which isn't too bad considering the main ingredient is meat. (30)

The second to last country we will be visiting is India! Most of the Indian population have religious constrictions causing them to not be able to eat foods containing beef, pork, or even any meat at all. The first dish though is butter chicken curry, which recently became popular in the US. Butter chicken curry contains mainly chicken and other ingredients like yogurt and spices to make the curry sauce. One cup (240 g) of butter chicken curry excluding the rice, contains 92 mg of cholesterol. (<u>31</u>) The next dish is another curry meal called korma. Korma is made with chicken breasts, bone broth, heavy cream, whole milk yogurt, and more. For 1 serving (around 2 cups, 319 g) of korma there is around 106 mg of cholesterol, which is pretty close to chicken butter curry. (<u>32</u>) The last dish from India is also a type of curry that's known as rogan josh. Rogan josh doesn't use chicken, but rather contains lamb shoulder, with other added ingredients and spices to cook the sauce. One cup (236 g) of rogan josh contains around 51 mg of cholesterol which is about half the other two curry dishes. (<u>33</u>)

The last country we will be reviewing is the one and only Japan. One of the most famous dishes that is known around the world is sushi. Although there are many combinations and different rolls, a very generic combination contains mayo, avocado, cucumber, sushi rice, sesame seed, imitation crab meat, and nori. One roll, or about 8 pieces of this sushi (211 g) contains only around 17 mg of cholesterol. (<u>34</u>) The next dish that originated in Japan and is very popular is chicken karaage. Chicken karaage is made up of chicken thighs and seasonings/spices that marinate the chicken. 1 piece of chicken karaage (37 g) has around 30 mg of cholesterol considering that they are bite-sized. (<u>35</u>) The last and final dish to wrap up our cholesterol ratings is wagyu steak. Wagyu is just a type of steak that can be seasoned with anything you

want, but it's also very expensive. Four ounces (114 g) of wagyu steak without any seasoning contains only 67 mg of cholesterol. $(\underline{36})$

Conclusion

We've reviewed 10 different countries and 30 various dishes or desserts and their cholesterol levels, so now when going to different restaurants you can watch how much cholesterol you're intaking with each bite. But although cholesterol can be high in some foods, other nutritional values can cause the dish to be considered "healthy." That's why although Korean foods tend to have high cholesterol levels, they're considered to be one of the healthiest cuisines to add to your diet. Mediterranean foods on the other hand tend to be a little lower in cholesterol than other countries, making these meals healthy and good to add to your diet.

Works Cited

[1] <u>https://www.cdc.gov/heartdisease/facts.htm</u>

- [2] <u>https://www.cdc.gov/cholesterol/ldl_hdl.htm</u>
- [3] https://www.ucsfhealth.org/education/cholesterol-content-of-foods
- [4] https://www.health.harvard.edu/heart-health/11-foods-that-lower-cholesterol
- [5] https://www.healthline.com/nutrition/high-cholesterol-foods#foods-to-eat
- [6] https://www.fatsecret.com/calories-nutrition/food/jambalaya/cholesterol
- [7] https://www.nutritionix.com/food/meatloaf
- [8] https://www.fatsecret.com/calories-nutrition/food/macaroni-and-cheese/cholesterol
- [9] https://recipes.heart.org/en/recipes/bulgogi-korean-beef-barbecue
- [10]https://mykoreankitchen.com/bibimbap-korean-mixed-rice-with-meat-and-assorted-vegetabl
- [11] https://www.myfitnesspal.com/food/calories/samgyetang-48494693
- [12] https://www.nutritionix.com/food/fettuccine-alfredo
- [13]https://www.nutritionix.com/i/usda/meat-lasagna-1-piece-center/513fceb775b8dbbc210030f
- [14]https://www.nutritionix.com/i/usda/meat-lasagna-1-piece-corner/513fceb775b8dbbc210030f
- [15] <u>https://www.nutritionix.com/i/parma/prosciutto-di-parma/64b914da7dc62400060a179f</u>
- [16] https://www.nutritionvalue.org/Beef_stroganoff_27113100_nutritional_value.html
- [17] https://www.nutritionix.com/food/borscht
- [18] https://www.allrecipes.com/recipe/140517/traditional-russian-pirozhki/
- [19] https://www.myfitnesspal.com/food/calories/peking-duck-140326952
- [20] https://www.nutritionix.com/food/sweet-and-sour-pork
- [21] https://www.nutritionix.com/food/kung-pao-chicken
- [22] https://www.nutritionix.com/food/taco
- [23] https://www.eatthismuch.com/food/nutrition/menudo_3155087/
- [24] <u>https://www.healthline.com/nutrition/are-tamales-healthy#nutrients</u>
- [25] https://www.eatthismuch.com/food/nutrition/beef-bourguignon,2694346/
- [26] https://www.nutritionix.com/food/creme-brulee
- [27] https://recipes.sparkpeople.com/recipe-calories.asp?recipe=217390
- [28] https://www.nutritionix.com/food/moussaka
- [29] https://www.nutritionix.com/food/dolmas
- [30]http://www.damngoodrecipes.com/nutritioncomparison.php?recipe_id=224&perunit=serving
- [31] https://www.nutritionix.com/food/butter-chicken-curry
- [32] https://www.nutritionix.com/food/korma
- [33] https://www.nutritionix.com/food/rogan-josh
- [34] https://www.nutritionix.com/food/sushi
- [35] https://www.nutritionix.com/food/chicken-karaage
- [36] https://www.nutritionix.com/food/wagyu

Effective Persuasion Strategies for Eliciting Concern About Environmental Issues by Sarah Phillips

Abstract

The combined efforts of citizens worldwide to address environmental issues have been insufficient to ensure the health of the global environment (Johansson & Kulin, 2018). In the face of this inaction, crises such as climate change continue to threaten many aspects of life, from economic productivity to human health and survival (McMichael & Lindgren, 2011). Thus, the aim of this paper is to identify persuasion strategies that are likely to be most impactful for spreading awareness and garnering concern about environmental issues by reviewing the literature on persuasion strategies that may be effective specifically in the context of pro-environmental messages. Mass media is a promising platform for the use of these strategies (narrative persuasion and central route persuasion, for example) based on its previous success encouraging widespread public attitude changes. Approaches to persuasion that are both tailored and varied will likely be most impactful.

It will grow increasingly important for public information sources to adjust their persuasion strategies to promote concern about the environment if environmental action across the globe continues to be inadequate. In the past, diverse efforts by the media to spark social change have been successful, and with recommendations like those outlined above, the media may be able to drive that kind of change again.

Methods

Literature on the impacts of different persuasion strategies, including strategies used to attempt to garner passion about the environmental crisis, was reviewed. To search for relevant papers, the following keywords were used: "persuasion", "environmental crisis", "climate change", "public response", and "media". Studies analyzing possible reasons for resistance to pro-environmental messages were considered, as were studies concerning persuasion strategies that might address those barriers. We also compared the relative advantages of different persuasion strategies in different contexts, considering, for example, the age of the audience and the stage of persuasion.

Resistance to Persuasion Strategies Implemented to Promote Environmental Advocacy *Resistance to Persuasion Strategies Employed by the Mass Media*

To influence citizens' attitudes and behavior, environmental advocates do not have a practical and equally far-reaching alternative to communicating with the public via the mass media (Eagly & Kulesa, 1997). Some scholars have suggested that communication via the media cannot greatly impact public mindsets. However, this is not a widely held view, and various historical examples suggest that the media does have the capacity to effectively alter public opinions. For instance, the anti-smoking campaigns of the late 1900s included public policy changes, health warnings on packaging, and a rush of new studies on the dangers of smoking,

amongst other strategies. As a result, not only has the number of smokers in the United States decreased significantly, but the general public's attitude towards smoking has become far more cautious. The impacts of social media filter bubbles (a term describing the process in which social media algorithms reinforce people's opinions by repeatedly suggesting content similar to content that has been viewed in the past) on users' mindsets are being increasingly explored (Bryant, 2011). A survey experiment involving hard propaganda messages demonstrated that even poorly received propaganda can powerfully influence citizens' behavior (Huang, 2018). Thus, the mass media is a potentially effective medium for directing widespread changes in pro-environmental behaviors and attitudes, and the resistance to persuasion strategies currently used by the media are likely not fully due to their platform.

Identity and Resistance to Persuasion

When a person perceives that an aspect of their identity or established convictions conflicts with pro-environmental attitudes or behaviors, defense mechanisms will likely be activated in response to pro-environmental messages (Ahluwalia, 2000; Ma & Hmielowski, 2022; Kolodziej-Smith et al., 2013). One of the principal theories regarding these conflicts and resistance to persuasion is the expectancy-value approach, which explains how the ways in which people process messages determine the persuasiveness of those messages (Ahluwalia, 2000). For instance, biased assimilation describes how people's established values and mindsets act as filters for new information; if a message is accepted, it will be taken in the context of the recipient's previous mindset in order to avoid contradictions with that mindset (Ahluwalia, 2000; Ma & Hmielowski, 2022). Another theory concerning identity conflicts and persuasion, the face negotiation theory, suggests that people feel the need to maintain the attitudes and behaviors that correspond to their identities to gain respect from their ingroups (Kolodziej-Smith et al., 2013). So, conflict avoidance when it comes to identity and persuasion is both intrinsically and extrinsically motivated. Messages promoting environmental advocacy may be perceived as threats to a person's identity (Ma & Hmielowski, 2022). For instance, strong and opinionated messaging from an outgroup (e.g., an opposing political party) about environmental action may be received as an attack because the ideas are coming from that outgroup, rather than because of the message itself. A more direct threat might be perceived if a person's political party is openly opposed to accelerated environmental action, and that person feels pressure to conform.

Narrative vs Statistical Persuasion Limits of Statistical Persuasion

Statistical evidence relies chiefly on quantitative information, while narrative evidence typically involves anecdotes, testimonials, personal experiences, or opinions (Han & Fink, 2012). One examination of several studies comparing the effects of narrative versus statistical persuasion found that most concluded that the former is generally more persuasive, particularly when attitude transformations were explored specifically (Han & Fink, 2012).

There is a limited number of studies focused specifically on persuasion strategies used to encourage environmental action or pro-environmental attitudes. However, studies concerning persuasion strategies used to influence public actions and attitudes regarding other social issues (i.e., gun control debate, public health promotion) can be informative.

Gun Policy

Because the gun control debate is a highly emotional social issue, thus far, researchers have largely focused on quantitative support for how easy access to guns for ordinary citizens impacts public safety (Kahan & Braman, 2003). However, efforts toward answering this question have had little practical impact. Most citizens are more in tune with political events concerning the gun control debate than they are with scientific findings concerning the issue, in part because politics usually has more media coverage than scientific research (Kahan & Braman, 2003). Therefore, even high-quality studies concerning the consequences of gun control policies have very limited influence. If this trend is reflected in the conflict over environmental policy, it might help explain why the pro-environmental efforts of most citizens have been insufficient thus far despite the consensus of the scientific community that climate change and other environmental issues are real and urgent (Johansson & Kulin, 2018).

In addition, researchers who seek to demonstrate the practical consequences of gun control policies are likely not targeting the concerns of most citizens (Kahan & Braman, 2003). Some researchers believe that this is because guns are social symbols. The conflict might be fueled more by passion about the meaning of guns, while their function is less significant. For some citizens, a change in gun policies could mean symbolic lifestyle changes or even alterations of identity. Other citizens might feel that they are faced with the same implications when they consider significant pro-environmental attitude and behavior changes.

Public Health

In recent years, there has been an abundance of misconceptions about public health distorting citizens' perceptions of the healthcare system. To address this trend, the strategies employed to spread this misinformation have been frequently analyzed (Peng et al., 2022). In one study examining articles containing misinformation and disinformation regarding public health, 12 types of persuasion strategies were identified, only two of which focused on misleading statistical evidence or targeted the audience's reasoning (Peng et al., 2022). The remaining 10 targeted the audience's emotions. A similar trend can be seen in articles containing legitimate information about public health (Atkin & Salmon, 2013). Health campaigns aimed at audiences who are most in need of change (and who are, therefore, most likely to be resistant to it) typically emphasize visual and sensational messages. In addition, though health campaigns typically have strong impacts on people's cognitive mindset changes they have little effect on people's attitudes and behaviors.

Thus, both due to a lack of emotion regarding the consequences of environmental destruction and intense emotion connecting people to their current lifestyles, the conflict over

environmental action is largely an emotional one (Appel et al., 2019). Scientific studies highlighting statistics are not designed to target people's values or emotions. Emotional reactions are rarely evoked when statistical persuasion techniques are employed because the emotional link between numbers and a lived experience is not easily made. Once somebody identifies emotionally with a group, statistical evidence does not target the source of that emotional connection and is therefore often ineffective in altering it.

Mechanisms of Narrative Persuasion

The persuasive power of narratives is strongly related to the emotions they elicit in their audiences (McCormack et al., 2021; Appel et al., 2019; Dal et al., 2004). This capacity of narratives to capture audiences' emotions may help to address environmental problems. For example, it may help to interrupt a cycle in which wildlife loss leads to reduced emotional investment in it, and therefore, further wildlife loss (McCormack et al., 2021; Dal et al., 2004). While some narratives encourage engagement because they provide hedonic experiences, or experiences that are rewarding due to the simple pleasures they provide, others encourage engagement because they provide eudaimonic experiences, which offer rewarding feelings of meaningfulness or connectedness (McCormack et al., 2021). Those kinds of pleasing feelings may help to combat the stress and guilt often present in discussions concerning difficult topics like environmental issues. Another powerful kind of emotion identified by researchers is event-congruent emotion, or emotion appropriate for each experience portrayed in a story (Appel et al., 2019). The results of one study demonstrate the capacity of narratives to elicit event-congruent emotions. Participants were shown a film, and their emotional experiences during six scenes likely to elicit event-congruent emotions were examined using software analyzing unconscious emotional facial muscle movements. Those who reported feeling more transported into the film (or those who felt the most intense empathy) were observed to have more acute facial expressions during those scenes.

Fiction narratives hold the capacity to alter established mindsets regarding environmental issues, which may indicate the capacity to address the destruction/disaffection cycle that weakens the connection between people and their world (McCormack et al., 2021). Some researchers who have explored why narratives can have this influence believe that narrative-style films about environmental issues tend to be more impactful than more factual, lecture-like approaches because the audience's viewing experience might help combat the lack of emotional connection to wildlife in communities in which contact with nature is rare. A few theories have been developed to explain how this may occur. Researchers postulate that narrative persuasion encounters reduced resistance in its subjects because participants become immersed in the narrative and are less aware of themselves and their own established mindsets and values. This idea is supported by the fact that, though understanding of, focus upon, presence in, and emotional investment in a narrative have all been identified as aspects of narrative engagement, the extent of emotional investment is the strongest indicator of the development of story-congruent attitudes (Appel et al., 2019). As opposed to challenging people's identities,

other researchers propose narratives can interact with their preexisting identities and values by portraying relatable characters (McCormack et al., 2021). In this way, they can overcome the internal conflict that arises when a person is asked to make a significant attitude or lifestyle change (Kahan & Braman, 2003; McCormack et al., 2021).

Outside of these studies, a large body of evidence has suggested that narratives can impact, not only people's emotions, but also people's beliefs, behaviors and identities (Dal et al., 2004). In one study, when people were asked to choose a single moment that made them cry, the first most common response referenced the death of a loved one, a real event, while the second most common response referenced a sad moment in a movie, an event within a narrative (Appel et al., 2019). In fact, roughly 44% of men and 80% of women named a book, movie, or TV show (narratives in different forms). This suggests that stories can evoke emotions with an impact comparable to that of real events. Beyond that, they can motivate action. Education entertainment, or the systematic use of narratives to increase a behavior within a population, has been encouraged by the United States government in the past. For instance, government officials have determined that the entertainment industry is essential in spreading anti-drug messages (Dal et al., 2004). Thus, rather than continuously attempting to force citizens to recognize and understand the practical consequences of current trends and policies, those who want to accelerate environmental action might find more success in targeting citizens' entertainment sources and emphasizing emotive storytelling.

Promoting Self-Transcendence to Reduce Defensive Responses

Self-transcendence can be defined as the transformation from a self-interested mindset to an altruistic mindset (Kang et al., 2018). Self-transcendent experiences can be regarded as advanced eudaimonic experiences as they are very pleasing, and people wish to experience them repeatedly (McCormack et al., 2021). Research has shown that self-transcendent values are conducive to pro-environmental behavior (Knowles, 2013). This might be because people are less likely to view their own behavior as defining themselves if persuasive messages appeal to self-transcendent values or promote activities that benefit others (Kang et al., 2018). Therefore, they are less likely to perceive and resist the idea that their previous negative behavior defined them too. In addition, when persuasive messages encourage behavior change by portraying that change as altruistic, they can promote feelings of self-confidence and the happiness and satisfaction that comes with compassion and benevolence.

Self-transcendent values can be activated in messages promoting environmental advocacy when those messages include broad universalism appeals to which the recipient may be more receptive than calls for environmental action (Knowles, 2013). For example, if an appeal for environmental action is united with the appeals of unity and justice it will likely be easier for the recipient to identify with the message's stated aims. Self-transcendent values can also be activated by fostering concern for people impacted by environmental issues, which may then indirectly foster concern for the environment in general. However, when certain benefits of a desired action are emphasized in a persuasive message, self-transcendent values tend to be deactivated. If a message highlights the financial benefits of environmental action, for example, it will likely activate achievement or wealth values, both of which conflict with pro-environmental mindsets. Using social pressure to encourage people to act may activate social recognition and public image values, which are not conducive to environmental action either.

Central and Peripheral Route Persuasion

Central route persuasion refers to any persuasion technique that relies upon argument quality to target the audience's reasoning or logic, and primarily employs factual evidence. Attitude shifts resulting from central route persuasion tend to be both resistant to change and predictive of behavior (Petty, 2013; Algarni, 2019). This resistance to change occurs in part because the recipient is motivated to consider the message in full, along with all its implications, and decide independently if it is convincing. In other words, successful central route persuasion involves the recipient adopting the views expressed by the message. However, these findings do not indicate that emotions elicited by persuasive messages do not also contribute to their endurance (Dillard & Seo, 2013). Multiple studies have suggested that strong affect in persuasion might help to guide people's long-term choices, such as voting and healthcare decisions (Dillard & Seo, 2013).

Peripheral route persuasion refers to any persuasion technique that employs cues unrelated to the central message to draw a positive reaction from the audience (e.g., hiring a well-respected public figure to advertise a product or using pleasing designs or color schemes on billboards;Petty, 2013). Attitude shifts resulting from peripheral route persuasion tend to be temporary and do not strongly influence behavior, contrasting those produced by central route persuasion techniques.

Whether a message is made more effective by emphasizing central route persuasion techniques or peripheral route persuasion techniques depends on the context, and the two strategies are most effective when employed together (Algarni, 2019; Petty, 2013). If a message is urging its audience to take action (e.g., environmental action) it will most likely be successful only if it involves some level of central route persuasion to ensure that the audience's motivation endures, as well as peripheral route persuasion to gain the audience's initial interest. A combination of central route and peripheral route strategies will be most impactful when presented with a strong emotional undertone (Dillard & Seo, 2013).

Tailored Persuasion Strategies

Within the categories of persuasion strategies described (i.e., narrative persuasion strategies, statistical persuasion strategies, persuasion strategies promoting self-transcendence, central route persuasion strategies, and peripheral route persuasion strategies) there are many specific strategies that have varying impacts among different demographics (Orji et al., 2014; Abdullahi et al., 2019). Two large-scale studies aiming to examine the relative efficacy of different strategies among different groups illustrated this phenomenon. (It is important to note that the strategies included in both studies, listed below, are ones which previous research has

shown to be generally effective in changing attitudes or behavior). Both studies concluded that demographic groups can have significantly different reactions to different persuasion strategies (Orji et al., 2014; Abdullahi et al., 2019). In the first study, the female participants found personalization, simulation, cooperation, customization, and praise techniques to be more persuasive than the male participants did, and for the remaining three strategies (reward, self-monitoring, and feedback), there was no significant difference in rankings between the sexes (Orji et al., 2014). In the second study, the female participants were more receptive to reward and trustworthiness strategies, while the male participants were more receptive to social learning strategies. (Abdullahi et al., 2019). It was also found that the children relied more upon the perceived trustworthiness of the source; teens and adolescents were especially receptive to social learning strategies; younger adults were most likely to respond to social learning and reward strategies; and older adults were more susceptible to trustworthiness strategies.

Disparities in the findings of the two studies may be attributed to the fact that, in the first, participants ranked the efficacy of every strategy after viewing a visual representation of each on a storyboard, while in the second, researchers categorized participants by sex and age and examined their different responses to persuasive educational technologies (Orji et al., 2014; Abdullahi et al., 2019).

Persuasive messages can be tailored in other ways that do not involve considering a person's demographic group (Teeny et al., 2021). One consistently impactful strategy is personalized matching, which focuses on the personality, beliefs, or values of a person, rather than broad categories. It matches an aspect of an appeal to an aspect of the personality, identity, appearance, etc. of the recipient. Several analysts have concluded that personalized matching is so effective that it likely influenced the outcome of the 2016 presidential election. Characteristics that may be included in personalized matching include affective states, cognitive states, goals, motivational orientations, attitudes, identities, personalities, and cultural orientation. For example, a person's affective state might be considered because a person in a positive mood will be more receptive to the positive outcomes of making a certain decision, while a person in a negative mood will be more receptive to the negative outcomes of not making that same decision.

Discussion

We aimed to identify types of persuasion strategies that may be well suited to encouraging widespread pro-environmental attitudes and behaviors by reviewing the literature on strategies effective in various contexts. The impacts of different persuasion techniques differ, for example, according to aspects of the audience's identity (e.g., age, gender, political stance) and the medium of persuasion. However, there are specific strategies that are consistently conducive to self-transcendent and likely pro-environmental attitudes, while others that tend to suppress those attitudes. As environmental crises continue to become more severe and impact every part of our world, the implementation of the most influential pro-environmental persuasion strategies will become increasingly important.

Limitations

Studies on social issues (e.g., gun control) were reviewed, but further studies directly investigating the effects of various persuasion strategies on pro-environmental attitudes are needed to determine whether the results of the former can be generalized to environmental issues. In addition, because the environmental crisis is a large-scale problem, it is unclear if persuasion strategies that are effective in smaller-scale studies will hold the same power for promoting widespread acceptance of and concern for environmental issues.

Future Directions

Because few studies focusing on analyzing persuasion strategies in the context of the environmental crisis were found, more research investigating the most impactful ways to influence public attitudes and behaviors regarding environmental issues might help to highlight the strategies that should be used in future campaigns conducted by environmental advocates. Also, the scientific community has given little attention to the psychology behind resistance to persuasion (Ahluwalia, 2000) and further research in this area may help to clarify which strategies might combat that resistance to persuasion, and which strategies might enhance it.

Conclusion

The present review synthesized various studies concerned with the influence of persuasion strategies in different contexts to assess which strategies (e.g., narrative persuasion and central route persuasion) might be effective in eliciting widespread concern about environmental issues. It is well supported that the mass media has the capacity to help direct public attitude. Thus, it may be effective for increasing widespread pro-environmental attitudes and behaviors in the future. However, pro-environmental messages might elicit defensive responses if a person feels that their identity contradicts environmentally friendly attitudes and behaviors. Narrative persuasion strategies are more impactful than statistical persuasion strategies in combatting those defensive responses, especially if those narrative persuasion strategies are personalized, or promote self-transcendence. In addition, peripheral route persuasion is more impactful than central route persuasion when it comes to persuading an audience to initially consider a pro-environmental message, while central route persuasion is more likely than peripheral route persuasion to leave a lasting impression on the audience. Citizens' efforts to combat environmental issues are inadequate. If this trend continues, public information sources may become essential mediums for promoting environmentally friendly attitudes and behaviors; thus, it is important that they employ the most effective persuasion strategies possible.

Works Cited

- Abdullahi, A. M., Oyibo, K., Orji, R., & Kawu, A. A. (2019). The Influence of Age, Gender, and Cognitive Ability on the Susceptibility to Persuasive Strategies. *Information*, *10*(11), 352. https://doi.org/10.3390/info10110352.
- Ahluwalia, R. (2000). Examination of psychological processes underlying resistance to persuasion. *Journal of Consumer Research*, *27*(2), 217-232.
- Algarni, A. (2019). What Message Characteristics Make Social Engineering Successful on Facebook: The Role of Central Route, Peripheral Route, and Perceived Risk. *Information*, 10(6), 211. https://doi.org/10.3390/info10060211.
- Appel, M., Schreiner, C., Haffmans, M. B., & Richter, T. (2019). The mediating role of event-congruent emotions in narrative persuasion. *Poetics*, 77, 101385.
- Atkin, C. K., & Salmon, C. (2013). Persuasive strategies in health campaigns. *The SAGE* handbook of persuasion: Developments in theory and practice, 278-295.
- Bryant, C. A. (2011). The social media bubble: an examination of social media user motivations and their implications for future users and communication technologies.
- Dal Cin, S., Zanna, M. P., & Fong, G. T. (2004). Narrative persuasion and overcoming resistance. *Resistance and persuasion*, 2(175-191), 4.
- Dillard, J. P., & Seo, K. (2013). Affect and persuasion. *The SAGE handbook of persuasion: Developments in theory and practice*, 150-166.
- Eagly, A. H., & Kulesa, P. (1997). Attitudes, attitude structure, and resistance to change. *Environmental ethics and behavior*, *415*, 122-153.
- Han, B., & Fink, E. L. (2012). How do statistical and narrative evidence affect persuasion?: The role of evidentiary features. *Argumentation and Advocacy*, 49(1), 39-58.
- Huang, H. (2018). The pathology of hard propaganda. The Journal of Politics, 80(3), 1034-1038.
- Johansson Sevä, I., & Kulin, J. (2018). A little more action, please: increasing the understanding about citizens' lack of commitment to protecting the environment in different national contexts. *International Journal of Sociology*, *48*(4), 314-339.
- Kahan, D. M., & Braman, D. (2003). More statistics, less persuasion: A cultural theory of gun-risk perceptions. University of Pennsylvania Law Review, 151(4), 1291-1327.
- Kang, Y., Cooper, N., Pandey, P., Scholz, C., O'Donnell, M. B., Lieberman, M. D., ... & Falk, E. B. (2018). Effects of self-transcendence on neural responses to persuasive messages and health behavior change. *Proceedings of the National Academy of Sciences*, *115*(40), 9974-9979.
- Knowles, B. (2013). Re-imagining persuasion: designing for self-transcendence. In *CHI'13 Extended Abstracts on Human Factors in Computing Systems* (pp. 2713-2718).
- Kolodziej-Smith, R., Friesen, D. P., & Yaprak, A. (2013). Does culture affect how people receive and resist persuasive messages? Research proposals about resistance to persuasion in cultural groups. *Global Advances in Business Communication*, 2(1), 5.

- Ma, Y., & Hmielowski, J. D. (2022). Are you threatening me? identity threat, resistance to persuasion, and boomerang effects in environmental communication. *Environmental Communication*, 16(2), 225-242.
- McCormack, C. M., K Martin, J., & Williams, K. J. (2021). The full story: Understanding how films affect environmental change through the lens of narrative persuasion. *People and Nature*, *3*(6), 1193-1204.
- McMichael, A. J., & Lindgren, E. (2011). Climate change: present and future risks to health, and necessary responses. *Journal of internal medicine*, *270*(5), 401-413.
- Orji, R., Mandryk, R. L., & Vassileva, J. (2014). Gender and persuasive technology: Examining the persuasiveness of persuasive strategies by gender groups. *Persuasive Technology*, 48-52.
- Peng, W., Lim, S., & Meng, J. (2022). Persuasive strategies in online health misinformation: A systematic review. *Information, Communication & Society*, 1-18.
- Petty, R. E. (2013). Two routes to persuasion: State of the art. *International perspectives on psychological science*, *2*(1), 229-247.
- Teeny, J. D., Siev, J. J., Briñol, P., & Petty, R. E. (2021). A review and conceptual framework for understanding personalized matching effects in persuasion. *Journal of Consumer Psychology*, 31(2), 382-414.

Should Media Channels Be Blamed for 'Framing' Disabled People in South Korea? By Taehyoung Jang

Abstract

The purpose of this research is to examine if the media channels such as News, Television series, movies and different online platforms and Social Network Services (SNS) have contributed in building the negative perception towards disabled people in South Korea (the target group) among the general population. According to different psychological theories, what has been presented may affect the perception development, however it may not be a dominant factor. Interestingly however, if what were presented contains negative factors, it may provide a bigger influence, and because the media channels portray the target group provocatively to attract more viewers (also because the target group has been used in the fight between the political parties) and that the target group is not people who can be encountered easily in real life, it is believed that what were presented through the media channels certainly played a role with development of the negative perception towards the target group in South Korea.

Introduction

The possession of information has been the legacy of the gifted for centuries. Its value, therefore, has been idealized and worshiped as much as money. It is well known that in the ancient battle between the Persians and the Greeks, a messenger of Greece nearly sacrificed his life to deliver the news of victory to his people. As shown here, as much as the importance of information itself, the responsibility of the messenger has never been underestimated throughout history. And while the potency of information has grown dramatically since recent times, its accessibility increased just the same. Thanks to the development in technology, nowadays anyone can freely and easily tap into information around the world regardless of boundaries. The main contributor to such a change is the debut of mass media. A great example is the invention of smartphones; over 10 years have passed since the invention of these portable computer devices capable of the internet and various types of communication, and it has permeated through our lives more than we realize. Statista found that the sales of these smartphones have expanded from 122.3 million in 2007 to over 1550 million in 2017, almost 13 times the original value(Statista, 2023). The penetration rate of smartphone ownership is also recorded to be 67 to 68 percent worldwide for the last 5 years(Statista, 2023). Despite such an outstanding development, there are many issues around it too. Therefore, this research focuses on how the media sources can affect the development of perception among the audience and how they contributed to the negative perception of the general population towards the disabled people in South Korea.

The accessibility of media sources in South Korea and the issues around the topic

Such an outstanding development could not be more true in South Korea, as the abundance of smartphones and internet access is higher than average. According to the Korean

Statistical Information Service (KOSIS), 0.94 smartphones per person is in the hands of the Korean population(KOSIS). If we include other forms of media windows, like television and computers, it isn't totally rough to say that everyone has access to mass media, not to mention that 93% of the Korean population has access to the internet(KOSIS). There are clearly some advantages to a high rate of media accessibility. First, the act of sharing and interacting with information becomes much easier. Also, communication becomes much more straightforward and frequent. These two aspects lead to equality in access to information, a common scene in contemporary society. However, though it sounds optimistic, side effects also exist. Going further, the advantages mentioned above might also act sideways in situations. Because spreading information is so easy yet influential, there is a higher chance of wrong, prejudiced information gaining power among society. There is reason to believe that because of this fact the disabled community in Korea is currently being discriminated against with a distorted perspective. This research focuses on how Korean media contributed to a negative perception towards disabled people and how it could be used appropriately to change this unfortunate situation.

Before talking further about the influence of media on the disabled community, a point that should first be acknowledged is the actual influence of media in Korean society. First, it can be found through advertisements. The Korean ministry of culture, sports and tourism has asserted that the market share of advertisement in South Korea in 2022 is measured to be 18.9 trillion won, an 8.6% increase from 2021(Ministry of Culture, Sports, and Tourism). The significant amount of money reflects how big the advertising industry is. Also, the Korean movie industry, as the Korean Creative Content Agency announced, is as big as 1.7 trillion won in 2022, 7th in size among the world(KOFIC). Considering the worldwide pandemic that has been ongoing for three years, and thus the fact that this number is only 68% of the market share in 2019, it is still a notable amount of influence in the Korean society. Gallup, a Korean research facility, recently found that 93% of Koreans have experience using Youtube. Among the younger generations, from 19 to 29, 66% had experience using facebook and 77% had experience using Instagram(Gallup). As seen from multiple angles, media has penetrated an unnoticeable amount of dependency in people's lives, making its influence hard to overlook.

Although what has been discussed above may seem negative as it may sound like the media is controlling our lives, however, the accessibility to those media sources is not a bad thing on its own. For example, as most people in South Korea have access to such media sources, it enables them to easily receive information, which enables the government and or the country to take care of them in case of an emergency such as a natural disaster, war and many more(McQuail) . On the other hand, 'easier delivery of information' itself could be a disadvantage as it could spread wrong information or inappropriate contents to the general population and more. Furthermore, those media sources in South Korea tend to focus on 'what happened and the result (or how it affected people)' rather than the cause of the issue itself to

draw more attention of the people (This argument will be discussed further in the later section of the paper).

According to Guerrero-sole in 2016, he claimed that different media sources such as news, advertising, different violence and pornographic contents on TV and the internet could could drive certain behavior of the audience and that the audience are likely to think or behave in a way which the media sources want them to act and think rather than how they would have when they encountered the issue on their own(Guerrero-sole). This is because many of the issues they encounter through the media sources are much unlikely to encounter in real life, so the only information that was given to them were through the media sources. This was further suggested by Stein, Friedrich and Stein in 1975, which they claimed that such chances are more likely when the media sources use the violent contents or anything that goes against the national culture and that it has a wide impact on the audience with increase in the risk of negative perception and violent behavior of the audience could be motivated by the media sources and the chance may be maximized when the contents focuses on the negative issues. Therefore, the next section of the research will discuss how this is the case by examining the way in which the target group has been presented to the audience through different media sources.

Examining how the target group was visualized to the audience and how that influenced the negative perception towards them.

The earlier section of the research discussed the impact of media channels and the influences which it can bring to our society. This section of the paper discusses how the media channels visualize the disabled people (the target group) to the audience and the issues around it.

One of the media channels which talk about the target group the most is the News. According to its original purposes, News aims to provide information, education, guidance and more to the general population and public to inform people about what is happening in the society. Nonetheless, the News channels in Korea have lost their original purpose and are used as political weapons. In fact, according to Song in 2019, he argued that each media channels have shown different political colors and are biased with what they broadcast through their own channels (Song), which was further supported by Kim and Jung in 2018, which they claimed that 13 different media channels (including both News and the other broadcasts) have shown their own political party preferences especially during the election season (Kim and Jung). This riggedness prevents accomplishing their original purposes by not delivering information, and the issues they broadcast often target to harm the other political parties and that they tend to exaggerate and emphasize the negativity to irritate the issue. Therefore, the target group became the victim of such wrong use of the media sources, because the issues around them were irritated which led to negative perception from the general population.

Nonetheless, when such media sources used and irritated the issues around the target group, they did not focus on 'cause and what happened', but rather focused on 'what happened and how it affected the general population'. This is quite straightforward as the political party

would want more of the general population to go against the other party and that one of the easiest ways to do so would be connecting the issue and how it negatively affected their lives. For example, there was a recent incident in South Korea where the number of disabled people from Solidarity Against Disability Discrimination (SADD) interrupted subway trains to protest against inequality and unfair treatment towards themselves (Park and You). Different media channels broadcasted such an issue, however, as suggested, the way they broadcasted in a way where it would persuade the viewers to believe that this would only harm their daily lives. For example, the title of this News article video said 'every single passengers had to get off the train at Yongsan station due to the protest by SADD' and there was a another News article video titled as 'Kukminuihim (It is a name of a political party): SADD still disrupts the traffic even after receiving financial aid'. As it can clearly be observed from both News article videos, they do not only show the political colors, but the way they present the issue clearly persuade the viewers to believe how their lives were affected due to the event. In addition, because they mostly focus on what happened and how it affected people, the audience starts to not care about why it happened, but rather the consequences which they have to undertake due to those disabled people who committed the protest, which highly could influence the audience when forming the negative perception towards the target group.

The impact of such action which leads to influence on negative perception development among the general population towards the target group can be observed further from the comments by the viewers. According to the study, which evaluated nearly 60,000 comments on relevant news articles, it discovered that more than 60% of the comments included discrimination, violent languages and abusive languages (Yoon). The study also emphasized that the sympathy towards the target group is starting to disappear and that people are starting to consider them as hostile and that many of these negative comments tend to appear at the top of the comments section which affects more people. Although the study does not suggest that those negative comments are solely due to what were presented in the articles, however, as suggested by Saddiqi and Silab in 2023, which they claimed that the audiences may believe in a way they were persuaded through what were presented by the media sources (Saddiqi and Silab), it could be argued that the negative perception towards the target group from the general population could have been the result of the wrong use of the media channels.

Nonetheless, the incident where SADD protested was not the only cause which would have affected the negative perception towards them from the general population. Another arguable use of media focusing on disabled people is how they are portrayed in movies or dramas. One of the latest and biggest drama hits in South Korea was the 'Extraordinary Lawyer Woo' where the main character suffers from autism, however still shows an unbelievable lawyer quality and becomes an outstanding lawyer. The first problem emerges from here, where she seems to be completely independent and became a lawyer which would allow her to make more salaries than many of the general population. This would have affected the negative perception towards them as according to the Ministry of Health and Welfare, There are a number of different governmental policies which aim to enhance the lives of the disabled people and that

even provide financial aids to them(Ministry of Health and Welfare). One of the objectives of the government is to ensure the well-being and lives of their people, so those policies are reasonable or further, even suitable, however, as it is hard for the individuals to witness the life of the target group in real life, their knowledge on how they live their lives sort of depends on how they are portrayed in the media, because that would be pretty much the only source to get a hint of it. But because the target group appears not so much like they need help as portrayed in the 'Extraordinary Lawyer Woo', it raises questions among the general population as those governmental policies and supports come from the general population with taxes.

Nonetheless, that is not what it is like to live as the target group in South Korea, in fact, Yoon reported in 2022 that even though the government seems to be running many policies and supports for the target group, they are still not enough and in fact, many of them are 'unrealistic and unlikely' and that the target group has to go through so many paper works and interviews to 'prove' that they are disabled people to receive minor support from the government (Yoon). The lack of governmental actions were emphasized further by Yeon and Kim in 2017, when they discovered that there are not enough special schools for the target group which led to only 1 out of 3 disabled students being accepted at those special schools (Yeon and Kim). Although it seems like the government is the one to be blamed for their inappropriate governmental actions, however, media sources should also take the blame for not focusing on real life issues around the target group. To add, it could also be concluded that the negative perception towards the target group from the general population would have been affected or gotten deeper, because the media sources did not portray them appropriately.

Conclusion

Although the actual influence of media when building ones' perception or behavior could be different to people and that some people are more likely to be affected whereas some may not, and that there are much more factors when building ones' perception. However, the way the target group was visualized in different media sources in South Korea never represented the real everyday lives of them and the problems they face everyday.

As mentioned earlier in the paper, one of the strongest advantages of the media sources was the 'delivery of information' and that it could be concluded that if the media sources could change the way they present the target group to the audience, it could stop the negative perception towards them.

Works Cited

- "Number of Smartphones Sold to End Users Worldwide From 2007 to 2022(in Million Units)." Statista
 - www.statista.com/statistics/263437/global-smartphone-sales-to-end-users-since-2007.
- "Global Smartphone Penetration Rate as Share of Population From 2016 to 2022." *Statista* <u>www.statista.com/statistics/203734/global-smartphone-penetration-per-capita-since-2005.</u>

"Survey on Broadcast Media Use Behavior." Korea Communications Commission

- "Internet Use Survey-Internet Use within the Past Month." Ministry of Science and ICT
- "2022 Advertising Industry Survey." Ministry of Culture, Sports, and Tourism

"Announcement of 2022 Korean film industry settlement of accounts." KOFIC

- "Market70 2022 (2) Usage Rate of 18 Media and Social Network Services." Gallup
- McQuail, Denis. "The Influence and Effects of Mass Media."
- Guerrero-Solé, Frederic. "The Influence of Media Type on the Third Person Effect." *Observatorio (OBS*)*, vol. 10, no. 4, Instituto Universitario de Lisboa (ISCTE-IUL), Dec. 2016. *Crossref*, <u>https://doi.org/10.15847/obsobs1042016941</u>.
- Friedrich, L. K., & Stein, A. H. (1975). "Impact of television on children and youth." Chicago: University of Chicago Press.
- Song, B. K. "Estimation of Partisan Bias in Media Coverage of Polling Results During the 2017 Presidential Election." *Korean Party Studies Review*, vol. 18, no. 4, The Korean Association of Party Studies, Dec. 2019, pp. 69–93. *Crossref*, https://doi.org/10.30992/kpsr.2019.12.18.4.69.
- Kim, Su-Jeong, and Yeon Goo Cheong. "A Study on the Characteristics of Political Bias of Korean Press : Focused on the Analysis of 19th Presidential Election Coverage." *Korean Journal of Communication & Information*, vol. 88, Korean Association For Communication and Information Studies, Apr. 2018, pp. 110–45. Crossref, <u>https://doi.org/10.46407/kjci.2018.04.88.110</u>.
- "Why Did SADD Resume the Subway Protest? The Meaning of '0.8%' of the Budget for the Rights of People with Disabilities." Park and You, Kyunghyang Shinmun https://m.khan.co.kr/national/national-general/article/202301031741001#c2b
- Kim. "For the second day, a surprise protest by SADD was held by blocking the bus lane... "Condemn Oh Se-hoon."" YTN
- Kang. 'Kukminuihim "Illegal traffic obstruction by SADD after receiving a subsidy from Seoul city." News A
- Yoon. "We Conducted a Thorough Survey of SADD Protest News Comments and Found These Results." Mediatoday <u>www.mediatoday.co.kr/news/articleView.html?idxno=309709</u>.
- Saddiqi, Qudratullah, and Safiullah Silab. "Negative Impacts of Mass Media on Social and Psychological Life of Human Beings." Sprin Journal of Arts, Humanities and Social Sciences, vol. 2, no. 01, Sprin Publisher, Feb. 2023, pp. 58–68. Crossref, <u>https://doi.org/10.55559/sjahss.v2i01.80</u>.

- "Policies > Disabled Persons > Disabled Persons Policy List | A lifelong friend who provides strength, the Ministry of Health and Welfare." Ministry of Health and Welfare, www.mohw.go.kr/react/policy/index.jsp?PAR_MENU_ID=06&MENU_ID=063701.
- Yoon. "Poor policies for the disabled are due to lack of government communication." Social Focus <u>https://www.socialfocus.co.kr/news/articleView.html?idxno=12888</u>
- Yeon and Kim. "89,000 disabled students... Only 1 in 3 children attend a special school." Financial News. <u>https://www.fnnews.com/news/201709261711375982</u>

From Words to Weapons: Japanese Ideology and Propaganda during World War II By Amaaya Agarwal

Abstract

During World War II, the Japanese government effectively utilized propaganda as a powerful tool, manipulating information to further their imperial ambitions and creating confusion between reality and fiction. They utilized it as a method of artistic manipulation, elevating their image in the public's perception, in a distinctive and unconventional manner. The paper will analyze a variety of wartime postcards, propaganda, illustrations, art work, cartoons, and comic strips. Specifically, it will look at the ideological content of these images and showcase how Japanese propaganda utilized the formats of comedy and advertisements to spread their message, while they creatively manipulated the masses. This paper will show how Japanese propaganda demonized the Western Powers and blurred lines of fact and fiction.

Introduction

Why do we focus on Nazism when we hear terms like ideology and propaganda during the Second World War? Why do we not consider the hidden prospects of Japanese Propaganda and their concept of the "Greater East Asia Co-Prosperity." There is a lot of research and documentation on German Propaganda and ideology in the Second World War, but there is little on wartime Japanese propaganda. Being a modern power meant being a colonial power to Japan, much like it did to the West.

In German propaganda, The Nazis used racial science, a fake science, to justify their concept of racial superiority and the need for expansion to establish a "Greater Germany." Nazism's ideology was shaped by Hitler's beliefs in German racial superiority. It rejected liberalism, democracy, the rule of law, and human rights. It emphasized the inequality of individuals and "races" and the right of the strong to rule the weak. We already know that Hitler worked towards a racially homogeneous society, considering the Aryan race superior, leading to persecution and genocide of the Jews. John Connelly says, " Jews were regarded as the anti-race; or, as Hitler is supposed to have said to Hermann Rauschning, 'The Jew is the anti-man, the creature of a; another god. He is a creature outside nature and alien to nature."¹⁰¹ The aggression of Nazi Germany, expansionist policies, and territorial ambitions played a significant role in causing WWII. Japanese propaganda during this era stood apart in various ways, from its artistic style to its nuanced messaging. This propaganda was more than just a tool for garnering domestic support; it was a complex and carefully orchestrated effort to shape global perceptions of Japan and its imperial ambitions.

World War II meant death, destruction, and bloodshed. To nations, For nations, it signified imperialism, expansion, nationalism, technological innovation, and ideological fervor.

¹⁰¹ John Connelly, "Nazis and Slavs: From Racial Theory to Racist Practice," *Central European History*, vol. 32, no. 1 (1999): 33.

¹⁰² The Second World War was not just fought on land, air, or water. There was another aspect of it. Beyond the conventional battlefields, another, more subtle war unfolded during the conflict. Film producers and poster designers aligned with both the Axis Powers and the Allied powers engaged in a psychological battle through propaganda. Through the power of propaganda, these psychological soldiers attempted to instill a love for their country.¹⁰³ This paper, in particular, scrutinizes the distinct nature of Japanese propaganda during World War II. It investigates how Japanese propaganda manipulated fact and fiction to craft a positive image of Japan while downplaying its wartime atrocities. It analyses propaganda pieces not just from the second world war, but from the early 1900s. Japan had been manufacturing reality since then. It sheds light on the background of Japan's initial relations with the West and propaganda images targeting them.

The Merriam-Webster Dictionary defines Propaganda as "ideas, facts, or allegations spread deliberately to further one's cause or to damage an opposing cause." Given the absence of comprehensive research on Japanese propaganda during the Second World War, there is ample opportunity to delve into primary sources and analyze the material available to shed light on this understudied aspect of World History. This paper aims to bridge this gap by conducting a comprehensive analysis of Japanese propaganda and ideology during the Second World War.

The Development of the Japanese Empire

Japan formed a puppet empire in Northern China, seized and colonized vast areas of South East Asia, and launched a brutal war against China, the United States, and the United Kingdom. Japan's people remained dedicated to defending and expanding their empire. The central theme of imperial expansion and "Greater East Asia Co-Prosperity" brought soldiers and civilians together to fight the war on the battlefield and through propaganda. Propaganda was vital to Japan's wartime empire. Neither the German nor American governments used propaganda quite like this. It was widespread, coming at once from various fields, including advertisement and comedy.¹⁰⁴ Additionally, the Japanese government understood that effective propaganda did not result from direct orders from its offices. Thus, propaganda that could be counted on to mobilize had to "grasp the hearts and minds of the people" was used. This strategy was called "*minchin ha'aku*." ¹⁰⁵ This resulted in a symbiotic relationship between the soldiers and civilians. Japanese Propaganda came from society instead of the government or central authority such as in Germany and Italy. Japanese included aspects of advertisement, postcards, cartoons, comics, and even movies to unify the country, envisioning a modern Japan.

¹⁰² John W. Dower, *War without Mercy: Race and Power in the Pacific War*, (New York: Pantheon, 1986)

 ¹⁰³ Chris Rudiger, "World War II and Propaganda," accessed July 21, 2023, https://web.stanford.edu/class/e297a/World%20War%20II%20and%20Propaganda.htm.

¹⁰⁴ Barak Kushner, *The Thought War: Japanese Imperial Propaganda*, (Honolulu University of Hawai'i Press, 2006.), p. 8.

¹⁰⁵ Ibid., p. 9.

Japan's close contact with the West dates back to 1853 when the American Commodore Matthew Perry sailed into Yokohama harbor with four battleships and demanded that Japan should open up trade with the USA. The Western powers had intentions of imperialism, and the signing of various treaties over the next five years was seen as a source of national humiliation. Over time, there was a growing desire for a modernized Japan. The government believed that to prevent Western powers from treating Japan like China, it was best to occupy neighboring territories after forming a unified and centralized empire. In 1919, after the First World War ended, Japan attended the Versailles peace conference and joined the League of Nations. Japan was officially recognized as a 'Big Five' world power.¹⁰⁶

During the 1920s, Japan saw corrupt politicians, a world economic crisis (the trade boom ended), and influential elite groups began to oppose democracy. After World War I, many European countries aimed to prevent another war. However, Japan did not experience as much suffering as some European nations, so their imperialist actions did not show a hesitation to go to war. Several factors combined to bring about significant changes in the early 1930s. Japan had control over the South Manchurian Railway and the banking system by 1931. The Japanese announced they had made Manchuria into an independent state called Manchuko, with Pu Yi as its leader. Pu Yi was the last emperor of China. They were not penalized. Manchukuo was established in 1932, but its origins can be traced back to 1905. During the Russo-Japanese War, Japan gained control over the southern part of Manchuria, which eventually led to the creation of Manchukuo. Japanese officials declared their intention to liberate Asia as early as 1933. In 1933, Japan started moving into northeastern China from Manchuria, even though they had no rightful claim to that territory. In March 1933, Japan officially left the League of Nations. By 1935, a significant portion of China, including Beijing, had come under Japanese political and commercial influence. After signing the Anti-Comintern Pact with Germany in 1936, the Japanese army used an incident between Chinese and Japanese troops in Peking to invade other parts of China. In 1938, the Japanese captured the cities of Shanghai, Nanking, and Hankoe.

Propaganda images from Manchuko

The news media played a significant role in promoting the war, even without any encouragement from the government. During the 1930s, Japanese officials viewed propaganda as a way to promote cultural ideals and attitudes that would be widely accepted by the public, rather than using forceful methods. The publishing and entertainment sectors have agreed to collaborate with army propagandists to help generate public support for the military occupation of Northeast China. They did it mainly because imperial warfare provided great opportunities for commercial

¹⁰⁶ Lowe, Norman. *Mastering Modern World History*, (Palgrave Macmillan, 2013.)

expansion and profit for mass culture producers. ¹⁰⁷ The war fever created the political and social backing that allowed the Kwantung Army to pursue aggressive military actions freely. ¹⁰⁸



Kenseishiryöshitsu, Manshü- koku nihongun sendenbutsu [1310, 5], National Diet Library, Tokyo. . Found in Kushner, The Thought War p.g. 123

This color poster from Japan serves as a striking example of the propaganda strategies employed by the Japanese government during their imperialist expansion, with a particular focus on Manchukuo, a puppet state established by Japan in Northeast China during the 1930s. At first glance, the poster radiates an aura of prosperity and a promising future for Manchukuo. It is meticulously crafted to portray a scene where civilians appear ecstatic, overjoyed, and harmoniously singing "Banzai!" This portrayal aims to convey the message that under Japanese governance, everyone in Manchukuo lives in a state of peace and contentment. In the top left section of the poster, the Kwantung Army is prominently displayed as heroes valiantly fighting off external enemies while ironically appearing as protectors of Manchukuo. This juxtaposition is deliberate and suggests that the Kwantung Army's actions are vital to safeguarding the peace and prosperity of the region. The image of individuals from various age groups coming together in jubilation implies a widespread acceptance of the new system established by Japan. It seeks to convey the idea that the Japanese presence is not only tolerated but embraced by the local population. The emphasis on prosperity is a calculated effort to rationalize Japan's occupation by suggesting that their governance has led to economic progress and an enhanced quality of life for the people of Manchukuo. Notably, the poster portrays Japanese soldiers purging bandits from the region, framing Japan as the guardian and enforcer of law and order. This depiction serves to justify Japan's military presence and occupation as a necessary measure to maintain security and protect the well-being of Manchukuo's inhabitants.

¹⁰⁷ Annika A. Culver, *Glorify the Empire: Japanese Avant-Garde Propaganda in Manchuko*, (University of British Columbia Press, 2013).

¹⁰⁸ John W. Dower, *War without Mercy: Race and Power in the Pacific War*, (New York: Pantheon, 1986)



Kenseishiryöshitsu, Manshü nihongun sendenbutsu [1310, 5], National Diet Library, Tokyo. Found in Kushner, The Thought War p.g. 124

In essence, this piece of propaganda is a concerted effort to present a favorable image of Manchukuo during the period of Japanese governance. By showcasing happiness, economic prosperity, and the maintenance of law and order, the poster seeks to legitimize Japan's imperialist expansion and occupation. It aims to persuade both domestic and international audiences that Japan's presence in Manchukuo is benevolent and in the best interests of the local population.



Kenseishiryöshitsu, Manshükoku nihongun sendenbutsu [1310, 6], National Diet Library, Tokyo. Found in Kushner, The Thought War p.g. 125

Two other pieces of Japanese Propaganda are depicted above. They, too, are from the time when Japan invaded Manchuria. This image underscores Japan's effort to convey the message that their presence in Manchuko was not driven by a desire for destruction but rather to nurture the growth of the region and foster unity among its diverse population. By highlighting harmony among races, Japan sought to portray itself as a benevolent force working towards the betterment of Manchuko's people. Japan had invaded Manchuria and made it a puppet state. Their main goal was imperialistic. However, in Japan, it was shown in a much different way. The second picture is of a poster from Manchuko written in Chinese. It has children of different races clearly shown with the same flag. "Creating harmony among the races" was the message.¹⁰⁹ Japan wanted to show that they were not there to start destruction, but to grow Manchuko and create harmony among the masses.

The following picture is of a Japanese soldier with a happy man from Manchuko. It reads, "Change the bad and install the good, for peace and prosperity" and the other side reads the response of the peasant - " we must correct the past and carefully listen to officials.¹¹⁰This widely circulated propaganda was designed to foster an appreciation for Japanese culture and customs in the region of Manchuria. This dialogue reinforces the idea that Japan's occupation was intended to bring about positive transformations, implying that the local population welcomed these changes. It suggests a harmonious collaboration between the Japanese military and Manchuko's residents. Japan's entry into Manchuria lacked a valid justification. Their act of crossing the borders was perceived as a display of aggression. However, the propaganda conveyed a different message. It is suggested that the Japanese intended to promote peace and harmony rather than aggression. They believed that the people of Manchuko should support them in implementing positive changes and rectifying any shortcomings.

Together, these pieces of propaganda show that Japan made up a story to justify its imperialistic actions in Manchuria. They wanted to make Japan look like a protector of peace, unity, and prosperity in the area. By focusing on ideas like racial harmony, positive change, and working together, Japan tried to show the rest of the world and its own people that it had good intentions. These messages were very important for controlling how the public saw Japan's expansionist plans and getting support for them.

¹⁰⁹ Translated text from a Japanese propaganda image, found in Kushner, *The Thought War*, p. 125.

¹¹⁰Translated text from a Japanese propaganda image, found in Kushner, *The Thought War*, p. 124



Kenseishiryöshitsu, Manshükoku nihongun sendenbutsu [1310, 6], National Diet Library, Tokyo.

Another piece of Japanese propaganda is shown above. It is a man, possibly a farmer reflecting on Manchuko's growth and development since the Japanese invasion. Even though Japan is the aggressor here, they are portrayed differently in Japan, raising national morale. The image of the contemplative man conveys a sense of introspection. He is portrayed as someone who is deeply thoughtful and perhaps even appreciative of the changes that have occurred in Manchuko under Japanese rule. This portrayal contrasts with the perception of Japan as an aggressor in international discourse. It suggests that Japan's presence and actions in Manchuria were not driven solely by conquest and subjugation but also by a desire to foster growth and development. This image is designed to humanize the Japanese occupation, showing it in a positive light, at least from a domestic perspective. One of the primary functions of such propaganda was to boost national morale within Japan. By showcasing images of contentment and growth in Manchuko, Japan sought to reassure its own citizens that their country's actions were just and beneficial. It aimed to create a sense of pride and unity among the Japanese populace, presenting the invasion of Manchuria as a noble endeavor.

The Britannica encyclopedia defines Propaganda as a more or less systematic effort to manipulate other people's beliefs, attitudes, or actions through symbols (words, gestures, banners, monuments, music, clothing, insignia, hairstyles, designs on coins and postage stamps, and so forth). And the Japanese propaganda did precisely this. They blurred the lines between fact and fiction. The propaganda and illustrations give the masses a picture of Manchuko, with citizens there happy on the arrival of the Kwauntang army. The one with the farmer portrays to the Japanese masses that Japan had gone into China and paved a road for ironical development there. The Japanese planned to send five million Japanese farmers to settle in the Manchurian

hinterland. The goal was to create a new generation of Japanese settlers with a more substantial influence on colonial society.¹¹¹

In reality, during the 1930s ,the silk industry saw a tremendous loss. The workers were out of a livelihood. Japan took this as an opportunity to use the land it took over in Manchuko for the silk farmers. The propagandists imagined Manachuko to be the heartland of Japan's heart new empire with space, minerals, land, and resources. In one of the cartoony scenes, in the top left section, the Kwantung Army is shown as heroes fighting off enemies protecting Manchuko, whereas, in reality, the Chinese needed protection from the Japanese imperialists in the 1930s. But, this was not the first time the Japanese had blurred fact and fiction to manipulate the masses and promote nationalist and militaristic ideologies. They had been doing this since the start and were good at it.



Propaganda images before the Second World War

The image above depicts a Japanese medical team tending to a wounded Russian. It is a staged photograph in a surgical theatre in the Russo-Japanese War. It was one of the earlier forms of propaganda in Japan. During the period in which Japan destroyed the Russian Empire in the Russo-Japanese War of 1904–1905. It is a misleading picture since it is not real. It instilled a sense of love for the Japanese military in the masses, as sympathetic and generous for helping out an injured Russian soldier.

¹¹¹ Annika A. Culver, *Glorify the Empire: Japanese Avant-Garde Propaganda in Manchuko*, (University of British Columbia Press, 2013).



This image is also of Japanese soldiers helping a wounded Russian soldier. It can be argued that this, too, is a staged photograph. These photographs served as propaganda as they depicted Japan as a country that helped its enemy countries and raised nationalistic feelings amongst the people. During the war, the Japanese often referred to themselves as the world's superior race ("shidominzoku"). ¹¹² fighting a war. This demonstrates the creativity in Japanese propaganda when they used false information like this to raise the spirit of a greater Japan. This is from the Sino-Japanese War (1894-1895). Japanese manipulation of facts was seen during the Second World War more clearly. Japan often depicted Western countries, particularly the United States, as imperialists and aggressors seeking to suppress Japan's rise as a world power. This portrayal aimed to rally the people against the perceived common enemy. In Dower's words "In fact, on the day of Pearl Harbor, the Japanese government approved a document stating 'It should be made absolutely clear to the Japanese people, this stated, that the enemy's 'selfish desire for world conquest' made war unavoidable, and Japan's cause was a moral one. The country's goal was to create a 'new world order' which would "enable all nations and races to assume their proper place in the world, and all peoples to be at peace in their own sphere."" ¹¹³

Japanese and the West

Various reasons can be given to explain the differences in racial and racist thinking between the Japanese and their Western enemies during Second World War. However, one general observation stands out: while racism in the West involved putting others down, the Japanese were primarily focused on elevating themselves. The Japanese were not skilled at belittling other races or using contemptuous stereotypes. Instead, they focused on understanding

¹¹² John W. Dower, *War without Mercy: Race and Power in the Pacific War*, (New York: Pantheon, 1986)

¹¹³ John W. Dower, *War without Mercy: Race and Power in the Pacific War*, (New York: Pantheon, 1986)

what it meant to be "Japanese" and how the "Yamato race" was distinct from other races and cultures. They believed that this uniqueness made them superior.¹¹⁴



May 1942 cartoon from the government-sponsored magazine Manga. Found in Dower, War without Mercy, p. 191.

The picture above is another creative piece of propaganda brainwashing the Japanese against the West. Combing out "dandruff" from one's head can be seen as a symbolic representation. It signifies eliminating unwanted thoughts and beliefs that the Japanese government deemed harmful to the nation's moral and social structure. The term "scurf" refers to specific characteristics such as extravagance, selfishness, hedonism, liberalism, materialism, money worship, and individualism. These were considered characteristics of Western societies that Japan aimed to counteract and replace with their values and principles. The cartoon aimed to establish a distinct contrast between Japan's values and those of Western nations by linking these traits to Anglo-American concepts. The objective was to cultivate a feeling of national pride and identity by portraying Japan as morally superior and ideologically different from the perceived indulgence of Western societies.

This propaganda piece, similar to the ones about Manchuria, was also ironic. The image depicts a man wearing a hat adorned with a map of the United Kingdom, intending to portray the UK in a negative light. During the war, the United Kingdom assumed control over India as imperialists. The propaganda depicts a man who is seen overpowering two individuals, specifically Indians. The individuals appear malnourished, whereas the British man presents a contrasting image. It could represent the resources that Britain utilized from India. This situation

¹¹⁴ Annika A. Culver, *Glorify the Empire: Japanese Avant-Garde Propaganda in Manchuko,* (University of British Columbia Press,2013).

caused great suffering among the ordinary Indians and benefited the British financially. One intriguing aspect is the man being stabbed by the sword. It has a bit of the Japanese flag. This demonstrates Japan's opposition to the British mistreatment of Indians and their willingness to assist, as evidenced by their support of the Indian National Army (INA). Interestingly, just as the British had colonized India, Japan was also engaging in a similar, and some may argue, even more severe, endeavor in China. This propaganda serves as a significant illustration for comprehending the Japanese mindset. It demonized their enemies for doing the same thing they did but ended up getting support from the masses from it.

It's noteworthy that while Japan was denouncing British colonialism in India, it was simultaneously engaged in a similar, and some might argue more severe, imperialistic endeavor in China. This propaganda serves as a significant illustration of the complexities in understanding the Japanese mindset during this period. It highlights Japan's selective use of moral arguments and how it could demonize its enemies for actions it was also involved in. This propaganda piece is a poignant reminder of the multifaceted nature of wartime messaging. It encapsulates Japan's strategic use of propaganda to not only vilify their enemies but also to galvanize support, even when Japan's own actions and imperialist ambitions mirrored those they condemned. It underscores the power of propaganda in shaping perceptions and mobilizing public sentiment during times of conflict.

Propaganda and Education

Education was another essential strategy utilized by the Japanese. Students in Japan were indoctrinated with nationalist and militaristic values through the country's education system during World War II. To present Japan in a more favorable light, revisions were made to historical textbooks, which either downplayed or omitted references to war crimes and atrocities committed by the Japanese military.

The picture below depicts a cartoon-like scene intended for an audience of Japanese children. A white flag is seen raised as a sign of Chinese defeat, and humorous illustrations portray Japanese victory and the Japanese flag. Japan often described the Japanese as pure, righteous, and loyal folks determined to liberate Asia from colonial oppression. But the reality was far from this. Japanese filmmakers, cartoonists, and illustrators raised the war morale in Japanese favor. They masked the reality—the reality of what they did in other countries. The atrocities and the mistreatment of the people of the territories imperialized. Dehumanizing and Demonising the West for it, the Japanese did it worse and hid it better.


Magazine Tabi (Travel), December 1937, p. 72. Found in Kushner, The Thought War p.g.

Reality and Manufactured Reality

Many atrocities and acts of brutality committed by the Japanese Imperial Army against civilians and prisoners of war during World War II were not widely known or recognized until after the war. The Japanese Imperial Army committed these atrocities and acts. During the war, the Japanese military carried out numerous atrocities, despite their outward appearance of glory. The Nanking Massacre, which occurred in 1937 and is also referred to as the Rape of Nanking, involved killing Chinese civilians and prisoners of war. It is estimated that hundreds of thousands lost their lives during this tragic event. The severity of these acts was frequently minimized or denied in Japanese propaganda, which exacerbated the feelings of resentment and distrust among the Allied powers.

A piece of illustration created by a man who, himself, was a prisoner of war to the Japanese demonstrates the stark contrast to the Japanese image that Japan created through Propaganda. Ronald William Fordham Searle was taken prisoner along with his cousin when Singapore fell to the Japanese in World War 2.In Searle's words, "I desperately wanted to put down what was happening because I thought if by any chance there was a record, even if I died, someone might find it and know what went on."¹¹⁵

¹¹⁵ "Ronald Searle - Wikipedia," *Wikipedia*, accessed August 6, 2023, https://en.wikipedia.org/wiki/Ronald_Searle.



This illustration shows a scene of a market, where Japanese soldiers mistreat food vendors. They are seen to assault the women fruit sellers who are, in all probability, natives of the territory they overtook. They portrayed in their propaganda that imperial Japan was a formidable and morally justified power with a perceived destiny to free Asia from Western imperialism.

Conclusion

This paper started by asking, "why do we focus on Nazism when we hear terms like ideology and propaganda during the second world war? Why do we not consider the hidden prospects of Japanese Propaganda and their concept of the "Greater East Asia Co-Prosperity."? While Nazism has garnered extensive scholarly attention, Japanese wartime propaganda presents a distinctive and unconventional narrative. It employed a sophisticated blend of artistry and manipulation, effectively elevating Japan's image in the public's perception. In the absence of comprehensive research on Japanese propaganda during World War II, this paper aimed to bridge the gap by conducting a comprehensive analysis of Japanese propaganda and ideology.

Japanese wartime propaganda encompassed a wide range of media, including postcards, illustrations, artwork, cartoons, and comic strips. These media forms served as powerful conduits for conveying ideological content and addressing complex issues of race and imperialism in Asia. Notably, Japanese propaganda employed creative techniques, such as humor and advertisements, to disseminate its message while skillfully manipulating the masses. One of the central themes explored in this paper was the manipulation of fact and fiction. Japanese propaganda adeptly blurred the lines between reality and manufactured reality, cultivating a sense of loyalty and allegiance among its viewers. This approach allowed Japan to present itself as a benevolent force while downplaying its wartime atrocities.

Throughout the years, Japanese artists, society, and government collaborated to create illustrations, postcards, cartoons, and comics that not only engaged the viewer but also induced a profound sense of connection and loyalty to Japan. The use of propaganda as a psychological tool is evident in these carefully crafted works of art. Understanding the fact-fiction dichotomy in Japanese propaganda is essential to grasp the complexity of historical events and the power of information in shaping perceptions during times of war.

Investigating AI's Challenges in Reasoning and Explanation from a Historical Perspective By Benji Alwis

Introduction

Imagine a scenario where an autonomous vehicle has been trained on an extensive dataset containing diverse driving situations, including numerous instances of pedestrians using designated crosswalks. This Artificial Intelligence (AI) model is designed to excel at recognizing crosswalks and navigating around pedestrians, prioritizing their safety. It has learned from this data that pedestrians typically cross the road at these marked locations, and it can discern the visual cues associated with crosswalks while accurately identifying pedestrian movements within them.

However, when faced with a novel and unfamiliar crosswalk, the AI system may encounter difficulties in accurately assessing the pedestrians' intentions. For instance, if a traffic signal at the crosswalk malfunctions, leading to confusion among pedestrians, the AI model might struggle to grasp the complexities of the situation and respond appropriately. This lack of the AI model's ability to understand and apply the underlying causes and effects in unfamiliar or unexpected situations could result in the autonomous vehicle failing to yield to pedestrians at crosswalks in specific circumstances. Such lapses in judgment could potentially lead to perilous situations, endangering the safety of both pedestrians and vehicle passengers. The primary issue at hand lies in the AI model's deficiency when it comes to causal reasoning, the ability to deduce outcomes based on cause-and-effect relationships. The neural network-based approach, which has powered significant recent advancements in AI, excels at identifying correlations within extensive datasets. However, it often falters in terms of interpretability and rational deduction, serving as a barrier to developing AI systems with human-like capabilities.

Hence, the imperative lies in bolstering AI with the capacity for causal reasoning, enabling it to address "what if?" and "why?" inquiries effectively. This becomes particularly crucial in safety-critical domains where understanding the underlying causes and potential consequences of actions is paramount. This essay aims to delve into the roots of this deficiency through a historical lens by tracing the evolution of AI. While this drawback has been scrutinized from a technological standpoint (Knight; Schölkopf), it is noteworthy that, to the best of my knowledge, this represents the first attempt to dissect it from a historical perspective. Building upon the argument put forth by Pinch and Bijker in their seminal work "The Social Construction of Facts and Artifacts," which contends that "technological determinism is a myth that results when one looks backwards and believes that the path taken to the present was the only possible path" (Bijker 28), I hold the view that the evolution of artificial intelligence is a complex process shaped not only by the inherent properties of the technology but also by an interplay of societal factors and human agency. Over the years, the development of technology has been profoundly influenced by a tapestry of social, cultural, and political forces. The framework of the "social construction of technology" (SCOT) offers a valuable lens through which we can understand this complex relationship between technology and society, with Pinch and Bijker laying its foundational stones. As explored later in this essay, the interplay between technology and society has played a pivotal role in shaping the trajectory of a nascent field like Artificial Intelligence during the pivotal period from the 1950s to the 1970s. Anderson and Rosenfeld elucidate some of the driving forces behind these dynamics, asserting that "bringing a new field into existence involves the participants in a bitter and sometimes brutal Darwinian struggle for jobs, resources, and reputation" (Anderson viii).

In this essay, I will adopt SCOT as the primary theoretical framework for dissecting the historical evolution of Artificial Intelligence. Throughout this analysis, I will leverage two fundamental principles integral to the SCOT framework.

The first critical factor examined is interpretive flexibility (Bijker 40). It suggests that technological innovations can be understood in various ways by different individuals or groups, leading to diverse perspectives and potential outcomes. This concept is a valuable tool for analyzing technology-related debates influenced by different social groups and their interests. It allows parties to frame technology differently, emphasizing certain aspects while downplaying others to advance their arguments. Moreover, it can be used strategically to evoke emotional responses and influence opinions.

In technology-related arguments, exploiting interpretive flexibility is a strategic communication technique that shapes the narrative around technology and its implications, influencing perceptions, opinions, and decisions.

The second critical factor is the role of relevant social groups in technology development and success. Various stakeholders, including engineers, designers, users, and policymakers, play a crucial role in negotiating and influencing the features and functions of technology. SCOT emphasizes the relationships and dynamics among these social groups and how they interact with the broader social context to understand how technology evolves and integrates into society. In this essay, I delve into the evolutionary journey of Artificial Intelligence during its formative phase, with a particular focus on its inception and the pivotal factors that have steered its developmental course. Merton's insightful observations shed light on the dynamics that govern the emergence of nascent scientific disciplines and the roles played by both insiders and outsiders in molding these domains (Merton 10). He notes that established scientists, often referred to as "insiders," typically enjoy a greater share of recognition and resources for their contributions in comparison to newcomers, aptly labeled as "outsiders." This disparity in recognition can give rise to a self-perpetuating cycle where established researchers continually accrue more opportunities, consequently fostering further progress and triumph in their field. The privileged status of insiders affords them the influential power to shape the trajectory of the discipline. They exercise this influence through their sway over critical determinants such as funding allocation, the establishment of publishing norms, and the acceptance of innovative concepts. Conversely, outsiders may encounter formidable obstacles when endeavoring to gain acknowledgment for their ideas, secure essential resources, and establish their credibility within the field. Nonetheless, they bring to the table a breath of fresh perspectives and innovative

concepts, challenging the prevailing paradigms and making indispensable contributions to the evolutionary path of the new field.

Merton's perspective underscores the pivotal role insiders play in delineating the contours of an emerging field, not only through their individual research endeavors but also through their collaborative ventures and interactions with fellow researchers. Moreover, external factors such as societal demands, technological breakthroughs, and interdisciplinary cooperation also exert substantial influence in molding the boundaries and the trajectory.

Actor-network theory (ANT), a concept pioneered by Bruno Latour, provides a framework for comprehending the genesis and legitimization of emerging scientific domains. ANT focuses on the web of interactions and collaborations involving an array of diverse actors, ranging from scientists and technologies to instruments, funding agencies, institutions, and even non-human elements. Within this framework, the alignment and coordination of these diverse actors are central to the development of shared interests and objectives (Latour 369). Unlike conventional perspectives that view scientific knowledge as the outcome of objective discovery, ANT posits that knowledge creation is a collaborative and co-constructive process involving both human and non-human entities. In essence, it asserts that the emergence of a nascent scientific field is characterized by a dynamic interplay of negotiations, controversies, and alliances among these multifaceted actors. According to actor-network theory, the conventional boundaries between scientific disciplines are not rigidly defined but are continuously subject to negotiation and construction. This perspective underscores the fluid nature of scientific boundaries, which are constantly evolving as a consequence of the interactions and negotiations among the various actors within the network.

Seidenberg characterizes the history of Artificial Intelligence research as a saga reminiscent of a long-running soap opera, populated by a cast of characters that may appear somewhat peculiar, even by the standards of academia (Seidenberg 122). In his vivid portrayal, this narrative unfolds as an extraordinary tale, replete with all the elements of a gripping drama – encompassing moments of tragedy, hubris, irony, humor, acrimonious intellectual battles, and, in a few instances, even the figurative "corpses" of ideas or projects that did not stand the test of time.

Alexander further delves into the underlying causes of these frictions and tensions within Artificial Intelligence research (Aleksander 29). He underscores that, in contrast to the linear and celebrated narrative of Watson and Crick's DNA discovery, the field of Artificial Intelligence is marked by a profusion of diverse and sometimes competing techniques and analytical methods. This inherent complexity, he contends, gives rise to a host of pressures and conflicts within the community of researchers. Among the significant catalysts of discord, Alexander identifies the relentless pressures to deliver tangible products, secure essential funding, the allure of mathematical rigor and analysis, and the desire to claim credit for innovative breakthroughs. These factors collectively contribute to the multifaceted and, at times, tumultuous nature of Artificial Intelligence research, creating a fabric of narratives that echo the human dynamics and motivations at play within the scientific arena. The history of Artificial Intelligence research, as described by Seidenberg and analyzed by Alexander, emerges as a captivating narrative mixed with all the hallmarks of a compelling storyline. It is a testament to the complexity of scientific exploration and the multitude of forces that shape the evolution of ideas in this ever-evolving field.

The Cybernetic Age: A New Frontier of Progress

The emergence of AI owes its inception to the efforts of a diverse array of exceptionally skilled and intellectually assured individuals. This inclusive group encompassed mathematicians, electrical engineers, psychologists, and neuroscientists. While certain members of this cohort never fully integrated into the mainstream of AI research, their contributions wielded remarkable influence in shaping the initial trajectory of the field.

Amidst the backdrop of the Second World War, the significance of collaborative problem-solving soared to new heights. The pioneering collective of researchers whose collaborative efforts paved the way for the first wave of AI was composed of notable mathematicians like Norbert Wiener and John von Neumann, engineers including Julian Bigelow and Claude Shannon, neurobiologists Rafael Lorente de Nó and Arturo Rosenblueth, neuropsychiatrist Warren McCulloch, along with the unconventional genius Walter Pitts, who lacked formal qualifications (Heims 11). Although often referred to as the cybernetics group, it was not until 1947 that this collective solidified its identity as a distinct scientific field. Cybernetics, a term coined by Norbert Wiener, delved into the exploration of control, communication, and regulation principles in both natural and artificial systems. During this period, the emphasis shifted towards the human sciences, prioritizing pragmatic problem-solving over abstract musings (Heims 1). Heims has portrayed Wiener as 'the dominant figure' within the cybernetics group discussions, highlighting his role as a brilliant visionary and provocateur of innovative ideas (Heims 206). Wiener's view was that intelligence materializes through the complex processing of information facilitated by feedback mechanisms. This position stood in contrast to some of the prevailing notions of his era, including Sigmund Freud's theory, which suggested that the mind primarily orchestrates biological energies (Crevier 28). Wiener's inclination to integrate psychology into the framework of cybernetic concepts diverged from the approach of another influential figure within this group, John von Neumann (Edwards 240). Despite the divergent approaches they adopted, the cyberneticians forged a potent cluster of influential thinkers during their time. The history of science shows that, particularly within human sciences, such elite groups played an instrumental role in shaping consensus on priorities, leveraging their collective resources and prestige to propel research agendas forward. The historical records of the Macy conferences on cybernetics, a sequence of multidisciplinary gatherings supported by the Macy Foundation and convened from 1946 to 1953, show the pivotal role undertaken by this collective during that era (Heims 12). This stands in stark contrast to the divisions and conflicts explored in subsequent sections of this essay.

Within the group of researchers who infused cybernetics into their initial theories of intelligence, there were those who embarked on a mission to replicate the complex mechanisms

of the brain. Their strategy involved the emulation of individual neurons through the use of electrical components. Neuropsychiatrist Warren McCulloch, a prominent figure among the cyberneticians, had been contemplating hypothetical engineering components designed to emulate the workings of the human mind and brain. He was known for his interdisciplinary approach, drawing insights from biology, mathematics, and philosophy to understand the brain and intelligence. In 1942, he met Walter Pitts. Upon their encounter, McCulloch, known for his benevolent nature, warmly offered him accommodation in his own residence, recognizing Pitts' homelessness (Anderson 3). Their collaborative efforts culminated in the creation of the McCulloch-Pitts (M-P) model, a computational framework depicting artificial neurons. This seminal innovation not only underpinned the inception of neural network theory but also cast a transformative influence on the landscape of computational neuroscience. The model's overarching objective was to encapsulate the fundamental operations of biological neurons alongside their prowess in information manipulation. Central to the M-P model was the introduction of artificial neurons configured as binary threshold units. These units took binary inputs, applied weighted connections, and produced binary outputs based on a threshold function. While the model was a simplification of real neural behavior, it demonstrated the potential for mathematical modeling of neural processes and information processing. It laid the foundation for subsequent developments in neural network theory and paved the way for the exploration of learning algorithms and more sophisticated neural network architectures. According to Jerry Lettvin, often considered the third vertex in the triangle of this collaboration (Kelly 55), Walter Pitts was a mere 17 or 18 years of age when the renowned McCulloch-Pitts paper titled "A Logical Calculus of Ideas Immanent in Nervous Activity" made its debut in the Bulletin of Mathematical Biophysics in 1943 (McCulloch). Lettvin has subsequently stated that

In no uncertain sense, Pitts was the genius of the group. He was also personally a very unhappy person. He was absolutely incomparable with the amount of knowledge he had (Anderson 9). To him the world was connected in a very complex and wonderful fashion. At the same time he was very very opposed to having his name known publicly, so much so that when they offered him the doctorate at MIT if he would just sign his name or translate a page from the German which he did very easily, he refused. Later on when they offered him a faculty position if he would just sign his name to a document, he refused (Anderson 9).

In 1951, a collaborative group comprising McCulloch, Pitts, Lettvin, and Pat Wall presented themselves as a unified front to MIT. Notably, during this timeframe, Norbert Wiener, who had by then gained widespread recognition as a pioneer in cybernetics, had risen to a position of considerable influence. Upon his affiliation with MIT, McCulloch willingly relinquished his full professorship, accepting instead the post of research associate along with a modest apartment in Cambridge. He envisioned the combination of information theory, neurophysiology, statistical mechanics, and computing machinery to understand the mystery of how the brain gives rise to the mind. Michael Arbib, who later became a research assistant in McCulloch's group, has recounted the influx of funding into this new area of research. There was lots of money around so that being an RA was not particularly onerous. Basically, the Navy and other agencies gave lots of money to MIT and funneled them to various people and Warren [McCulloch] was one of the good guys so he had quite a lot of money to support bright young students. (Anderson 216)

He further corroborated the opinions voiced by Lettwin regarding Pitts' intellectual prowess.

I think, where Pitts was the child and yet, in some ways, intellectually the more powerful of the pair though McCulloch knew an incredible amount about the brain and had been a very successful anatomist and still was at that time. (Anderson 218)

During their time at MIT, the research trajectories of McCulloch and Pitts began to diverge. As recounted by Lettwin,

McCulloch became seduced into what can be done theoretically with nerve networks. Pitts by this time had more or less set himself against the concept of doing a synthetic job. To him it was much more important to come up with analytical notions of how such things were possible (Anderson 9).

The McCulloch-Pitts model, although valuable in its own right, fell short in adequately capturing the intricacies of the biological brain, and thus it failed to elicit substantial enthusiasm among brain scientists. Recognizing this limitation, Wiener, drawing upon his mastery of statistics and probability theory, aimed to steer Pitts toward refining his brain model to attain a more realistic representation. Against this backdrop, Pitt's collaborations with Wiener gained substantial traction, and he started writing an extensive thesis delving into randomly connected probabilistic three-dimensional neural networks.

What transpired subsequently needs to be examined within the context of several influencing factors. As outlined in one of Norbert Wiener's biographies (Wiener 55), He was such a misfit in school that his father, Leo Wiener, a stringent Harvard languages professor, opted for homeschooling. Unfortunately, if Norbert fell short of expectations, he was occasionally labeled with derogatory terms such as "donkey," "brute," "ass," and "fool" in a multitude of languages—over forty, to be precise. These hurtful recollections remained a haunting presence throughout Norbert's lifetime. Despite these challenges, Norbert Wiener managed to complete his doctoral studies at Harvard by the age of eighteen, driven in the direction his father had encouraged. However, detaching himself from this imposed path took some time. Numerous sources shed light on Wiener's vulnerability to depression. An account from one of his MIT students notes that "his profound immersion in his own thoughts often rendered him unaware of his surroundings (Gangolli 772)," Delving into Wiener's biography by Conway and Siegelm, a complex tapestry of attributes comes to the forefront (Conway). This includes a fusion of "astounding brilliance, a childlike sense of awe and trust, a humanist perspective stemming from resolute idealism, and, regrettably, his struggles with insecurity and a turbulent personal life." Walter Pitts' father and brothers considered him an outsider. When he reached the age of 15, he took the significant step of running away from home, effectively severing all communication ties with his family (Smalheiser 217). It is noted that he held Warren McCulloch and Norbert Wiener

in the light of paternal figures within his life (Anderson 9). Wilson, who extensively studied the complex dynamics between Pitts, McCulloch, Lettwin, and Wiener, arrives at the conclusion that

The affective inclinations in the group were perhaps too muddled and too muffled to withstand the force of conventional patriarchal fury, and Pitts was too fragile and too isolated to recover from the intellectual and emotional shock (Wilson 847) resulting from the forthcoming incident.

Unexpectedly, Wiener severed all connections with the McCulloch group, including Pitts, sending shockwaves through their interactions. In a formal letter addressed to the President of MIT, he articulated a series of grievances against them, highlighting concerns such as the alleged misallocation of research funds. Speculation surrounding the true catalyst for this abrupt rupture has given rise to several theories (Anderson 9, Smalheiser 223). Nonetheless, in a biography penned by Conway and Siegelm, drawing from insights provided by Lettvin, an alternative narrative unfolds (Conway, 219). According to their account, Wiener's wife, Margaret, emerges as a pivotal figure in precipitating this division. Allegedly, she wove a fabricated tale out of her aversion to Wiener's association with the group, characterized by Bohemian inclinations and an unconventional lifestyle. Furthermore, it is posited that McCulloch's well-documented penchant for alcohol, and the extent to which he indulged in it, might have exacerbated Margaret's concerns due to Wiener's already weak emotional state. In essence, the reasons behind this sudden and drastic transformation in Wiener's relationships and alliances remain multi-faceted and open to interpretation.

This event left Pitts utterly devastated, bearing the brunt of its impact more than anyone else. Losing Wiener was akin to losing a father figure for him. Lettwin's account sheds light on the depth of this impact. Pitts had been preoccupied in the development of three-dimensional neural networks, a concept that was meticulously documented in his thesis, spanning hundreds of pages. Shockingly, he destroyed this painstaking work, a decision that Lettwin attributes to the emotional turmoil of the moment. The blow was so profound that, as Lettwin recalls, Pitts never managed to fully recover from it. Lettwin touchingly notes, "From that point on, there was no way of getting him interested in things (Anderson 9)." This continuing sadness endured until his tragic passing in 1969, seventeen years later. As recounted by Smalheiser, Pitts' response to the upheaval went beyond mere emotional distress (Smalheiser 223). Rather, he engaged in an unprecedented experiment with substances. Pitts, known for his exceptional intellect, took an unconventional path by synthesizing novel analogues of barbiturates and opiates within his laboratory. He delved further by subjecting himself to experiments involving long-chain alcohols, a testament to his complex coping mechanisms. Notably, in June 1954, Pitts' brilliance garnered recognition, as Fortune magazine distinguished him in its roster of Ten Top Young Scientists in U.S. universities (Smalheiser 223). Conway and Siegelm, in their analysis, underscore the pivotal role of the research trio-Wiener, Pitts, and McCulloch-and its subsequent dissolution. Their separation, according to the authors, emerges as a central reason for the unfulfilled potential of cybernetics. Conway and Siegelm lament that this division

prevented cybernetics from achieving the remarkable success they believed it was destined for (Conway 233).

Cybernetics, as a discipline, was driven by a profound objective: to replicate the intricate workings of the human brain through computer hardware (Edwards 239). This ambition stemmed from their view of human intelligence as a dynamic interplay of information—an internal world of closed loops. In their eyes, intelligence emerged through the manipulation of information, a process empowered by the feedback loops. This perspective was rooted in the realization that intelligence, whether displayed by humans or other systems, wove information processing and adaptive responses in the pursuit of objectives. Their approach revolved around the creation of self-organizing machines poised to attain complex behaviors by engaging with their surroundings—a representation of closed-loop dynamics.

The Epoch of Symbolic AI: Pioneering Intelligence Using Software

The subsequent wave of progress emerged through a group of researchers whose perception of computers went beyond their pragmatic utility. They regarded these machines not merely as instruments for pragmatic problem-solving, but rather as automated representations of mathematical models with profound intellectual attraction. This intellectual effort resulted in the form of Artificial Intelligence (AI), a term formally coined in 1956 (Crevier 50). Departing from the ambition to simulate cognitive functions through hardware replication, AI pursued a different trajectory by attempting to exhibit intelligent behavior within software constructs. Scientists such as Allen Newell, Herbert A. Simon, Marvin Minsky, and John McCarthy stand among the pioneers of AI research. Their contributions paved the way for the first wave of artificial intelligence (Crevier 32-44).

The 1956 Dartmouth Conference, a summer school held at Dartmouth College in Hanover, New Hampshire, is widely acknowledged as the pivotal origin of AI as an academic discipline (Crevier 48). This two-month event, co-convened by Marvin Minsky and John McCarthy, aimed to explore the notion that all aspects of learning and intelligence could be comprehensively explained to the extent that machines could replicate them precisely. The documented discussions reveal that Minsky emphasized topics like learning theory and the necessity for precise descriptions of the principles behind the brain's physiological structure as significant focal points during the gathering (Penn 172).

One of McCarthy's objectives was to create a hybrid logical and natural language for AI, aiming to provide machines with a foundational comprehension of the world. Between 1956 and 1958, he successfully realized this goal through the development of a programming language named LISP (Penn 154). LISP manipulates lists and programs written in LISP are inherently structured as lists themselves. This language, which emerged as the lingua franca of symbolic AI in its early stages, enabled the field to make significant strides.

The advent of digital computers in the 1950s and the subsequent widespread adoption of high-level programming languages played a pivotal role in advancing and shaping symbolic AI. These programming languages introduced a higher level of abstraction, enabling researchers to

focus on directly translating symbolic and logical concepts into code. Symbolic AI revolves around the manipulation of explicit symbols and rules to represent knowledge and perform reasoning tasks. In symbolic AI, knowledge is typically conveyed through symbols, logical statements, and rule-based systems. The primary objective is to manipulate these symbols to deduce conclusions and solve problems. Symbolic AI systems are rule-driven, relying on formal logic for reasoning. They excel in well-structured and clearly defined domains, where explicit rules and logical relationships can be easily articulated. One of the early achievements of symbolic AI was the creation of expert systems, which encoded human expertise and knowledge in the form of rules to solve specific problems. However, symbolic AI has inherent limitations when it comes to handling uncertainty and processing vast amounts of unstructured data, which makes it less suitable for tasks like image recognition and natural language understanding. As later elaborated in this essay, the early AI pioneers aimed to establish a distinct identity separate from cyberneticians. However, it is important to note that this perspective is not entirely accurate. What is intriguing is that the impact of cybernetics on this group of researchers remained largely unexplored until the publication of Paul Edwards' book, "The Closed World," in 1996 (Edwards 239).

Among the influential AI researchers of the time were Allen Newell and Herbert A. Simon, creators of the Logic Theorist in 1956, a program capable of proving mathematical theorems using symbolic logic. Notably, Oliver Selfridge, a prominent disciple of Norbert Wiener and recognized as the "Father of Machine Perception," exerted a significant influence on Newell's intellectual journey. Selfridge's pioneering programs occupied the intersection of cybernetics and symbolic information processing, representing a pivotal transitional phase in the evolution of computational models. This transitional quality of Selfridge's work not only resonated with Newell's own intellectual inclinations but also provided him with a conceptual framework to bridge the gap between biologically inspired ideas and symbolic AI approaches (Edwards 250).

Marvin Minsky was one of the early proponents of symbolic AI and the development of expert systems. He believed that intelligence could be replicated through the manipulation of symbols and logical rules. His contributions were integral in shaping the nascent stages of the field's evolution. Nonetheless, Jonathan Penn has highlighted a noteworthy aspect regarding Minsky's academic journey. During his tenure as a doctoral researcher in mathematics at Princeton University in 1950, Minsky extensively immersed himself in cybernetic theory (Penn 160). It is worth noting that Minsky's transition toward symbolic reasoning commenced around 1954, a mere two years prior to the pivotal Dartmouth Conference that sought to establish the roadmap for AI research.

The Dawn of Neural Networks: Revolutionizing Intelligence

Frank Rosenblatt, an AI researcher deeply engaged in learning theory at Cornell University during that period, was conspicuously absent from the list of invitees to the Dartmouth Conference (Penn 140). In 1957, Rosenblatt made a groundbreaking contribution by publishing a technical report in 1957 and a pivotal paper a year later on "Perceptrons," a term he introduced which now corresponds to what we commonly refer to as neural networks (Rosenblatt). Combining his background in psychology with a strong reliance on statistical methodologies, Rosenblatt's perceptron project was centered around the concept of training a machine through associative logic. His work marked the inception of the first model capable of acquiring weights from examples, thereby advancing the concept of learning through practice. The initial form of the model emerged as a simulation within an IBM 704 computer (Penn 82). Rosenblatt's model, while admittedly a simplification of the nervous system, was rooted in the foundational framework of McCulloch and Pitts neurons. This approach, inspired by the symbolic AI community of that era. The fundamental distinction lay in how symbolic AI perceived knowledge: as a hierarchical system of predefined rules and procedures. In contrast, the approach taken by perceptron research embraced a perspective where knowledge was acquired organically, emerging from intricate interactions with the environment, and developing from the ground up (Penn 82).

Rosenblatt emerged as not only a brilliant scientist but also a captivating figure with a knack for media navigation. As mentioned by Mikel Olazaran, he possessed qualities that would make a press agent's dreams come true (Olazaran 105). Interestingly, in contrast to the unfolding events that lay ahead, his earlier years held an intriguing connection: during their time as fellow students at the Bronx High School of Science, he shared a friendship with Marvin Minsky that traced back to their childhood days (Gravier 102).

The scientific community's frustration originated from Rosenblatt's presentation, marked by a unique flourish, of his work to the media. This was followed by the unfortunate misrepresentation of his findings in the subsequent reporting. One such example was how the prestigious Science magazine featured a headline titled "Human Brains Replaced?" that suggested "Perceptron may eventually be able to learn, make decisions, and translate languages." (Gravier 103) The New York Times covered an event involving a primary sponsor of the project

The Navy revealed the embryo of an electronic computer today that it expects will be able to walk, talk, see, write, reproduce itself and be conscious of its existence. Later perceptrons will be able to recognize people and call out their names and instantly translate speech in one language to speech and writing in another language (Olazaran 100). The New Yorker also quoted Rosenblatt as expressing:

The Perceptron can tell the difference between a dog and a cat, though so far, according to our calculations, it would not be able to tell whether the dog was to the left or to the right of the cat. We still have to teach it depth perception and refinements of judgment (Gravier 103). The challenge of image classification under various demanding conditions persisted as a formidable problem for decades to follow. It was only within the past decade that neural networks successfully reached these significant milestones. Critics leveled accusations at Rosenblatt, asserting that he had not upheld scientific standards and had instead employed the media in a biased manner (Olazaran 103). Nevertheless, when addressing scientific audiences, Rosenblatt exhibited caution in linking his work to prior research.

Minsky, a prominent advocate of the symbolic AI approach during that era, had actually delved into his own experimentation with neural networks while at Harvard. Additionally, he engaged in thorough theoretical analysis during his tenure at Princeton. While Rosenblatt's work stands as the most renowned non-symbolic AI project of its time, it was part of a broader trend that commenced in the early 1950s and gained momentum leading up to the late 1950s. Minsky was among some of the prominent scientists who were concerned about this growing trend. Later he claimed that

schemes quickly took root, and soon there were perhaps as many as a hundred groups, large and small, experimenting the model either as a 'learning machine' or in the guise of 'adaptive' or 'self-organizing' networks or 'automatic control' systems. (Olazaran 110). Advocates of the neural network approach readily acknowledged its limitations. Foremost among these constraints was its single-layer architecture, which rendered it incapable of executing numerous essential functions. During that period, the absence of a methodology to train multilayer networks hindered the practical utility of this algorithm. The proponents of this approach asserted that single-layer networks represented just the initial stage, and while acknowledging their significant limitations, they remained confident that more intricate systems would eventually surmount these challenges. However, these seemingly exaggerated claims about its potential and capabilities sparked numerous, often intense debates within scientific circles. Among those voicing skepticism was Minsky, who prominently led discussions against the perceptron approach. Amidst the fervent debates of the 1960s, a particularly heated period, Marvin Minsky and Seymour Papert, both associated with MIT at the time, undertook a noteworthy and resource-intensive endeavor. They chose to 're-enact' the perceptron's outcomes, a meticulous process involving replicating every step the original author had taken. Unavoidably, the undertaking turned out to be a protracted endeavor, surpassing the initially anticipated timeframe. The culmination of this effort, along with its subsequent analysis, eventually saw the light of day in 1969 with the release of an unpublished technical manuscript and the publication of a revised and de-venomized book titled "Perceptrons (Minsky)."

It is widely acknowledged that the critique presented in the book, coupled with the influential stature of Minsky and Papert during that era, exerted significant influence in temporarily stalling the progress of neural-network research in the United States (Olazaran 183). This pause in advancement saw Symbolic AI reclaim its previously dominant position, maintaining its supremacy until the resurgence of neural network research in the 1980s. In hindsight, Papert later conceded that this redirection was largely a mistake, given that nearly half of the findings presented in the book actually supported the potential of Perception. Similarly, Minsky later acknowledged that the book might have been an "overkill." (Bernstein) It is widely acknowledged that the initial optimism surrounding the advancement of AI may have been excessive. Nevertheless, it is equally important to recognize that the backlash against neural networks during this time may have been too extreme.

Today, it is worth noting that neural networks have become the driving force behind the vast majority of AI success stories, underscoring the remarkable turnaround in perception and the undeniable impact they have had on the field of artificial intelligence.

Unifying the Pinnacle of Intelligence: Neuro-Symbolic AI

A fusion of philosophical, historical, and social influences has often led to the conventional belief that symbolic AI and neural network approaches were fundamentally and irrevocably separate entities (Schneider). However, Vasant Honavar has compellingly challenged this seemingly insurmountable divide (Honavar). He has emphasized the alignment between the foundational philosophical assumptions and scientific hypotheses that have molded both approaches in the realm of modeling cognition and engineering intelligent systems. He has pointed out that both approaches share the core working hypothesis that cognition, or the processes of thought, can, at some level, be effectively modeled through computation. Neural networks have indeed demonstrated remarkable proficiency in processing and discerning patterns from raw data. Nevertheless, they often lack the explicit representations of background knowledge essential for tasks such as abstraction, analogical reasoning, and long-term planning. In contrast, symbolic knowledge-based AI excels in modeling knowledge, facilitating traceability, and enabling auditability of AI system decisions. The emerging neuro-symbolic paradigm seeks to harmonize and synthesize the strengths of both approaches, presenting a highly promising avenue for advancing artificial intelligence by enhancing its capacity for explainability and causal reasoning (Sheth).

A pressing question that naturally arises is why this integration was not ventured into at an earlier juncture. I contend that one of the primary impediments to the exploration of integrating these two approaches lies in the enduring historical schism that persisted between these two scientific communities. This divide made collaborative endeavors challenging during the formative stages of development, ultimately resulting in the establishment of two parallel streams of research.

Conclusions

It is natural for pioneers in a field to be concerned with documenting their own history. Typically, such efforts focus on developing a historical narrative from an intellectual standpoint. However, as the SCOT framework suggests, the emergence and evolution of new fields are the outcomes of a complex interplay among technology, societal factors, and human agency. Some of the foundational ideas of cybernetics found their roots in the Macy Conferences, a series of multidisciplinary gatherings held between 1946 and 1953, supported by the Macy Foundation. In the wake of World War II, numerous scientists had returned from participation in multidisciplinary military research projects, and their achievements were held in high regard. For instance, Norbert Wiener had incorporated feedback control systems into anti-aircraft gun fire control systems to enhance targeting accuracy during the war. Consequently, this generation of scientists possessed valuable experience in engaging in multidisciplinary research projects, making it relatively easier to replicate such collaborative efforts in academic settings. This contrasts with the relatively unproductive Dartmouth Conference (Minsky), which coined the term "Artificial Intelligence" and took place a decade later in a different socio-political context. Moreover, the cybernetics movement gained momentum at a time when some of the scientific and technical advances of the war years—such as the modern general-purpose computer and models based on it—were just becoming publicly available. This occurred within the broader context of postwar practical requirements, political discussions, and social networks, all of which played a pivotal role in shaping the trajectory of cybernetics.

A significant portion of pioneering cybernetics research was carried out by a close-knit group of scientists who worked together within the same university for an extended period. This group, which included luminaries like McCulloch, Wiener, Pitts, and Lettvin, not only collaborated professionally but also shared strong social bonds. McCulloch, in particular, stood out as an intellectually open, charismatic, warm, and personally informal figure. His hospitality and generosity extended to many young scientists, including one noteworthy example, Pitts. He, a prodigious talent, was homeless, in need, shy, and somewhat eccentric. The remarkably productive collaboration between McCulloch and Pitts might never have transpired without the emotional support McCulloch provided to Pitts.

On the other hand, Wiener, another influential 'father' figure in Pitts's professional and personal life, presented a contrasting personality. Wiener, though brilliant, was socially insecure and awkward. Unfortunately, their close social ties eventually contributed to the breakdown of their scientific collaborations, resulting in a tragic personal loss and a setback to the progress of science. It's worth noting that Pitts, initially an outsider, had been greatly aided by the support of these insiders, ultimately benefiting the field of science.

Rosenblatt, in the years that followed, would build upon the McCulloch and Pitts model to develop his ideas of perceptrons, which marked the foundational point for the neural networks we use today. However, by the time of the relationship breakdown, Pitts was already working on an improved version of the model. Lettwin, who enjoyed a close professional and personal association with Walter Pitts during that era, provided insightful commentary on Pitts' pioneering work. He remarked, "Walter was ahead of his time. He envisioned a layered device, a three dimensional net..nobody else was tackling it.. and got some very interesting results (Conway 232-233)." One can only imagine the potential implications if this enhanced model had been available to Rosenblatt at that crucial juncture.

What's evident is that exceptional individuals are necessary to pioneer new scientific fields. Beyond intelligence and creativity, they must also possess the skills to secure funding, gain media attention, and build teams. Some of these unconventional individuals may be highly sensitive, and this essay illustrates how social factors can hinder their progress. The majority of modern general-purpose computers are often referred to as Von Neumann machines, owing to their foundational reliance on the stored-program concept proposed by John von Neumann, a prominent figure in the field of cybernetics. This architectural paradigm,

outlined in his seminal work "First Draft of a Report on the EDVAC" in 1945, cited only one published report, the 1943 McCulloch-Pitts paper (Conway 150). However, Conway and Siegelman have postulated that John von Neumann may have been exposed to certain visionary ideas through his close collaboration with Norbert Wiener. He had submitted forward-thinking suggestions to Vannevar Bush, the presidential science advisor at the time, in 1940, which proposed five key features in the EDVAC's eventual architecture. They even cite informed sources of the era who assert that "Most of the elements of the Von Neumann machine, save the stored program, are present in Wiener's memorandum," and suggest that, had Bush circulated Wiener's memorandum widely, we might now refer to the "Wiener-Von Neumann" or even the "Wiener machine" instead of the "Von Neumann machine (Conway 151)."

This historical narrative, intertwined with the inception of computer architecture, underscores the interpretive flexibility that has often been exploited in attributing credit, particularly in the nascent stages of fields like Artificial Intelligence. The early development of AI spanned diverse academic departments, and its findings were disseminated through various publication channels, given that it had not yet crystallized into a well-defined discipline. One illustrative case is that the debate revolves around the attribution of credit for the development of the backpropagation algorithm, which is now a cornerstone of contemporary deep learning. In this complex historical narrative, several individuals have been associated with its invention, each with their own claims. One perspective attributes the pioneering work to Paul Werbos, who, as a mathematics PhD student at Harvard in the early 1970s, devised a technique known as dynamic-feedback for neural network-type models (Werbos). Another viewpoint credits Seppo Linnainmaa, who introduced a similar concept in 1970 but without direct reference to neural networks (Schmidhuber). Additionally, David Rumelhart, who independently reinvented the algorithm in 1986, claimed ignorance of Werbos' contributions and coined the term "backpropagation algorithm," thus adding another layer to the controversy (Synced). This complex debate serves as a testament to the intricate nature of emerging fields. It is crucial to recognize the historical context within which Werbos and Linnainmaa conducted their research. At the time, neural networks as a discipline were in their infancy, lacking the development and prominence they enjoy today. Consequently, these early innovators did not explicitly position their work within the neural network domain, partly due to limited interest and practical challenges. Moreover, the technological landscape of the era posed significant hurdles. Computers were markedly slower than today's counterparts, impeding the efficient implementation and validation of their algorithms. For instance, Paul Werbos encountered difficulties in convincing his thesis committee at Harvard, as skepticism about the algorithm's validity prevailed. He was even advised to seek the opinion of someone with more expertise and credibility. In a telling example, Werbos turned to Marvin Minsky for counsel, only to receive a lukewarm response (Olazaran 248). Nearly two decades later, Minsky retrospectively justified his skepticism by citing the slow convergence of the algorithm (Olazaran 249), which was not surprising given the state of computing technology at the time. This example underscores issues of historical recognition and the challenges faced by early pioneers in an emerging field, where

limited resources and understanding often hindered the full appreciation of groundbreaking contributions.

As cited by John von Neumann, his architectural framework drew inspiration from the McCulloch-Pitts model (Conway 150). However, this model harbored certain imperfections. It is worth noting that had these flaws been rectified, a scenario that Walter Pitts was actively pursuing before an unfortunate decision to destroy his own PhD thesis, both the Von Neumann architecture underpinning contemporary computers and the present-day neural networks, which were inspired by the McCulloch-Pitts model, might have attained even greater levels of sophistication and effectiveness.

The clash between symbolic AI and neural network approaches unfolded within a distinct socio-technological landscape compared to the era of cybernetics. During this period, key stakeholders, including scientists, funding agencies, the media, and the broader public, had become increasingly aware of the emerging AI innovations. By the time perceptrons and neural networks began to gain prominence, the leaders of the symbolic AI movement had already solidified their pioneer status and earned considerable prestige. They occupied the position of insiders, whereas the neural network researchers found themselves on the outside. Their reactions were motivated by several factors, including the aspiration to steer the narrative and shape the trajectory of technology, fierce competition for funding, a determination to challenge what they perceived as unverified assertions, and a degree of exasperation with the manner in which these claims were being presented.

Creating a fresh narrative marks a pivotal milestone in pioneering a nascent domain. As exemplified by McCarthy, one of the AI pioneers, the inception of the term 'artificial intelligence' was driven by the desire to disentangle from the web of 'cybernetics.' He notably stated, "I wished to avoid having either to accept Wiener as a guru or having to argue with him (Penn 131)." However, once such distinction is attained, safeguarding it takes precedence. As pioneers, Minsky and Papert were eager to encourage more researchers to align with their approach and grew concerned as neural network research gained traction. They sought to halt what they perceived as an unwarranted diversion of resources into an area they deemed scientifically and practically questionable. The rhetoric was to "kill the perceptron (Olazaran 168)." Their objective was to restore the equilibrium of AI funding and research in favor of their own approach.

The current AI hype, to some extent, is substantiated by tangible achievements. Yet, during the 1960s, the discourse predominantly revolved around the prospects and potential of various approaches. This created more room for interpretive flexibility to play a significant role in the debates. This meant that the way technology and its potential were presented to funders, the media, and the public carried greater weight. Harnessing the power of interpretive flexibility required crafting the technology narrative in a manner that resonated with the values held by the target audience. Despite the fact that the specific criticism primarily targeted single-layer perceptrons on an objective basis, it had a broader, negative undertone directed towards the

entire neural network paradigm. Owing to the sway of these influential voices, it was this overall critical tone that gained prominence and influence.

This contributed to an environment teeming with heightened emotions and tensions, leaving behind a sustained, negative impact. The symbolic AI community and the neural networks community were often seen as two distinct camps. This schism had a significant impact, with relentless criticism directed towards the neural network approach casting a pall over research endeavors, commercial enthusiasm, and funding prospects. Rosenblatt, a prominent figure in the neural network domain, relied heavily on financial support from the Office of Naval Research (ONR) and Advanced Research Projects Agency (ARPA). Regrettably, the pervasive skepticism surrounding the potential of neural networks played a pivotal role in dwindling funding opportunities for many neural network projects. In the context of unrelenting criticism, declining funding, and the notable shift of key commercial supporters to alternative approaches, coupled with influential researchers transitioning to different domains, we can view this complex landscape through the lens of Actor Network Theory (ANT). These interconnected events created a network effect, culminating in a situation where, when the decisive attack in the form of the publication of the perceptrons book occurred, Rosenblatt found himself inadequately positioned to mount a robust defense, primarily due to a lack of supportive alliances.

From a retrospective, objective perspective, it raises questions as to why previous efforts were not undertaken to bridge the gap between symbolic AI and neural networks. It underscores that technological progress is not solely a product of technical feasibility; rather, it is molded by the intricate interplay of social dynamics, technological advancements, institutional influences, and human choices. History vividly illustrates how the network effects generated by these diverse actors often lead to winners and losers. During the symbolic AI's ascendancy, the neural network movement found itself on the losing side, and vice versa. This polarity did little to foster a collaborative environment conducive to exploring groundbreaking unified architectures. Each camp stuck to its chosen path, even though both faced unique challenges.

However, in an era unburdened by the baggage of past debates, it appears that the time has arrived for unrestricted exploration of unified approaches.

Works Cited

- Aleksander, Igor Pioneering brain workers, Times Higher Education Supplement, 1998 (1354), p.29
- Anderson, James A., and Edward Rosenfeld, eds. *Talking nets: An oral history of neural networks*. MiT Press, 1998. Viii
- Bernstein, Jeremy. "Marvin Minsky's Vision of the Future." *The New Yorker*, 7 Dec. 1981, www.newyorker.com/magazine/1981/12/14/a-i.
- Bijker, Wiebe E., et al. The Social Construction of Technological Systems, Anniversary Edition: New Directions in the Sociology and History of Technology. MIT Press, 2012.p
- Conway, Flo and Jim Siegelman. Dark Hero of the Information Age: In Search of Norbert Wiener, the Father of Cybernetics. New York, Basic Books, 2005.
- Crevier, Daniel. *AI: the tumultuous history of the search for artificial intelligence*. Basic Books, Inc., 1993.
- Edwards, Paul N. *The closed world: Computers and the politics of discourse in Cold War America.* MIT press, 1996.
- Gangolli, Ramesh. "Dark Hero of the Information Age: In Search of Norbert Wiener, the Father of Cybernetics. By Flo Conway and Jim Siegelman." *The American Mathematical Monthly* 113.8 (2006): 767-74.
- Heims, Steve Joshua. The Cybernetics Group. Cambridge: MIT, 1991. The MIT Press. Web.
- Heims, Steve J., and Robert Andersen. "John von Neumann and Norbert Wiener: from mathematics to the technologies of life and death." (1981)
- Honavar, V. . Symbolic Artificial Intelligence and Numeric Artificial Neural Networks: Towards a Resolution of the Dichotomy. In: Sun, R., Bookman, L.A. (eds) Computational Architectures Integrating Neural And Symbolic Processes. The Springer International Series In Engineering and Computer Science, vol 292. Springer, Boston, MA (1995).
- Kelly, James G. "Talking Nets: An Oral History of Neural Networks." *Oral History Review* 28.2 (2001): 154-57.
- Latour, Bruno. "On actor-network theory: A few clarifications." Soziale welt (1996): 369.
- McCulloch, W.S., Pitts, W. A logical calculus of the ideas immanent in nervous activity. Bulletin of Mathematical Biophysics 5, (1943) 115–133
- Merton, Robert K. "Insiders and outsiders: A chapter in the sociology of knowledge." *American journal of sociology* 78.1 (1972): 10.
- Minsky, M. and A. Seymour. P. "Perceptrons." Cambridge, MA: MIT Press 6 (1969): 318-362.
- Minsky, Marvin. "The Beginning of the Artificial Intelligence Community." *Web of Stories*, www.webofstories.com/play/marvin.minsky/45.
- Olazaran Rodriguez, Jose Miguel. Historical Sociology of Neural Network Research (1991)
- Penn, Jonathan. Inventing Intelligence: On the History of Complex Information Processing and Artificial Intelligence in the United States in the Mid-Twentieth Century (2020)
- Rosenblatt, F. "The Perceptron: A Probabilistic Model for Information Storage and Organization in the Brain." *Psychological Review* 65.6 (1958): 386-408.

- Knight, Will. "An AI Pioneer Wants His Algorithms to Understand the 'Why." WIRED, 8 Oct. 2019, www.wired.com/story/ai-pioneer-algorithms-understand-why.
 Sheth, Amit, Kaushik Roy, and Manas Gaur. "Neurosymbolic AI Why, What, and How." (2023). Web..
- Schmidhuber, Jürgen *Who Invented Backpropagation?* people.idsia.ch/~juergen/who-invented-backpropagation.html.
- Schölkopf, Bernhard, et al. "Toward Causal Representation Learning." Proceedings of the IEEE, vol. 109, no. 5, Institute of Electrical and Electronics Engineers, May 2021, pp. 612–34. https://doi.org/10.1109/jproc.2021.3058954.
- Seidenberg, Mark S. "Talking Nets: An Oral History of Neural Networks Edited by James A. Anderson and Edward Rosenfeld." *Trends in Cognitive Sciences* 3.3 (1999): 121-22
- Smalheiser NR. Walter Pitts._Perspectives in Biology and Medicine February 2000 Winter;43(2):217-26
- Synced. "Who Invented Backpropagation? Hinton Says He Didn't, but His Work Made It Popular." *Medium*, 14 Dec. 2021, medium.com/syncedreview/who-invented-backpropagation-hinton-says-he-didnt-but-hiswork-made-it-popular-e0854504d6d1.
- Werbos, Paul J. "Backpropagation through time: what it does and how to do it." Proceedings of the IEEE 78.10 (1990): 1550-1560.
- Wiener, Norbert. Norbert Wiener# A Life in Cybernetics: Ex-Prodigy: My Childhood and Youth and I Am a Mathematician: The Later Life of a Prodigy. MIT Press, 2018.
- Wilson, Elizabeth A. "Would I Had Him with Me Always": Affects of Longing in Early Artificial Intelligence." *Isis* 100.4 (2009): 839-47.

Proposal to Adopt an Australian Prevention Model For Child Sex Abuse in America By Ivori Hinton

Abstract

This paper is a compilation of suggestions and ideas based on thorough research with the goal of proposing a public health model for the prevention of child sexual abuse. In order to construct the best possible solution, a public health model from Australia was chosen to be examined for usage in America. This model is primarily based on education and intervention, with the goal of reducing sexual offenses against children as well as raising the public's awareness of child sexual abuse. Examining state laws, nation-wide statistics, and the current resources provided in America versus the ones provided in Australia is what makes up a large portion of this paper. This article examines the current state of child sexual abuse, identifies areas for improvement, and attempts to a build a contextualized framework based on other effective interventions.

Introduction

The Center for Disease Control defines Child Sexual Abuse (CSA) as the "involvement of a child (under 18 years old) in a sexual activity that violates the laws or social taboos and that he/she: does not fully comprehend/does not consent to or is unable to give informed consent to or/is not developmentally prepared for and cannot give consent to." The CDC also describes child sexual abuse as a public health problem and identifies it as an adverse childhood experience. The effects of child sexual abuse can range from physical health concerns including injury and sexually transmitted diseases or infections, it also causes emotional and mental health affects including post-traumatic stress disorder, depression, and behavioral problems later in life such as drug abuse, risky sexual behavior, suicide, etc. Victims of childhood sexual abuse find themselves a part of a vicious cycle, by being at an increased risk to perpetrate sexual crimes later on in life (*Fast Facts: Preventing Child Sexual Abuse, CDC* 2022). In order to prevent the further victimization of children, there is a need to implement prevention strategies, public education, and safety nets within a public health model.

The differences in perpetration and punishment of child sexual abuse across the world will cause prevention models differ based on local laws, population size, education, culture, intervention methodology etc. In America, the population is over three hundred million. The public health model examined in this article is from Australia, whose population is roughly 8% of the US. The variances in urban spread and population sizes, can make true comparisons of situations challenging, however assessed practices amongst similar social cultures can give worthwhile indications into effective interventions and support. According to a 2010 study from the U.S. Department of Health and Human Services' Childrens' Bureau, 20% girls and 5% boys experienced sexual abuse before the age of 18 (*Child Maltreatment 2010, 2011*). Rates of incidence have increased in the last decade, with the 2023 Australian Child Maltreatment Study (ACMS) publishing a paper stating around 25% of children in Australia were sexually abused,

with it happening more frequently to girls at a rate of 37.3% compared to the frequency of 18.8% of boys (Mathews B et al., 2023).

Australia only recently introduced a new plan for the prevention of child sexual abuse with the new prevention program, dubbed the National Strategy to Prevent and Respond to Child Sexual Abuse. It intends to span from 2021-2030. This detailed plan was worked on by academics, victims of child sexual abuse, clinical professionals, and many other groups of people specializing in child sexual abuse. This strategy includes a more developed model of Quadara et al.'s public health diagram, which was a research report made in 2015 proposing a prevention model. (Fig. 1). The National Strategy's model contains an additional quaternary prevention method (Fig. 2), which is used to ensure the effectiveness of the prior prevention methods (*National Strategy to Prevent and Respond to Child Sexual Abuse 2021-2030*, 2022.)

Figure 1: Quadara et al.'s approach to linking risk factors of perpetration to prevention efforts (A. Quadara, 2015).



Figure 2: National Strategy's approach outlining four levels of defense (National Strategy to Prevent and Respond to Child Sexual Abuse 2021-2030, 2022).

QUATERNARY

Evaluates how effective tertiary interventions are to make sure they are delivering the right results.

TERTIARY INTERVENTION

Aims to respond to child sexual abuse and prevent it from happening again.

SECONDARY PREVENTION

Aims to address the early warning signs of child sexual abuse and change the end result for people who are at risk of experiencing or perpetrating child sexual abuse.

PRIMARY PREVENTION

Responses are aimed at the whole community and address the underlying causes of child sexual abuse.

In America there are multitudes of organizations, affiliate networks, nonprofits, and efforts by public health departments to stop child sexual abuse, but there are few resources directly from the federal government. Australia plans to take action against CSA, the United States currently does not. Australia's program is also multi-phasic and spans over several years, which strengthens the program, as more time allows for the program to expand.

A public health model in Australia was explained in an extended research report, "Conceptualising the Prevention of Child Sexual Abuse", highlighting the "three lines of defense" (*Quadara et al., 2015*). The primary level is the sexual education of children and teenagers; the secondary level is intervention for those exhibiting worrying sexual behavior; and the tertiary level is treating those who have already offended and committed a sexual crime.

This report would later be quoted by other researchers (*McKibbin et al., 2017*), who sought to reform the three lines of defense proposed by Quadara et al. These three lines of defense have been implemented into a, Australian national program to prevent child sexual abuse. The definitions of each line of defense are inexact, instead allowing for fluidity and development based on the context of implementation. An examination of the workings of the current systems of prevention and treatment will serve to help better develop programs for not

only education, but for the early identification and treatment of those at risk of committing sexual crimes and sufferers of sexual disorders. There are a large number of personal factors that act as risk indicators of sexual violence, such as early sexual initiation, aggressive behaviors, hostility towards women, etc. There are also familial, relational, societal, and community-based risks that can increase the likelihood of offending (*Risk and Protective Factors*|*CDC*, 2022).

The second line of defense also mentions paraphilic disorders and interventions around worrying sexual behaviors. A distinction must be made here, as those with paraphilic disorders are not automatically at risk of problematic sexual behavior, *and not all those who commit sexual crimes have paraphilic disorders*. The risk indicators of sexual violence vary greatly, and placing the blame on paraphilics further contributes to stigma and a reluctance to get help

Primary Line of Defense

As defined in the introduction, the primary line of defense is the education of children, teenagers, and parents. Across different state lines, there are different curriculums and practices for sexual education. This can even vary based on school and school district, as well as the grade level of students. According to a CDC summative study from 2022, Kentucky, a semi-southern state, has no laws regulating sexual education. 96% of secondary schools (grades 9-12) taught HIV and STD prevention, while only 69% taught age appropriate sexual health strategies (CDC, 2017). Examining a west coast, majority democratic state such as California will yield results such as having laws that require sex education to be comprehensive, taught, and accurate, with 93% of schools teaching HIV and STD prevention and 81% of secondary schools teaching age appropriate sexual health strategies (CDC, 2017). An article on AmericanProgress.org written in 2017 listed out twenty-five states based on their sex education requirements; only six required comprehensive sex education (including healthy relationships and consent), while others only required one or the other or even none of the aforementioned topics in sexual education (President et al., 2022). The lack of federal sex education laws makes sex education in schools a very muddy, hard to analyze topic. In some states students are being taught about healthy relationships and safe sex, while in others they are taught an abstinence-only curriculum.

Sex education isn't just for children and teens though. Parents being educated on their children's sexual development is crucial for the safety of kids. In an analysis of several studies, many parents do not actually understand what educating their children on CSA is, and once they know, they are more receptive to letting their children learn and are valuable assets in reporting and advocating for children (Wurtele, 2008). Reporting rates are also low, with an estimated 86% of cases of child sexual abuse going unreported (Childusa, 2020). Parents getting involved with professional sources to help educate themselves on the signs of sexual abuse can identify warning signs and get their child help. Many children do not say anything about abuse, and a parent having the knowledge to recognize that their child might be a victim of abuse is incredibly important.

So what does the National Strategy suggest? The National Strategy has a list of five themes for how the model should be formed. The education section lists items one through six,

which include awareness campaigns, annual reporting frameworks, and how to enhance the arrangements that are used to share information on child safety. The goal is to expand the sexual education of the public. This can be done through many channels and isn't limited to just community resources. Health agencies publishing infographics, colleges having pamphlets for students to take, teachers being able to teach sex education, and doctors educating parents on signs of sexual abuse are all valid streams of information. Commercials and PSAs could also be utilized by health agencies and the government.

Secondary Line of Defense

The secondary prevention method is identifying and treating those who are at risk of sexual offending but have not yet offended. Risk factors vary wildly, and there is no one way a sexual offender will act. Many people share the idea that every sexual offender is somewhat of a "boogeyman," an intangible person who is unfamiliar and violent. In actuality, 93% of sexual offenders are known to the victim and the victim's family (*Child USA*, 2020). There are many factors that make someone at risk of sexual offending, with four categories: individual, societal, community, and relationship (CDC, 2022). A majority of these behaviors are marked by poor emotional control, lack of proper familial relationships, poor socialization, and the normalization of sexual violence. Identifying adolescents and young adults with these kinds of behaviors is crucial to the safety of children.

The CDC also states "coercive sexual fantasies" can be a risk factor. A paraphilic disorder does not immediately equate to abnormal sexual fantasies; according to the DSM-V, a sufferer must either feel distress over the sexual interest not due to societal disapproval (such as someone with a standard sexual fetish for objects, this fetish brings them distress) or has sexual fantasies that are considered harmful, such as those involving a lack of consent, the suffering or distress of other people, or persons who cannot legally give consent (*Office of Justice Programs*, 2000).

In a 1992 analysis of child molesters, the National Center for Missing and Exploited Children made a distinction between pedophiles and child molesters. Most people do not make the distinction between the two, so there must be clarity on what the difference is. A pedophile is a person with a paraphilic disorder. This means they have sexual thoughts and fantasies about children. A child molester is someone who sexually assaults or abuses children. Not all child molestors are pedophiles and not all pedophiles are child molestors. This document states that the lack of distinction between the two can cause confusion, which becomes important in treatment of those who have pedophilic disorder (*National Center for Missing and Exploited Children*, 1992).

When there is such a stigma around a mental disorder, it becomes difficult for those suffering to get help. Pedophilic disorder must be treated as any other mental illness. Many people are against the treatment of people with pedophilic disorder as a whole, using arguments such as the "ticking-time bomb," in which they state that all persons with pedophilic disorder will offend and are all a danger to children, and some will argue that there is no way to reform or cure a pedophile. There are very few mental illnesses that have cures, what they do have is treatment; treatment can include medication and different forms of therapy (*National Institutes of Health*, 2007), and pedophilic disorder is no different. The societal stigma around pedophilia is one of the factors that make this disorder so difficult to treat, addressing that is one of the many important things in the conversation around child sexual abuse. It is, however, important to acknowledge that some people with pedophilic disorder will act on their attractions, and these people should not be excused because of their mental illness.

The treatment of adolescents who show signs of paraphilic disorders is important, but it is not the only factor to take into consideration, as paraphiliacs are not the only group to offend. Examining research, a picture of the traits that exist within juvenile sex offenders can be formed. In 2017, Brynna Fox and Matt DeLisi formed the first statistical typology report of juvenile offenders. There are 6 classifications made inside of this report—four types in males, two in females. The typologies that could be considered most obvious and easiest to look out for are the 'Impulsive Unempathetic', who are characterized by low levels of regret and impulsive behavior. Male Victim Offenders are consistently (over 60% of the time) categorized as depressed. Early intervention in depressive behavior of young men could be beneficial. The primary age of offending onset was 13-15. Traits measured were empathy for victims, levels of impulsivity, depression, if they had hallucinations, and more (Fox & DeLisi, 2017). Using these and future typologies of juvenile offenders can also aid in the education of what traits indicate risk for sexual offending as a minor, and an intervention can be had if traits are alarming. Interventions need to be handled by multiple people, and there needs to be a formulaic way to handle such interventions.

Risk factors of offending (as described by the CDC that are not indicative of paraphilias) are often due to circumstances of how a child is raised; finding a solution for this is complex. People outside of the family should be encouraged to aid a child how they can, but there is only so much that can be done. It is an unfortunate reality that there are certain things that cannot be prevented, simply because the government does not possess the legal power to interfere. Protecting children from poor home lives is the responsibility of CPS, but in the U.S. there are several problems with the organizations the U.S has protecting children. A study of 155 girls in foster care showed that 81% of them had experienced sexual abuse, and this is a system that is closely linked with CPS (Dowdel, 2009).

As a community and as the government, there is only so much interference that can occur; even the National Strategy acknowledges this, and states that there needs to be more research put towards this subject. There still needs to be something put in place to help with intervention, even with a lack of research. The National Strategy suggests that a framework should be made to aid those with these behaviors; youth justice and therapeutic aid need to be a focus, as well as public education from the government. The government also aims to set up a national clinic and create standards for how to deal with children who have problematic sexual behavior. (*National Strategy, 2022*)

Tertiary Line of Defense

What is there to do when someone does offend? There is no way to effectively eliminate crime. When the justice system is faced with it, there must be a solution they have to go to when a sexually based offense is committed. The American justice system is complex and multifaceted. Instead of focusing on decriminalization, specific types of criminal charges, or anything that comes before the punishment, there will be specific focus on what they do with those who have been convicted of a crime. Much can be said about how sexual crimes are handled in the justice system, but the scope of that is more focused on the legal aspects of sexual offending and not the medical and psychological aspects, which is what the public health plan is most highly concerned with.

Currently, there are two types of post-conviction penalties for sex offenders, these being punishment or treatment. Depending upon what state an offender is in, the penalty may be different. All fifty states including the District of Columbia have sex offender treatment programs, 80% of which are community-based (Przybylski, 2017). And of course, all states have laws against sexual crimes, with punishments ranging from jail-time to a very recent Florida bill signed into law, declaring that a state can seek the death penalty for sexual battery cases towards minors twelve and under (*Death Penalty Information Center*; 2023). Convicted sex-offenders will sometimes receive treatment inside of prison; however, similar to state laws, these are difficult to track since prison systems vary based on state or region, and some states have private prisons. Most people convicted of a sexual offense will have some kind of treatment required as a part of their sentencing (*National Institute of Justice*, 2015). After prison, sex offenders are also expected to register themselves on the sex offender registry and can face punishment, ranging from a fine to a prison sentence of up to ten years (U.S. Code, 2006).

Australian laws are somewhat similar, having sexual offenders register on a registry and complete jail time for sexual offenses. In Australia, there are treatment programs based on cognitive-behavioral interventions, which help offenders grow victim empathy and social skills, challenge any cognitive distortions they may have that led to offending, and focus on controlling thoughts and urges (Craissati, 1998). While not inside every prison, there are multiple organizations and programs that operate throughout the country.

What, ultimately, is the goal of treatment? One part of it is the hope that it will reduce recidivism; studies still remain unclear on whether or not treatment affects recidivism. Treatment programs are not the end-all to the greater legal aspects of sexual offenses though. The national plan suggests other methods of improving the legal system around sexual offenders, such as expanding and improving the victim database, furthering training for law enforcement on how to handle sexual crimes and victims of sexual crimes, and examining laws and research to better strategies based on the two.

Author's Position

It is incredibly difficult to condense the layered topic of childhood sexual abuse into a concise but informed essay. There are many things that had to be overlooked or not even

considered in order to keep everything relevant. Entire papers have been written on statistical reoffense rates of sex offenders or on the topic of sex education in schools; the national strategy itself is seventy-six total pages. The main goal of this paper is to make a suggestion—to offer a first step into developing a public health plan for this problem. The national strategy itself most likely took years to develop, as the concept of the three lines of defense have been around since 2015, introduced by Quadara. The Quaternary prevention method introduced in the National Strategy is an essential piece of reviewing how the public health plan is working, although it was not mentioned in any main paragraphs, that does not denote its importance.

Childhood sexual abuse can happen to anyone, even though many people have the idea that it will not happen to their children. Sexual abuse is often an uncomfortable and personal topic, but the reluctance to discuss it is at the detriment of every child and parent who might have to one day deal with it. A public health approach to this problem would make it easier for parents to identify and help their children, thus keeping children from being victimized further.

America is fraught with political tension and problems, and sexual education has always been part of those issues. The epidemic of child sexual abuse and its prevention should be entirely apolitical. Identifying this as a public health crisis would be beneficial in depoliticizing the topic, to allow medical and psychological professionals more say in how this should be handled. In order to actually protect children, there need to be national standards based on what research and professionals say benefits children and their parents. The implementation of a public health program involves effort from communities as well. It would take a great deal of effort to actually put in place a nationwide program for the prevention of sexual abuse, but the benefit is worth the cost, even if it helps prevent one child from being sexually abused.

Works Cited

'Paraphilic Disorders - Psychiatry.org'. American Psychological Association, 2013.

- 'Fast Facts: Preventing Child Sexual Abuse |violence Prevention|injury Center|CDC'. Centers for Disease Control and Prevention, 2022.
- 'Risk and Protective Factors |violence Prevention|injury Center|CDC'. Centers for Disease Control and Prevention, 2022.
- 'Kentucky Summary Report. Analysis of State Health Education Laws'. *Center for Disease Control*, 2017.

California Summary Report. Analysis of State Health Education Laws. 2017.

Schachter, Michael. *Therapeutics*. WORLD SCIENTIFIC (EUROPE), 2025, https://doi.org10.1142/p574.

Craissati, J. Child Sexual Abusers: A Community Treatment Approach. Psychology Press, 1998.

Dowdell, Elizabeth B., et al. 'Girls in Foster Care: A Vulnerable and High-Risk Group'. *MCN. The American Journal of Maternal Child Nursing*, vol. 34, no. 3, May 2009, pp. 172–178,

Failure to Register, 18 U.S.C § 2250 (2006) https://www.law.cornell.edu/uscode/text/18/2250

Florida legislature rescinds unanimous-jury requirement in death sentencing. Death Penalty Information Center. (2023, April 18).

https://deathpenaltyinfo.org/news/florida-legislature-rescinds-unanimous-jury-requiremen t-in-death-sentencing

Mathews, Ben, et al. 'The Prevalence of Child Maltreatment in Australia: Findings from a National Survey'. *The Medical Journal of Australia*, vol. 218 Suppl 6, no. S6, Wiley, Apr. 2023, pp. S13–S18, <u>https://doi.org10.5694/mja2.51873</u>

Mckibbin, G., et al. Talking about Child Sexual Abuse Would Have Helped Me": Young People Who Sexually Abused Reflect on Preventing Harmful Sexual Behavior. 2017.

- National Strategy to Prevent and Respond to Child Sexual Abuse 2021-2030. National Office for Child Safety. 2022.
- ^cChild Molesters: A Behavioral Analysis Office of Justice Programs'. *National Center for Missing & Exploited Children*, 1992.

'Bethesda (MD): National Institutes of Health (US)'. *National Institutes of Health (US)*, 2007.

Sexual Assault of Young Children as Reported to Law Enforcement. 2000.

'Practice Profile: Treatment for Adults Who Have Committed Sex Offenses'. *CrimeSolutions*, CrimeSolutions.

'---'. CrimeSolutions, National Institute of Justice,

https://crimesolutions.ojp.gov/ratedpractices/30. Accessed 15 Sept. 2023.

Simhoni, Shanee. 'Sex Education Standards across the States'. *Center for American Progress*, 9 May 2018,

https://www.americanprogress.org/article/sex-education-standards-across-states/.

'Chapter 7: Effectiveness of Treatment for Adult Sex Offenders'. Office of Sex Offender Sentencing, Monitoring, Apprehending, Registering, and Tracking, https://smart.ojp.gov/somapi/chapter-7-effectiveness-treatment-adult-sex-offenders. Accessed 15 Sept. 2023.

Quadara, A., et al. Conceptualising the Prevention of Child Sexual Abuse. AIFS, 2015.

Wurtele, Sandy K. 'Behavioral Approaches to Educating Young Children and Their Parents about Child Sexual Abuse Prevention'. *The Journal of Behavior Analysis of Offender and Victim Treatment and Prevention*, vol. 1, no. 1, American Psychological Association (APA), 2008, pp. 52–64, https://doi.org10.1037/h0100434.

Processing Languages Naturally and Intelligence Artificially By Nikita Parakala

Whether celebrating life's greatest highs or coping with the lows, or just every mood in between, music has outlined my existence from as long as I can remember.

While my parents argue that Walkmans, CDs and portable mp3 players transformed the music world, I believe that today's online streaming applications like Spotify, have truly revolutionized how music lovers consume music, by reading their minds, and providing them the quick fix they need anytime, anywhere. Soon after Spotify and I, quite literally discovered each other, I was dying to know how it all worked. A few weeks of obsessive research led me to learn about how its Artificial Intelligence (AI) and Natural Language Processing (NLP) capabilities have hyper personalized music.

AI is defined as the capability of machines to imitate intelligent human behavior. AI typically uses the development of algorithms and computer programs to perform tasks that need human intelligence. Various aspects of AI include Natural Language Processing, Machine Learning, Deep Learning, Robotics, Expert Systems, Computer Vision, and Ethics.

Of these, Natural language Processing (NLP) is a huge leap forward in AI technology, possibly because it is getting rid of the communication barrier that has existed between machines and humans.

Here's how that communication barrier existed.

In the past, computers could only work with structured languages. The language had to be precise and clear-cut. To program a computer to perform a task, you had to give it clear instructions, using only the commands that it understood. The syntax had to be precise as well. NLP is removing the need for being so precise. Instead of us having to learn the computer's language, computers are now learning ours! Since it removes the communication barrier between humans and computers, the potential for the application of NLP is almost limitless.

So how does NLP work?

NLP models work by finding relationships between the parts of language like the letters, words, and sentences found in a text dataset.

Natural language processing is hard, mainly because human languages are complex and understanding them needs an understanding of the concepts and the words, and how they're connected to make sense. For us, it is just regular communication, but everyone knows that words come with a deeper context and when we say something to another person, that person can actually understand what we mean, and all of this communication grows with experience.

So how can we offer that experience to a machine?

The answer is, we need to provide it with a lot of data to help it learn through experience. The first working step of an NLP system depends on that particular system's application. For example, voice-based systems, like Google Assistant or Alexa, translate words into text. Usually, this is done using the Hidden Markov Models (HMM) system. The HMM use mathematical models to figure out what a person has said and translate that into text that can be utilized by the NLP system.

The next step is the actual understanding of the context and the language. Though the techniques vary a little bit from one NLP system to another, they mostly follow a similar format. The systems attempt to break every word down into its noun, verb and other parts of speech. This happens through a series of coded rules which depend on certain algorithms. These algorithms integrate statistical machine learning, in order to help figure out the context. For NLP systems other than speech-to-text, the system skips the initial step and directly moves into analyzing the words, utilizing the algorithms and grammar rules.

The final step is the ability to categorize what a person says in different ways. The results get utilized in several ways depending on what the NLP system is actually trying to do.

Since we are talking about how a Natural Language Processing system works, let us look at its key components, Syntactic and Semantic analysis. Syntax stands for the arrangement of words in a sentence, so that they can make grammatical sense. Syntactic analysis is used to assess the way the natural language gets aligned with the grammatical rules. Syntactic and Semantic Analysis differ in the way text is analyzed. In the case of syntactic analysis, the syntax of a sentence is used to interpret a text. In the case of semantic analysis, the overall context of the text is considered during the analysis.

Two popular methods are applied to implement an NLP system – machine learning and statistical interference.

NLP systems have a wide range of applications today, which are constantly growing and transforming as the world transforms.

Chatbots for customer call assistance, **language translation programs** for translating languages before a human translator gets involved, **sentiment analysis** for analyzing the emotional state, attitude, and mood of people posting messages on social media platforms and **descriptive analytics** for capturing customer feedback for products or services. Applications like **search autocomplete** and **search autocorrect** are widely used to locate correct search terms, or automatically correct incorrect terms.

Did you know that spell check is also a gift of an NLP application?

My greatest NLP gifts come in the form of my daily Spotify music picks. Spotify's NLP algorithms constantly scan the web to find blogs, articles or any other text about music, and come up with a profile for each song. With all this scraped data, the NLP algorithm can classify songs based on the kind of language used to describe them and can match them with other songs that are discussed in the same way. Artists and songs are assigned to classifying keywords based on the data, and each term has a sort of "weight" assigned to it. A vector representation of the song is created, and Viola! That is used to suggest similar songs! Of course, these systems rely a lot on user data to curate personalized playlists. Spotify's algorithm analyzes your listening history, favorite genres, and the time of day you listen to music.

In conclusion, NLP is a crucial aspect of AI that is rapidly changing the world, by helping computers understand and generate our natural language.

All this is awesome, but shouldn't the notion of intelligence include its creative, and wild elements? Surely there are unpredictable elements in our intelligence and language that data-processing algorithms may find elusive? How likely is it that algorithms will be able to acquire these unpredictive qualities that are needed to solve the problems humanity is facing? And if they can't, would Artificial Intelligence remain an oxymoron?

I hope not. For now, I'll enjoy my music!

Works Cited

- "A Complete Guide to Natural Language Processing," *DeepLearningAI*, January 11, 2023. https://www.deeplearning.ai/resources/natural-language-processing/
- Sen, Ipshit. "How AI helps Spotify win in the music streaming world," *Outside Insight*. https://outsideinsight.com/insights/how-ai-helps-spotify-win-in-the-music-streaming-wor ld/
- Svensson, Jakob. "Artificial intelligence is an oxymoron: The importance of an organic body when facing unknown situations as they unfold in the present moment," *National Library Of Medicine, National Center for Biotechnology Information,* November 5, 2021. https://pubmed.ncbi.nlm.nih.gov/34754144/
- Overby, Stephanie. "Artificial intelligence vs. natural language processing: What are the differences?" *The Enterprisers Project*, February 26, 2020. https://enterprisersproject.com/article/2020/2/artificial-intelligence-ai-vs-natural-languag e-processing-nlp-differences
- Giattino, Charlie, Mathieu, Edouard, et al. "Artificial Intelligence," *Our World in Data*. https://ourworldindata.org/artificial-intelligence
- Miller, Evelyn. "How do Natural Language Processing systems work?" *MagniMind Academy*. https://magnimindacademy.com/blog/how-do-natural-language-processing-systems-work
- Kaput, Mike. "How Spotify Uses Artificial Intelligence-and What You Can Learn from It," *Marketing Artificial Intelligence Institute*. September 19, 2022. https://www.marketingaiinstitute.com/blog/spotify-artificial-intelligence
- Tambekar, Akshad. "How Spotify Uses Machine Learning Models to Recommend You the Music You Like," *Great Learning*. August 29, 2022. https://www.mygreatlearning.com/blog/how-spotify-uses-machine-learning-models/

Coherence and Chaos within within Fiction Narrativization By Xingyi Li

Abstract

As Linda Hutcheon suggests, 'The process of narrativization has come to be seen as a central form of human comprehension, of imposition of meaning and formal coherence on the chaos of events', it is both meaningful and inspiring to explore ways how novelists balance coherence and chaos through the process of narrativization. Given that, this paper aims at analyzing the effectiveness of incorporating multiple narrative perspectives, conflicting values under consistent themes, and the mixture of reality and illusion within storytelling.

Introduction

Exploring the nature of narrativization is like reflecting upon the "very nature of culture" and that of "humanity"(White). With its "international, transhistorical, transcultural" (Barthes) qualities, it acts a vital role to human comprehension, as it drives storytelling in more human-specific directions than cultural ones. As such, narrativization serves as a "metacode" that instills meaning in texts: that is, it translates 'knowing' into 'telling' in delicate ways, subsequently lowering, minimizing, and even diminishing transcultural messages for readers with cultural barriers.

This paper argues that novelists, in their process of narrativization, achieve a balance between coherence and chaos by various means, among which the following stand out-- the incorporation of multiple narrative perspectives during a chronological sequence of events, the introduction of conflicting values under consistent themes, and the mixture of reality and illusion within storytelling. Through these approaches, an author is able to achieve the goal of narrativization-- to make stories accessible to readers despite cultural barriers-- despite his/ her employment of creative story-telling tactics such as stream of consciousness.

Multiple narrative perspectives

To begin with, while novelists foster a coherent narrative structure by following the chronological sequence of events, they might also weave in chaotic elements such as "braided narratives" (Bancroft), which feature multiple narrators within a single event to create instability. Intertwining various narrative perspectives not only conveys a story in a more comprehensive manner, but also fosters stronger interconnection between the readers and the text (Berve); that is, such a narrative style would train readers to process and evaluate various-- sometimes even conflicting-- perspectives simultaneously, allowing them to gain a firmer grasp on the event details and form critical judgments. At this point, the author gradually removes himself/ herself from the story to allow events "tell" themselves.

A case in point would be William Faulkner's work *As I Lay Dying*, a polyphonic novel that tells how the Bundren family embarks on a journey of carrying the dead body of the family matriarch Addie to Jefferson, Mississippi, for burial. While this book is told in a linear structure following the funeral procession-- the wake, the night before taking off, the incident of the
wagon and coffin, and so on-- a distinctive narrativization feature falls upon its bountiful narrative point of views (Ross): having a total of fourteen characters to compile fifty-nine sections of first-person narrative in total.

Constant switching of perspectives and different narrative styles can introduce chaos, challenging readers' perception of events. Within each narrative, the author adopts the technique of 'interior monologue' (Hoffman), or the 'stream-of-consciousness'-- the "presentation of psychological aspects of character" in novels (Humphrey). These inner thoughts are weaved in such unorganized sequences to characterize the spontaneity of each individual's thinking process, therefore creating a chaotic effect. For instance, Verdaman's -- the youngest Bundren son—narrative is filled with illogical and naive thoughts, which resemble those of a young child. Across different narrative sections, his mind jumps randomly from describing her dying mother as the "fish in the dust" (Faulkner) surrounded by trees that "look like chickens" (Ibid.), to later on suggesting his mother is "not a rabbit" (Ibid.) since she's going to be nailed in a box. While the unusual way of likening his mother as animals appears strange and abnormal, Faulkner is able to bring the unfettered association of this "grief-crazed child" (Wagner) together into a single image: "My mother is a fish" (Faulkner).

Differently, the author portrays Darl as a character with the "propensity to indulge in metaphysical reflexions" (Delville) as he possesses strong intellectual awareness that somehow results in his alienation from the community around him. Frequently, Darl's reflections on human existence are featured by binary dialectics-- alternation of sentence structures-- such as "I don't know what I am. I don't know if I am or not" and "if it is was, it cant be is. Can it?" As such, Darl is depicted as almost clairvoyant with a strong analytical nature. However, in contrast to Darl's contemplation, that of Cash is rather straightforward and logical, without being tangled in excessive emotion. This is especially evident in a section where, instead of narrating Addie's tragic death, Cash neatly lists thirteen steps of crafting his mother's coffin like writing an instruction book.

"I made it on the bevel.

1. There is more surface for the nails to grip.

2. There is twice the gripping-surface to each seam.

•••

12. So I made it on the bevel.

13. It makes a neater job." (Faulkner)

The simpleness of his narrative style, in turn, fits Cash's nature of being a man who rarely uses words to express his often simple and plain emotions. Rather than expressing sadness through words, Cash transforms his grief into a physical object: the coffin. As such, Faulkner not only completes the story through the lens of various characters, but also unveils their unique personalities through different narrative tones, allowing the readers to experience these differences themselves.

Amid the disarray created by frequent transitions of different narrative perspectives, however, Faulkner is able to maintain the coherence of the work by following the chronological

order of Addie's burial, therefore minimizing the confusion through the continuity of the entire plot (Berve). That is, the author structures different pieces of the narration from the preparation phase of the Burden family's journey to Jefferson to the actual process and the eventual arrival. Apart from members of the Bundren family, perspectives of outside narrators are also incorporated, such as their neighbor the Tull family, who offers more factual material to supplement the readers' understanding regarding the setting of the story. As such, the author ensures readers stay on track of the storyline. It is, therefore, through the incorporation of multiple narrative perspectives that novelists create chaos, yet by the chronological structure within the narrativization, a unified and coherent story is created.

Conflicting Values Under Consistent Themes

Another way novelists balance coherence and chaos is by maintaining thematic consistency throughout the work while providing conflicting responses from the characters. Indicating "a struggle between opposing forces" (Algert), conflict usually takes form between a 'protagonist' and 'antagonist', or between 'individuals' and 'society' in terms of prevailing opinions. In literature, not only does the emergence of conflicts ensemble values held by different social groups, it also serves as a crucial narrative mechanism that accelerates the plot of story.

An example would be Margaret Atwood's dystopian novel *The Handmaid's Tale*, which tells the story of a Handmaid, Offred, in a highly patriarchal totalitarian society of Gilead, where women's value lay solely on providing reproductive sources for Gilead's powerful man, often against the handmaids' own will. Naturally, a reoccurring theme is female's lack of autonomy over pregnancy. While conflicts can be categorized into various types-- including intrapersonal, interpersonal, intergroup, etc. (Al-Mamary & Hussein)-- one of the overarching discord in this book is "self-society conflict": namely, how characters in Gilead respond differently to the social dominance of patriarchal power (Naji and Abbas), which inevitably create a sense of chaos among the narrative. Aunt Lydia, for instance, upholds the social hierarchy that sustains Gilead's inhumane policy of reproduction, as she instructs the Handmaids that women plagued with infertility "were dirty women" and "slobs", and that "fertility is a gift given right by God" (Atwood). In contrast, the author also creates resisting and rebelling individuals, such as the Handmaid Moira who jabs something "hard and sharp and possibly metallic" into the ribs of the Aunts regulating her behavior, threatening that "I'll puncture your lung" (Atwood). There are also characters like the Handmaid Janine, who are forced to confess her sins for the gang-rape incident. A chaotic environment is formed when incessant blame pour from her fellow Handmaids, chanting "Her fault", "She did", and "Crybaby" (Ibid.). Not only does this group condemnation scene confront females' vulnerability directly against masculine domination, but it also fosters an overly disorganized scene filled with blame and the antithesis of feminist ideals. The mixed viewpoints from the same gender, who are supposed to all be victims yet now harbor disparate responses towards the patriarchal regime, boost the story's tension, thus creating deep-layered chaos.

Meanwhile, novelists may also create intrapersonal conflict filled with chaotic ideas to boost the complexity of plot development. For instance, throughout *The Handmaid's Tale*, the author frequently weaves in Offred's flashbacks of her earlier marriage, current captivity, and reflection upon her existence, such as how she used to picture her body "as an instrument of pleasure" (Atwood) to, gradually, witnessing "the flesh arranges itself differently" (Ibid.) to become a "mound of flesh surrounding a womb" (Naji and Abbas); then, her mind moves on to depict the empty apartment to her running across dead branches with her daughter. Arranging these fragmented stream-of-consciousness of the main character, Atwood successfully conveys a sense of alienation, not only from her early life as a free human, but also alienation from her self-identity-- she has too much experience from her early life to be a submissive Handmaid, yet also too many memories of her days in the Handmaids community to disown this identity utterly.

Despite so many highlights on chaos-making conflicts, be it the conflicting views on the loss of their autonomy of pregnancy amongst the same gender and same social group of Handmaids, or the conflicting memories that are essential to Offred's construction of an everchanging self-identity, the author still manages to keep the reader focused on a consistent struggle by coherently uniting the aforementioned conflicts under the same topic-- rebellion against an extremely patriarchal regime. Thus, a series of internal struggles penetrating through the novel is used to expose the disarray and randomness of the character's inner struggle under the recurring theme that is coherent throughout the novel.

Mixture of reality and illusion

Apart from incorporating multiple narrative perspectives and conflicting values, novelists also employ a mixture of reality and fantasy throughout narrativization to create chaos, which are then balanced by incorporating coherent threads such as recurring symbols. Symbolism is a commonly seen device that uses "concrete images to convey abstract ideas", (Glatch), generating deeper level and less evident meaning such as extended metaphors. Novelists create symbols to merge the boundaries between life and imagination in a poetic manner (Wiehardt), inviting readers' own interpretation. While ambiguity is therefore created, symbolic elements navigate readers through the plot, achieving a coherent story. Such device has been frequently spotted in Garcia Marquez Gabriel's magical realism works including *A Hundred Years of Solitude* and *Chronicle of a Death Foretold*, as well as Toni Morrison's works such as *Beloved*, in which readers would often be greeted by conversations between the dead and the living, an unrealistic event merging the readers' senses of reality and delusion. Nevertheless, both authors successfully keep the coherence of the stories by constructing peculiar cultural and religious contexts in which ghosts conversing with the living is possible.

Edgar Allan Poe's short story, *The Fall of the House of Usher*, is another great example, as it induces delicate narrativization to make the "impossibility of absolute discernment" omnipresent (Perry and Sederholm). The perspective of the narrator is confusing as he fails to distinguish between reality and "what must have been a dream" (Poe), leaving a chaotic narration at the moment, such as when describing the dilapidated house that still remains intact.

"...when I again uplifted my eyes to the house itself, from its image in the pool, there grew in my mind a strange fancy-- a fancy so ridiculous, indeed, that I but mention it to show the vivid force of the sensations which oppressed me. I had so worked upon my imagination as really to believe that about the whole mansion and domain there hung an atmosphere peculiar to themselves and their immediate vicinity-- an atmosphere which had no affinity with the air of heaven, but which had reeked up from the decayed trees, and the gray wall, and the silent tarn-a pestilent and mystic vapour; dull, sluggish, faintly discernible, and leadenhued." Here, the narrator describes the house of Usher as everywhere deteriorating-- with "decayed trees", "fungi overspread", and "bleak walls"-- but at the same time, structurally intact as a whole, which is counterintuitive. However, it is worth noticing that since his description of the mansion mainly comes from his "strange fancy"-- which originates from observing the structure's reflection in the water-- the narrator's comment on the house becomes an "edifice of his own unconscious imagination" (Perry and Sederholm). In such a way, Poe blurs the reality of the setting, introducing the psychological fantasy of the narrator and, later as the story progresses, that of Roderick Usher.

Meanwhile, the Usher mansion serves as a prominent symbol throughout the work: it implies both the physical and mental state of the declining Usher family. As the tangible house is described as old and decrepit, it corresponds to the illusory fate and deteriorating health of Madeline and Roderick-- the last living twin heirs of the family. In addition, by inventing this "dual character"-- whose living conditions are interdependent-- Poe associates Roderick's insanity with the abstract 'mind' and Madeline's death with the tangible 'body', suggesting the mystical relationship existing among mind and body: they are inseparable parts. Gradually, the novelist is able to link the final collapse of the house to Madeline's death, as well as "Roderick Usher and the lament of the end of his family line" (Yamina), which reinforces the correlated relationship between the house and the family. Therefore, while ambiguity inevitably occurs through the chaotic merge of reality and imagination, Poe maintains the narrative's coherence by effectively using the Usher house as an important symbol throughout the whole story.

Conclusion

To wrap up, as narrative "ceaselessly substitutes meaning for the straightforward copy of the events recounted" (Barthes), it serves as a crucial tool for novelists to maintain a balance between coherence and chaos. While there are various means to achieve overall consistency amidst disorienting events, some of the most prominent ones include having various distinct narrators telling the same story through chronological order, incorporating disputable opinions between characters, and fusion of reality and intangible imagination within the story. Narrativization, therefore, acts as an effective "metacode" in endowing meaning within the text in an effective way, facilitating and enriching human comprehension in the long run.

- Algert, N. E. "Conflict in the workplace." *Proceedings: Women in Engineering Advocates Network, Denver,* CO (1996): 123-127
- Atwood, Margaret. *The Handmaid's Tale*. First Anchor books movie tie-in edition. New York, Anchor Books, a division of Penguin Random House LLC, 2017.
- Bancroft, Corinne. "The braided narrative." Narrative 26.3 (2018): 262-281.
- Barthes, Roland. "Introduction to the structural analysis of narratives." *Narrative theory: Critical concepts in literary and cultural studies* (2004): 65-116.
- Berve, Caitlin. "Multiple Points of View: Benefits, Pitfalls, and Uses." *Ignited Ink Writing*, 12 Mar. 2018.
- Delville, Michel. "Alienating Language and Darl's Narrative Consciousness in Faulkner's" As I Lay Dying"." *The Southern literary journal* 27.1 (1994): 61-72.
- DiMatteo, Tiffany. "Beloved: A Case Study in Storytelling Analysis."
- Faulkner, William. As I lay dying. Vintage, 2011.
- Glatch, Sean. Symbolism in Literature: *What Symbolism Is, and How to Use It in Your Writing Finding Meaning in Images*, 14 July 2022.
- Hoffman, Frederick J. Freudianism. "the Literary Mind. 1945." Reprint, Baton Rouge (1959).
- Humphrey, Robert. *Stream of consciousness in the modern novel*. Univ of California Press, 1958. Márquez, Gabriel García. *Chronicle of a death foretold*. Penguin UK, 2014.
- Márquez, Gabriel García. "One hundred years of solitude." *Medicine and Literature, Volume Two.* CRC Press, 2018. 255-272.
- Morrison, Toni. "Beloved. 1987." New York: Vintage (2004).
- Morrison, Toni. "The Bluest Eye. 1970." New York (1994): 751-59.
- Naji, Ola Razzaq, and Nawal Fadhil Abbas. "Conflict in Atwood's The Handmaid's Tale: A Critical Discourse Approach." (2022).
- Perry, Dennis, and Carl H. Sederholm. Poe, "*The House of Usher,*" and the American Gothic. Springer, 2009.
- Poe, Edgar Allan. The fall of the house of usher. Vol. 661. Prabhat Prakashan, 1973.
- Ross, Stephen M. ""Voice" in Narrative Texts: The Example of As I Lay Dying." *PMLA* 94.2 (1979): 300-310.
- Wagner, Linda W. "" As I Lay Dying:" Faulkner's All in the Family." *College Literature* 1.2 (1974): 73-82.
- Weidhardt, Ginny. "'Symbolism in Fiction Writing." owl. purdue. edu 25 (2019).
- White, Hayden. "The value of narrativity in the representation of reality." *Critical inquiry* 7.1 (1980): 5-27.
- Williams, Jessica Horvath. "Unlike the Average Mental Disability as Narrative Form and Social Critique in Morrison's The Bluest Eye." *Studies in American Fiction* 45.1 (2018): 91-117.
- Yamina, Touahir. The Use of Symbolism in Poe's The Fall of the House of Usher. Diss. 2013.

Symptoms and Countermeasures for Spaceflight-Associated Neuro-Ocular Syndrome (SANS) By Samarth Kumar

Abstract

Spaceflight Associated Neuro-Ocular Syndrome (SANS) is currently a big topic of research for scientists. The effect of SANS can cause optical disturbances and be risky for astronauts in space for a long period of time. There are many potential causes of SANS, with popular theories involving Intracranial pressure (ICP). This paper gives an overview of SANS, provides potential countermeasures for prolonged space travel, and delves into further areas of research that still need to be done.

Introduction

SANS is a problem that can occur for astronauts after a prolonged time spent in space. It has a wide range of effects, and its symptoms can occur to different degrees for individuals (Stenger et al. 2017). Currently, about 96% of ISS crew members experience some level of SANS (NASA) Long Term Surveillance of Astronaut Health n.d). Symptoms can start in space and continue even after coming back to Earth, symptoms may start within 3 weeks of microgravity exposure (Mader et al.). Most International Space Station (ISS) crew members go into six-month missions with only a handful going into missions lasting around a year (Lee et al.).

Symptoms of SANS

Symptoms of SANS tend to impair one's vision. A common occurrence is choroidal folds occurring in the eye (Shen et al.). This means an astronaut can have retinal folds in his posterior pole or peripheral retina of the eye (Shen et al.). These folds can also potentially lead to other orbital or ocular diseases including scleritis, tumors, and hypotony. While in space with limited medical resources, it should be important to minimize the risk of disease for astronauts. SANS may also lead to cotton wool spots in the eye which can lead to vision loss and make an astronaut more susceptible to diabetes, mellitus, systemic hypertension, and a handful of other diseases that could potentially compromise a mission (Ioannides et al.). SANS can be split into four thresholds depending on symptom severity ranging from mild to advanced, currently about 72% of ISS crew members are at the first threshold (mild) which has mild but reversible effects. Symptoms such as vision loss and headaches fade away within a couple of months of arriving on Earth (Lee et al.). It is important that some changes in the eye caused by SANS can be prevalent years after returning to Earth, these include choroidal folds and globe flattening. 18% of crew members reach the 2nd threshold (moderate) where the symptoms are a bit more clinically concerning but shouldn't have a big impact on the astronaut's long-term health or the mission. 6% reach the 3rd threshold (severe) which can mean acute impact on the astronaut's health and ability to function in space. For now, no cases have had an impact on long-term vision health (advanced). However, it is important to note that an extended time in microgravity may lead to a

more severe level of SANS, something that is a growing concern for physicians and scientists. (NASA Long Term Surveillance of Astronaut Health).

Why does SANS occur?

To understand why SANS occurs there are some important terms you need to know. Intracranial pressure (ICP) is a measurement of pressure in your skull. Intraocular pressure (IOP) is the measurement of the fluid pressure in one's eye. These two can interact with each other and their difference (IOP-ICP) is called the translaminar pressure difference (TLPD) (Shen et al.).

So how does ICP interact with IOP? A healthy eye needs balance with a stable IOP and ICP level but space travel can lead to changes in pressure in the skull. The exact mechanisms of IOP and ICP's effects on SANS are unknown but experiments conducted on mice can show us certain effects caused by pressure changes in the head. Specifically, results from a recent study in 2020 by Shen *et al.* demonstrated that when both IOP and ICP were increased the mice did not show signs of scotopic vision (object visibility) loss that we see in SANS, instead, there was a loss of photopic contrast sensitivity (vision that helps see color). A prevalent symptom of SANS is loss of scotopic vision. This shows that increasing IOP and ICP at the same time may cause problems but likely won't cause SANS, instead, it is the imbalance between the two that leads to vision loss. This can be seen by the higher likelihood of a loss of scotopic contrast sensitivity (Shen et al.).



Figure 1: Showing distribution of bodily fluids after an extended period of time in space.

Why does going into space lead to changes in TLPD? This is a topic that's up for debate and one that's still being researched today. A common theory for why this occurs is headward fluid shifts (Figure 1) (Marshall-Goebel et al.). Scientists assume that a long period spent in microgravity can lead to blood and other bodily fluids rising into the skull (Marshall-Goebel et al.). A lack of gravity to pull these fluids down could potentially lead to a buildup in the head which could mean increased intracranial pressure at a rate that is faster than the rate of increase for intraocular pressure. Since TLPD is the difference between these two, a disproportionate increase could lead to a change in TLPD contributing to the development of SANS. The increase of fluid in the head could put stress on the eyeball leading to globe flattening as the eye is pushed outward away from the skull, something that can cause changes in vision (Figure 2) (Mader et al.).





Figure 2: Diagram of changes in eye shape due to headward fluid shifts (globe flattening).

Other potential causes of SANS include cytotoxic oedema which hypothesizes that an inflammatory stress pathway mechanism might lead to SANS. The choroidal expansion that occurs in an eye upon reaching a microgravity environment may be another reason. Similar to the headward fluid shift theory, fluid shifts would increase IOP and this increased pressure on the eye could lead to globe flattening (Galdamez et al.).

While SANS may be less problematic for short duration missions, scientists are not sure how it will affect astronauts on long duration missions away from Earth. In addition, Martian gravity is 38% of Earth's gravity while lunar gravity is about 17% of Earth's gravity (Broome). A big question is if Martian and lunar gravity will help alleviate the symptoms caused by SANS. It's important to find a solution to this problem before planning Mars or other distant missions. Symptoms like visual impairment or ocular disease in space can hinder crew members and could potentially compromise a mission, making it a high-priority risk for NASA's proposed Mars missions (Human Research Roadmap). For example, if a crew member specializing in medical assistance has visual impairment it could make it difficult for the crew to respond to a medical emergency. Additionally, if the pilot suffers from visual impairment, it could make it difficult to take manual control of the spaceship and land it on Mars, causing the mission to be potentially unsuccessful.

Potential Countermeasures for SANS Development

Currently, there aren't any working countermeasures to SANS that scientists are confident in. Many ideas have been proposed for potential countermeasures but there isn't comprehensive data to back their efficiency. There's still a lot of testing and research to be done when it comes to SANS countermeasures to make a proper decision on what works best. This section overviews potential countermeasures that can be used to mitigate the effects of SANS.

Lower body negative pressure (LBNP) is a technique that redistributes blood in one's body, specifically by bringing more blood down to the legs and lower body area (Crystal and Salem). Since a likely reason SANS occurs is fluid shifts in the body, LBNP can be a way to simulate gravity on Earth while an astronaut is in space. On Earth, most fluids in the body are pulled down towards the legs due to gravity but in a microgravity environment, these fluids will become more evenly spread out in the body and therefore accumulate in the head, something that can cause globe flattening. While LBNP may not completely simulate gravity, its effects can play a role in reducing the change in TLPD, something commonly associated with SANS. Ways of making LBNP easily accessible in space are currently being researched, one popular idea is integrating a LBNP device into wearable trousers (Bird; Ashari and Hargens).

Another potential countermeasure would be swimming or equinox balance goggles. Equinox balance goggles work by making a vacuum around the eye which can help normalize pressure (Berdahl). Lowering this pressure can help bring TLPD levels back to normal. This can help prevent potential optical diseases from occurring while in space. The effectiveness of the solution can be debatable though, there still needs to be research done on how much of an effect these goggles have on IOP and ICP (both important when calculating TLPD) (Shen et al.). There have been promising studies though such as one run by Scott et. al, which showed that swimming goggles when combined with exercise can increase IOP (Scott et al.). If goggles do turn out to be an effective countermeasure, they can be cost-effective and easy to implement.

Thigh Cuffs, which are circular straps that go around the thigh and can be tightened, are another countermeasure that should be considered. Thigh cuffs serve a similar purpose as LBNP, they both work to stop the headward fluid shifts that occur during space travel. Thigh cuffs could be used to constrict blood vessels which can slow or even block the flow of fluids. Since fluids have a harder time circulating, they won't be able to build up in the head and cause a change in pressure. Poor blood circulation can have other potential side effects on the body though (Cleveland Clinic). Astronauts may experience muscle pain, numbness, and tingling sensations. A 5 day study run by Robin et. all showed that most astronauts didn't feel too much discomfort after use of thigh cuffs, but long-term use may provide different results (Robin et al.). While thigh cuffs may seem like a cost-effective and easy-to-implement solution, when compared to LBNP the potential side effects that could occur just don't seem to outweigh the benefits. Thigh cuffs are something that should have further research on it because a feasible way to implement them could save a lot of time and money on long space missions.

Conclusion

Out of all the countermeasures, the best option is LBNP. For one, there has already been a lot of research around LBNP (found in head-down tilt studies) compared to the equinox balance goggles and thigh cuffs. LBNP as a countermeasure would likely produce promising results when it comes to preventing SANS on longer-term spaceflight missions. The biggest drawback to LBNP is figuring out how it should be implemented. As mentioned above, NASA is working to make compact LBNP pressure devices for astronauts and people are also looking at implementing LBNP into wearable trousers (Bird; Ashari and Hargens). Examining the effectiveness of LBNP devices as well as researching potential side effects are big areas of research that should continue to be done to mitigate the risk of SANS on long spaceflight missions. It's also important to note the side effects of LBNP which can include hypotension, decreased heart rate and dizziness (Goswami et al.).

Swimming goggles would be a cheap and easy to implement solution for SANS as a study found promising results on the effects of exercise and swimming goggles on intraocular pressure. 20 healthy men were used for the study in which some exercised with goggles while others exercised without swimming goggles. The exercise decreased IOP, and then when swimming goggles were worn it subsequently increased it (Scott et al.). If a proper exercise regimen is established with the addition of swimming goggles the difference between ICP and IOP can potentially be decreased leading to lower TLPD and countering SANS. The main problem lies in the fact that not enough research has been done on these effects. Research needs to be done on if the change in IOP is significant enough to produce noticeable results. Also, side effects of the goggles would also need to be researched.

Thigh cuffs are another cheap and easy solution. The problem with thigh cuffs lies in the amount of side effects that result from their use. A study run by Robin et al. showed promising results when it came to a solution using both LBNP and thigh cuffs (Robin et al.). For one, the tolerance for LBNP with or without thigh cuffs remained about the same. There was also a decrease in fluid shifts when thigh cuffs were used. While the subjects felt discomfort on the first day of utilizing this solution, a couple days into the study many of the symptoms were alleviated. Thigh cuffs were only applied intermittently during this study. Limiting the use of thigh cuffs to make sure discomfort doesn't get out of control and astronauts don't experience other potentially dangerous side effects is also an important part of this solution. So, while thigh cuffs may work, especially alongside the use of LBNP more research needs to be done on a way to implement this solution in a safe and effective manner.

More research is needed to better understand the underlying biological mechanisms of SANS development and its potential effects when astronauts are exposed to extended periods of microgravity. These countermeasures listed need further examination. Importantly, we aren't quite sure why SANS occurs at different magnitudes for different people. We also need to research why symptoms of SANS don't occur at all for others. Determining factors that could make SANS more likely or more harmful could be an important step when analyzing potential countermeasures for SANS.

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Works Cited

- Ashari, Neeki, and Alan R. Hargens. "The Mobile Lower Body Negative Pressure Gravity Suit for Long-Duration Spaceflight." *Frontiers in Physiology*, vol. 11, 2020, p. 977, https://doi.org/10.3389/fphys.2020.00977.
- Berdahl, John. "Equinox Balance Goggles: The Effects of Local Orbital Pressure Changes on Intraocular Pressure." *National Space Biomedical Research Institute*, http://nsbri.org/index.html@p=21972.html#:~:text=The%20Balance%20Goggles%20fun ction%20by,and%20intraocular%20pressure%20(VIIP). Accessed 20 July 2023.
- Bird, Elizabeth. Compact Flexible Lower Body Negative Pressure Device for Integrated Exercise Microgravity and Fluid Shift Countermeasure. 4 Sept. 2018, https://www.nasa.gov/directorates/spacetech/strg/nstrf_2018/Compact_Flexible_Lower_ Body_Negative_Pressure_Device/.
- Broome, Kate. "What Is The Gravity On Mars Vs. Moon Vs. Earth." *Science Trends*, 12 Dec. 2017,

https://sciencetrends.com/gravity-mars-vs-moon-vs-earth/#:~:text=Kate%20Broome&tex t=We%20all%20know%20that%20gravity,17%20percent%20of%20Earth's%20gravity.

- Cleveland Clinic. "Poor Circulation." *Cleveland Clinic*, https://my.clevelandclinic.org/health/diseases/21882-poor-circulation#:~:text=How%20d oes%20poor%20circulation%20affect,%2C%20fingers%2C%20feet%20and%20toes. Accessed 13 Aug. 2023.
- Crystal, George J., and M. Ramez Salem. "Lower Body Negative Pressure: Historical Perspective, Research Findings, and Clinical Applications." *Journal of Anesthesia History*, vol. 1, no. 2, Apr. 2015, pp. 49–54, https://doi.org/10.1016/j.janh.2015.02.005.
- Galdamez, Laura A., et al. "Origins of Cerebral Edema: Implications for Spaceflight-Associated Neuro-Ocular Syndrome." *Journal of Neuro-Ophthalmology*, vol. 40, no. 1, 2020, https://journals.lww.com/jneuro-ophthalmology/Fulltext/2020/03000/Origins_of_Cerebra 1 Edema Implications for.12.aspx.
- Goswami, Nandu, et al. "Lower Body Negative Pressure: Physiological Effects, Applications, and Implementation." *Physiological Reviews*, vol. 99, no. 1, Jan. 2019, pp. 807–51, https://doi.org/10.1152/physrev.00006.2018.
- Human Reasearch Roadmap. "Risk Of Spaceflight Associated Neuro-Ocular Syndrome (SANS)." *Human Research Roadmap*, 15 Aug. 2022, https://humanresearchroadmap.nasa.gov/risks/risk.aspx?i=105.
- Ioannides, Antonis, et al. "Isolated Cotton-Wool Spots of Unknown Etiology: Management and Sequential Spectral Domain Optical Coherence Tomography Documentation." *Clinical Ophthalmology (Auckland, N.Z.)*, vol. 5, 2011, pp. 1431–33, https://doi.org/10.2147/OPTH.S16272.
- Lee, Andrew G., et al. "Spaceflight Associated Neuro-Ocular Syndrome (SANS) and the Neuro-Ophthalmologic Effects of Microgravity: A Review and an Update." *Npj Microgravity*, vol. 6, no. 1, Feb. 2020, p. 7, https://doi.org/10.1038/s41526-020-0097-9.

- Mader, Thomas H., et al. "Optic Disc Edema, Globe Flattening, Choroidal Folds, and Hyperopic Shifts Observed in Astronauts after Long-Duration Space Flight." *Ophthalmology*, vol. 118, no. 10, Oct. 2011, pp. 2058–69, https://doi.org/10.1016/j.ophtha.2011.06.021.
- Marshall-Goebel, Karina, et al. "Mechanical Countermeasures to Headward Fluid Shifts." *Journal of Applied Physiology (Bethesda, Md. : 1985)*, vol. 130, no. 6, June 2021, pp. 1766–77, https://doi.org/10.1152/japplphysiol.00863.2020.
- Robin, Adrien, et al. "DI-5-CUFFS: Venoconstrictive Thigh Cuffs Limit Body Fluid Changes but Not Orthostatic Intolerance Induced by a 5-Day Dry Immersion." *Frontiers in Physiology*, vol. 11, 2020, p. 383, https://doi.org/10.3389/fphys.2020.00383.
- Scott, Jessica M., et al. "Association of Exercise and Swimming Goggles With Modulation of Cerebro-Ocular Hemodynamics and Pressures in a Model of Spaceflight-Associated Neuro-Ocular Syndrome." *JAMA Ophthalmology*, vol. 137, no. 6, June 2019, pp. 652–59, https://doi.org/10.1001/jamaophthalmol.2019.0459.
- Shen, Guofu, et al. "Modeling a Potential SANS Countermeasure by Experimental Manipulation of the Translaminar Pressure Difference in Mice." *NPJ Microgravity*, vol. 6, 2020, p. 19, <u>https://doi.org/10.1038/s41526-020-00109-5</u>.

How is Inflation Shaping the Post-Pandemic US Economy? By Yash Bansal

Abstract

Today, the federal funds rate sits at 5.25%-5.50%, a record high since February 2001. The Federal Reserve Bank has been increasing interest rates largely because of stubborn inflation. Since 2021, America has seen high inflation, prompting the Fed to raise rates. This has had a ripple effect on the entire US economy, affecting both consumers and businesses. This literature review was written to understand the cause of the inflation and the effects that inflation has had on businesses, banks, consumers, workers, and families. In conclusion, it can be deduced that increased consumption as a result of the stimulus checks contributed to the high inflation, and when the Fed raised rates, that triggered a series of layoffs, bank failures, and change in consumer behavior.

Keywords

Stimulus Package, CPI, Federal Reserve, Rate Hikes, Layoffs, Unemployment

Introduction

The decisions that those in authority make today will have a profound impact on tomorrow. For example, when the Federal Reserve Bank raised interest rates after the Covid-19 pandemic, inflation had the potential to harm both corporations and the average American citizen. Corporations were faced with expensive credit and consumers faced layoffs as inflation caused more difficult conditions for employment (Alisa 1).

Key Definitions

CARES Act: An act implementing a variety of programs to address the issues onset by the COVID-19 pandemic ("About the CARES Act and the Consolidated Appropriations Act") *COVID-19 Pandemic*: Global outbreak of coronavirus starting in December 2019, an infectious disease caused by the SARS-CoV-2 virus ("Coronavirus disease (COVID-19) pandemic"). *CPI*: The Consumer Price Index measures the change in prices of a basket of goods typically consumed by urban households

Monetary Inflation: Rate of increase in prices over time (Oner)

Dovish: Opposite of hawkish; monetary policy favoring achieving maximum levels of employment. Typically achieved by the Fed lowering interest rates (Rodini)

Rate Hikes: When the Federal Reserve Bank increases its federal funds rate

Interest rate: Income earned on the funds utilized by the person holding the same .

The Federal Reserve: Central Bank of the US. It provides the nation with a stable monetary system.

The Covid-19 Pandemic Bailout

Recent inflation concerns began when the world locked down in the wake of the March 2020 COVID-19 pandemic. Stores and factories temporarily closed, with many businesses in limbo. The general public's expectation was that the world would reopen after a few weeks, but as weeks turned into months, the world became anxious. More importantly, businesses became concerned as the jobs deemed non-essential-those not in healthcare or in government-forced workers to "stay-at-home."

Moreover, United States economic activity came to a halt, with the GDP falling 4.6% quarter over quarter ("Annualized growth of real GDP in the United States from the first quarter of 2013 to the second quarter of 2023"), which prompted a government bailout. A \$2.2 trillion stimulus plan, called the CARES Act (Coronavirus Aid, Relief, and Economic Security Act), provided Americans earning less than \$75,000 individually or \$150,000 as a household with \$1,200 or \$2,400 stimulus checks, respectively (Sauter).

This included \$260 billion in increased unemployment benefits, \$350 billion in forgivable loans to small businesses to help cover employee salaries, and \$500 billion to large corporations for the same purpose (Snell). According to the Congressional Budget Office, this bill would add \$1.7 trillion to the deficit from 2020-2030. A subsequent \$900 billion stimulus bill was passed in January 2021, which gave an additional \$600 per person or \$1200 per household, further increasing the deficit.

The Federal Reserve During the Covid-19 Pandemic

The federal body in charge of controlling the flow of money within the economy is the Federal Reserve. The Federal Reserve also monitors the country's inflation rate. To explain, the inflation rate refers to the rate at which a standard basket of household goods increases in price from one year to the next. In a stable economic climate, as companies hire workers and households have additional income, demand increases, which increases these prices. This is considered healthy inflation, and the federal reserve's inflation target rate is about 2% year over year. This ensures that the US dollar remains stable, with demand and prices remaining predictable. It also encourages the US dollar to remain strong in the global economy.

The Effects of the Stimulus Checks in 2020

However, in 2020, people received thousands of dollars in stimulus checks and benefitted from extended unemployment benefits. This prompted some affected employees to choose to not return to work (Ferguson). This was damaging to an economy that was trying to reopen after the pandemic. Most companies were on a hiring spree as they hoped to return to pre-pandemic profits. Instead, corporate America found previous wages no longer sufficient to hire (Haddon 2). This forced firms to increase wages. Businesses passed on this added cost to consumers in the form of rising prices. These price increases are recognized as inflation.

Another impact of the stimulus checks is that it helped create an unsustainable, artificial level of demand. For many people, the stimulus money exceeded their previous income. So what

became of this additional disposable income? In many cases, it became a temporary spike in household savings ("United States Personal Savings Rate") and luxury spending (Baker et al. 2). Increases in demand caused prices to rise, spiking inflation. However, this increase in demand was artificial and unsustainable. As the stimulus money ended, many consumers were no longer able to afford these products. Prices, however, continued to increase ("12-month percentage change, Consumer Price Index, selected categories").

These price increases were reflected in the monthly Consumer Price Index (CPI) data. The CPI is the general indicator that investors and experts use to gauge inflation in America. According to the Bureau of Labor Statistics (BLS), the year-over-year percent change of the CPI exceeded the target rate of 2% in April 2021, when the CPI reported a 4.2% increase in prices year over year (2021). However, the Federal Reserve Bank remained dovish, opting not to raise interest rates so as to not stymie the labor market recovery (Schneider and Saphir).

The Fed's "interest rate" is the federal funding rate, and it serves as the rate at which banks can borrow money from the government. This rate is used as a benchmark for banks when lending to consumers. The rate from March 2020 to March 2022 was 0.25%, a historically low amount. This meant that banks, after taking into account inflation, had a negative or near-zero real interest rate.

Companies Take Advantage of Low Rates

Additionally, one way for the Fed to close the deficit is to increase this interest rate. But, the Fed did not want to raise interest rates too quickly out of fear that this would exacerbate unemployment. America was just coming out of the pandemic; businesses were finally opening back up, people were returning to work, and unemployment was going down. The Fed did not want to stunt and possibly reverse this recovery by increasing rates. Fed Chairman Jerome Powell testified before a House panel in June 2021 that he believed the price pressures from the rising demand and bottlenecks in supply would ease on their own.

As a result of the low cost of borrowing, many businesses, especially in tech, energy, and finance, initiated a hiring frenzy. Microsoft increased their workforce by 22% from June 2021 - June 2022, Meta increased theirs by 30% in 2020, and Alphabet added 15% to their workforce in 2021 (Leswing and Cortés). Low interest rates made it possible for companies, both big and small, to borrow large sums of money. Cheap capital allowed companies, especially start-ups, to grow their businesses meteorically. As a result, there was a rapid increase in demand in the job market. In the 4th quarter of 2021, the unemployment rate was 4.2%, down 2.8% year-over-year, with 5.4 million new jobs being added in 2021 (Edwards et al,.). This data further indicated that America was recovering from the pandemic. The Fed used this as rationale to keep interest rates low. However, at the start of 2022, CPI data began to show persistent inflation. This forced the Fed's hand into raising rates.

The Fed Makes Moves

When the Fed started raising interest rates, they increased it aggressively. Between March 2022 and May 2023, the Fed met ten times. From those meetings, the Fed raised rates from 0.25% to 5.25% (Tepper). Following some of these meetings, the Fed went as far as raising 0.75% in one instance. During this period, the CPI data continued to show persistent inflation. For example, from April 2021 to June 2022, annual price inflation increased from 4.2% to 9.1%. 9.1% inflation has not been reached in the US in the last 40 years.

This rapid increase was paused in June 2023 when inflation finally showed signs of cooling, and interest rates were left at 5.25% before resuming again in July (Tepper). The Fed opted to pause the increase to allow time for the rate hikes to fully take effect on inflation. Effects of interest rate hikes typically take anywhere from between 6 months to over 1 year to be felt in the economy.

Impacts of the Rate Hikes

However, inflation is not the only thing on which rate hikes had an impact. Rate hikes also left a profound mark on American businesses and consumers. Prior to the rate hikes, companies enjoyed low borrowing rates. Small businesses–especially tech startups–reaped the benefits of this opportunity. In 2020, small businesses received loans from banks at an average annual percentage rate (APR) of 2.77% (Mak). From 2021 to present day, interest rates for small business loans from banks have steadily climbed to 5.5% APR (Porter). For small businesses, the rate increase diminished the benefits of borrowing. A lack of capital brought the growth of many small businesses to a grinding halt; they were no longer able to afford their rapid expansion (Griffith).

As these businesses now lacked capital, they were forced to lay off workers. 17.6 million workers were laid off in 2022 alone ("U.S. labor market shows improvement in 2021, but the COVID-19 pandemic continues to weigh on the economy"). Tech companies were hit especially hard by this, including Meta, Google, and Microsoft (Trueman 2). A sea of layoffs and startup closures soon followed. Since this constriction in January of 2022, 250,000 jobs in the tech sector have been cut ("The Crunchbase Tech Layoffs Tracker").

Furthermore, companies that opted not to rapidly downsize may have passed increased costs to consumers in the form of higher prices. This trend is reflected by the persistent inflation consumers continue to experience ("12-month percentage change, Consumer Price Index, selected categories"). The core inflation rate (inflation rate without food and energy, both of which tend to fluctuate greatly) has followed a volatile pattern, varying between 4.3% and 6.6% (as of August 2023) since the Fed first started raising rates in March 2022. As consumers continue to grapple with higher costs, many have changed their spending patterns. To explain, when inflation increases, consumers "trade down" (finding cheaper alternatives to what was previously purchased) in 5 ways: choosing lower prices or lower quantities, switching to inferior goods, prioritizing promotions and discounts, buying in bulk or delaying purchases, and avoiding big-ticket items (Draxl).

Small Banks Collapse

A second ramification of the rate hikes was the failure of small banks. Bank failures occur when the institution is unable to meet its obligations to its depositors and lenders. In the past couple of years, there were numerous startup companies that needed loans to continue expanding. Mostly regional banks, like Silicon Valley Bank (SVB) and First Republic Bank (FRB) were willing to underwrite high leverage loans. Banks needed assets to fill out their balance sheet to meet investors' return requirements. However, higher rates, and less profits as a result of the recessionary environment meant that many of these startup companies defaulted on their loans. Consequently, banks had less capital, which meant they could not pay back their lenders. These defaulting borrowers contributed to pushing banks into a liquidity problem. Compounding the defaulting borrowers was the decrease in the value of treasury bills which hurt the banks' balance sheets. In March of 2023, the recessionary environment and the increasing withdrawals continued to strain the regional banks' reserves. Ultimately, some crumbled like Silicon Valley Bank and Signature Bank, with FRB collapsing in May.

In the aftermath, these collapsed regional banks were purchased by national banks like JP Morgan. As a result of 2023's bank failures, the FDIC agreed to fully insure all depositors. This was done to prevent panic (and potentially bank runs), and increase consumer confidence in the banking industry. Unfortunately, these behaviors also encourage banks to take more risk (Hakenes et al. 2). For example, in the 2008 financial crisis, banks' irresponsible lending practices were ultimately absorbed by the US government.

Conclusion

In conclusion, post-COVID inflation forced the Federal Reserve Bank to raise rates. This increase hurt both corporations and citizens, as corporations dealt with costly credit and citizens suffered layoffs. Stimulus money directly given to consumers led to many unemployed workers who would not return to work. This created unhealthy wage growth which contributed to inflation, as corporations were forced to pass on the added cost of labor onto the consumers. Inflation also forced the Federal Reserve to aggressively increase interest rates. This put pressure on businesses, who were no longer able to continue their rapid growth as a result of high borrowing costs.

In fact, many startup companies defaulted on their loans. This put many small banks at risk, being the most likely to give out these high-leverage loans. These defaulting loans contributed to a wave of bank failures in March 2023. Due to a lack of capital, revenue dipped and businesses were forced to lay off employees. Those that chose not to lay off workers were instead forced to increase prices, passing on the costs to consumers. This further increased inflation.

A shift in consumer behavior followed, as they opted to trade down to combat rising costs. This catastrophic domino effect impacted people at all economic levels. Preventing a repeat of these events will require government decision-makers, the Federal Reserve Bank, businesses, and consumers to do their part. While the Covid Stimulus garnered great support

early on, the longer term impact on the economy ultimately served to crush those it was intended to protect. Controlling inflation and maintaining economic stability and growth is key to preventing the recurrence of the hyperinflation.

Works Cited

"About the CARES Act and the Consolidated Appropriations Act | U.S. Department of the Treasury." *Home.treasury.gov*, 2020,

home.treasury.gov/policy-issues/coronavirus/about-the-cares-act.

- Alisa, Maximova. "The Relationship between Inflation and Unemployment: A Theoretical Discussion about the Phillips Curve." *Journal of International Business and Economics*, vol. 3, no. 2, Dec. 2015, pp. 89–97, https://doi.org/10.15640/jibe.v3n2a7.
- Baker, Scott R., et al. "Income, Liquidity, and the Consumption Response to the 2020 Economic Stimulus Payments." SSRN Electronic Journal, 2020, https://doi.org/10.2139/ssrn.3587894.
- Daniel, Edwards,Roxanna;Essien,Lawrence S. ;Levinstein,Michael. "U.S. Labor Market Shows Improvement in 2021, but the COVID-19 Pandemic Continues to Weigh on the Economy : Monthly Labor Review: U.S. Bureau of Labor Statistics." *Www.bls.gov*, June 2022, www.bls.gov/opub/mlr/2022/article/us-labor-market-shows-improvement-in-2021-but-th e-covid-19-pandemic-continues-to-weigh-on-the-economy.htm#:~:text=June%202022-.
- Ferguson, Stephanie . "Understanding America's Labor Shortage." *Www.uschamber.com*, 7 Feb. 2022, www.uschamber.com/workforce/understanding-americas-labor-shortage.
- Griffith, Erin. "Fear and Loathing Return to Tech Start-Ups." *The New York Times*, 11 May 2022, www.nytimes.com/2022/05/11/technology/tech-start-ups.html. Accessed 16 Sept. 2023.
- Haddon, Heather. "RESTAURANTS SERVE up SIGNING BONUSES, HIGHER PAY to WIN BACK WORKERS." The Wall Street Journal, 25 Apr. 2021.
- Hakenes, Hendrik, et al. *Annual Conference of the German Economic Association in Dresden*. 2004.
- Mak, Adrian. "The Average Small Business Loan Interest Rate (2021)." *AdvisorSmith*, 12 Oct. 2021,

advisorsmith.com/data/average-small-business-loan-interest-rates/#:~:text=For%20fixed %2Drate%20loans%20to. Accessed 16 Sept. 2023.

- News, Crunchbase. "Tech Layoffs: US Companies with Job Cuts in 2022 and 2023." *Crunchbase News*, 15 Sept. 2023, news.crunchbase.com/startups/tech-layoffs/#:~:text=In%202023%3A%20More%20than %20169%2C524. Accessed 16 Sept. 2023.
- Oner, Ceyda. "Inflation: Prices on the Rise." *International Monetary Fund*, 2023, www.imf.org/en/Publications/fandd/issues/Series/Back-to-Basics/Inflation.
- Penn,Rick;Huang,Victor. "Job Openings Reach Record Highs in 2022 as the Labor Market Recovery Continues : Monthly Labor Review: U.S. Bureau of Labor Statistics." *Www.bls.gov*, May 2023,

www.bls.gov/opub/mlr/2023/article/job-openings-reach-record-highs-in-2022-as-the-labo r-market-recovery-continues.htm.

Porter, T. J. "Average Business Loan Interest Rates." *Bankrate*, 23 Aug. 2023, www.bankrate.com/loans/small-business/average-business-loan-rates/#average.

- Rodini, Laura. "Hawkish vs. Dovish: Definitions, Examples & What They Mean for Investors." *TheStreet*, 27 June 2023, www.thestreet.com/dictionary/h/hawkish#:~:text=high%20interest%20rates.-. Accessed 16 Sept. 2023.
- Schneider, Howard, and Ann Saphir. "Fed Will Not Raise Rates on Inflation Fears Alone, Powell Says." *Reuters*, 22 June 2021,

www.reuters.com/business/us-lawmakers-likely-press-powell-feds-hawkish-turn-2021-06 -22/.

Snell, Kelsey. "What's inside the Senate's \$2 Trillion Coronavirus Aid Package." NPR.org, 26 Mar. 2020,

www.npr.org/2020/03/26/821457551/whats-inside-the-senate-s-2-trillion-coronavirus-aid -package.

- Statista. "U.S. Real GDP Growth by Quarter 2020." *Statista*, 2023, www.statista.com/statistics/188185/percent-change-from-preceding-period-in-real-gdp-in -the-us/.
- Tepper, Taylor. "Federal Funds Rate History 1990 to 2022." *Forbes Advisor*, 3 May 2023, www.forbes.com/advisor/investing/fed-funds-rate-history/.
- Trueman, Charlotte. "Tech Layoffs in 2023: A Timeline." *Computerworld*, 12 May 2023, www.computerworld.com/article/3685936/tech-layoffs-in-2023-a-timeline.html?page=2.

U.S. BUREAU OF LABOR STATISTICS. "12-Month Percentage Change, Consumer Price Index, Selected Categories." *Bls.gov*, 2009, www.bls.gov/charts/consumer-price-index/consumer-price-index-by-category-line-chart. htm.

- "United States Personal Savings Rate | 1959-2020 Data | 2021-2022 Forecast | Historical." *Tradingeconomics.com*, tradingeconomics.com/united-states/personal-savings.
- World Health Organization. "Coronavirus Disease (COVID-19) Pandemic." *Www.who.int*, World Health Organization, 2023, www.who.int/europe/emergencies/situations/covid-19.

How Palliative Care Addresses Physical and Existential Suffering in Symptomatic and Terminally III Patients By Suraj Murugarajan

Abstract

Palliative care and hospice care are medical specialties focused on enhancing the quality of life and alleviating physical, mental, and spiritual suffering among patients with advanced and/or terminal illnesses. These two fields of medicine were initially conceived about 120 years ago, and the widespread implementation of these fields into the global practice of medicine only began about 70 years ago. These fields have continued to grow worldwide, as has the research on their effect on the physical and existential well-being of patients who are terminally ill. Physical symptoms are generally relieved through various medications, but other non-pharmaceutical therapies are available. Doctors and nurses working in palliative care are key figures in addressing existential suffering, and other therapies are also available. The main focus of this literature review is to show people a newer field of medicine that is not being discussed as widely as it could be.

Keywords: Translational Medical Sciences; Disease Treatment and Therapies; Palliative Care; Hospice Care

Introduction

For as long as humans have existed, disease has caused suffering and death. From the Spanish Flu in 1918 to COVID-19 one century later, scientists have found hundreds of treatments for various diseases. Scientists have also developed treatments for many diseases without curative therapies to keep the condition from progressing. However, sometimes, these treatments are unavailable or are too painful, costly, or insufficient to stop the progression of the disease. In these cases, where the patient has no treatment options or decides they no longer wish to undergo treatment, hospice care may be offered. Similarly, palliative care may be provided to patients undergoing treatment who need assistance with symptom management or who have quality-of-life concerns.

Palliative care first gained attention in the 1950s, when much of the focus of medicine in the oncological field was on discovering a cure for cancer. Those with advanced-stage diseases or deemed incurable were mainly forgotten about and left to die alone. During the 1960s in the United Kingdom, questions were raised about how to handle near-impossible cases. Cicely Saunders is one of the prominent names in the rise of hospice care for cancer patients in the UK. In the late 1950s, she was working on her first major medical publication. Her chapter on "The Management of Patients in the Terminal Stage" was the only work to discuss end-of-life care in a six-volume series on Cancer. During this time, there were very few hospice facilities in the UK. Of the few in existence, nearly all were run by religious organizations. In 1999, the British government appointed Mike Richards to reform and improve cancer services. His efforts led to what is known as palliative care today (Clark, 2007).

Fortunately, palliative and hospice care look very different in the modern era than they did one hundred years ago. Today, palliative care focuses on alleviating suffering, including physical, spiritual, and existential. Physical suffering consists not only of pain but also symptoms such as nausea, vomiting, neuropathy, and diarrhea. Through therapies such as medication, surgery, or radiotherapy, great strides have been made in the last few decades to reduce patients' physical discomfort (WHO Geneva. 1990). While physical pain management is a huge part of palliative care, other factors must also be considered when addressing all aspects of suffering. At the end of life, patients often experience profound existential thoughts, which cannot be relieved by the methods mentioned previously. Instead, other methods that address existential issues are more efficacious, such as counseling, religious participation, and psychotherapy. This review paper aims to compile the numerous studies and methods by which palliative care aims to address the whole person, as well as alleviate suffering at the end of life.

Discussion–*Physical Suffering*

The goal of palliative care is to reduce suffering caused by disease. One of the most integral parts of this is reducing physical pain. To see if the treatment is effective, there must first be qualitative and quantitative ways to assess pain or discomfort in palliative care patients. A common method to quantify pain is by asking a patient to state the severity of their pain, with a number usually between 1 and 10, with 1 being minimal to almost no pain, 4-5 being moderate pain, and 10 being unbearable pain. Another model that is used is displaying faces with different expressions, ranging from a smiling face to a strained one to one that is crying uncontrollably. The patient is asked to match their pain level with the one they feel most represents how they feel. These models are useful for describing pain because, although it is relative, it allows the patient to describe what they are feeling accurately. Additionally, this same pain scale can be used while administering the therapy to evaluate the effect on the patient's symptoms. The new value the patient uses will be compared to their old assessment, allowing providers to determine if there is any positive or negative effect on the patient. Using adjectives is also useful in determining what kind of therapy should be used. Different types of sensations suggest different kinds of problems in the body. Another important factor in assessing pain is determining the location of the pain. This makes it easier to decide what measures should be taken to reduce the pain because the location allows the examiner to determine the nature of the pain and how to reduce it (Perron & Schonwetter, 2001). After the type of pain has been identified, physicians can begin administering therapy.

The main form of therapy today is medication. The general guideline for administering pain medication to cancer patients was established by the World Health Organization in 1986 but later revised in 1996. This method is still utilized today. The Analgesic Ladder breaks down pain medication management into two sections: one section for the level of pain and one section for the usage of the medication. The section for the pain level is broken down into mild pain, mild to moderate pain, and moderate to severe pain, with each level requiring different types of medication. The section for medication usage is broken down into medication by mouth, by the

clock, by ladder, by an individual basis, and with attention to detail. Generally, the main medication consists of opioids and adjuvants, but for lower levels of pain, acetaminophen is used instead of opioids. This is because the goal of the medication is to make the patient feel better with as little medication as possible. As time progresses, however, stronger and stronger opioids may be required to compensate for patients' increasing opioid tolerance, and medication such as morphine or oxycodone may be required. This structure gives physicians a general framework for administering medication as this basis is widely accepted (Perron & Schonwetter, 2001). Within two years of its proposal, the Analgesic Ladder was validated in 80-90% of its cases, proving that it was a highly effective way of determining what kind of medication was required for the patient (Yang *et al.* 2020)

Research has also been conducted on the usage of cannabinoids in pain management. Although the results suggested using cannabinoids alongside the use of other treatments did have a positive effect on the patients, the results did not suggest that there was any definitive effect on the patients to consider cannabinoids as a therapeutic measure to be used alone. The study mentions that the results should be regarded "as an individual therapeutic trial" and should not be taken alone but alongside other therapeutic measures.

Somatic pain is generally responsive to opioids but sometimes may require additional therapeutic measures. The prevailing medication currently is nonsteroidal anti-inflammatory drugs (NSAIDs). However, NSAIDs have their own side effects, such as nausea and vomiting (Jenkins & Bruera, 1999). Neuropathic pain is generally not responsive to opioids, and different medications should be used. Generally, tricyclic antidepressants and antiseizure medications are used. Anticonvulsant medication can be utilized if the patient does not benefit from these types of drugs. Traditionally, the treatment for pain has been the use of medication. However, there are many nonpharmacological approaches to reducing pain in patients. "Physical interventions include massage, acupuncture, exercise, stretching, passive range of motion, heat therapy, transcutaneous electrical nerve stimulation, and immobilization. Psychosocial interventions include relaxation techniques, imagery, support groups, family counseling, education, biofeedback, and psychotherapy" (Perron & Schonwetter, 2001).

Palliative care also focuses on relieving non-pain-related suffering. For example, many patients who undergo chemotherapy experience long and uncomfortable nausea. To treat this discomfort, there are generally two approaches to drug selection: empirical and mechanistic. The empirical approach allows physicians to choose antiemetic drugs based on previous experience. It is akin to the doctor using a one-size-fits-all approach to prescribing medication without considering the cause of the nausea. However, the mechanistic approach uses current knowledge of an empirical approach and how chemicals in the brain and nervous system interact with substances to choose the best medication for the patient based on how it will interact with the receptors in the brain. The mechanistic approach relies on understanding the disease and what causes it to come up with treatments, while the empirical approach relies on clinical experience to suggest medication even if the underlying mechanisms of the disease or the drug are not fully understood. Similar to physical pain, a second medication should be added if the patient is

unresponsive to one type of treatment. Many drugs are available for treating nausea and vomiting, including prokinetic agents and antagonist medications, such as antihistamines. For many end-of-life patients, delayed gastric emptying is a common symptom, often secondary to their medications or underlying medical issues. When delayed gastric emptying goes untreated, it can lead to many symptoms, including nausea and vomiting. Prokinetic drugs aim to increase the contraction of muscles in the gastrointestinal tract to stop delayed gastric emptying. This way, they help prevent nausea and vomiting (Lewis *et al.*, 2016). Antihistaminic agents work by targeting parts of the brain. They work mainly by blocking H1 receptors in a part of the medulla that facilitates vomiting and the chemoreceptor trigger zone, the part of the medulla that receives emetic signals and sends this information to the vomiting center of the brain, thereby inducing emesis (MacDougall & Sharma, 2023; Glare *et al.*, 2011).

Another very common form of discomfort in palliative care patients is constipation, especially as patients are on significant analgesics. Constipation is relieved through medications, including genocides, bisacodyl, and methylcellulose (Suh *et al.*, 2011). The most common medication to treat constipation in palliative care patients is macrogol. It has been shown to be the most effective medication for constipation and works for a wide age range of patients (Klaschik *et al.*, 2003).

Existential Suffering

Unfortunately, many times, patients need healing beyond their physical symptoms, and healthcare workers have reported feeling underprepared to deal with the transition of life (Rushton *et al.*, 2007). Hospice nurses have developed strategies to help patients deal with existentialism. Something to note is that before their existential needs can be addressed, patients' physical suffering must first be relieved since constant pain and nausea will exhaust them to the point where spiritual and existential concerns cannot be properly addressed.

Experienced nurses from a prominent hospice in Norway were invited for an interview, each with extensive experience and qualifications for end-of-life care. Two key themes were determined over the course of the interviews: sensing the existential suffering the patient was experiencing and consoling the patient (Tornøe *et al.*, 2014). Determining what the patient needs is an extremely difficult process since, many times, the patient's suffering is a mix of both physical and emotional, making it difficult to discern what the patient truly needs. Nurses talked about sensing the emotions in patients' rooms, specifically when other family members were present. They reported various emotions in the rooms' atmospheres, from intense dread to being joyful and lively (Tornøe *et al.*, 2014).

Nurses can provide consolation by talking with the patient but, more importantly, by employing active listening techniques. Many times, silence is a very consoling experience for patients. By simply being present and offering a comforting touch, nurses can show compassion in a calm and peaceful manner. Other times, nurses could support the patient emotionally by allowing them to process their feelings by encouraging patients to talk about their feelings about

future passing. The nurses noted that patients who talked about their feelings seemed to pass away more peacefully than those who did not.

Hospice care workers are vital when helping families share and express grief. Many patients do not wish to share difficult information with their families. For instance, dying parents hide their emotions not to scare their children, or spouses may withhold information from one another over the fear of causing them distress. When patients find it difficult to talk to their families, nurses are able to facilitate the conversation.

During times of despair, many patients find comfort in their religion. Hospice workers can help patients by allowing them to connect with their religion. For example, nurses can refer patients to hospice chaplains to help them with religious support, or they can directly support patients by providing them with the things they need to practice their religion. The nurses in the interview stated that for Christian patients they would pray for the patients and their families and read from the Bible if requested. Nurses are also able to help patients with religions that they are not very familiar with. For example, although the nurses interviewed were not very well versed in the Muslim faith, they were still able to provide religious consolation by providing them with things such as halal food and a prayer space (Tornøe *et al.*, 2014).

Patients can also engage in other activities like drawing, painting, listening to music, or playing with animals. Data on art therapy has been collected on numerous populations with different diseases and symptoms, from cancer to dementia, and the results show that art therapy has a tremendously positive impact on end-of-life patients. Most patients who participate in any kind of art-based activity have been shown to have a better quality of life after engaging in them. These patients report not only less emotional symptoms, such as anxiety and depression but also physical symptoms, such as reduced fatigue and pain (Iguina & Kashan, 2022). The use of music therapy has also shown a positive effect on the lives of patients in hospice care. As an evidence-based therapeutic treatment, it has been shown to decrease depression, stress, and anxiety in patients (Gao *et al.*, 2019). Music therapists analyze the needs of patients and then use various methods such as compositional, improvisational, receptive, and re-creative therapy to facilitate a healing environment. In each of these methods, patients can either create or listen to music, allowing the patient to express themselves or be more relaxed (Drury University, 2022).

The use of animal companionship as a form of therapy has proven helpful in other settings, such as pediatric wards and correctional facilities, and they have a similarly positive effect on hospice patients. A study was conducted in a day hospice in England in which two trained cocker spaniels were brought to visit the patients, as well as a resident budgerigar and some tropical fish. While the bird and the fish received positive yet mixed reviews from the patients, the dogs received an overwhelmingly positive response, with more than 86 percent of the patients reporting a "very keen" attitude to the dogs. Many patients had previously had an animal companion, making them much more open to meeting the animals. Still, even patients who had not previously had pets were willing to meet with the animals. Physical contact with the dogs made the patients feel more relaxed and happier, and affectionate dogs brightened the

atmosphere significantly. The presence of dogs makes the hospice environment feel less clinical and more friendly, greatly improving the moods of the patients (Phear, 1996).

Conclusion

Before hospice and palliative care, most patients were left to die if they were considered to be past the point of saving. Thanks to the work of people like Nurse Cicely Saunders, palliative and hospice care have grown from being nonexistent to now being an established field of medicine with an ACGME-accredited fellowship. Palliative care providers help patients in the advanced stages of their disease by addressing physical and existential suffering. To properly treat physical suffering, it is important to first quantify it in a way that makes it easy to determine what the proper therapy should be. It is also important to determine the location of the discomfort for the best treatment. The creation of the Analgesic Ladder by the World Health Organization was a monumental step in standardizing how patients receive proper treatment based on the level of pain they are experiencing.

To address physical pain, the general approach is to use different types of medication. However, other nonpharmacological approaches can also be used, such as massage or acupuncture. Other non-pain-related symptoms are also very common among palliative and hospice care patients. Other types of somatic symptoms include nausea, vomiting, and constipation. These symptoms are treated with different types of medication.

In addition to addressing physical suffering, palliative and hospice care place a large importance on addressing existential suffering as well. Hospice nurses are trained to sense patients' feelings and console them through various methods, such as active listening and a comforting presence. Nurses are also vital to facilitating conversation between patients and their loved ones, as it may be difficult for the families to discuss their feelings. Patients can also engage in other activities, such as art therapy, music therapy, and animal companionship. Massive strides have been made and are continuing to be made in the field of palliative and hospice care. As new fields in the vast ocean of medicine, it is important to highlight the importance and impact they have had on numerous patients and their families. By combining medical knowledge with human compassion, these new fields have developed and continue to develop that provide quality and dignified care to all types of patients regardless of who they are, bringing all of us closer together.

Works Cited

- "Cancer Pain Relief and Palliative Care : Report of a WHO Expert Committee [meeting Held in Geneva from 3 to 10 July 1989]." *World Health Organization*, World Health Organization, 1 Jan. 1990, apps.who.int/iris/handle/10665/39524.
- Clark, D. "From Margins to Centre: A Review of the History of Palliative Care in Cancer." *The Lancet. Oncology*, U.S. National Library of Medicine, 2007, pubmed.ncbi.nlm.nih.gov/17466900/.
- Gao, Y, et al. "The Effectiveness of Music Therapy for Terminally Ill Patients: A Meta-Analysis and Systematic Review." *Journal of Pain and Symptom Management*, U.S. National Library of Medicine, 2019, pubmed.ncbi.nlm.nih.gov/30389608/.
- Glare, Paul, et al. "Treating Nausea and Vomiting in Palliative Care: A Review: CIA." *Clinical Interventions in Aging*, Dove Press, 12 Sept. 2011, doi.org/10.2147/CIA.S13109.
- Iguina, M, and S Kashan. "Art Therapy." *National Center for Biotechnology Information*, U.S. National Library of Medicine, 2022, pubmed.ncbi.nlm.nih.gov/31747178/.
- Jenkins, C, and E Bruera. "Nonsteroidal Anti-Inflammatory Drugs as Adjuvant Analgesics in Cancer ..." Anti-Inflammatory Drugs as Adjuvant Analgesics in Cancer Patients, 1999, journals.sagepub.com/doi/10.1191/026921699666671383.
- Klaschik, E., et al. "Constipation-Modern Laxative Therapy Supportive Care in Cancer." *SpringerLink*, Springer-Verlag, 20 Sept. 2003, link.springer.com/article/10.1007/s00520-003-0525-x.
- Lewis, K, et al. "The Efficacy and Safety of Prokinetic Agents in Critically Ill Patients Receiving Enteral Nutrition: A Systematic Review and Meta-Analysis of Randomized Trials." *Critical Care (London, England)*, U.S. National Library of Medicine, 2016, pubmed.ncbi.nlm.nih.gov/27527069/.
- MacDougall, M, and S Sharma. "Physiology, Chemoreceptor Trigger Zone StatPearls NCBI Bookshelf." *Physiology, Chemoreceptor Trigger Zone*, 2023, www.ncbi.nlm.nih.gov/books/NBK537133/.
- Perron, V, and R Schonwetter. "Assessment and Management of Pain in Palliative Care Patients." *Cancer Control : Journal of the Moffitt Cancer Center*, U.S. National Library of Medicine, 2001, pubmed.ncbi.nlm.nih.gov/11176032/.
- Phear, D. *A Study of Animal Companionship in a Day Hospice*, 1996, journals.sagepub.com/doi/10.1177/026921639601000410.
- Rushton, C, et al. "Contemplative Practices for Compassionate End-of-Life Care." *Am. Nurse Today*, 2007, www.researchgate.net/publication/242750788_Contemplative_practices_for_compassion ate_end-of-life_care.
- Suh, D, et al. "Use of Medications and Resources for Treatment of Nausea, Vomiting, or Constipation in Hospitalized Patients Treated with Analgesics." *The Clinical Journal of Pain*, U.S. National Library of Medicine, 2011, pubmed.ncbi.nlm.nih.gov/21368666/.

- Tornøe, Kirsten A, et al. "The Power of Consoling Presence Hospice Nurses' Lived Experience with Spiritual and Existential Care for the Dying BMC Nursing." *BioMed Central*, BioMed Central, 3 Sept. 2014, doi.org/10.1186/1472-6955-13-25.
- "What Are the Four Methods of Music Therapy?" *Drury University*, 8 Aug. 2022, www.drury.edu/music/what-are-the-four-methods-of-music-therapy/.
- Yang, J, et al. "The Modified Who Analgesic Ladder: Is It Appropriate for Chronic Non-Cancer Pain?" *Journal of Pain Research*, U.S. National Library of Medicine, 2020, pubmed.ncbi.nlm.nih.gov/32110089/.

Borderline Personality Disorder: Dissecting Gendered Stigmas, Historical Context, and Media Impact By Victoria Lai

Intro

Borderline Personality Disorder (BPD) is a complex mental health condition that presents unique individual challenges and exerts significant societal impacts. Notably, its prevalence is strikingly high among women, with approximately 75% of cases affecting females (American Psychiatric Association, 2013). This gender disparity raises questions about causation and correlation, potentially tracing it back to its historical roots. Early symptoms of the disorder have been documented in medical literature, spanning thousands of years. The emergence of official research on BPD, which scholars believe to have evolved from hysteria, was diagnosed by Sigmund Freud and many other researchers. These diagnoses marked a turning point in understanding hysteria, albeit one that portrayed it negatively; despite the progress made since the Victorian era, when unsubstantiated treatments aimed to cure "spontaneous uterus movement" or hysteria, misconceptions about the modern DSM-5 criteria of BPD persist in modern society.

This paper addresses the critical issue of the lack of education about borderline personality diagnosis and the perpetuation of stereotypes in the media, which further stigmatize individuals with BPD. These misrepresentations intensify the gendered stigma surrounding BPD and exacerbate the overall stigma associated with mental illness. Recent studies reveal that individuals with BPD encounter higher levels of discrimination and prejudice than those with other mental health diagnoses (Sheppard et al., 2023). The criteria for diagnosing individuals along the BPD spectrum encompass numerous symptoms, often leading to misdiagnosis and complications. These symptoms include disturbances in self-identity, such as an unstable self-image, dissociation, harsh self-criticism, heightened interpersonal sensitivity, abrupt shifts between idealization and devaluation of others, oscillating between over-involvement and withdrawal in relationships, erratic mood fluctuations, experiences of depression and anxiety, impulsive behaviors, and episodes of hostility (DSM-5; American Psychiatric Association, 2013).

Through this paper, I hope to advocate for more accurate and informed portrayals in the media and public discourse to contribute to the destigmatization of BPD and raise awareness about this complex mental health condition. I will explore how this stigmatization can lead to self-stigma among individuals diagnosed with BPD, examining its impact on their interpersonal relationships. Addressing these issues requires a multifaceted response that includes improved education, spreading awareness, and promoting more responsible media portrayals and open conversations about mental health. By critically analyzing the multifaceted nature of BPD, uncovering the historical and societal contexts that have shaped perceptions, and advocating for more accurate and empathetic portrayals of this disorder, we can spread more information and awareness about this nuanced mental health condition in hopes of destigmatization.

The Impact of Emotional Dysregulation on Interpersonal Relationships in BPD

BPD is a complex and debatable diagnosis, with uncertain evidence regarding its cause. Nonetheless, shared traits among individuals with BPD suggest that genetic and environmental factors, including emotional vulnerability, childhood abuse, and insecure attachment, may play a role (Klein et al., 2022). The symptoms of BPD significantly hinder daily functioning and form the central point of this discussion. This section overviews BPD symptoms and diagnostic criteria, examining the disorder's repercussions on everyday life and interpersonal connections. It highlights the significance of emotional dysregulation and self-destructive behaviors within BPD's framework. BPD manifests through a spectrum of symptoms characterized by intense emotional and behavioral fluctuations.

The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) characterizes diagnostic criteria for BPD as disturbances in identity, self-image, and relationships. Key features include unstable self-perception, acute abandonment fears, impulsivity, mood volatility, and a chronic sense of emptiness (American Psychiatric Association, 2013). Complicating matters, those with BPD are at elevated risk of self-harm and suicide, with up to 10% of patients facing this terrible outcome (Paris et al., 2019). This combination of symptoms creates an inner turmoil that impedes daily management and interpersonal bonds. Emotional dysregulation within BPD enhances impulsive and self-destructive actions such as self-harm, suicidal ideation, gambling, irrational choices, and substance misuse. Notably, 73% of BPD patients meet the criteria for a lifetime substance use disorder (Grant et al., 2008), exacerbating their mental health challenges. However, it is vital to acknowledge that these actions stem from the intense agony and despair experienced at the moment, which compels them to adopt toxic coping mechanisms. Such impulsive conduct further strains interpersonal relationships, fostering perceptions of instability and prompting potential ostracization due to perceived difficulty and unpredictability, which triggers BPD patients' core wound of the fear of abandonment. The persistent feelings of emptiness and identity instability within BPD hinder the pursuit of long-term goals and cohesive self-development. The comorbidity of BPD with other major mental disorders exacerbates its complexity and susceptibility to misdiagnosis. A study scrutinizing BPD misdiagnosis through structured interviews found significantly increased odds of prior bipolar misdiagnosis among BPD patients (Ruggero et al., 2011). Almost 40% of individuals with BPD were incorrectly diagnosed with bipolar II (Healthline).

Additionally, disordered eating behaviors are commonly expected, with prevalence rates up to 53%, linked to BPD's emotional regulation difficulties, alexithymia—the struggle with identifying and describing one's emotions, and an externally oriented thinking style (Sifneos, 1973). These trends underscore the urgency of improved education and training for mental health professionals in managing this complex condition. Central to BPD lies emotional dysregulation, evident in intense responses to minor triggers and the struggle to manage emotions effectively. This fundamental characteristic is closely intertwined with how the disorder affects relationships and social interactions. People with BPD frequently develop intense emotional dependencies on a "favorite person" (FP), characterized by intense and frequently insecure attachments. This

favorite person role encompasses friends, romantic partners, or family members. Within these relationships, BPD individuals oscillate between two extremes, shifting from idealization to devaluation, thus encapsulating the dual nature of craving intimacy and fearing rejection. The emergence of interpersonal aggression, particularly in response to social rejection cues, compounds relationship challenges by disrupting effective interpersonal functioning (Jeong et al., 2022).

BPD individuals are trapped in uncontrollable emotions, propelling them to focus on their F.P. increasingly. Paradoxically, this fixation causes their F.P. to gradually lose faith in sustaining the relationship and meeting the BPD individual's needs. This recurring pattern triggers a profound emotional response within individuals with BPD, tapping into their core wounds and activating their deep-rooted fear of abandonment. Consequently, their reaction to this fear manifests as clinginess and an urgent pursuit to avoid rejection. Ironically, these actions intended to secure the relationship often yield the opposite outcome, further straining the connection. The uncertainty of emotional responses and behaviors highlights the complexity of relationships for individuals with BPD. The emotional turbulence from oscillating between idealization and devaluation confuses interactions, frequently culminating in conflicts. The heightened sensitivity to cues of rejection, combined with challenges in emotion management, fuels a cycle of interpersonal difficulties. As individuals with BPD grapple with their fear of abandonment while attempting to preserve the relationship, their actions inadvertently contribute to the distancing they fear. The dynamics surrounding favorite person attachments within BPD show the contradictory aspects of the disorder, from the individual's yearning for intimacy to their subsequent tendency to push their favorite person away through shifting emotions. This impacts their relationships and social interactions, which perpetuate instability and isolation. A greater understanding of these interconnected facets raises awareness and humanizes the challenges posed by this disorder.

The Gendered Historical Progression and Stigmatization of BPD.

The striking similarities in symptoms between BPD and hysteria have prompted speculation regarding a potential evolutionary or close connection between these disorders. Historically, hysteria has been associated primarily with individuals possessing a uterus, and ancient civilizations, such as the Egyptians and Greeks, believed that the womb could influence the body's overall health (McGill, 2017). This historical perspective attributing various health issues to the uterus has complicated diagnosing and treating BPD and hysteria. The historical link between uterine factors and health complications has added complexity to the challenges individuals with these disorders face. The shared symptoms, including emotional instability, impulsivity, and relationship difficulties, have frequently led to diagnostic and treatment confusion. Researchers and clinicians have grappled with distinguishing between these conditions, as evidenced by statements like, "Borderline personality disorder sometimes exhibits certain hysterical symptoms. In our clinical practice, we encounter patients for whom differentiating between BPD and a hysterical disorder in terms of psychopathological aspects is

challenging" (Tatsuo Oshima, MD, Ph.D., 2000). However, some researchers propose that "borderline personality disorder simply replaced hysteria, reflecting contemporary values regarding women's behavior." This perspective characterizes BPD as a psychiatric diagnosis often perceived as "feminized" due to its higher prevalence among women, with a ratio ranging from 3:1 to 7:1 (Becker, 2000). The criteria for diagnosing BPD frequently encompass symptoms associated with traditionally considered "feminine qualities" (Jimenez, 1997). The historical context surrounding understanding and treating disorders like hysteria and BPD has significantly shaped the challenges individuals face today.

In the past, when ethical interventions and solid scientific evidence were lacking, especially women with these disorders endured unfounded and often cruel treatments. The false belief that these conditions were exclusively linked to femininity led to stigmatization, witchcraft accusations, and misguided therapies, such as ritualistic burnings (R. Porter, 1988). Even Sigmund Freud's proposed solution, suggesting that women should "get married and have sex," centered around women's sexuality and reflected the biased perspectives of the time, perpetuating stigma associated with conditions stereotypically associated with femininity (McGill, 2017). This gendered narrative persisted over time, with hysteria evolving to reflect shifts in societal perceptions. Initially attributed solely to the "frustrated uterus" affecting widows and virgins, hysteria was a disorder exclusively ascribed to women or even linked to the absence of male genitalia. Over time, hysteria evolved into a medically recognized condition affecting a person's brain (Bogousslavsky, 2011).

In the 19th century, it remained common yet misunderstood in Europe, posing significant challenges to the medical field. French neuroscientist Jean-Martin Charcot played a pivotal role in unraveling hysteria through his innovative approach, "the great neurosis," involving comprehensive patient observations. Charcot identified critical features like "convulsions, contortions, fainting, and impairment of consciousness," which he termed "hystero-epilepsy," linking the condition to disruptions in neurons and challenging prevailing notions (Waraich & Shah, 2017). Charcot's perspective shifted the understanding of hysteria from being solely a female affliction to a neurological condition that could affect individuals, regardless of gender or traditionally masculine roles, such as railway engineers or soldiers. This historical transformation of Hysteria from a gender-bound concept into a recognized medical diagnosis highlights a recurring pattern in which women's mental health has been misconstrued and mischaracterized. The clinical descriptions of individuals with BPD, which often switch between extreme dysfunction and manipulative charm, reflect this enduring pattern, deeply influenced by ingrained misogynistic beliefs (Masland et al., 2022; Robert et al. Center, 2022). Such portrayals serve as derogatory labels and contribute to concrete stigmas that disproportionately affect women.

The Impact of Labeling on Mental Health and the Stigma Surrounding BPD

Within the broader context of discussing the impact of labeling on mental health and the stigma surrounding BPD, it is essential to recognize a compelling link between trauma,

especially abuse, and the diagnosis of BPD in women. Notably, 81% of individuals diagnosed with BPD have a history of past abuse, and many women diagnosed have been sexually abused in childhood (Ussher, 2011). Paradoxically, the BPD diagnosis can unintentionally divert attention from the abuse, instead emphasizing the victim's perceived "disordered personality." Many diagnosed with BPD often feel their traumatic experiences are downplayed despite substantial evidence linking such incidents to the disorder. This connection highlights the need to consider how labeling and stigmatization can have far-reaching consequences on mental health. Sly Sarkisova, a psychotherapist specializing in trauma, characterizes BPD as "a label that is often misused and applied, especially to women, to pathologize them for emotional expressions of suffering." noting that BPD is sometimes misused as a label to pathologize emotional responses to suffering (Shimo, Alexandra 2019). Many psychologists share concerns that BPD diminishes women's suffering by affixing pejorative psychiatric labels to them, diverting attention from a society riddled with traumatic experiences for women. Clare Shaw asserts that "the real issue is the pervasive abuse of women and girls in this society coupled with the continuing silencing and invalidation of women's experiences." (C. Shaw, 2018). This disproportionate gender bias also manifests in the process of diagnosis. Carol S. North's work in 2018 demonstrates that women are diagnosed with BPD between three and seven times more frequently than men. This can be attributed, at least partly, to the modern criteria for BPD, which encompass symptoms that align with stereotypical "feminine qualities," including internalized negative emotions like depression and emotional volatility. Clinicians describe some women with BPD as pathologically dysfunctional, often labeling them as "difficult" or "problematic" (Masland et al., 2022), while others depict them as attractive, successful, and charming manipulators who seduce others, including therapists, into destructive relationships. These depictions serve as pejorative markers and literal stigmas, predominantly affecting women. Tragically, these traits that society associates with BPD are often perceived as making women "both damaged and dangerous." The historical archetype of the "demanding, angry, aggressive woman" labeled as "mentally disordered" perpetuates the gendered nature of this condition (Jimenez et al., 1987).

Many researchers and psychologists believe diagnosing BPD can inadvertently downplay the gravity of women's suffering with the BPD label, which is heavily associated with stigma. Dr. Joel Dvoskin, a forensic psychologist affiliated with Georgetown Law, believes that action must be taken to remove the stigma associated with the term "BPD" in diagnosis. He emphasizes the real impact of the "BPD" label when applied to an individual, highlighting that "not all mental health diagnoses promote treatment" and singles out BPD as a diagnosis that "significantly harms people." He critiques the term because it often results in sub-standard treatment for those diagnosed with the disorder. For instance, mental health professionals frequently label the unwanted behaviors of BPD clients as "manipulative" and in need of punishment. He candidly recalls his early career experiences when he accepted the BPD label without critical examination, using it to explain a range of disruptive behaviors observed within prison settings. He encountered male and female inmates who exhibited patterns of seeking and rejecting intimacy and dependency, overreacting to seemingly minor emotional triggers, and occasionally engaging in self-injurious behaviors. "These people, I was told, engaged in these behaviors because they were 'Borderlines." And we knew that they were 'Borderlines' because they performed these behaviors. This tight circle of logic had the advantage of letting me, as a prison psychologist, completely off the hook when I failed to help them because 'Borderlines," I was told, were difficult or impossible to treat." (Joel A. Dvoskin, Ph.D., A.B.P.P.1996) Through this perspective, Dr. Dvoskin sheds light on the broader issue of labeling, demonstrating how the diagnosis of BPD can become a catch-all explanation for complex behaviors, resulting in lowered expectations for successful interventions and potentially perpetuating a cycle of stigmatization and inadequate care.

Within mental health, language holds profound significance beyond mere semantics. Words like 'disorder' can hinder a deeper understanding and shape thought and practice, discouraging individuals from seeking help and fostering self-stigmatization, where people internalize negative beliefs about themselves. Researchers have found that individuals with personality disorders, especially those with BPD, tend to stigmatize themselves more than individuals without such disorders. The heightened self-stigmatization experienced by individuals with BPD is believed to be rooted in the fact that they "expect and perceive social rejection more intensely than the general population" (Grambal et al., 2016). Their heightened sensitivity to social rejection can lead to increased self-stigmatization. Individuals with BPD may internalize negative societal perceptions and judgments, further impacting their self-esteem and self-worth. Moreover, researchers believe that "individuals with BPD also exhibit negative and unstable self- and other evaluations compared to healthy individuals." These factors could be associated with a higher level of self-stigma and shame due to the nature of BPD, given that "persistent challenges in social interactions, intense and unstable interpersonal relationships, and exaggerated efforts to avoid abandonment constitute core features of BPD" (Grambal et al., 2016).

Furthermore, these components of stigma, including labeling, stereotyping, separation, status loss, self-shame, and discrimination, have significant implications in the context of mental health disorders like BPD. In the case of BPD, individuals can find themselves labeled and stereotyped due to their condition, which can lead to feelings of self-shame (Link & Phelan, 2001). Society's tendency to separate and stigmatize those with mental health disorders, including BPD, perpetuates this self-shame and contributes to the broader stigma surrounding mental health. This is why spreading awareness and educating the masses about BPD and mental health is vital to challenging societal norms and attitudes contributing to stigma. Understanding the multifaceted nature of stigma, as outlined by Link and Phelan (2001), underscores the importance of addressing these issues on both an individual and societal level to create a more compassionate and inclusive society.

The gendered aspects of BPD extend beyond their impact on women's perspectives on mental health and have profound implications for our society. Despite the progress in moving away from the constraints of a patriarchal society that once limited women to domestic roles, specific gender disparities persist, particularly in mental health. It is crucial to recognize that the gendered stigma surrounding BPD affects not only women but also men, albeit in different ways. For women, the stigma surrounding BPD often revolves around characterizations of being overly emotional, complicated, or manipulative. These labels hinder their willingness to seek help and perpetuate harmful stereotypes about women's mental health.

Conversely, the gendered stigma associated with BPD may manifest differently for men, potentially leading to underdiagnosis or misdiagnosis. Men with BPD may encounter challenges seeking support due to societal expectations of traditional masculinity, discouraging vulnerability and emotional expression.BPD is an exemplar, illustrating how inequalities persist in our society despite societal advancements. The stereotype associating BPD with femininity reinforces societal norms that hinder progress, possibly contributing to the fact that the DSM-5 reports 75% of diagnoses as women. The perception that BPD predominantly afflicts women creates a significant predicament for men grappling with this disorder. The notion that BPD and mental health support are associated with femininity or weakness may deter men from seeking help, as they fear being labeled as "feminine" or "weak" (Karim et al., 2019). This reluctance to seek assistance exacerbates their condition and perpetuates the stigma surrounding BPD, ultimately undermining their mental well-being.

The complex dynamics we observe in today's society can be traced back to historical accounts that shed light on the challenges men face. For instance, the long-held belief that Hysteria was exclusively a "woman's disease" and intricately tied to the essence of femininity, as articulated by Laycock (1840) and Otto Weininger's assertion in 1903 that "hysteria is the organic crisis of the organic mendacity of woman" (Bronfen, 1998), evolved to include the nervous system but still contributed to the enduring stigma around men accessing mental health support. This historical context plays a crucial role in shaping contemporary dynamics deeply entrenched in stigmatizing men who seek help for their mental health concerns (Sagar-Ouriaghli et al., 2019). Another historical example involves British neurologist Sir John Russell Reynolds in the 18th century, who perpetuated gendered perceptions by attributing men and boys with Hysteria as having a "feminine constitution." Similarly, Emile Batault's analysis of male Hysteria in the late 1800s revealed prevailing perceptions of these men as "coquettish and fearful... preferring ribbons and scarves to labor" (Gilman et al., 1993). These stereotypes hindered the accurate diagnosis of Hysteria in men and aligned with the conventional masculinity of the time. These historical examples vividly illustrate how societal attitudes and gender norms have long stigmatized men seeking assistance for mental health concerns. This profoundly ingrained stigma, rooted in the association of emotional vulnerability with femininity, has far-reaching implications for men's mental well-being.

Today, men are often conditioned to suppress emotions and maintain an image of strength and resilience. Consequently, seeking help for mental health issues is perceived as taboo and incongruent with traditional masculinity (McKenzie et al., 2018). This dynamic, compounded by the misconception that BPD is a predominantly feminine disorder, creates an environment that prevents men from reaching out for support. These societal stigmas continue to exert influence,
and the historical negative perception surrounding Hysteria also resonates with the present reputation of BPD.

It is important to emphasize that although there are negative consequences for men stemming from the gendered perceptions of BPD, women remain the prime targets of these stereotypes and are the ones mainly affected. Women continue to live with the stigma associated with BPD, facing the double challenge of dealing with the disorder and its societal bias. While men may encounter barriers in seeking help, women often endure the weight of being labeled as unhinged, manipulative, or esoteric due to their BPD diagnosis. To address these issues, our society needs to break down these gendered perceptions along with more unbiased evaluation tools and enhanced education to promote an environment that encourages both men and women to prioritize their mental health without fear of judgment. While acknowledging the challenges faced by men in seeking mental health support, it is crucial to remember that the overarching impact of BPD's gendered stigma primarily falls upon women, and addressing this gender bias should remain a central focus in our efforts to improve mental health awareness and support for all individuals.

The Media's Perpetuation of Mental Health Stigmatization and the Role of Accurate Portrayals

In contemporary society, the 'Hot Crazy Matrix' has garnered scholarly attention due to its widespread presence in the media and its substantial impact on societal perceptions of attractiveness. Originally introduced as an internet-derived theory, this matrix has shaped popular culture and public awareness through gendered stereotypes. This theoretical framework posits a correlation between a woman's perceived attractiveness level and her emotional stability, or " craziness." According to the matrix, as a woman's perceived attractiveness increases on a 10-point scale, there is an associated rise in her perceived emotional volatility. Researchers such as Blanchard and their colleagues assert that specific traits are commonly associated with borderline personalities positioned on the 'crazy' end of this spectrum.

Consequently, the theory suggests that women must navigate a delicate equilibrium between being deemed attractive and not excessively so, as an overabundance of attractiveness may render apparent emotional instability less acceptable to men. This unique perspective raises intriguing questions regarding the threshold at which 'craziness' becomes acceptable or even appealing, particularly in women characterized by certain perceived attractiveness levels, including those with BPD (Blanchard et al., 2021). These considerations extend to the fetishization and romanticization of women with BPD,

reinforcing a gendered archetype and emphasizing the imperative of educational initiatives aimed at dispelling the misconceptions perpetuated by theories like the "Hot-Crazy Matrix."



Figure 1: Example image illustrating the "hot crazy matrix" theory, derived from <u>https://scienceintegritydigest.com/2021/02/12/the-hot-crazy-matrix-paper/</u>

In the 21st century, the media's pervasive presence and substantial influence have significantly shaped public perceptions of mental health disorders, often perpetuating stereotypes and misconceptions. This influence extends beyond news media, encompassing the entire entertainment industry. Researcher Kubrak's (2020) meta-analysis, which examined the impact of films on young people's attitudes, highlights the profound reach of the entertainment industry in molding beliefs and opinions, particularly on topical social issues. Kubrak's work emphasizes the capacity of movies to significantly impact specific areas, such as gender and ethnic stereotypes, thereby effectively transforming societal perceptions and generating new opinions on various subjects. She suggests that movies, as an immersive experience driven by narrative transportation, are responsible for their significant impact on viewers' beliefs and attitudes, including those related to mental health (Kubrak, 2020). When movies portray mental health positively, they foster empathy and understanding among viewers. Conversely, negative portrayals can reinforce stereotypes and biases, perpetuating harmful attitudes and stigma. This insight underscores the responsibility of the entertainment industry to depict mental health issues accurately and sensitively, given its potential to influence societal perceptions and attitudes.

Expanding upon Kubrak's insights, Green and Sestir (2017) introduce the concept of transportation theory to explain the immersive power of film narratives. Transportation theory describes how individuals mentally immerse themselves in the world of a narrative, shifting their focus from the real world to the fictional one. This immersion results in a strong sense of absorption, encompassing emotional and cognitive responses to the narrative content that closely mirrors reactions to real-world events. Those transported into a narrative may also experience vivid mental imagery, further blurring the line between fiction and reality (Green & Sestir, 2017). This state of narrative transportation underscores the persuasive impact of storytelling in films, as influenced individuals often exhibit increased beliefs, attitudes, and behaviors consistent with the story's content. This concept underscores the potency of storytelling through film, as it can effectively shape public perceptions and contribute to both positive and negative societal attitudes, depending on how mental health issues are portrayed on screen.

The media's influence on shaping perceptions becomes especially evident when examining the portrayal of BPD and other cluster B personality disorders. Dr. Michael E. Thase, a distinguished professor of Psychiatry and director of the Penn Medicine Mood and Anxiety Program, highlights the enduring misunderstandings surrounding BPD, partially attributing this to its complex diagnostic history and its often unfavorable depiction in media (Wust, 2018). Dr. Thase notes that movies and T.V. shows tend to represent individuals with BPD as overly colorful, theatrical figures with unpredictable mood swings and potentially dangerous behavior, particularly when angered. One notable example is the portrayal of the 'bunny boiler' character by Glenn Close in "Fatal Attraction," which epitomizes this broad and exaggerated representation. He emphasizes that such portrayals should not be viewed as accurate reflections of BPD but rather sensationalized depictions that "fail to capture the complexity of this genuine mental health condition" (Wust, 2018). These examples show that the perpetuation of misconceptions through media misrepresentations contributes to the stigmatization of BPD, highlighting the necessity for more precise and nuanced portrayals in media outlets.

In filmmaking, directors and screenwriters grapple with challenges when attempting to convey the complex nature of BPD within the confines of a two-hour movie. The demand for dramatic portrayals and entertainment value often precedes the need for accuracy. The film analysis conducted by Alexis Ian Rainey on 'A Textual Analysis of Mental Illness in Film' offers valuable insights into the portrayal of mental illness in cinema, and she critiques various films depicting mental illness and analyzes them, specifically in the film "Girl Interrupted." Girl Interrupted presents an illustrative example of BPD on screen, portrayed theatrically. While the film is based on author Susanna Kaysen's real-life experiences during her 18-month stay at a mental hospital in the late 1960s, the director James Mangold, known for his dramatic works, adapted this movie, which resulted in creative discrepancies between the book and the film (IMDb). While the film draws inspiration from author Susanna Kaysen's real-life experiences with BPD, it is essential to note that Susanna's symptoms, as portrayed in the film, deviate from an official diagnosis of BPD at the time. This discrepancy underscores how the film misrepresents BPD by depicting actions that do not align with the diagnosis.

Furthermore, in Rainey's (2015) analysis, she notes her observations on the character of Susanna, which is quite noteworthy. Susanna, the protagonist at one point in the movie, arrives at the hospital with diagnostic paperwork labeling her as 'depressed' and 'promiscuous,' along with a note of a suicide attempt. What is particularly interesting is that Susanna is the only character who eventually leaves the hospital in a seemingly mentally stable state, capable of resuming life outside the hospital walls. This state exceeds the mental well-being of other patients. While not diagnostically accurate, this portrayal of Susanna significantly normalizes her character, making her more relatable and accessible to the audience. This observation underscores the film's potential to destigmatize BPD and mental illness by presenting characters who challenge stereotypes and evoke empathy from the viewers. (Rainey 2015). The movie "Girl Interrupted" exemplifies how filmmakers may resort to dramatic portrayals to capture the essence of a mental health disorder, even at the cost of sacrificing accuracy for entertainment purposes.

Consequently, these inaccurate portrayals in movies contribute to misconceptions about mental health, as the exaggerated nature of films primarily designed for entertainment perpetuates stereotypes and hinders public understanding (IMDb). By highlighting Dr. Thase's insights and the challenges filmmakers face, it becomes apparent how media depictions of BPD can diverge significantly from the reality of the condition, ultimately impacting societal perceptions and attitudes. These portrayals influence how the general public understands BPD and underscore the importance of responsible and accurate depictions to combat stigmatization and promote empathy and understanding.

Filmmakers resort to dramatization for various reasons. Firstly, drama and exaggeration are fundamental elements of storytelling and entertainment, designed to captivate audiences and maintain engagement. Given the intricacies of mental health disorders like BPD, which are characterized by subtle nuances, filmmakers may feel compelled to accentuate specific traits or behaviors to make the narrative more compelling. Henry J. Steadman, Ph., an expert in criminal justice and behavioral health, corroborates this notion by noting that mental illnesses are often portrayed in films and media with "exaggerated, inaccurate, and comical images used to depict individuals with psychiatric disorders, along with providing incorrect information about mental illness" (Steadman et al., 1981). Television, including films, plays a significant role in teaching people about behaviors, social conventions, and rules of conduct. It frequently reinforces social norms regarding how individuals with psychiatric disorders should be treated. This phenomenon aligns with Albert Bandura's (1977) social learning theory, which suggests that people learn through direct experience and observation (Saul Mcleod,2023). Without personal experiences with individuals with mental illnesses, many people rely on media portrayals to form their perceptions of those with mental health conditions.

Addressing these issues necessitates a concerted effort by the entertainment industry to responsibly and accurately depict mental health issues. Furthermore, it calls for greater public awareness and media literacy to help viewers distinguish between cinematic and theoretical stereotyped portrayals and the real-life experiences of individuals with mental health conditions. Ultimately, the paramount goal should be the promotion of empathy and understanding through accurate portrayals to reduce the stigma surrounding mental illness.

Conclusion

In conclusion, Borderline Personality Disorder is inextricably linked with pervasive societal stigma, giving rise to a web of complex challenges that individuals living with this disorder navigate. The complex interaction of historical factors, societal misconceptions, and internalized self-stigma significantly shapes the experiences of individuals affected by BPD. This dynamic is rooted in the historical perception of BPD as primarily affecting women, thus contributing to gendered stigmatization that continues to influence our collective consciousness. Although more pronounced for women, these gendered stereotypes involve negative perceptions such as being overly emotional, manipulative, or unstable, which can negatively impact men's willingness to access mental health resources. When individuals receive a BPD diagnosis, these

stereotypes can trigger self-stigma, shifting the focus from potential underlying trauma and adversity to perceived inherent personality flaws. This shift exacerbates self-stigmatization as those affected may feel that their suffering is dismissed or misattributed.

Moreover, society significantly perpetuates BPD stigma through a lack of education and awareness regarding this complex mental health condition. Frequently sensationalized and inaccurate media portrayals have further entrenched these stereotypes, making it exceedingly challenging for individuals with BPD to find understanding and support within their communities. Despite the presence of legitimate diagnostic criteria for BPD in the DSM-5, it remains misunderstood, misdiagnosed, and heavily stigmatized. This stigmatization also extends to men, raising questions about whether societal values and expectations of individuals contribute to the observed gender disparity in BPD diagnoses. This gendered nature of diagnosis criteria, exemplified by instruments like the Beck Depression Inventory (BDI) for depression, introduces an additional layer of complexity to mental health disparities. The BDI's potential to inadvertently inflate the presence of depressive symptoms in women due to its alignment with traditional expressions of depression symptoms can distort conclusions about gender disparities in mental health. Confronting the historical and societal biases that have contributed to the stigmatization of BPD is crucial for cultivating a more inclusive and empathetic society. As a society, we must address the gender disparities in mental health diagnoses to advocate for the well-being of individuals affected by BPD and mental illness and bring us a step closer to destignatizing mental illness. Achieving this goal necessitates a concerted effort to educate the public and media about the realities of this condition, promote accurate portrayals in the media, and implement comprehensive educational initiatives to dispel misconceptions and cultivate empathy. By engaging in these efforts, we can contribute to breaking the cycle of stigmatization and establishing an environment where individuals with BPD receive acceptance and active support on their path to recovery and well-being.

Works Cited

- Ahmedani, B. K. (2011). Mental Health Stigma: Society, Individuals, and the Profession. Journal of Social Work Values and Ethics, 8(2), 41–416.
- Ali, A., & Adshead, G. (2022). Gender bias in the diagnosis of depression: A systematic review. *International Review of Psychiatry*, 34(2), 97–107. doi:10.1080/09540261.2021.1903147
- American Psychiatric Association. (2013). Borderline Personality Disorder Diagnostic Criteria 301.83 (F60.3) In Diagnostic and Statistical Manual of Mental Disorders (5th ed.). https://doi.org/10.1176/appi.books.9780890425596.CautionaryStatement
- P. Antolin, "Challenging Borders: Susanna Kaysen's Girl, Interrupted as a Subversive Disability Memoir." *European Journal of American Studies*, vol. 15, no. 2, June 23 2020, <u>https://doi.org/10.4000/ejas.16051</u>.
- Armstrong, J., & Nacu, S. (2023, February 10). Opinion: What is wrong with "Girl Interrupted." The Cougar Press. URL Feb.10
- Boone, T., Reilly, A. J., & Sashkin, M. (1977). SOCIAL LEARNING THEORY Albert Bandura Englewood Cliffs, N.J.: Prentice-Hall, 1977. 247 pp., paperbound. *Group & Organization Studies*, 2(3), 384–385. <u>https://doi.org/10.1177/105960117700200317</u>
- Berenson, K. R., Downey, G., Rafaeli, E., Coifman, K. G., & Paquin, N. L. (2011). The rejection-rage contingency in borderline personality disorder. *Journal of Abnormal Psychology*, 120(3), 681–690. <u>https://doi.org/10.1037/a0023335</u>
- Bik, Elies. "The Hot-Crazy Matrix Paper." *Science Integrity Digest*, February 12. , scienceintegritydigest.com/2021/02/12/the-hot-crazy-matrix-paper/.
- Blanchard, A. E., Dunn, T. J., & Sumich, A. (2021). Borderline personality traits in attractive women and wealthy, attractive men are relatively favored by the opposite sex. Personality and Individual Differences, 169. doi:10.1016/j.paid.2020.109964
- Bogod, E. (2010). What is in a Name? Borderline Personality Disorder Label Creates Stigma. Community Mental Health Worker, In Recovery from BPD. Retrieved from <u>https://icmha.ca/wp-content/uploads/2015/01/Bogod2010BPD.pdf</u>
- Bronfen, E. (1998). The knotted subject: Hysteria and its discontents. Princeton University Press.
- Dorfman, N., & Reynolds, Joel Michael (forthcoming). The New Hysteria: Borderline Personality Disorder and Epistemic Injustice. *International Journal of Feminist Approaches to Bioethics*.
- Dvoskin, Joel A, (1996). "The Abuse of Psychiatric Diagnosis in Prisons." www.vachss.com/guest dispatches/ dvoskin.html.
- Eaton, N. R., Krueger, R. F., Keyes, K. M., Skodol, A. E., Markon, K. E., Grant, B. F., & Hasin, D. S. (2011). Borderline personality disorder comorbidity: Relationship to the internalizing-externalizing structure of common mental disorders. Psychological Medicine, 41(5), 1041-1050. doi:10.1017/S0033291710001662
- Farrell, M. D. (2012). The portrayal of schizophrenia in contemporary mass media. Psychiatric News, 47(5), 27-29.

- Feingold A. (1992). Gender differences in mate selection preferences: a test of the parental investment model. *Psychological Bulletin*, 112(1), 125–139. <u>https://doi.org/10.1037/0033-2909.112.1.125</u>
- Ferguson, Sian. "Signs of Bipolar Misdiagnosis." *Healthline*,1 Feb. 2023, www.healthline.com/health/bipolar-disorder/Bipolar-misdiagnosis.
- Gadassi, R., Snir, A., Berenson, K., Downey, G., & Rafaeli, E. (2014). Out of the frying pan, into the fire: mixed affective reactions to social proximity in borderline and avoidant personality disorders in daily life.
- Journal of Abnormal Psychology, 123(3), 613-622. https://doi.org/10.1037/a0036929

Gilman (1994) L. The Case of Sigmund Freud: Medicine and Identity at the Fin De Siècle. Baltimore, Johns Hopkins Univ. Press, 1994. press.jhu.edu/books/title/2522/case-sigmund-freud.

- Green, Melanie & Sestir, M. (2017). Transportation Theory. 10.1002/9781118783764.wbieme0083.
- Grambal, A., Prasko, J., Kamaradova, D., Latalova, K., Holubova, M., Marackova, M., Ociskova, M., & Slepecky, M. (2016). Self-stigma in borderline personality disorder cross-sectional comparison with schizophrenia spectrum disorder, major depressive disorder, and anxiety disorders. Neuropsychiatric Disease and Treatment, 12, 2439–2448. doi:10.2147/NDT.S114671
- Henry J. Steadman, A situational approach to violence, International Journal of Law and Psychiatry,
- 5(2)(1982),https://doi.org/10.1016/0160-2527(82)90004-8.
- Karim, Hiba & Shirazi, Elham & Nohesara, Shabnam & Sadeghi, H.M. & Saeb, A. & Alavi, Kaveh. (2019). Comparison of gender roles in male and female patients with borderline personality disorder (BPD) with control group and its correlation with severity of clinical symptoms. Revista Latinoamericana de Hipertension. 14. 1-7.
- Kubrak T. (2020). Impact of Films: Changes in Young People's Attitudes after Watching a Movie. *Behavioral sciences (Basel, Switzerland)*, 10(5), 86. https://doi.org/10.3390/bs10050086
- Grambal, A., Prasko, J., Kamaradova, D., Latalova, K., Holubova, M., Marackova, M., Ociskova, M., & Slepecky, M. (2016). Self-stigma in borderline personality disorder cross-sectional comparison with schizophrenia spectrum disorder, major depressive disorder, and anxiety disorders. *Neuropsychiatric disease and treatment*, *12*, 2439–2448. https://doi.org/10.2147/NDT.S114671
- Jeong, H., Jin, M. J., & Hyun, M. H. (2022). Understanding a Mutually Destructive Relationship Between Individuals With Borderline Personality Disorder and Their Favorite Person. Psychiatry Investigation, 19(12), 1069–1077. doi:10.30773/pi.2022.0079

- Jimenez, M. A. (1997). Gender and Psychiatry: Psychiatric Conceptions of Mental Disorders in Women, 1960-1994. Affilia, 12(2), 154–175. https://doi.org/10.1177/088610999701200202
- Karim, S., Arshad, M., & Matin, A. (2019). The gendered nature of borderline personality disorder and mental health: A comprehensive analysis. *Journal of Gender Studies*, 28(6), 698–712. doi:10.1080/09589236.2018.1562422
- Klein, P., Fairweather, A. K., & Lawn, S. (2022). Structural stigma and its impact on healthcare for borderline personality disorder: A scoping review. *International Journal of Mental Health Systems*, 16(1), 48. doi:10.1186/s13033-022-00558-3
- Lambert, V. (2020). Pathological Femininity and the Western Construction of Selfhood: A Genealogy of the Borderline Subject. Retrieved from <u>https://researchspace.auckland.ac.nz/bitstream/handle/2292/53466/Lambert-2020-thesis.p</u> <u>df?sequence=5</u>
- Lampropoulos, G., Anastasiadis, T., Siakas, K., & Siakas, E. (2022). The impact of personality traits on social media use and engagement: An overview. International Journal on Social and Education Sciences (IJonSES), 4(1), 34-51. <u>https://doi.org/10.46328/ijonses.264</u>
- Link, B. G., & Phelan, J. C. (2001). Conceptualizing stigma. *Annual Review of Sociology, pp. 27,* 363–385. <u>https://doi.org/10.1146/annurev.soc.27.1.363</u>
- Mcleod, S. Albert Bandura's Social Learning Theory. *Simply Psychology* (2023), <u>www.simplypsychology.org/bandura.html</u>.
- Munson, K. A., Janney, C. A., Goodwin, K., & Nagalla, M. (2022). Cultural Representations of Borderline Personality Disorder. *Frontiers in Sociology*, p. 7, 832497. https://doi.org/10.3389/fsoc.2022.832497
- New, A., Rot, M., Ripoll, L., Perez-Rodriguez, M. M., Lazarus, S., Zipursky, E., ... Siever, L. (2012).
- Empathy and Alexithymia in Borderline Personality Disorder: Clinical and Laboratory Measures. Journal of Personality Disorders, 1-16. <u>https://doi.org/10.1521/pedi_2012_26_037</u>
- North, C. S. (2015). The Classification of Hysteria and Related Disorders: Historical and Phenomenological Considerations. *Behavioral Sciences*, pp. 5, 496–517. doi:10.3390/bs5040496
- Ohshima, T. (2001). Borderline personality traits in hysterical neurosis. *Psychiatry and Clinical Neurosciences*, 55(2), 131–136. <u>https://doi.org</u>
- Sansone, R. A., & Sansone, L. A. (2010). Fatal attraction syndrome: stalking behavior and borderline personality. *Psychiatry (Edgmont (Pa.: Township))*, 7(5), 42–46.
- Alaska, Candice. (2020). "Why We Need Responsible Representation in the Film Industry." *National Alliance for Mental Health*, December 16, 2020, www.nami.org/Blogs/ NAMI-Blog/December-2020/
 - "Why-We-Need-Responsible-Representation-in-the-Film-Industry.
- A.I. 2015 Stigma on the Screen: A Textual Analysis of Mental Illness

in Film. U of Georgia, MA thesis. getd.libs.uga.edu/pdfs/ Rainey alexis i 201505 ma.pdf.

Freeman, Ronald Roesch, Richard J., (1989). Mental disorder and the criminal justice system: A review, International Journal of Law and Psychiatry, 12(2-3),105-115

0160-2527, https://doi.org/10.1016/0160-2527(89)90002-2.

- Sagar-Ouriaghli, I., Godfrey, E., Bridge, L., Meade, L., & Brown, J. S. L. (2019). Improving Mental Health Service Utilization Among Men: A Systematic Review and Synthesis of Behavior Change Techniques Within Interventions Targeting Help-Seeking. *American journal of men's health*, *13*(3), 1557988319857009. https://doi.org/10.1177/1557988319857009
- Shaw, C. & Proctor, G. (2005). I. Women at the Margins: A Critique of the Diagnosis of Borderline Personality Disorder. Feminism & Psychology 15. 483–490. 10.1177/0959-353505057620.
- McKenzie, S. K., Collings, S., Jenkin, G., & River, J. (2018). Masculinity, Social Connectedness, and Mental Health: Men's Diverse Patterns of Practice. *American journal of men's health*, *12*(5), 1247–1261. <u>https://doi.org/10.1177/1557988318772732</u>
- Sheppard, H., Bizumic, B., & Calear, A. (2023). Prejudice toward people with borderline personality disorder: Application of the prejudice toward people with mental illness framework. *International Journal of Social Psychiatry*. <u>https://doi.org/10.1177/00207640231155056</u>
- Boozer, Jack, editor. *Authorship in Film Adaptation*. University of Texas Press, 2008. *JSTOR*, https://doi.org/10.7560/702851. Accessed September 14, 2023.
- A.(2019) "Are Sexual Abuse Victims Being Diagnosed with a Mental Disorder They Do not Have?" *The Guardian*, March 27, 2019, www.theguardian.com/ lifeandstyle/2019/mar/27/

Are-sexual-abuse-victims-being-diagnosed-with-a-mental-disorder-they-dont-have.

"The Gender Gap in Mental Health."(2022) *News Medical Life Sciences*, 21 Jan, www.news-medical.net/health/

The-Gender-Gap-in-Mental-Health.aspx#:~:text=Women%20have%20a%20significantly%20 higher,to%20genetic%20and%20biological%20factors.

- Ussher, J. M. (2011). *The madness of women: Myth and experience*. Routledge/Taylor & Francis Group. <u>https://doi.org/10.4324/9780203806579</u>
- Waraich, M., & Shah, S. (2018). The life and work of Jean-Martin Charcot (1825-1893): 'The Napoleon of Neuroses.' *Journal of the Intensive Care Society*, *19*(1), 48–49.

Wust, M. "Zero Shades of Grey: Living with BPD." U Penn Medicine, May 2018, www.pennmedicine.org/news/news-blog/2018/may/ Zero-shades-of-grey-living-with-bpd.

At the Juncture of the Body and the Brain: Using Neuroscience to Excel at Sports by Steffi Kim

Sports are a cornerstone of modern society, with athletic ability being heralded at the professional and recreational levels alike. Although sports are often associated with brute muscle rather than intelligent thought, this notion that bodily finesse is unrelated to brainpower is a fundamental misconception. In reality, the brain controls every muscle and is inseparable from the body. Elite athletes don't just possess astounding control over their muscles—whether arms, feet, legs, or so forth—but also display remarkable neural control that allows them to perform such agile motions in the first place. Sports are more than just entertaining games; they are a pursuit to stretch the confines of the human body, striving towards maximum endurance, speed, prowess, and grit. At the surface level, it is tempting to attribute the successes of great athletes to a superior, preternatural physique. Yet this idea that athletes are built from a fundamentally different mold than everyone else fractures under scrutiny. For instance, the top two contenders for the 2017 American League MVP were physically disparate—José Altuve (at 5'6", 165 pounds) and Aaron Judge (at 6'7", 282 pounds; Schonbrun). Elite athletes are great due to a baseline of physical talent being augmented through neural acuity, enabling them to reach new heights and become masters of their craft. These athletes possess a wealth of underlying neural skills such as extraordinary proprioception, spatial awareness, and efficient neural circuitry that allow them to see and react to the competition on a whole different level. If success in sports solely depended on physical superiority, NBA star Steph Curry, who stands at an unremarkable 6'2" and 185 pounds, would never have stood a chance against his freakishly tall and brawny counterparts. When distinguishing the traits that separate top-tier athletes from everyday people, the mental edge plays a vital role. So, how can neuroscience be used to maximize athletic potential?

The foundation of any pursuit of excellence must stem from proper motivation, and improvement in sports is no exception. Determination derived from intrinsic sources surpasses extrinsic motivation like money and fame, provided that one's basic needs have been fulfilled. The five predominant intrinsic motivators are curiosity, passion, purpose, mastery, and autonomy (Kotler). Tapping into these sources of motivation has positive implications for one's attitude and alters the body's underlying neurochemistry. When correctly activated, these intrinsic drivers work to flood the body with rewarding neurochemicals like dopamine, norepinephrine, and oxytocin, which accelerate one's skill development, and, as a bonus, make the ceaseless hours of practice no longer feel burdensome. The brain is more likely to recall emotionally salient events; as such, increasing the neurochemicals present during an experience increases the chances of it being solidified within long-term memory (Kotler). The presence of dopamine and other rewarding neurochemicals while one practices translates to heightened focus and improved memory, two critical aspects of skill development. In addition to optimizing the effects of the nervous system, these intrinsic motivators can also alter the functioning of the brain. Having a purpose reduces the sensitivity of the amygdala (responsible for emotional control) thereby

mitigating anxiety, and also reduces the size of the medial temporal cortex, indicating that having a purpose changes the brain's perception. Furthermore, leading a purpose-driven lifestyle is linked to a greater volume of the right insular cortex, which relates to well-being and keeps depression at bay (Kotler; Lewis et al.).

After establishing these five intrinsic drivers, the paramount way to amplify motivation is by setting ambitious yet attainable goals (Kotler). Specific and difficult goals enhance performance by providing an anchor point for one's focus, and by guiding one's attention away from unrelated tasks (Houston). Unsurprisingly, goals correlate with higher rates of persistence. With that being said, NYU studies have found that publicly discussing a goal reduces the likelihood of it being completed, because a "social reality" is established where one is self-deceived into thinking they've already fulfilled the ambition (Gollwitzer et al.). Similarly, picturing oneself at the podium can be constraining, causing one to underestimate the hard work needed to get there (Bronson and Merryman). Motivation can be maximized by regularly accomplishing small but rewarding tasks, which will produce a series of dopamine boosts culminating in momentum (Kotler). Indeed, researchers have found that the greatest decline in motivation occurs when there is a lack of small accomplishments or measurable progress. However, without the resolve and grit to overcome adversity, motivation is a moot point. As defined by psychologist Angela Duckworth, grit is the junction of passion and perseverance, and relies on the workings of the prefrontal cortex, which is also involved with self-discipline and goal orientation (Kotler). The brain releases dopamine as a reward for completing challenges. As such, grit can be built up by repeatedly surmounting obstacles, which will train the brain to associate the reward of dopamine with exertion and perseverance (Kotler).

Whether one adopts a gain-oriented or prevention-oriented mindset dramatically alters the workings of the body and the brain. Perceiving a scenario as a threat (prevention-oriented mindset) results in one becoming more apprehensive, timid, and self-conscious. The amygdala, responsible for the fight-or-flight response, becomes highly reactive towards perceived dangers, whether real or imaginary (Bronson and Merryman). Moreover, the medial prefrontal cortex displays heightened neural activity, suggesting that decision-making has shifted from the instinctively unconscious to the labored and time-consuming. When one perceives a scenario as a challenge (gain-oriented mindset), reward networks become highly active, hormones suppress the amygdala's fear response, and decision-making becomes instinctive (Bronson and Merryman). Having a challenge or threat mindset is synonymous with playing to win versus playing not to lose. In prevention-oriented situations where a missed penalty kick would result in losing the game, professional soccer players' success rate was only 62%. If the identical shot occurred in a gain-oriented scenario where a successful kick would result in a win, the players scored 92% of the time (Jordet and Hartman). Playing not to lose, or trying not to make mistakes, often begets errors, due to the hesitant playing style and second-guessing involved.

Mindset changes everything in sports. A fixed mindset is characterized by believing talent is inveterate, while a growth mindset involves challenging oneself and believing practice is conducive to improvement. One's attitudes can influence the workings of the brain; people who

approached a difficult problem with a fixed mindset showed a complete dearth of neural activity, indicating that their brains did not even attempt to absorb new information (Kotler). Maintaining a growth mindset, or open-minded approach to learning, is linked to increased work ethic and persistence. Those with a fixed mindset tend to dwell on mistakes, which causes them to make new ones. Competition is riddled with mistakes-athletes stress over every blunder, errors are the moments that everyone remembers—and, in this way, errors are a predominant aspect of the game. As a rule of thumb, the winning team is simply the team that has fewer missteps. So how does the brain process errors? Research has shown that the brain is on high alert for mistakes, often realizing one has committed an error before the person is even consciously aware. After making a mistake, the anterior cingulate cortex (ACC) experiences a decline in voltage within the first 50-70 milliseconds, followed by a period of neuroplasticity and recovery where the brain processes what went wrong (Bronson and Merryman). In the heat of high-stakes competition, a small mistake can cause a much greater drop in the ACC's voltage and a subsequently weaker recovery, indicating that the brain has become overtaxed. Rather than remaining flexible and adapting to the situation, the brain becomes fixated on the mistake and unable to recover (Bronson and Merryman). Once an error has been made, adopting a growth mindset is critical. A growth mindset allows the brain to analyze what went wrong and facilitates neuroplasticity, which is the brain's ability to alter its activity in response to new stimuli. On the other hand, assuming a closed mindset prevents the brain from dissecting the error and reshaping it into a learning experience. A single mistake during figure skating can be fatal to competition. As a result, many skaters struggle to recover from their first flaw and tend to fall multiple times (Bronson and Merryman).

While motivation and mindset have an undeniable effect on athletic performance, the primary way the brain impacts sports is through movement itself. The central nervous system, comprised of the brain and spinal cord, controls all motions and thereby dictates athletic performance (Schonbrun). Some motions are reflexive, enacted solely by the reciprocal nature of antagonistic and agonistic muscles. For instance, when the patellar tendon is tapped with a hammer the leg involuntarily kicks outwards, because as one muscle contracts the other is forced to stretch and vice versa (Knierim). While monosynaptic reflexes occur in the spinal cord, all deliberate motions involve the motor cortex, which resides on the frontal lobe, directly in front of the central sulcus (Knierim). The motor cortex consists of three main subregions, the primary motor cortex (M1), the supplementary motor area (SMA), and the premotor cortex. When these brain regions are exposed to electricity, movement is triggered in various body parts. The specific body part that moves corresponds to the area of the cortex that was stimulated. In conjunction, these brain structures are responsible for the planning, control, and execution of all voluntary movements. While the premotor cortex and SMA are implicated in the planning and coordination of motions, the breadth of motor control lies in the primary motor cortex (Knierim). Signals to move originate in the primary motor cortex as electrical impulses and travel down to the spinal cord on nerve fibers. Once in the spinal cord, these electrical impulses reach speeds of up to 100 meters per second, racing down the corticospinal tract before synapsing with the

muscle fibers, triggering movement (Schonbrun). The neurons of the primary motor cortex fire up to 100 milliseconds before a movement is initiated, and encode within the signal the force, direction, speed, and distance the muscle should move (Knierim). Faster, more dramatic motions require larger neural signals (Schonbrun).

Although this neurobiological triggering of movement may seem straightforward enough, no two human motions are identical. The reason for this lack of precision is noise, or variability in nerve signals. All human motions are susceptible to this neural noise, which causes each action to have a unique motor pattern. In the words of Russian physiologist Nikolai Bernstein, human motions are "repetition without repetition" (Schonbrun). With each movement neurons are prone to firing at inconsistent intervals, or otherwise experiencing variations during travel, resulting in the muscles receiving slightly altered instructions each time. While minute, these nerve signal deviations can substantially affect the muscles, resulting in inconsistent, imperfect movements (Schonbrun). This is why—despite innumerous hours of practice—it is impossible to make every single layup or place the exact same pitch in baseball down to the minutiae. At the upper levels of a sport, mitigating this variability is vital. Athletes can minimize this nerve-signal noise by employing smooth, continuous motions, like a baseball pitcher's windup, rather than a series of discrete actions. Motions have a speed-accuracy tradeoff, and oftentimes maintaining composure and slowing down allows for increased precision (Schonbrun).

There are two stages to learning a new skill: declarative knowledge and procedural knowledge. Declarative knowledge, the initial learning phase, relies on receiving step-by-step instructions telling one what to do. During this stage the brain instinctively uses chunking, where the coalesced motion is broken down into a series of chunks, for instance, groups of three actions, that are performed (Schonbrun). Complex movements can be thought of simply as a chain of discrete actions linked together in a sequence. The first movement of a chunk is up to 40% more defined than the sequential motions and leaves a larger impression on the primary motor cortex. The initial action reflexively triggers the sequential chunks to continue the chain of movement, which is why basketball players perfectly time the first dribble of their free-throw routine, to set the motor chunking down the right path (Schonbrun). Certain manners of chunking are more ergonomic. However, habits are binary—a habit either exists or does not—and hard to break, so learning the correct motor sequence from the onset is critical (Schonbrun).

The aim of deliberate practice is to correctly reproduce a movement until it becomes habitual and second nature. The more a motion is repeated, the more accurately the brain comprehends how the movement should be executed (Schonbrun). Once these mental representations of a movement have been rotely rehearsed, perfected, and ingrained, one can shift from declarative (conscious actions) to procedural (intuitive) knowledge. Upon attaining procedural knowledge the skill itself has become automatized, allowing the brain to focus its energy on other details, like tactics (Schonbrun). Choking during sports—when an athlete underperforms during high-stakes competition—results from weakly established procedural knowledge being combined with heightened self-focus. The importance of training under competition-like circumstances cannot be overstated. Essentially, choking occurs when, "The automaticity of a task is temporarily lost because the procedural knowledge is disrupted due to the athlete becoming anxious and self-conscious" (Marshall et al. 2). During high-pressure situations athletes tend to overthink, over-analyzing their movements rather than trusting the instinct of automatization, which causes them to freeze up or else perform sloppily. Elite athletes are those who have achieved robust automatization at the highest level and under varied conditions, to the point where simple skills require little to no conscious effort. A fMRI scan of Neymar's brain showed that when Neymar flexed his foot he exhibited significantly less neural activity when compared to other professional soccer players. This data suggests that years of practice had increased Neymar's skill efficiency, allowing him to exert less cognitive energy on the movement itself and devote more focus towards decision-making and tactics (Naito and Hirose).

Neymar was able to flex his foot with minimal brain activation because the motion had become automatized to the point of "muscle memory." This broadly used term is somewhat of a misnomer in the sense that muscles themselves do not have memory-only the brain does (Schonbrun). Muscle memory is the result of a movement being repeated over and over again until the brain reconfigures and strengthens the neural connections used to perform that specific action. In other words, it occurs when a movement becomes fine-tuned and solidified into long-term memory (Schonbrun). What actually transpires during "muscle memory"? The brain changes its architecture by coating certain nerve fibers in myelin, a whitish fatty-protein sheath that wraps around the nerve fiber, similar to rubber insulating an electrical cord. Myelin allows nerve impulses to travel down the fiber faster, thereby allowing an action to execute more efficiently. Having myelinated neural connections will allow one to retain skills longer, expend less energy, and boast faster reaction times (Knierim). After all, fast reaction time is rooted in efficient neural circuitry—it is the minimum time needed for the brain to perceive and process sensory information and initiate a motoric response. With the upsides to muscle memory being so appealing, why doesn't the brain automatize more actions? This comes down to a storage issue; the brain has limited real estate, and only the nerve fibers of repeatedly performed actions get bolstered by myelin, which takes up a significant amount of space. The goal of all training should be to repeat a correct movement time and time again, until the brain myelinates those fibers and the action becomes instinctive (Schonbrun). The caveat to this is once an action has become ingrained, practicing it rotely will not foster more than incremental improvement. It is in one's best interests to constantly practice tasks just above their skill level, rather than repeat the same old familiar drills that have already become automatized. Exercises that hit the challenge-skills sweet spot will push one to stretch themselves, pay heightened attention, and advance their abilities—without the risk of facing discouragement (Kotler).

Contemporary research has shown that physically practicing a movement is not the only way to reinforce those corresponding neural pathways and attain "muscle memory." Visualization, an increasingly popular technique in sports psychology, involves an athlete sitting still and mentally picturing themselves performing an action. The premise for Visualization lies in The Action Observation Network (AON), an interlinked system of brain structures comprised of the superior parietal cortex, areas of the cerebellum, the ventral premotor cortex (PMV), the superior temporal sulcus (STS), the supplementary motor area (SMA), and the inferior parietal lobule (IPL; Schonbrun). The Action Observation Network activates when executing an action, or when observing another person perform that same action. During fMRI scans of female ballet dancers' brains, the AON was active when watching both female and male ballet moves. Nevertheless, their AONs lit up the strongest when they watched dances they had physically performed before, particularly the female ballet moves (Calvo-Merino et al.). This research indicates that the AON can discern movement it has embodied from movement it has merely observed, and displays the greatest neural activity when it is a movement the athlete has frequently performed (Schonbrun). In this way, visualization is most effectively used to train skills the athlete already has a solid physical grasp and physical experience of. By employing visualization, athletes can strengthen the same neural pathways they'd use if they were physically performing the motion. Visualization, sometimes referred to as mental imagery or motor imagery, is supported by a significant body of research. Studies have found that when stroke patients merely visualized their paralyzed limbs moving, blood rushed into the damaged parts of the brain and aided with motor recovery (Poveda-García et al.). Another study found that golfers who coupled physical drills with visualization showed greater improvements on the course, when compared to a physical-drills-only control group (Brouziyne and Molinaro). Moreover, among basketball players, motor imagery training was linked to increased free-throw shooting percentages, and even increased winning percentages for teams that regularly utilized visualization (Cannon). The inferior parietal lobe (part of the AON) is responsible for mirror processing, where simply watching an action causes the motor neurons in charge of that action to fire (Bronson and Merryman). In this way, visualization allows athletes to rehearse and reproduce actions more quickly and adroitly, enhancing focus and confidence along the way.

When it comes down to the day of the competition, the fields of sports psychology and neuroscience offer many insights into handling pre-match somatic and cognitive anxiety. Contrary to popular belief, anxiety in and of itself does not hinder and may improve athletic performance. Everyone has an Individual Zone of Optimal Functioning or an anxiety level where they perform at their best (Bronson and Merryman). Depending on a variety of factors including the type of COMT gene one has, certain people thrive under pressure, while others become easily overwhelmed. Researchers have found that the anxiety levels of elite athletes before a competition varied from 26 to 67 (on a scale from 20 to 80; Bronson and Merryman). Professionals are not immune to stress but rather harness it into increased focus, remaining confident in their abilities. This is not to say that stress can only aid one's performance. Even among seasoned athletes, the detrimental effects of stress can be crippling during high-stakes competition. If anxiety leads to a threat mindset, participants undergo harsh physiological effects. The body responds by releasing a blend of stress-induced hormones, most notably noradrenaline and adrenaline, which control respiratory activity, glucose levels, and the constriction and dilation of blood vessels (Bronson and Merryman). Many athletes are all too familiar with these stressful sensations—one's pulse pounds as heart rate increases, the veins constrict and blood

pressure rises, and compressed lungs result in muscles receiving less oxygen and energy sources rapidly depleting. These debilitating effects also involve the brain; "When under threat, your working memory becomes impaired, meaning you have trouble making sense of and acting on new information, become more prone to recalling and reliving negative emotional experiences, and consciously overthink behaviors that should be second nature" (Meister and Lavanchy). The physical discomfort of a queasy stomach, racing heart, and tight muscles detracts from the body's capacity to react and perform optimally, leading one to panic and further exacerbate the situation. Fortunately, pinpointing the kinesthetic location of malaise and completely dwelling on that sensation-heavy heart, lump in the throat, and so forth-can dispel the feeling of dread (Kotler). Nevertheless, competing in the threat mindset is an extremely unpleasant, arduous experience. This can be circumvented altogether by employing a challenge mindset, or viewing a competition as an opportunity, which will enable the body to perform in a radically different manner. A challenge mindset causes the body to convert noradrenaline (a neurotransmitter that constricts veins) into adrenaline, resulting in veins dilating and blood flow revamping, as heart rate rises and much-needed oxygen is pumped to the muscles (Bronson and Merryman). Glucose production in the liver is boosted, providing cells with their primary energy source and aiding cellular respiration. Rather than produce stress-inducing hormones such as cortisol, the body releases quadruple the amount of adrenaline than that of noradrenaline, providing athletes with a rejuvenating energy burst (Bronson and Merryman).

Reframing a stressful competition as a challenge and opportunity rather than a threat allows one to channel performance anxiety, which has potent physical effects, into a positive force. When trying to combat pre-game nerves positive self-talk has its upsides, but if not rooted in reality these false platitudes tend to backfire (Bronson and Merryman). Self-pep talks are often uninspiring, and some negative thinking may help with predicting and avoiding future errors. Likewise, having inklings of doubt can curb dangerous overconfidence. Finding the right balance between confidence and humility is key. Studies have shown that the morning before an event, testosterone (which increases motivation and suppresses fear) levels of athletes significantly rose, in anticipation of future physical exertion (Bronson and Merryman). Nevertheless, the body's intuitive pre-game testosterone boost only occurred in athletes who took a future competition seriously and felt anxiety, rather than overconfidence.

Ultimately, neuroscience governs how the athlete perceives, learns, and reacts to the ever-changing demands of the game. Aligning intrinsic motivators and setting clear goals allows one to maximize motivation and use neurochemicals to their advantage. Interpreting situations as challenges, rather than threats, can empower the body by affecting the blend of neurochemicals the brain releases. Along the same thread, reframing a competition using a growth, rather than closed, mindset determines which brain regions are activated and how the brain will respond to and recover from mistakes. Deliberately practicing in a neuroscience-based manner—minimizing action noise/variability, being cognizant of chunking, and reinforcing correct habits through repeated practice—can help accelerate skill development and facilitate the transition from Deliberate to Procedural Knowledge. By harnessing psychological techniques like visualization,

one can ingrain the proper mental representations of a skill into their mind. Furthermore, recognizing that pregame anxiety is not inherently detrimental and learning how to channel this formidable influence to one's advantage will have a profound impact on athletic performance. Because in the end, sports come down to more than just a test of physicality or a battle of grit. Sports lie at the intersection of the body and the mind, the combination of physics and neuroscience, of technique and tactics. Sports are just one facet of society, of many more to come, that is having its underlying neuroscientific workings brought to light.

Works Cited

- Bronson, Po, and Ashley Merryman. *Top Dog: The Science of Winning and Losing*. Grand Central Publishing, 2014.
- Brouziyne, M., and C. Molinaro. "Mental Imagery Combined with Physical Practice of Approach Shots for Golf Beginners." *Perceptual and Motor Skills*, U.S. National Library of Medicine, pubmed.ncbi.nlm.nih.gov/16350625/. Accessed 4 Sept. 2023.

Cannon, Jamaal Edward. *Effects of Imagery Use in Basketball Free Throw Shooting*, June 2008, scholarworks.lib.csusb.edu/cgi/viewcontent.cgi?article=4438&context=etd-project.

- Calvo-Merino, Beatriz, et al. "Seeing or Doing? Influence of Visual and Motor Familiarity in Action Observation." *Current Biology*, vol. 16, no. 19, Oct. 2006, pp. 1905–1910, https://doi.org/10.1016/j.cub.2006.07.065.
- Houston, Elaine. "What Is Goal Setting and How to Do It Well." *PositivePsychology.Com*, 9 Apr. 2019, positivepsychology.com/goal-setting/.
- Gollwitzer, Peter M., et al. "When Intentions Go Public." *Psychological Science*, vol. 20, no. 5, 2009, pp. 612–618, https://doi.org/10.1111/j.1467-9280.2009.02336.x.
- Jordet, Geir, and Esther Hartman. "Avoidance Motivation and Choking under Pressure in Soccer Penalty Shootouts." *Journal of Sport and Exercise Psychology*, vol. 30, no. 4, 2008, pp. 450–457, https://doi.org/10.1123/jsep.30.4.450.
- Knierim, James, et al. "Neuroscience Online: An Electronic Textbook for the Neurosciences." *Neuroscience Online: An Electronic Textbook for the Neurosciences* nba.uth.tmc.edu/neuroscience/index.htm. Accessed 4 Sept. 2023.
- Kotler, Steven. The Art of Impossible. HarperWave, 2021.
- Lewis, Gary J, et al. "Neural Correlates of the 'Good Life': Eudaimonic Well-Being Is Associated with Insular Cortex Volume." *Social Cognitive and Affective Neuroscience*, U.S. National Library of Medicine, May 2014,

www.ncbi.nlm.nih.gov/pmc/articles/PMC4014105/.

- Marshall, Dave VJ, et al. "The Effects of Self-Talk Cues on the Putting Performance of Golfers Susceptible to Detrimental Putting Performances under High Pressure Settings." *International Journal of Golf Science*, vol. 5, no. 2, Dec. 2016, pp. 116–134, https://doi.org/10.1123/ijgs.2016-0001.
- Meister, Alyson, and Maude Lavanchy. "The Science of Choking under Pressure." *Harvard Business Review*, 7 Apr. 2022, hbr.org/2022/04/the-science-of-choking-under-pressure.
- Naito, Eiichi, and Satoshi Hirose. "Efficient Foot Motor Control by Neymar's Brain." *Frontiers*, Frontiers, 16 July 2014, www.frontiersin.org/articles/10.3389/fnhum.2014.00594/full.
- Poveda-García, Ana, et al. "The Association between Mental Motor Imagery and Real Movement in Stroke." *Healthcare (Basel, Switzerland)*, U.S. National Library of Medicine, 17 Nov. 2021, www.ncbi.nlm.nih.gov/pmc/articles/PMC8620455/.
- Schonbrun, Zach. *The Performance Cortex: How Neuroscience Is Redefining Athletic Genius*. Dutton, 2019.

The Advantages and Disadvantages of MMT By Amanda Tian

Introduction

From the 1980s to the Global Financial Crisis, many prominent central banks embraced the principle that a stable macroeconomic environment should be achieved by pursuing steady money growth and exercising fiscal restraint. However, the tremendous economic hardship after 2007 formally brought "modern monetary theory" (MMT) to sight.

To prevent economy-wide credit contraction, numerous governments adopted expansionary fiscal policy, which required massive spending that tax revenue simply could not meet. By partly funding government expenditure with central bank credit, MMT allowed governments to break free from tax income constraints to counter extraordinary economic downturns. Despite the controversies surrounding monetizing debt generated by government spending, MMT soon attained popularity among certain politicians and scholars, giving rise to the idea that government budgets can be fully funded by monetary authorities.

Although the concept of a government printing fiat money almost costlessly sounds attractive to many, such financing method should go hand in hand with government budget constraint and structural reforms to sustain long-term growth. For without those, most advantages offered by free money printing will be more than offset by the downside. The sections below outline the pros and cons of extending MMT to its extreme in order to illustrate why fiscal restraints and growth policies are necessary for central-bank-funded governments to realize its advantages while forestalling the vices.

Over the years, central banks significantly increased financing for government spending, MMT is getting more extreme. (See fig.1).



Fig.1. Changes in different kinds of total asset

Three Benefits of Relying Solely on Central Bank

First, a quintessential benefit of replacing tax revenue with money printing is that the government attains fiscal flexibility. Counter-cyclical fiscal support and public goods and services provision fall into this category. Second, using central bank money allows the government to take decisive and exceptional measures when facing liquidity crises. Third, unrestricted money supply empowers the government to manipulate long-term interest rate, potentially speeding up economic recovery.

Fiscal flexibility is a classic advantage bolstered by abundant examples. For instance, to avoid excessive damage to private balance sheets during the 2020 pandemic, the U.S. government directly transferred over 600 billion dollars to families and 360 billion to enterprises through the CARES Act, thanks to monetary support from the Federal Reserve (Lessons Learned from Economic Impact Payments). As the pandemic forced businesses to close and sent the unemployment rate soaring, contracting tax revenue simply could not afford such large-scale spending. Had the Federal Reserve refused to lend to the treasury, it would not have been able to conduct counter-cyclical fiscal policies to preserve private income and demand for credit. In this case, fiscal flexibility provided by central bank funding helped the government to prevent a "balance sheet recession" coined by Richard Koo, resulting in a recession lasting only 2 months, the shortest in U.S. history (The Escape from Balance Sheet Recession and the QE Trap). Another potential advantage of fiscal flexibility is that governments can provide superior public infrastructure and services to citizens absent tax income limitations. Not only do infrastructure construction and public service expansion serve as short-term stimulus to the economy, these programs can also facilitate long-term productivity growth (Infrastructure and the Economy). This is not to argue for unlimited public investment with central bank money to crowd out private actors, but that governments are able to spend more on programs with high externalities to generate sustainable development absent tax-income limitations. Therefore, if used properly, central bank credit provides the government with fiscal flexibility to counter economic downturns and finance productivity-enhancing public expenditures.

Government transfer payments supported by money from the Fed more than offset decrease in income, facilitating a fast recovery from the pandemic. (See fig.2).



Fig.2.USA: Personal Income

The second advantage of central bank backing up all government spending is that authorities will not hesitate to inject liquidity to prevent financial crises from escalating because they face less accusations of "wasting the taxpayers' money". After all, there is no tax collection to start with. During the Global Financial Crisis, the treasury department under Hank Paulson initially ruled out rescuing Lehman Brothers with taxpayers' money to avoid moral hazard. However, the downfall of Lehman triggered an unseen global liquidity crisis, compelling the Federal Reserve to pump money to important financial institutions eventually. Should the government use central bank money instead of taxes, political opposition to the necessary liquidity provision would have been much less pronounced.

CARES Act stands as a recent example of counter-cyclical fiscal policy supported by central bank money. (See fig3.).



Fig.3. A Visualization of the CARES Act

The third advantage is that governments can use central bank money to perform quantitative easing (QE) to maintain financial stability and lower long-term interest rate, reducing disinflationary pressure. By purchasing large amounts of long-term securities with printed money, central banks can reduce the long-term cost of financing even when short-term policy rates are at the zero lower bound. Reduced cost encourages private actors to increase borrowings both to invest and to consume, thereby creating demand and growth. QE has been practiced in Japan, the U.S. and the Eurozone after financial crises with varying degrees of success, and

many researchers agree that QE encourages investment and spending to avert disinflation (Quantitative Easing and the 'New Normal' in Monetary Policy).

The U.S. government's debt issuance is absorbed by the Fed, lowering interest rate in the process to support credit demand. (See fig.4).



■Others - trillions of \$

Fig.4. U.S. government's issuance

To add on to the three concrete advantages, central-bank-funded government spending means zero taxation, but the potential benefit is at best dubious. A tax-less environment naturally attracts enterprises and human capital if the government keeps its currency value stable. Nevertheless, a tax-free country can cause an international "race to the bottom", diminishing any excess attraction of zero tax rate in return. A simple thought experiment may help: Suppose there exist two countries; all else equal, country A cuts its tax rate to zero and country B still has above-zero rate. Then, theoretically, most if not all enterprises and tax-payers would flee to country A, and the only way for B to maintain its competitiveness is to cut to zero as well. The process is much like producing in a perfectly competitive market, in which no excess profit exists. One can argue that while zero tax in major countries, like the U.S., can cause international "race to the bottom", less developed regions and small economies might profit from this strategy without dragging the global tax rate down to zero. However, an attractive business environment is not only about taxation, it also requires conditions like proper law enforcement and expedient public infrastructure, all of which requires tax funding. If people were to fund these institutions and programs with unlimited central bank money instead, then vices like inflation, the crowding

out of private investment and moral hazards become the sword of Damocles. Even if a zero-tax environment is viable, fiscal restraint should be exercised to prevent the downsides, as argued below.

While there are many noteworthy benefits of a central-bank-financed government, the advantages listed above still require government budget constraints and policies to enhance long-term growth; otherwise, the drawbacks below will outweigh these benefits.

The Concerns about Relying Solely on Central Bank

A major concern about a central-bank-funded treasury with little to no budget constraint is that nearly unlimited money supply will cause inflation, if not hyperinflation. The most recent example would be the U.S. inflation outbreak starting 2021. Although supply-chain issues partly contributed to the persistence of high U.S. CPI growth, the cheaply available money printed by the Federal Reserve combined with expansionary fiscal policies stimulated credit generation. Thus, the bout of inflation was accompanied by high M2 growth. A more classic and severe case of uncontrolled money printing was the 1922-23 hyperinflation in the Weimar Republic. To cover expenditures and pay the reparation debt, the Weimar government unleashed too much paper-mark notes to the international and domestic market. From 1919 to 1923, wholesale price level increased 1.813 percent, the mark-dollar exchange rate plunged to a trillion to one in less than two years, and the unemployment rate skyrocketed (90 Years Ago: The End of German Hyperinflation). The Weimar disaster manifested that there must exist some fiscal discipline to limit central bank printing, or uncontrolled government spending will devastate economic stability with hyperinflation, rampant currency depreciation, making rational planning and production impossible.



Central bank printing led to significant U.S. M2 growth, which contributed to the ensuring bout of inflation. (See fig.5).

Fig.5. US CPI and M2 index

Moreover, if governments have no budget constraints, they could issue too much debt as to jeopardize the functioning of its government debt market, undermining currency stability in the process. Without tax revenue, all government expenditure will be financed by issuing debt, which will be held by the central banks and other investors. However, central banks constantly purchasing government bonds means that the interest rates on the bonds will become unacceptably low to investors, gradually pushing them out of the government bond market. As a result, central banks become the only buyer of government bonds, which are no longer market-priced and fail to act as a benchmark reflecting the true cost of borrowing. The attractiveness of government bonds also underpins the stability of its currency. Were government bonds no longer attractive, investors would have sold them, causing its currency to lose purchasing power.

The two great inflation episodes are both related to high money growth facilitated by the Federal Reserve (See fig.6).



Fig.6. US CPI index

A third problem is that cheap central bank money creates moral hazard in economic activities. If a government enjoys unlimited liquidity from the central bank and spends carelessly, excess liquidity enters the private sector to make the cost of borrowing close to none. Then both the government and private actors tend to invest irresponsibly. Even if a speculative financial bubble bursts and private liquidity dries up under higher interest rate, the government can always

instruct the central bank to print more money and flood the market with liquidity again to encourage another speculative cycle.

Even as governments exercise fiscal restraint, the unconditional monetary cooperation from central banks can make authorities overdependent on monetary policies to cope with short-term economic adversities, overlooking structural adjustment that improves fiscal balances and long-term growth. Masaaki Shirakawa, former head of the Bank of Japan (BOJ), has compelling criticisms regarding Japan's overreliance on central-bank money printing ("Tumultuous Times: Central Banking in an Era of Crisis"). He demonstrates that the stagnation of Japanese GDP growth was mainly the result of its shrinking working-age population and declining enterprise competitiveness. Yet, many politicians and businessmen had the erroneous belief that Japan's slow economic growth in the early 2010s was due to the government failing to spend and the BOJ failing to print. Under such belief, the Abe Shinzo administration initiated vield curve control (YCC) in 2016. YCC allows the government to purchase its own debt without limit to cap long-term interest rate at near zero, hoping to stimulate private demand. Nevertheless, constant government stimulus using central bank money had little impact on Japanese growth and CPI as of 2022. It seems that what should have been done were structural reforms to attract immigration, improve birth rate and enhance labor productivity. However, the government's direct control of BOJ creates the false impression that money printing can have sustained long-term effects on growth. This problem does not necessarily occur when central banks fund all government expenditures, but its damaging effect of delaying long-term structural reforms should not be overlooked.



Despite the Japanese government's reliance on BOJ funding and the high rate of monetary base growth, its GDP and CPI growth remain stagnated for structural reasons. (See fig.7).

Although the growth rate of Service CPI increases recently, BOJ money is not the cause; low base-year level created by the pandemic is. (See fig.8).



Fig.8.Service CPI index

Conclusion

In a nutshell, governments fully funded by central banks enjoy advantages such as fiscal flexibility, the ability to inject liquidity during financial crisis with less political opposition and the capacity to lower long-term interest rate to improve growth. Still, these advantages rest upon two premises: first, governments should exercise fiscal constraint; second, they should not over-rely on easily available monetary policies as to give up on long-term structural reforms. Otherwise, uncontrolled government spending may bring hyperinflation, dysfunctional government bond markets, unstable exchange rates and moral hazard in economic activities. Overdependence on money printing also delays structural reforms that can improve productivity and fiscal balance, undermining economic growth in the long-run.

Works cited

- Bowman, David, et al. "Quantitative Easing and Bank Lending: Evidence from Japan." By David Bowman, Fang Cai, Sally M. Davies, Steven B. Kamin :: SSRN, 23 July 2011, doi.org/10.2139/ssrn.1893068.
- Domar, Evsey D."The 'Burden of the Debt' and the National Income." The American Economic Review, vol. 34, no. 4, 798–827. 1994.

Greenspan, Alan. The Age of Turbulence: Adventures in a New World. Penguin Books, 2008.

- Infrastructure and the Economy CRS Reports, crsreports.congress.gov/product/pdf/R/R46826. Accessed 13 Sept. 2023.
- Kanopiadmin. "90 Years Ago: The End of German Hyperinflation: Thorsten Polleit." Mises Institute, 14 Nov. 2013, mises.org/library/90-years-ago-end-german-hyperinflation.
- Kiley, Michael T. "Quantitative Easing and the 'New Normal' in Monetary Policy." Board of Governors of the Federal Reserve System, doi.org/10.17016/feds.2018.004. Accessed 13 Sept. 2023.
- Koo, Richard. The Escape from Balance Sheet Recession and the QE Trap: A Hazardous Road for the World Economy. Wiley, 2015.
- Levin, Andrew T., et al. "Quantifying the Costs and Benefits of Quantitative Easing." NBER, 12 Dec. 2022, www.nber.org/papers/w30749.
- Michael Gelman and Melvin Stephens Jr. "Lessons Learned from Economic Impact Payments during COVID-19." Brookings, 18 June 2023, www.brookings.edu/essay/lessons-learned-from-economic-impact-payments-during-covid-1 9/.
- Shirakawa, Masaaki. Tumultuous Times: Central Banking in an Era of Crisis. Yale University Press, 2021.
- "A Visualization of the Cares Act." Committee for a Responsible Federal Budget, www.crfb.org/blogs/visualization-cares-act. Accessed 13 Sept. 2023.

Epimedium Suppresses the Proliferation of Human Glioblastoma multiforme cell lines in vitro By Sanem Naz Kafalı¹, Buse Kurdoğlu²,Sude Kurdoğlu³, Erkan Yurtcu⁴

Abstract

Aim: To investigate the anti-neoplastic effect of epimedium on Glioblastoma multiforme (GBM) cell lines

Methods: The cells utilized were human glioblastoma multiforme cells (T98-G). Cell viability was measured using the Tryphan blue test. Epimedium's cytotoxic concentrations were determined using MTT (Sigma, St. Louis, Missouri, USA). Epimedium extract was administered at 1, 2.5, and 5 mg doses. At 540 nm, an enzyme-linked immunosorbent assay (ELISA) reader (Biotech Instrument ELx800, Winooski, Vermont (VT), USA) assessed the optical density of the chromogenic product. Tumor cell viability was calculated using the optical densities of epimedium-treated cells.

Results: The MTT test was used to determine how epimedium affected the growth of T98-G cells. T98-G cell growth was suppressed by epimedium in a concentration-dependent manner. T98-G cell viability at 1 mg concentration epimedium was 99.62/0.07; however, at 2.5 md and 5 md epimedium, it was 98.69/0.08 and 88.09/0.14, respectively.

Conclusion: Epimedium reduced T98-G cells' proliferation in a concentration-dependent manner. Epimedium's anti-neoplastic effects may not be considerable or sufficient for clinical usage as a single.

Keywords: anti-neoplastic effect, epimedium, Glioblastoma multiforme (GBM) cell lines

Introduction

Cancer has been the most serious health concern in human history. Glioblastoma multiforme (GBM) is one of them, accounting for 15% of all primary brain tumors. It occurs in around 3-4 instances per 100,000 people (1). Surgery, chemotherapy, radiation, and immunotherapy are the most common clinical cancer treatment options. GBM tumor cells quickly penetrate surrounding tissue, making effective tumor removal nearly impossible. Adjuvant radiation and chemotherapy are frequently required in addition to surgical resection, although the present treatment method does not offer long-term remission (2). As a result, several therapy modalities for GBM should be researched.

Many Chinese herbal medicines have lately been utilized to treat cancer. Among these is Epimedium. Epimedium is extensively dispersed in China (4) and has been used as an herbal medicine for over two thousand years (5). The preparations of Epimedium included about 260 components (6). Epimedium became famous due to its effects on reproductive function and anti-aging (7, 8). However, Epimedium has been shown in recent years to be an antineoplastic drug because it inhibits tumor cell growth and migration and induces apoptosis. (9). Epimedium's antitumor properties against cancers such as lung cancer, prostate cancer, hepatocellular carcinoma, and esophageal cancer have recently been evaluated (10)

Although Epimedium's antineoplastic impact on Glioblastoma multiforme has been explored, information on GBM cell lines is scarce. As a result, this investigation was conducted by high school students under the supervision of Prof. Dr. Erkan Yurtcu.

Results

The MTT test was adopted to assess the effect of epimedium on the proliferation of T98-G cells for 48 hours. Epimedium suppressed T98-G cell proliferation in a concentration-dependent manner (table 1,3). T98-G cell viability at 1m g concentration epimedium was 99.62/0.07, but at 2,5 md and 5m epimedium viability was 98.69/0.08 and 88.09/0.14, respectively (Table1). We discovered that the mean optic density of the untreated group (both medium and cell) was 0.29 and 0.99 0.70, respectively, but the mean optic density of the epimedium-treated group was 0.990 \pm 0.70, 0.980 \pm 0.69, and 0.910 \pm 0.62 (Table2).

Epimedium concentration (mg)	% viability (Mean ±Std Dev)
5	88.09 ±0.14
2,5	98.69± 0.08
1	99.62±0.07

Table	1.	%	viability	ofe	nim	edium	-treated	cells
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Table 2 [.] Mean	optic density	of untreated ((control)	and er	pimedium-tro	eated cells
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	Mean optic density/ Std Dev
Medium Control	0.29
Cell Control	0.99 ± 0.70
Epimedium 5 mg	0.91± 0.62
Epimedium 2,5 mg	0.98± 0.69
Epimedium 1 mg	0.99± 0.70



Table 3: % viability of Epimedium Treated cells

Discussion

There is extensive scientific data supporting the use of Epimedium for cancer treatment. Icariin, the main component in Epimedium, has enormous promise for treating many diseases, such as breast cancer, hepatocellular carcinoma, esophageal cancer, and lung cancer (11).

Many recent in vitro and in vivo studies have shown that icariin can decrease the growth of breast cancer cells. Icarin, for instance, has been shown to suppress the development of breast cancer cells and cause apoptosis (12). In addition to its antineoplastic properties, icariin can increase the treatment resistance of human breast cancer cells. Cheng et al. demonstrated that icariin therapy enhanced tumor cell-acquired resistance to tamoxifen.

Tian et al. studied the effect of icariin treatment on colon cancer cells and discovered that icariin inhibited the growth and migration of colon cancer cells. In another study, icariin was reported to have a robust antineoplastic effect on colon cancer cells but did not affect normal colon epithelial cells (14)

Icariin has been utilized in the treatment of esophageal cancer stem cells. Han et al. discovered that icariin could suppress the development of esophageal cancer stem cells in vitro, and that cell survival rate dropped progressively in close connection to icariin concentration. (15).

Icarin's antineoplastic impact on hepatocellular cancer was recently examined. Li et al. demonstrated that icariin may decrease the development of human liver cancer cells throughout time and at different doses (16).

There is additional information about the Glioblastoma cell line and the application of icariin. Icarin inhibits glioblastoma cell adhesion, motility, and invasion via inhibiting extracellular matrix metalloproteinase. (17)

In the case of GBM, icariin may sensitize GBM cells to apoptosis, inhibiting invasion and epithelial-to-mesenchymal transition (18, 19). L. Yang et al. discovered that icariin has a substantial adverse effect on the development of U87MG cells (20).

Our research discovered that Epimedium suppressed the development of T98-G cells in a concentration-dependent way. At 1m g concentration epimedium, the viability of the T98-G cell was 99.62/0.07. On the other hand, at 2.5 md and 5m, epimedium viability of T98-G cell was 98.69/0.08 and 88.09/0.14, respectively. The anti-neoplastic effect of epimedium may not be

significant and insufficient for clinical use solely, but it may be because epimedium concentration or epimedium was roughly used. This study was carried out by high school students who aspire to be doctors in the future and were accompanied by a senior researcher.

Works Cited

- Batash R, Asna N, Schaffer P, Francis N, Schaffer M. Glioblastoma multiforme, diagnosis and treatment; recent literature review. Curr Med Chem. 2017;24:3002-3009
- Olin MR, Pluhar GE, Andersen BM, et al. Victory and defeat in the induction of a therapeutic response through vaccine therapy for human and canine brain tumors: a review of the state of the art. Crit Rev Immunol. 2014;34:399-432.
- S.H. Chen, et al., Comparative study of two types of herbal capsules with different Epimedium species for the prevention of ovariectomised-induced osteoporosis in rats, J. Orthop. Transl. 4 (2015) 14–27. [16] Y. Xu, et al.,
- The taxonomic relevance of flower colour for Epimedium (Berberidaceae), with morphological and nomenclatural notes for five species from China, PhytoKeys 118 (2019) 33–64.
- S. Wang, et al., Icariin, an up-and-coming bioactive compound against neurological diseases: network pharmacology-based study and literature review, Drug Des. Dev. Ther. 15 (2021) 3619–3641.
- H. Ma, et al., The genus Epimedium: an ethnopharmacological and phytochemical review, J. Ethnopharmacol. 134 (3) (2011) 519–541.
- J. Sun, et al., Icariin promotes mouse Leydig cell testosterone synthesis via the Esr1/Src/Akt/Creb/Sf-1 pathway, Toxicol. Appl. Pharm. 441 (1159) (2022) 69.
- J. Zheng, et al., Icariin improves brain function decline in aging rats by enhancing neuronal autophagy through the AMPK/mTOR/ULK1 pathway, Pharm. Biol. 59 (1) (2021) 183–191.
- C. Zhang, et al., Antitumor effects of icaritin and the molecular mechanisms, Disco Med. 29 (156) (2020) 5–16.
- Xiao-fang WANG1,Jun WANG2 Icaritin suppresses the proliferation of human osteosarcoma cells in vitro by increasing apoptosis and decreasing MMP expressio Acta Pharmacologica Sinica (2014) 35: 531–539;
- Yufang Liu et al., Icariin as an emerging candidate drug for anticancer treatment: Current status and perspective. Biomedicine & Pharmacotherapy 157 (2023) 113991
- L. Song, et al., Icariin-induced inhibition of SIRT6/NF-κB triggers redox mediated apoptosis and enhances anti-tumor immunity in triple-negative breast cancer, Cancer Sci. 111 (11) (2020) 4242–4256.
- X. Cheng, et al., Icariin induces apoptosis by suppressing autophagy in tamoxifenresistant breast cancer cell line MCF-7/TAM, Breast Cancer 26 (6) (2019) 766–775.
- M. Tian, et al., Icariin reduces human colon carcinoma cell growth and metastasis by enhancing p53 activities, Braz. J. Med Biol. Res 51 (10) (2018), e7151.
- S. Han, et al., Effects of Icaritin on the physiological activities of esophageal cancer stem cells, Biochem Biophys. Res Commun. 504 (4) (2018) 792–796.
- S. Li, et al., Icariin, a natural flavonol glycoside, induces apoptosis in human hepatoma SMMC-7721 cells via a ROS/JNK-dependent mitochondrial pathway, Cancer Lett. 298 (2) (2010) 222–230.

- Xu, B et al. Icaritin inhibits the invasion and epithelial-to-mesenchymal transition of glioblastoma cells by targeting EMMPRIN via PTEN/AKt/HIF-1α signalling. Clin. Exp. Pharmacol. Physiol. 42 (2015) 1296–1307.
- Han H, Xu B, Hou P, Jiang C, Liu L, Tang M, Yang X, Zhang Y and Liu Y. Icaritin Sensitizes Human Glioblastoma Cells to TRAIL-Induced Apoptosis. Cell Biochem Biophys 2015; 72: 533-42.
- Xu B,et al. Icaritin inhibits the invasion and epithelial-to-mesenchymal transition of glioblastoma cells by targeting EMMPRIN via PTEN/AKt/HIF-1alpha signalling. Clin Exp Pharmacol Physiol 2015; 42: 1296-1307.
- Lijuan Yang Yuexun Wang Hua Guo Meiling Guo. Synergistic Anti-Cancer Effects of Icariin and Temozolomide in Glioblastoma Cell Biochem 2013-014-0360-30