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Table Of Contents

An Analysis of the Current Understanding of Cancer By Rishi Rajendran

Abstract

Despite decades of research, a "cure for cancer" remains elusive. As the second leading cause of death in the world, cancer is a notorious scourge. As humans have made significant progress in understanding and combating cancer throughout the years, many wonder why we have not been able to "cure" cancer once and for all. However, cancer is actually a multitude of different diseases. The current amount of available knowledge of the pathology of each of these different cancers varies. Similarly, the effectiveness of current treatments for these different cancers can also vary. The presence and extent of a given cancer in society is also driven by factors beyond the cancer itself. Cancer epidemiology can shift as the human environment shifts and level of public health awareness can further shape and adjust the epidemiology of different cancers. Overall, these components establish cancer as a multifaceted problem, requiring an equally multifaceted solution to ultimately resolve.

Intro

Cancers have been around for as long as humans have. Many people wonder given this amount of time why we have not "found a cure" for cancer yet. Put simply, there is not one single cure for this multitude of diseases. Cancer is an umbrella term for a multitude of diseases. There are over 100 forms of cancer. Numerous cancers have been discovered and are now divided by organ type or even subdivided into genetic variants. There are many factors that contribute to whether an individual will develop cancer. These include hereditary genetic mutations as well as genetic mutations from environmental damage, chemical carcinogens, viruses, and more. Approximately 39.5% of people are expected to be diagnosed with cancer in their lifetimes, or two out of every five people. Cancer is estimated to be the second highest leading cause of death in the world.

The core definition of cancer is the uncontrolled division of abnormal cells. The process by which cancers form is called malignant transformation. First, DNA damage is caused by the hereditary or environmental factors previously mentioned. Over time, these genetic insults damage two important categories of genes: tumor suppressor genes and proto-oncogenes. The job of the tumor suppressor genes is to regulate cell proliferation, or the increase in cell numbers, whereas proto-oncogenes drive that proliferation and the cell-cycle forward. When the accumulated damage mutates these genes, it hinders the tumor suppressor genes and it exacerbates the proto-oncogenes, resulting in unchecked cell growth and proliferation. Then, these dysregulated cells are unable to communicate appropriately with other cells in the body and begin causing disorganization of tissue. This continued heavy proliferation forms masses of cells, known as tumors. However, not all tumors are necessarily cancerous. Tumors are classified as either benign, which means they are non-spreading and not cancerous, or malignant, which means they are cancerous tumors capable of spreading to other areas of the body. This process of cancerous spread from the original site is known as metastasis. Malignant tumors are known to

us as cancer. Tumors can either begin as malignant, or sometimes benign tumors can become malignant, representing the two forms of malignant transformation. Malignant transformation can occur quickly, taking weeks to months, or a long time, possibly even decades, depending on the form of cancer.

Popular media and news often speak of "the cure for cancer" when speaking of cancer research. However, despite often sharing core features and symptoms, the numerous different forms of cancer differ in their ability to be diagnosed, epidemiology, physiological behavior, level of public health awareness, and specific treatment methods. There is still much to learn about cancer in our modern times.

Depth of understanding

One reason why cancer is so difficult to cure is because different cancers have varying levels of signs to indicate they are present, meaning that some are more difficult to diagnose. Some cancers have telltale signs early on in their disease course, while other cancers can get severe before there is any sign of them. The absence of signs delays diagnosis, leading to a greater severity of disease by the time the cancer is detected. Certain cancers are not noticeable until they metastasize to other organs and cause noticeable dysfunction in those organs. Cancer is classified into four stages from one to four and the increasing numbers signify the cancer has grown and possibly spread to other areas of the body. This is a problem because as the cancer spreads, it becomes more difficult to wholly remove as it now involves more than one organ. Cancers that are difficult to diagnose are especially dangerous because if detected at a late stage, they are harder to treat.

A prime example of a cancer that humans still have more to learn about, and as a result often can not detect until the disease becomes severe, is pancreatic cancer. This cancer has a significantly high mortality rate, where on average 10.9 people out of every 12.5 diagnosed die. The world wide five year survival rate (the number of people alive five years after diagnosis) is 6%, which is extremely low. The reason for these low numbers is because pancreatic cancer is often only detectable once it has spread to, and caused dysfunction in, multiple organs. This late stage makes it much more difficult to treat. The only curative treatment for pancreatic cancer is surgical resection, surgery that removes an organ or tumor. Only 20% of patients have cancer still confined to the pancreas and thus surgically resectable. The other 80% have metastatic cancer and resection alone will not be enough to eradicate it from the body (Zhang et al., 2018; McGuigan et al., 2018). As a result, patients often look into other, more damaging treatment methods. Despite years of research, we are still unable to detect this cancer well. One reason for this is because common symptoms are non-specific and could be mistaken as caused by another condition, such as weight loss and jaundice. One area of current pancreatic area research is identification of biomarkers that may signal that the cancer is present at earlier stages. This would be used as a screening tool for earlier intervention and treatment.

Contrary to pancreatic cancer, Hodgkin's lymphoma is a cancer that humans have made significant progress in understanding and treating. Lymphoma takes place in the lymph nodes

located in the neck, armpit, chest, and other areas throughout the body. Along with common cancer symptoms, a defining characteristic of lymphoma is the swelling of these areas. Compared to pancreatic cancer which has vague symptoms that overlap with other various diseases, the characteristic symptoms of lymphoma make it easier to recognize. In addition to defining characteristics, Hodgkin's lymphoma spreads in an orderly fashion through the lymph system (NCI, 2023). Once discovered early, there is less difficulty treating it, compared to a cancer that is diagnosed in the late stages. The five year survival rate for Hodgkin's lymphoma is 89%. Humans have become adept at treating cancers with telltale signs, such as lymphoma. In the end, the ability to diagnose cancers play a big part in curing them and there is still much to learn. Additional scientific and financial investments are required for the medical community to make strides in being able to more readily discern, and more effectively treat pancreatic cancer and other intractable cancers.

Current treatment

Another contributing factor to the difficulty of curing cancer is the diverse treatments needed for different cancers, and sometimes even different stages of the same cancer. As of now, humans have developed treatment methods that can destroy cancer, but cause collateral damage in other areas of the body. Treatments such as surgical resection, chemotherapy and radiotherapy are commonly used. Chemotherapy, largely the predecessor of more modern treatments, dates back to the 1940s. More precise methods were yet to be discovered so broad treatments targeting fast dividing cells were the first drugs found to truly make inroads against cancer and therefore used to treat many cancers. Although chemo was often successful in ameliorating cancer, it was not suitable for all cancer and also caused nasty side effects. As time progressed, more strategic methods were sought and developed. Chemotherapy often remains firstline treatment for many cancers. Chemotherapy targets cancer by identifying its fast proliferation rate and destroying DNA replication, ultimately killing the cells. These medications can be taken by injection or pills. However, because these drugs target cells with fast proliferation rates, chemo can destroy healthy cells that also divide quickly. For this reason, hair loss is a common side effect of chemo because it can destroy healthy hair follicles alongside cancer cells. Other side effects include anemia, low platelets, and memory and sleep problems (NCI, 2022). Radiotherapy treats cancer by utilizing high doses of radiation to kill cancer cells and thereby shrink tumors. Similar to chemo, radiotherapy side effects include hair loss, fatigue, and skin changes (NCI, 2019). While treatments such as chemotherapy and radiotherapy can have adverse side effects, newer, more targeted treatments, such as immunotherapy, are less harmful. Immunotherapy uses a patient's immune system to attack cancer cells (Riley et al., 2019).

Over time, cancer treatment has evolved from broad-based treatments such as chemotherapy to more precise treatments. For example, one recently developed treatment that uses immunotherapy principles is CAR T-cell therapy. In this treatment, T-cells, a type of immune cell found in the patient's blood, are removed and genetically reprogrammed with chimeric antigen receptors (CARs), entities that can recognize and kill tumor cells. The Food and

Drug Administration (FDA) has approved two CAR-T cell therapies for clinical use that target specific lymphomas and leukemias, which are cancers in the blood cells and lymph system, respectively (Riley et al., 2019). Because of successful treatments, researchers have been inspired to experiment with targeting other areas to get rid of different cancers. Despite success, CAR T-cell therapy remains expensive and time-intensive, and side-effects are still being researched. As seen through how CAR T-cell therapy is being used to treat specific B cell leukemias and lymphomas, different cancers require separate treatments with their own relative biomarkers yet to be discovered. Cancer treatment has evolved in many ways, but not for every cancer, and as new treatment methods are being researched, humans are once again reminded that cancer is not just a single disease, but numerous diseases.

Level of Public Health Awareness

The level of public health awareness for a given cancer can greatly influence the education and management of that cancer. An example of how the public's perception of a cancer has changed over time can be observed through oropharynx cancer and human papillomavirus. Human papillomavirus (HPV) is known to cause both oropharynx cancer and cervical cancer. Because women have cervices, women can get cervical cancer while both women and men can get oropharynx cancer. In the 2000s, cervical cancer was more common than oropharyngeal cancer and as a result, public health campaigns were made for young women to be vaccinated against HPV. Over time, cervical cancer rates in women dropped while oropharyngeal cancer rates in men grew noticeably (Chan, 2022). This relationship is likely to be due to the encouragement of women to get vaccinated from HPV. Now that this knowledge is available to the public, both women and men have been encouraged to be vaccinated from HPV in recent years. Until then, it was assumed that it was unnecessary for men to be vaccinated from HPV because of the lack of knowledge, but now HPV is publicly associated with multiple cancers. This example of oropharyngeal cancer, a cancer that was once overlooked, demonstrates how lack of public awareness can reduce disease protection and education.

Another example that demonstrates the criticality of public awareness is asbestos. Asbestos is a carcinogenic mineral, meaning it has the ability to cause cancer, but this information has only become known in recent decades. This mineral was originally used in construction because of its desirable properties such as resistance to heat, electricity, and corrosion. From the 1940s to 1970s it was commonly used in textured paint and insulation, and as such, was found in ceilings and other areas of many houses. However, after noticing negative health trends, it was discovered that if exposed to these minerals, the individual would have a higher probability of developing lung cancer. Asbestos has a special synergy with tobacco smoke, whose own exposure was common during those times (Klebe et al., 2019; Park et. al, 2008; Dahlgren et al., 2016). This risk is also greater in people with a family history of lung cancer, as well as a history of smoking or other exposure to lung carcinogens. In addition to lung cancer, asbestos exposure was also proven to cause malignant mesothelioma, a deadly cancer occurring in various organs. Once the dangers of asbestos, a carcinogen commonly found in

housing and other construction, came to light, awareness of this danger spread, and usage was largely banned in most countries. The hazardous effects are thus well-known in well-developed countries, though not as well-known in countries with reduced public awareness. The case of asbestos, a material previously thought to be harmless, demonstrates how public awareness is crucial to prevent people from developing cancer. In this way, awareness can change the epidemiology, the incidence of cancer. Education around cancer causing factors is just one of the ways in which the dangers of cancer can be reduced.

Epidemiology

Epidemiology is the branch of medicine that seeks to understand the factors contributing to both the incidence and resolution of diseases. Part of the reason cancer is difficult to cure is that the incidence, and factors contributing to the incidence, of various cancers fluctuate over time. These fluctuations are influenced by society and the environment that humans create for themselves. As the second leading cause of death, cancer is an infamous disease. However, many people contribute to the development of their cancer because of their lifestyle habits. In addition to environmental factors, cancer can develop as a result of certain lifestyles and environments. For example, the consequences of an unhealthy lifestyle are showcased through pancreatic cancer. The International Agency for Research on Cancer estimates that pancreatic cancer has the highest incidence rate in Western countries such as those in Europe and North America. Risk factors of pancreatic cancer include smoking, usage of alcohol, obesity, and diabetes. The higher risk of obtaining pancreatic cancer can be tied to the higher incidence of some of these habits in Western countries. In modern times, there has been a rising incidence of obesity and other diseases driven by unhealthy habits and the culture of Western countries. It is probable that modern habits such as these contribute to pancreatic cancer in these countries (McGuigan et al., 2018).

An example where a Western environment diet may be influencing cancer epidemiology is colorectal cancer, also known as colon cancer, or rectal cancer. Though colorectal cancer has been decreasing in older patients since the 1990s, the incidence has been rising in young adults in recent years. From 2014 - 2018, incidence of colorectal cancer increased 1.4% per year for people younger than 50, and decreased 2% per year for people older than 50. Common factors that contribute to developing colorectal cancer include having a high fat, low carb diet, consuming a low amount of green food, being overweight or obese. On average, 3 in 4 patients diagnosed have no genetic predisposition for colorectal cancer, indicating that diet and other lifestyle factors are contributing to this strangely increased incidence in younger individuals. The colorectal cancers in younger people have been found to behave differently from those of older patients. For example, in terms of tumor location within the colon (Stoffel et al., 2019; Beaumont, 2019).

Considering a more positive epidemiological trend, the last several decades have seen a reduction in lung and bladder cancers, secondary to smoking. As the health detriments of smoking have become much better publicized and widely known over the decades, smoking

habits have declined, and therefore the rates of their associated cancers have also declined. The epidemiologic influences on cancer incidence are difficult, if not impossible, to reasonably predict, posing a perennial challenge to the management of certain cancers.

Conclusion

People commonly refer to the "cure for cancer" as if there is a single piece of information, or single treatment, that is yet to be discovered. However, there are actually several factors that contribute to cancer and its treatment. These factors include depth of understanding, effectiveness of treatment, breadth of public health awareness, and fluctuating epidemiology.

Cancer is an umbrella term for many different diseases. The depth of knowledge medical science has at their disposal varies from cancer to cancer. This leads to a dynamic landscape where some cancers are now easily curable while others such as pancreatic cancer are still very dangerous killers. Further research into these cancers are the best asset to improving future treatments.

Cancer treatment has evolved tremendously over the last century, in tandem with the evolution of the diversity of the diseases called cancer. Medicine moves towards the goal of more effective cancer treatments through the increased understanding and more strategic targeting of aspects specific to each given cancer, and sometimes aspects even specific to different people. Continued development of targeted effective therapies will both improve patient outcomes as well as reduce negative side effects.

Cancer incidence and prevalence can also be modulated by social factors. There have been strong examples throughout the 20th and 21st century where public health campaigns have increased awareness about certain cancers and their causes, to great effect. These include awareness campaigns about smoking, HPV and the HPV vaccine, and asbestos. Increasing public education about these diseases and the factors that contribute to them ultimately has resulted in fewer cases and deaths from these cancers, making the strong case that future public health campaigns are a great resource to help reduce other avoidable cancers.

Finally, many other environmental factors contribute to the fluctuating epidemiology of different cancers. Often, as in the case of smoking and lung cancer, these factors may only be identified, and properly associated, after several years of studying. As our world is dynamic, so is the incidence of, and susceptibility to, various cancers. As society currently strives to understand the recent rise in incidence of colorectal cancer in younger individuals, it remains important to continue both fundamental and epidemiologic research into these various cancers.

Overall, "cancer" represents many, many different diseases, each with their own specific knowledge requirements, treatment, specifications, points of public awareness, and environmental influences. The multifaceted nature of the problem of cancer requires that the solutions we continue developing be just as thoughtful and multifaceted.

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What are the Implications of Myopia on Teen Basketball Players?
By Nandan Anandakrishnan

Abstract

   The study investigates the effects among American teenage basketball players of myopia. Nowadays, it is difficult to directly see into the future, but one can certainly say that the development of sports medicine is partly because the most common visual eye condition, myopia, has affected the performance of teenage basketball players. Through this work, I hope to refine our understanding of how myopia modifies spatial ability and shooting accuracy in basketball, and how these effects influence performance. My focus of the investigation is aimed at ascertaining that basketball players who focus only on the short term may be better off compared to those who see the long-term picture. To gather a thorough picture, the investigation applied a multimethod approach, involving both quantitative and qualitative assessments. For the quantitative assessment, accuracy and reaction time on shooting tasks as well as vision metrics were measured. My drawbacks include those that I possess to a very limited degree which is I have no detailed information on how basketball players' experiences and skills are affected by lack of vision since this makes it difficult to come up with appropriate interventions and advice and, therefore, unable to advance new innovative methods.

   The qualitative results of interviews with myopic athletes demonstrate a relatively problematic situation in such a sphere that comprises the impossibility of following the ball, feeling its depth, and predicting the movement of your opponent. Quantitative data analysis supports the vindication of this conclusion to a great extent. As players' myopic vision is negatively correlated with their pitch, their shots, and their gameplay goals, their shooting accuracy also decreases. The conversation covers possible appliances of a technique to coaches, players nutrition as well and the financial condition of players. The main purpose of this research is to put a spotlight on the problem of blind players and to add knowledge to the lens worn in the sports area by considering what difficulties caused due to myopia in basketball.

Introduction

   Several studies have gone on for many years trying to uncover the phenomenon of the rise of myopia joining the global health statistics. In this age which becomes more info all the time, the complex interdependence between visual acuity and athletic performance has been the main consideration of the research with professional sports used in this way as the place where the findings are carried out. This particular project proposes an in-depth assessment of the myriad of things that myopia brings to the young players when it comes to basketball in the contemporary and demanding milieu of Texas exemplifying its possible impacts on playmaking skills, shooting accuracy, reaction time, and spatial awareness.

   Taking into account that physical appearance plays a critical role for any athlete, the research intends to debunk a hypothesis that coats or lenses by known brands could be a guiding factor in advancing in one or the other academic fields or sports disciplines.

It's evident that the value of good visual performance comes with no question among athletes; thus, this study seeks to shed light on the under-researched relationship between myopia and basketball mastery. Through focusing on the Texas area, the locale of hundreds of small youth teams who are training to mature into a large pool of skills, we are confident we will not only find such localized insights but will also get information that goes beyond geographical boundaries which helps immensely in both sports science and the sports industry as a whole. The region of North America is an example of the area that is igniting interest for the study that we do, because of the relative importance of this area in the league of NBA. Given that we have various teams and there is a culture of everything being strictly basketball among the congregation, Youth Teams can provide us with a local angle by which we can focus and examine the consequences of myopia in the visual performance of young athletes. While we are upbeat about this exceptional project on the horizon, the inquiry will cover a wide scope in terms of training programs, technology options, and envisioning mental health issues linked to sports. The study probes the layers of myopia as a complicated degenerative condition where in great depth it seeks to decipher the mechanisms in sports in which the condition can subtly hinder the performance of athletes. A myopic player vs a non-myopic player when it comes to deceiving techniques such as "snake eyes" obviously leads the myopic player to be a weaker player and leads to discrimination against myopic players overall in the basketball leagues.

Literature Review

All studies have shown a correlation between myopia and a worse performance in a player and also showed a correlation between common solutions and common causes

Study #1 "Sports and Myopia: An Investigation on the Prevalence and Risk Factors of Myopia in Young Sports-Related Groups in Tianjin, China"(Zhang 2022)

This study takes place in Tianjin China and examines the "relationship between sports and the prevalence of myopia in youth sports"(Zhu 2022), it does this by taking sample athletes at Tianjin's Vocational College of Sports. The study uses cluster sampling and qualitative and quantitative survey measures which included epidemiological questionnaires and ophthalmic examinations. According to the study, the myopia rate among males and females was 50.08% and basketball had the 2nd highest in myopia players over all other sports.

Furthermore, the study focused on many trends within the subjects of the people they were surveying they took into account their age and the correlation between UCVA and SER which is a unit of measurement in myopia, and found that "the bell curves shift left with lower and wider shapes which indicates a bigger variance and myopic shift of the SER"(Yan 2022). Advanced technologies were used in this study to "analyze overall myopic progression such as spot photoscreener to have good consistency with another test called the cycloplegic refraction test"(Sun 2022). which can detect myopia early on in children, the test is easy to use on large populations, requires minimal effort by the patient and is quick and easy to use making it easy to make it a widespread tool to fight myopia.

Study #2 "Parental History of Myopia, Sports and Outdoor Activities, and Future Myopia"(Jones 2007)

This study talks about myopia in North America and how to prevent its spread, it also mentions in small sections how athletics is affected by it. One of the main focuses of the study is to analyze the genetic percentage chance of myopia could be passed down, another was if this myopia was preventable and able to be corrected especially in the realm of sports. The study found that of the parents who had myopia, about 21.6% of their children were diagnosed with myopia(Jones 2007). The study used logistic models to paint the picture of how important it was to get daily sunlight, test subjects who were exposed to sunlight daily were significantly less likely to develop myopia, this statement is also mirrored by the study done in China. The study's method using "Univariate and multiple logistic regression analyses were performed, and receiver operator characteristic (ROC) curves were generated." (Zadnik 2007) "Differences among the areas under the ROC curves were compared using the method of multiple comparisons with the best." (Mutti 2007)."

Hypothesis

I hypothesize that a myopia player has a significant disadvantage to a non-myopic player even with corrective equipment, they will struggle with shooting accuracy, spatial awareness, and accurate depth perceptions. They will also experience higher rates of turnover due to misjudging distances and failing to anticipate opponent players' moves due to deceptive practices. I also hypothesize that this is due to the lack of sunlight and increase in the use of electronic devices and a high emphasis on academics from an early age in today's youth. Due to these reasons, a child's cornea is being made to focus on objects that are closer to the eye so it stretches out leading to myopia.

To contextualize this inquiry, it is crucial to understand the broader implications of myopia on athletic achievement. How does diminished visual acuity impact the precision required in shooting? What role does myopia play in the split-second decision-making inherent in basketball? By addressing these questions, we seek not only to expand our understanding but also to lay the groundwork for informed interventions and practices that can optimize visual performance.

The journey through this research will navigate a terrain where sports science, ophthalmology, and the unique characteristics of the North American basketball landscape converge. The exploration will unfold in three distinct phases: an extensive review of existing literature, a meticulous collection of empirical data, and a comprehensive analysis that aims to distill patterns, correlations, and potential mitigating factors.

In delving into the existing body of knowledge, we will explore the historical evolution of myopia research, highlighting seminal studies that paved the way for contemporary inquiries. Understanding the nuances of myopia, its etiology, and its prevalence within the broader population sets the stage for a more nuanced examination within the specific context of teen players in Texas.

The empirical phase of this research involves the collection of data from a diverse sample of players in the North American area, encompassing factors such as visual acuity measurements, shooting performance metrics, reaction time assessments, and qualitative insights through interviews and surveys. This comprehensive approach aims to capture a holistic picture of how myopia manifests among elite basketball players and its potential implications for their on-court endeavors.

The subsequent analysis phase involves a statistical examination of the gathered data, employing methodologies that discern correlations, identify trends, and tease out the nuanced interactions between myopia and performance metrics. This process not only scrutinizes the immediate impact of myopia but also considers potential confounding variables, ensuring the robustness and reliability of the findings.

As we navigate this research, it is essential to recognize the evolving landscape of technology and its role in augmenting visual performance. From advanced corrective lenses to cutting-edge training methods, technology presents a spectrum of interventions that can mitigate the challenges posed by myopia. This study will explore these technological advancements, evaluating their efficacy in enhancing the visual capabilities of players in Texas and, by extension, their overall athletic performance.

Beyond the physiological aspects, the research will delve into the psychological dimensions of myopia in professional sports. How does the awareness of a visual condition influence the mindset of players? Does it contribute to resilience, adaptability, or conversely, present psychological hurdles? These questions aim to unravel the intricate interplay between the physical and mental aspects of myopia within the competitive realm of basketball.

Methodology

Approach: Mixed (Quantitative and Qualitative) Approach

Prevalence and Causes of Myopia in Teen Basketball Players

Myopia a.k.a. nearsightedness is the most widespread sports eyesight related and especially among the younger players. Timewise, players usually dedicate longer hours at a time checking screens, be it game footage, watching smartphones, or playing video games. Constant screen use may lead to nearsightedness due to the higher volume of close work and reduced time spent outdoors. Also, it is genetics that determine a lot in the development of myopia and anyone can inherit the condition, for instance, when that person has family members with myopia. Besides, high school and college players expend many hours in their training schedules, which may entail extended practice of the basketball exercises and brainstorming about strategic play. This restricted experience of outdoor sunlight often coupled with an intense stare while playing can cause the eyes to become more nearsighted. Unhealthful diet habits that include a diet insufficient in nutrients necessary for eyes such as vitamin A, can also be the trigger for the development of myopia. In addition, players due to their packed schedules may skip regular eye

check-ups or ignore disorders related to vision, thus letting the myopia proceed and evolve in an uncontrolled way.
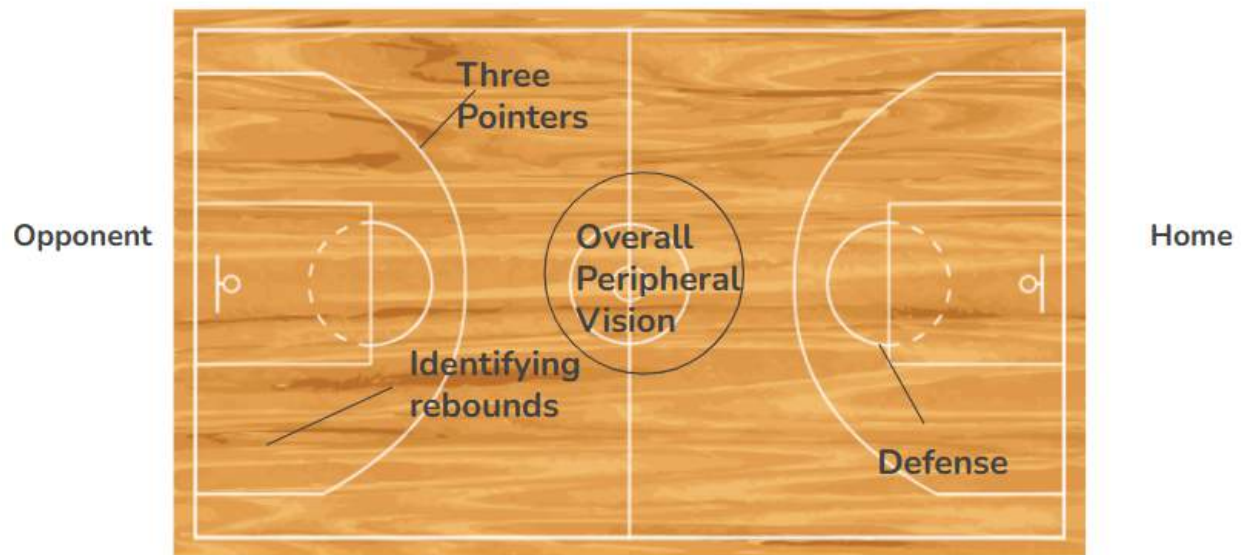
The diagram represents the struggle areas of a myopic player on the court:

This diagram was also present during my presentation and shows the areas that myopic players struggled in the most during previous studies research the basic explanation of the diagram is that myopic players struggle with peripheral vision and reaction time while dribbling on the court, the struggle with shooting three-pointers and if a teammate shoots the ball, they can have trouble locating it. Finally, they can have trouble defending because of the swift actions of the opponent.

Quantitative Data Collection and Analysis

The researchers in this study used a direct method on test subjects who played basketball elaborately and comprehensively, the data was organized in multiple forms such as in table form to represent different variables in each athlete such as their age, their sport, family history, etc. They graphed the data into a multivariable logistic regression model and also utilized flow charts to separate the different stages of quantitative data they were using. They used variables associated with a higher chance of myopia that are not traditionally used such as educational level and family household income which adds to the diversity of this study.

Image 1:

Variables	OR(95%CI)	P value
Female vs Male	1.150(0.888, 1.490)	0.288
Age(>=18 vs <18)	0.765(0.441, 1.327)	0.340
Use electronic screen(often vs not often)	1.406(1.028, 1.923)	0.033
Family history of myopia(yes vs no)	2.022(1.480, 2.763)	<0.001
Indoor sports vs Outdoor sports	1.788(1.391, 2.297)	<0.001
Reading (often vs not often)	1.108(0.848, 1.447)	0.452
Family income	1.008(0.894, 1.137)	0.890
2000-5000 vs above 5000	1.073(0.831, 1.385)	0.591
1000-2000 vs above 5000	1.334(0.935, 1.903)	0.112
below 1000 vs above 5000	0.746(0.489, 1.137)	0.173
BMI	1.034(0.999, 1.070)	0.059
Sleep deficiency(yes vs no)	0.950(0.743, 1.214)	0.681
Unbalanced nutrition(yes vs no)	1.148(0.860, 1.533)	0.350
Drinking(yes vs no)	0.803(0.586, 1.102)	0.174
Smoking(yes vs no)	1.105(0.787, 1.553)	0.564
Daily training time (hours/day)	0.893(0.800, 0.997)	0.043
1-2 hr vs <1 hr	0.684(0.415, 1.126)	0.135
2-4 hr vs <1 hr	0.620(0.371, 1.035)	0.068
4-6 hr vs <1 hr	0.539(0.310, 0.938)	0.029
> 6 hr vs <1 hr	0.466(0.257, 0.844)	0.012
Education level	1.162(0.849, 1.590)	0.348
junior high school vs primary school and below	2.332(0.851, 6.389)	0.100
senior high school vs primary school and below	2.683(0.994, 7.244)	0.051
university and above vs primary school and below	2.506(0.744, 8.439)	0.138
Study locations	1.946(1.543, 2.453)	<0.001
students from TUS vs athletes	1.654(0.902, 3.032)	0.104
students from TVCS vs athletes	3.544(1.862, 6.746)	<0.001

OR (axis: 0.0 0.5 1.0 1.5 2.0 2.5 3.0 3 6 9 12)

"The table uses multivariate logistic regression analysis to use multiple variables to find a correlation in the risk of myopia." (Zhao 22).

Qualitative Data Collection and Analysis

The qualitative portion of these studies was very similar in that they commenced a journey through immersive interviews and questionnaire-type surveys with a rich panel of diverse coaches and players, additionally, a questionnaire was provided to the test subjects to gather information on their personal experiences, this ranged from how well they believe they did and what they could do to improve their skills, to asking the real raw question of did they think their myopia was preventing them from growing more in the sport, additionally, certain coaches who also participated in the study were also given a questionnaire to rate each player myopia and non-myopia on specific tests performed in front of the coaches, they also were interviewed privately to gain insight on the specific disadvantages myopia players face on the court.

The interviews conducted, which were to a set of coaches and players, were recorded and transcribed efficiently to a text sheet to ensure the authenticity and recognize the value of each participant's narratives. The raw transcripts provided the rich material for subsequent analysis by the researchers; and each interview provided a wealth of raw qualitative data for the researchers' interpretation and analysis.

To analyze the interview the researchers used thematic analysis which is a qualitative research method used to uncover the underlying themes and recurring patterns within the interviews, the researchers sifted through the interviews identifying the small details that indicate whether a coach was "sugarcoating" or when they were not exaggerating.
After analysis, certain opinions were common among most of the participants, which was that multiple disadvantages were common, including many from my hypothesis such as shooting accuracy, spatial awareness, and on-court dribbling.

To ensure the credibility of the conclusions, the researchers used multifaceted approaches(which means getting multiple perspectives) for validating and verifying the

information. They used secure forms to hold information and recorded information in more ways than raw data to ensure its credibility.

From the cross-sectional approach, researchers developed a robust result and argument from the information provided which was that myopic players severely suffered due to their condition and could not perform with no corrective equipment and still perform worse than a non-myopic player with corrective equipment.
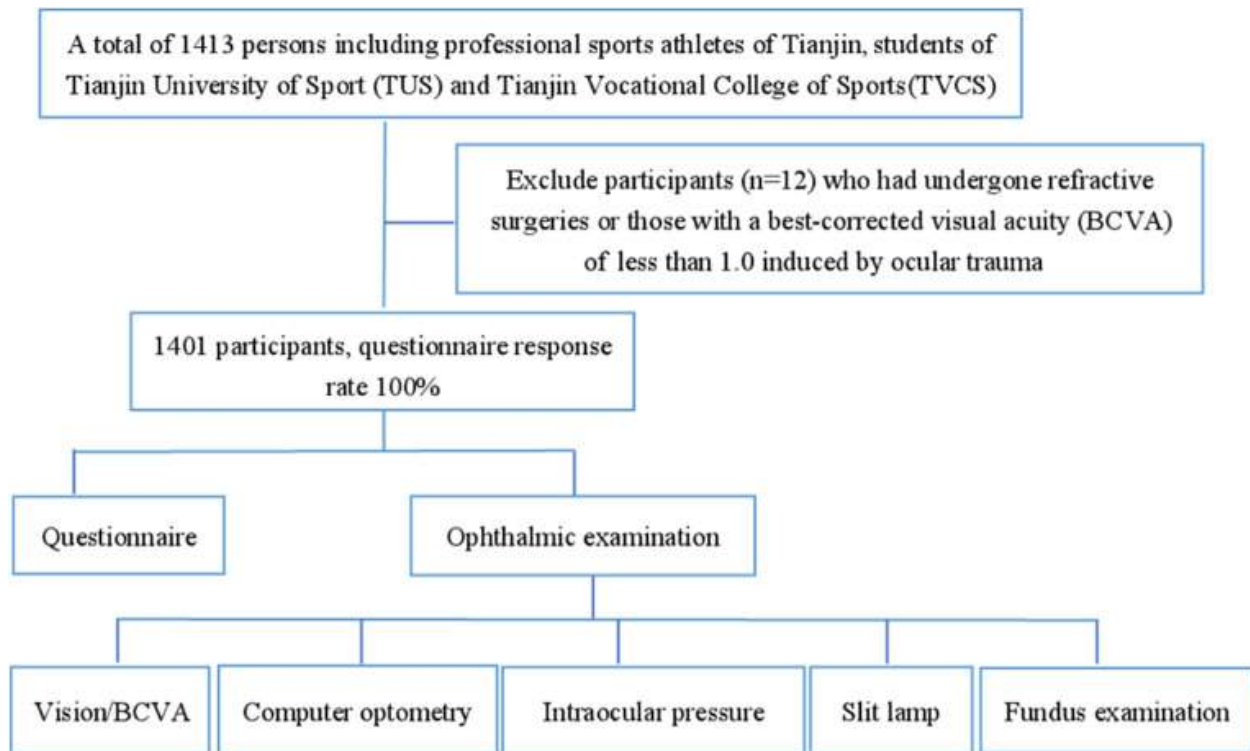
"This Flow diagram summarizes the systematic search and review process. BCVA, best-corrected visual acuity." (shu 2022)

Results and Discussion of Results

The current findings are that over 40% of basketball players in America are suffering from myopia, and a similar percentage is expected in North America. This staggering statistic underscores the urgency of addressing this issue and understanding its implications for teen basketball players.

When more kids spent more time outside playing sports even with their parents being diagnosed with myopia saw a concave downward spiral of myopia development - See Appendix C

Summary

The results show that a large percentage of teenage basketball players in the U.S. suffer from myopia and that there is a staggering amount of help that is needed to treat and solve their performance issues on the court. This includes many positions and many aspects of sports, there

are also many innovative medical solutions for people who are at risk of myopia and for people who have myopia.

Implications

There are many implications I discovered, the Court Performance being a big after where multiple aspects of basketball including shooting accuracy, overall reaction time, and spatial awareness were affected by myopia, I also discovered many new revolutionary medical advances such as orthokeratology and atropine eye drops. Direct government aid would be required for this to spread to more communities because these are innovations with promising results in the testing stage and just passed and are ready for use. Another result is that sunshine influences children's growth, including their eyes. Adding to my hypothesis, East Asian countries that mandated at least two hours of outside time in schools slowed the myopic rise curve in each respective country.

Implications for On-Court Performance

1. **Shooting Accuracy**: Myopia in athletes significantly impacts shooting accuracy, since the correct angle for the ball to be shot and hit the backboard and into the hoop has to be precise, a hand technique line of direction, etc have to be perfect, but with only a blurred vision of the hoop to work with it makes it challenging to precisely gauge distances and alignments. As a result, this leads to missed shots, particularly from long-range such as 3-pointers, and can affect a team's scoring potential.

2. **Reaction Time**: On the court swift reaction times are essential in basketball, as players need to anticipate and react to movements and changes whether slow or fast-paced. Unfortunately, myopia impairs a player's ability to capture and process the minor visual cues an opponent might make, making it harder to make a reaction without audio support from other players, and leading to a higher chance of missed opportunities.

3. **Spatial Awareness**: Everyone needs to have spatial awareness, it's what we use to sense where we are and what we are around, it's highly needed in basketball as players need to navigate the court with obstacles known as the opponent and anticipate movements to steal the ball and make split-second decisions on where to go. Myopic players have distorted depth perception and in some cases peripheral vision, this can hinder a player's ability to maintain situational awareness to make movements on the court.

4. **Defensive Positioning**: Defensive positioning is statistically what many myopic players take to stay safe, however even this position relies heavily on visual acuity and the ability to track the movements of opponents. Myopia comprises this ability, a player faces challenges when attempting to accurately access the positioning of opponents approaching the home team hoop

and react accordingly, this can potentially lead to a missed block and many score opportunities for the opposing team.

Psychological and Emotional Implications

 Confidence and Self-Esteem: Confidence on the court is a big factor when playing and the impact of myopia can affect this and their self-esteem. In practice, missed shots, slower reaction times, and lapses of failure due to their sight can lead to frustration, depression, and a diminished belief in themselves.

 Anxiety and Stress: When players constantly struggle with myopic visual issues on the court it can create pressure anxiety and stress leading to worse performance overall, the fear of missing a big crucial shot or defending the hoop and failing due to their myopic status can impact their overall mental well-being and focus on the game

 Motivation and Determination: When dealing with a disability of any kind, motivation is key and that extends to myopia as well, the sheer will to overcome challenges is tough and some players may experience a decline in motivation and determination, this is due to the sense of helplessness and the sense of falling behind which can affect their commitment to the sport.

Potential Solutions and Interventions

 When we address myopia in young athletes, several innovative solutions can be implemented. Educational initiatives are able to be implemented to raise awareness among players about the utter importance of eye health, the risks to myopia and risks associated with myopia, and most importantly the preventative measures they can take. Furthermore, teenage players can be encouraged to limit screen time outside of basketball and school-related activities and while in use, incorporate regular breaks to alleviate eye strain. They can also install red lights on their phone and home, and blue light filters on their electronic devices to alleviate eye strain and reduce the risk of myopia progression. Incorporating outdoor time into players' daily routines can increase exposure to natural sunlight, in studies done in China more time spent outside daily has been shown to have preventive effects against myopia. Additionally, providing players with their daily nutritional guidance ensures they can maintain a balanced diet rich in protein, zinc, and other eye-friendly nutrients such as vitamin A, lutein, and also zeaxanthin. Facilitating access to comprehensive eye examinations for players includes screenings for myopia and other vision-related diseases yearly. When it comes to myopia it is crucial for early detection and intervention, doing this can help manage myopia effectively and prevent its progression. In myopia, prevention is 10x more effective than treatment.

Technological Advancements and Vision Correction Options

 1. Specialized Corrective Lenses: Current advancements in lens technology have led to custom-made specialized lenses, that are corrective lenses for each athlete. These lenses have all the benefits of normal contact lenses like visual acuity, enhanced depth perception and wider full

of view and also cater to different forms of myopia and are a preferred and more comfortable lens for players with myopia.

2. "Orthokeratology(Ortho-K): Orthokeratology, which is also known as corneal refractive therapy"(Mukamal, 2023), is a "myopic player wearing specialized rigid gas-permeable contact lenses overnight to slow the progression of myopia"(Mitchell 2007) by temporarily reshaping the cornea, this potentially can reduce and/or eliminate the need of any corrective lenses during the day. This approach is a new medical development that doesn't know long-term effects, however, it is beneficial for athletes who prefer not to wear glasses or traditional contact lenses during the day and gameplay.

3. Laser Eye Surgery: A common myopia treatment is Laser eye surgery procedures, one example is "LASIK(Laser-Assisted IN Situ Keratomileusis) and another is PRK (Photorefractive Keratectomy)"(Shortt, 2013), both offer a solution for myopia for a limited period of about 10-15 years. The laser does this by reshaping the cornea to correct the passage of light into the eye, the procedures can improve visual acuity and reduce and possibly eliminate the need for corrective lenses in the future and completely change the game in a player's performance on the court.

4. Vision Training Programs: A Specialized vision training program is specifically designed for myopic athletes, and is focused on improving visual skills such as depth perception, peripheral awareness, and hand-eye coordination. These programs include a wide variety of methods to do this such as VR headsets, special eye movements done daily, exercise, and drills during training. These are designed to challenge and enhance specific aspects of visual performance to possibly mitigate the impact of myopia on an athlete's performance.

5. Pharmaceutical interventions(Atropine eye drops): There are several pharmaceutical interventions that we use to treat myopia, a brand new one includes atropine eye drops which temporarily paralyze the eye during the night hours when said athlete would be sleeping, thus reducing myopia progression in the youth years and enhancing overall focus of the eye when awake.

Acknowledgment of Limitations

During the collection of my quantitative data, the precise age group was slightly not covered by the data studies I used, the location and units of measurement were also different, one of the studies was done in China and the other encompassed North America but did not having a focus on sports, in my qualitative data analysis many Interviews were conducted in a crowded room in one of the studies, due to that some of the messages were cut and not able to be used for my research. I also wanted to incorporate more qualitative data in my research, however, most studies focus on qualitative data because it is easier to rank and come up with a direct result. Due to this, I could not incorporate more real-life experiences into my article. Another limitation is that the sample size was much smaller than my sample size, because the research done in China covered one college campus, while mine covers the teenage basketball players within North America. The data is still valid even with these limitations, the research would have been through had these limitations not been present.

Areas for further research

While this study successfully sheds light on the consequences of myopia, there exist some other aspects that need more in-depth research like Psychosocial Factors, this can be done by studying the psychosocial effect of myopia on teenage basketball players, including how it affects self-esteem, body image, and decision-making process to participate in sports competitively. Such a task would be accomplished by using a mix of research methods including interviews and surveys to extract insights from players, coaches, and parents. Myopia is an ongoing disease, causing the eye's vision to get worse by 1 year to qualify as a dangerous risk factor when the patient is older. Long-Term Visual Health: Find out how the prevalence of myopia among basketball players develops and worsens consistent with their age. Also, shed light on the different severe ocular complications, including retinal detachment, glaucoma, and macular degeneration. Another fantastic outcome found during the research is the utilization of atropine eye drops. Atropine eye drops are an eye prescription that has few limitations but a child only can remove his glasses when using these kinds of eye drops as atropine is usually prepared for powerless use. Also, there are those children who end up having blurry vision after taking atropine drops and a follow-up prescription of multi-focal glasses or glasses One of the statements coming clear from one of the studies discussing atropine results is that atropine eye drops being very fragile needs great care and caution when administered, as to let too much of it in can have serious consequences, thus then little drops should be given at a time of the intake even when you don't see the results coming up. Moreover, Another category that has not been studied adequately is Multifocal Lenses or Orthokeratology which is a much safer approach than Atropine. Finally, I believe that there are no studies for this singular phenomenon which is Environmental and Lifestyle Factors: It would be interesting to study environmental factors related to indoor lighting conditions, screen time, and outdoor activities, and how these factors contribute to the development of myopia in teenage basketball players. This implies studying populations over time to reveal modifiable risk factors which tag is the basis for developing targeted interventions. Generally, myopia was not commonly the case for our ancestors and I think it is because we had a wild lifestyle. A vision treatment that depends on sun exposure and nature-based interventions can be a great plan.

Conclusion

As the number of basketball teams involving youth communities expands, the caution on the eyesight of these players is highly recommended. As part of the long-term goals of the team, I think having that is paramount. By telling and making teen players aware of the dangers as well as the knowledge about how they can prevent myopia, they ensure that they will reduce myopia. Moreover, local organizations should understand the causes of myopia and implement solutions to help the myopic players regain their strength further on and also off the court. Ranging from players and coaches to doctors, parents, and administrative staff, this is a way to bring everyone together. We can create a culture of preventive eye care and influence those who demonstrate myopia to reach the same high standards of running excellence. The Texas NBA can lead by

emphasizing the visual health of its players and using evidence-driven strategies that will not only serve as an example for the players within the state but also for the entire world by creating a culture of sportsmanship in which all players will be concerned about the health of their neighbors.

       In essence, myopia presents teenagers who play basketball on the court a critical challenge, affecting their game and the overall health of their bodies. By determining the causes of myopia and implementing the precautionary steps to fight them, oculists can guarantee the visual health of different players and prolong their careers in this game. A multipronged approach of educational programs, lifestyle modification, and the provision of good eye care will help us to effectively deal with this condition in our youth athletes and to ensure that by doing this, the players continue to excel on the track for years to come.

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Appendix

Appendix A: Figures from "**Parental history of myopia, sports and outdoor activities, and future myopia"(Zadnik, 2007)**

Figure 1: Description of which subjects were excluded and the reason for exclusion.(Zadnik, 2007)
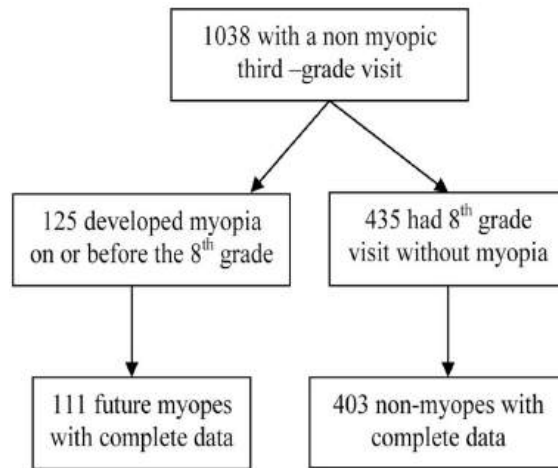
Appendix B- ROC curves associated with sphere, axial length, corneal power, sports and outdoor hours, reading hours, and parental myopia.(PMC 2007) Key included in image
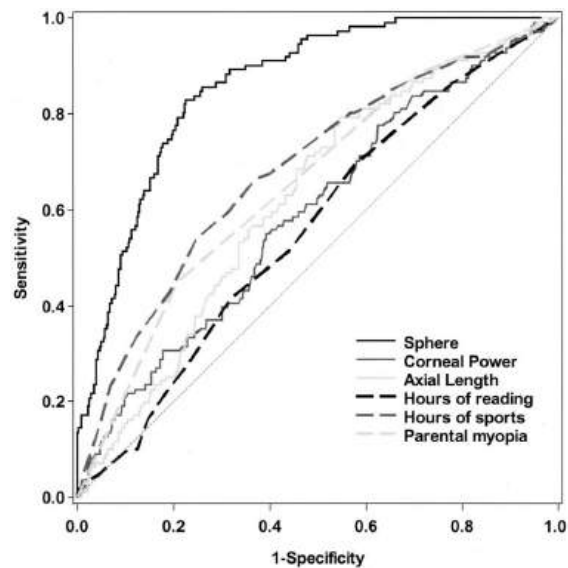
Appendix C: Current width of the 95% CI associated with the probability of myopia among the levels of sports and outdoor activity stratified by the number of myopic parents.(Zhang, 2007)
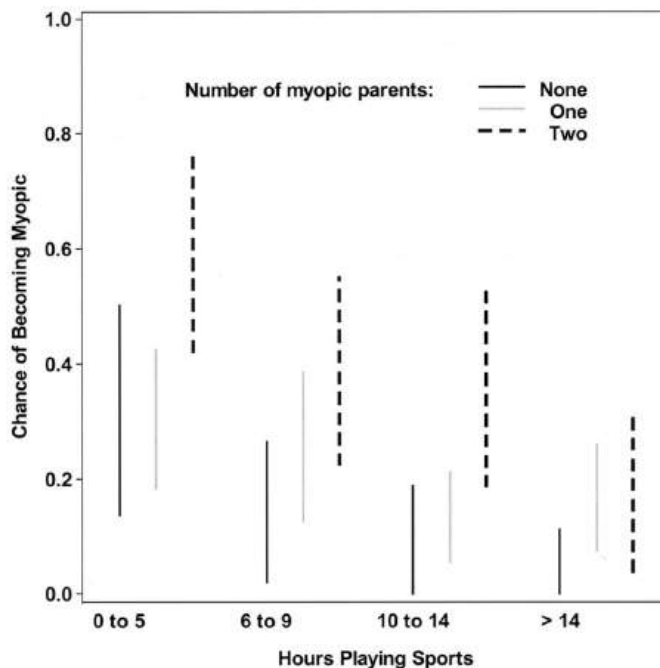
2: The prevalence of myopia in different sports. The number in the parentheses was the young sports-related groups (myopia/total) for each sport.(Yan 2022)
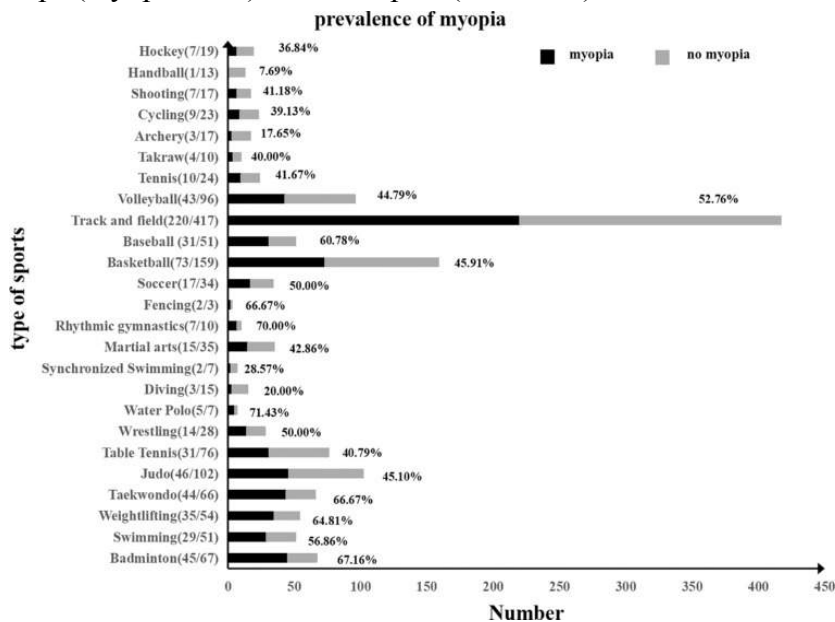
Appendix D: ROC curve for a model using sphere, axial length, corneal power, number of myopic parents, sports and outdoor activity hours, and interaction of myopic parent number and sports and outdoor activity hours compared with a model including only sphere, axial length, and corneal power.(Mitchell 2007)
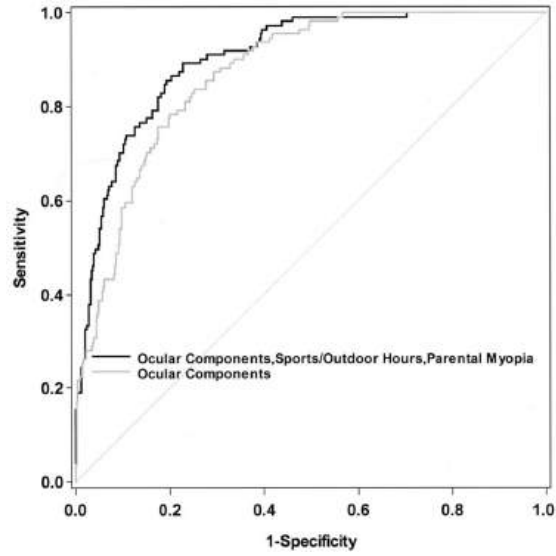
Appendix E: Probability of myopia by quartile of sports and outdoor activity hours per week and the number of myopic parents.(Moeschberger 2007)
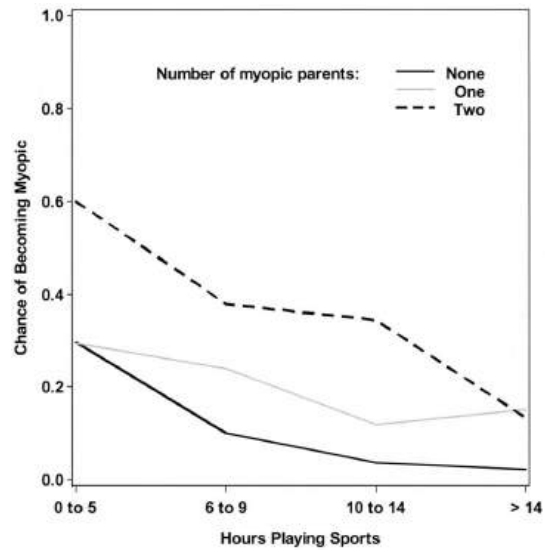
Using AI and Combining Strategic Algorithms to Win UNO
By Joo Young Cheong

Abstract

UNO is one of the world's most popular card games and has been extensively studied for optimal play. In this paper, we attempt to bring a new approach to UNO gameplay by analyzing the effectiveness of an aggregated strategy: an algorithm that selects from contrasting, human strategy patterns with a weighted probability distribution to result in gameplay stronger than its individual parts. This strategy achieves a win rate of up to 51.71% against random agents, proving its effectiveness. We develop a strategy that can combine simple strategies using a method that comes from the field of game theory which is based on the Multiplicative weight update. In this way, we can combine different strategies and get better results than just applying individual strategies.

Introduction

UNO is a card game popular around the world that has sold over 150 million copies. In UNO, the player's objective is to get rid of their whole hand first before other players. (Mueller) They can do so by taking turns to play cards that match in number/type or color with the card on top of the discard pile, and drawing a card when they are unable to do so to end their turn. In addition to the number cards of 0-9 for each color (red, yellow, green, blue), there are special cards that have different effects and do not have numbers. These cards include a Draw 2 card, which skips the next player's turn and forces them to draw 2 cards, a Skip card, which skips the next player's turn, and a Reverse card, which reverses the turn order players take, for each color. Finally, there are Wild cards, which have no numbers, are playable on any card, take the color of the player's choice, and skip the next player's turn. These are accompanied by Wild Draw 4 cards, which act the same as Wild cards but also make the next player draw 4 cards.

Figure 1: An official image of the different types of cards in UNO. Note that the middle 2 cards in the second row are custom, and are not present in this study's version of the game.

Many popular strategies have been used. When playing with the scoring system, the player that discards their hand first collects points for each card in their opponent's hand, with different types of cards scoring different amounts of points. As special cards and cards with higher numbers score more, one strategy is to play "greedily" to rid of all of your high-value cards so that opponents will score less from your hand. (Uno Rules) Another strategy is to save a Wild card as your last card to ensure that it will always be playable. (Amlen)

With this amount of popularity, UNO has been analyzed for optimal play with many different lenses. Among different approaches include reinforcement learning, (O. Brown et al.) mathematical game theory and NP-completeness, (Erik D. et al.) and game refinement theory using hard-coded algorithms.(Alfian Ramadhan et al.)

However, many of these studies have not touched upon 2-player UNO. As playing special cards skips the next player's turn, it will immediately become your turn again in 2-player UNO. This may change strategies used in 2-player UNO, as chaining several special cards together can get rid of cards from different colors and make the opponent draw several cards, creating a faster pace.

In this paper, we aim to create an algorithm for 2-player UNO that provides a middle ground between past work. This algorithm does not use a neural network or artificial intelligence, but functions by choosing between independent strategies with a weighted probability distribution. the paper aims to answer the following hypothesis: Can an algorithm combine simple strategies in an intelligent way?

Results

To create the probability distribution for the aggregated strategy, each simple strategy's win rate was analyzed. 10000 games were played between each different simple algorithm, with a different turn order between the same algorithms counting as a new matchup.

Algorithm 1	Algorithm 2	Win Rate of Algorithm 1
enemy0	enemy1	51.73%
enemy0	enemy2	50.49%
enemy1	enemy0	50.75%
enemy1	enemy2	50.16%
enemy2	enemy0	52.05%
enemy2	enemy1	52.31%

Table 1: Win rates of each simple algorithm matchups

These results were compiled into the following table to determine the total win rate of each algorithm, taking into consideration both turn orders.

Algorithm	Total win rate
enemy0	~49.85%
enemy1	~49.21%
enemy2	~50.93%

Table 2: Total win rate of each simple algorithm

Using these above win rate values as the distribution for the "enemyCombined" algorithm, the following values were achieved:

Algorithm 1	Algorithm 2	Win Rate of Algorithm 1
enemyCombined	enemy0	51.45%
enemyCombined	enemy1	51.70%
enemyCombined	enemy2	51.52%
enemy0	enemyCombined	51.51%
enemy1	enemyCombined	50.63%
enemy2	enemyCombined	51.41%

Table 3: Win rate of enemyCombined in every matchup

From this, we find that the total win rate of enemyCombined is ~50.19%.

To study the effect of the first-move advantage, each algorithm's win rate for going first and last has been listed below:

Algorithm	Win rate for being first to play	Win rate for being second to play
enemy0	51.24%	48.56%
enemy1	50.51%	48.09%
enemy2	51.92%	49.28%
enemyCombined	51.6%	48.8%

Each algorithm was also played against itself 1000 times to analyze the first-move advantage.

Algorithm	First-move advantage
enemy0	1.20%
enemy1	3.06%
enemy2	1.18%
enemyCombined	2.98%

Table 5: First-move advantage of each algorithm against itself

Finally, each algorithm's total win rate against a completely random algorithm was compiled below.

Algorithm	Total win rate against random algorithm
enemy0	51.20%
enemy1	50.47%
enemy2	51.95%
enemyCombined	51.71%

Table 6: Total win rate of each algorithm against random algorithms

Discussion

From a total of 120000 games played between each algorithm, the hypothesis was proven. A win rate of 51.71% against random agents and 50.19% against all strategies is significant, winning a majority of the time. It outperforms "enemy0" and "enemy1", and by combining these strategies we have gotten better results than using just one of these algorithms.

The algorithm itself poses new questions. How does this algorithm compare to human players? There are official UNO tournaments held, as well as a UNO app for virtual games. The algorithm could be tested in these environments to determine its effectiveness. It is also capable of learning and adapting new strategies. More strategies can be aggregated, and the selection by win rate will naturally filter out the new strategy if it is detrimental. How much more effective would the algorithm be if high-level players contributed their strategies to it?

Tables 4 and 5 show that, much like chess and many other games, there is a clear advantage in moving first in UNO. This could be further explored. Which algorithms could

maximize the potential of moving first, and which algorithms minimize the disadvantage of moving last?

This study could have been expanded upon in several ways. Firstly, more than 2 agents could have been simulated in a 3-player or more game, which would change strategies dramatically as special action cards would not immediately give the player an additional turn. Next, the algorithm itself could be improved upon. The algorithms that are combined could make use of additional information such as counting the number of cards played for each color to make more informed decisions and simulate realistic play. They could also choose whether they announce "UNO," which would introduce a strategic element of choosing to draw more cards. On a related note, more extensive simulations could have been ran to determine the true win rate of the algorithms.

Finally, different rule variants of UNO could have been experimented with. Official rules such as custom Wild cards and first face-up cards applying to the first player could be implemented, and popular house rules such as "stacking" Draw 2 cards could also be explored. How would these small changes in gameplay affect the probability distribution and win rate of each strategy?

Materials and Methods

There are many variants of UNO and even official rules between versions vary. (Uno Rules; Mattel Inc.) Differences include custom wild cards and having the first face-up card apply to the first player if it is a special card. In this study, these rules have been ignored, and the following deck is used:

Type	Amount
0	1 for each color
1-9	2 for each color
Skip, Reverse, Draw 2	2 for each color
Wild	4
Wild Draw 4	4

3 strategies were selected, modeled after human play. Each of these strategies was made into hard-coded algorithms. The first strategy, "enemy0", plays cards as much as possible, randomly choosing with a set of weights for each card type that prioritizes Wild Draw 4 cards the most and basic number cards the least. The second strategy, "enemy1", attempts to play as many cards as possible in a turn. Every turn, it looks through a decision tree for which cards it can play consecutively and chooses the longest line. The third and final strategy, "enemy2", plays more

conservatively. It prioritizes playing lower-value cards (first the number cards, then the special cards, then the Wild cards, and then finally Wild Draw 4 cards) until it can find a line in the decision tree where it can play all of its cards. The algorithms are designed to play without the scoring system.

The titular UNO comes from players needing to announce the word "UNO" after playing their second-last card. If they fail to do so before others, then they receive a penalty of drawing 2 cards. Here, the algorithms are assumed to announce "UNO" immediately, and will never draw 2 more cards.

Before initializing the game, these algorithms are pitted against each other 10000 times. From this, the win rate of each algorithm is determined and then used to make a weighted probability distribution. The aggregated strategy, "enemyCombined", chooses from the other base strategies according to the weighted probability distribution and has an additional 10% chance to ignore all strategies and choose a random move.

The program is modeled similarly to the OpenAI Gymnasium environment so that future work could easily expand on this using machine learning provided by OpenAI.

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Arguments for and Against Prison Abolitionism By Eva Fang

Abstract

The ongoing debate on prison abolitionism overshadows a deep problem at the level of society. It is a problem related to the effectiveness and ethics of the current carceral systems. Prison abolitionism is an adamant cry for the abolishing of prisons for alternate justice models, which emphasize harm reduction and human rights. This essay evaluates the debate between the arguments for and against prison abolition, based on real outcomes of imprisonment, such as its social effects and concerns about human rights, and weighed up by arguments in favor of prisons continuing to serve in retribution, deterrence, rehabilitation, and protection of society. According to abolitionists, too often do prisons increase crime, prevent successful reintegration, and suppress basic human rights, where adverse impacts outweigh the desiderata. In contrast, the advocates of the present system insist on retribution, deterrence, and protection of the public, claiming that abolition of prisons will demolish social control together with crime. The essay thus concludes that indeed prison abolition based on thinking does raise worthy issues, but in effective pragmatic practice replacing prisons is in doubt. This, in turn, would suggest that reform of existing systems may offer a more pragmatic approach, reinforcing the constant need to explore alternative justice measures while addressing some of the inherent challenges at the heart of current carceral practices.

Introduction:

The recent debate surrounding prison abolitionism reflects a significant societal dilemma. Prison abolitionism, as a political and analytical framework, seeks to replace carceral systems to alternative models of justice that prioritize harm reduction (Dastile and Agozino). Public perception often associates prisons with the confinement of individuals convicted of serious offenses, such as attempted murder, manslaughter, aggravated assault, rape, sexual assault, robbery, and conspiracy to commit robbery. Therefore, the concept of prison abolition is frequently met with resistance, fueled by the belief that incarceration remains the sole mechanism for controlling criminal behavior and protecting society.

This essay will appraise the arguments both supporting and against prison abolition, exploring potential avenues for reforming existing criminal justice structures. Arguments for abolition often center on the assertion that prisons should be dismantled if they fail to fulfill their intended objectives, result in negative social impacts, or infringe upon fundamental human rights; whereas proponents of incarceration hypothesize that prisons could perform numerous functions including retribution, rehabilitation and deterrence, and protection the public from incarceration.

Arguments For Prison Abolitionism

I.Real Effect of Prisons

The notion of prisons as "breeding grounds for crime" and "schools for crime" (*Sentencing drug offenders*) is widespread. Prolonged prison sentences, by their very design, may expose individuals to a multitude of criminal elements, thereby facilitating criminal experience and intent (University of Law). The forced cohabitation in prison life renders it exceedingly easy for individuals to be influenced by the thoughts and actions of their incarcerated peers. In addition, when offenders are confined to 'cages' and constantly reminded of their transgressions and punishments, they may abandon rehabilitation. A meta-analysis of 116 studies has presented that custodial sanctions have little to no effect on recidivism rates, and may even contribute to a slight increase when compared to the effects of noncustodial sanctions such as probation (Petrich et al.).

Research has also established a correlation between lengthier prison sentences and minor increases in recidivism rates for both low-risk and high-risk offenders. Specifically, low-risk offenders demonstrated a higher likelihood of recidivism than high-risk offenders following release. This finding indicates that, in many cases, prisons fail to effect meaningful change in offenders. A November 1999 study analyzing the effect of imprisonment on criminal behavior analyzed 300,000 offenders and found no evidence that incarceration reduced recidivism (Public Safety Canada). Therefore, if the sole function of prisons is merely the short-term confinement of offenders, they cannot effectively contribute to broader societal improvements through crime reduction.

II. Social Impacts

The high rate of recidivism raises a crucial question: Why are individuals released from prison likely to re-offend? Incarceration results in a permanent record of imprisonment, a mark that carries significant social stigma. This stigma creates a barrier to reintegration as former prisoners encounter pervasive negative perceptions. Therefore, they may face a myriad of challenges upon release, including unemployment, social stereotyping, homelessness, and inadequate living conditions from low income. It is unreasonable to expect rehabilitation and a life free from crime when the justice system prioritizes punishment over offering genuine opportunities for reform and self-improvement post-release (University of Law).

Unemployment poses a particularly significant obstacle for individuals transitioning back to society after imprisonment. While prisons offer educational programs, their impact appears limited. Studies indicate that approximately two-thirds of former prisoners remain unemployed following release. For instance, data from the Ministry of Justice indicates that over a third of working-age individuals with a criminal record, including convictions, cautions, and prison sentences, had no recorded employment for nine years following their release (Ministry of Justice). This lack of stable employment perpetuates a cycle of low income, substandard living conditions, and a higher risk of re-offending.

Disturbingly, even when former prisoners secure employment, their earning potential remains significantly depressed. Research from the Ministry of Justice highlights that individuals serving community sentences earned a median income of £5,100 one year post-release, the

lowest among all offender categories. In contrast, individuals who received fines for similar offenses earned more than double, with a median income of £11,400 (Ministry of Justice). This income gap highlights a criminal record and the lasting challenges faced by former prisoners attempting to rebuild their lives. The multitude of obstacles they encounter upon re-entry to society lends credence to calls for prison abolition and alternative approaches to justice.

III. Human Rights

In contrast to the general protections afforded by the Human Rights Act, prisoners experience a curtailment of certain rights. This, however, has sparked debate, with proponents arguing for the preservation of fundamental freedoms and basic human rights for incarcerated individuals.

The Prison Rules of 1999 outline specific regulations that govern the lives of those incarcerated. Imprisonment involves a reduction in freedom and civil liberties compared to the general populace, with actions subject to stringent control. This includes limitations on freedom from forced labor, restricted privacy, and reduced control over personal property (Dannreuther). While personal privacy holds significance, the realities of prison life often mean individuals may be subject to searches at any time, and their communication with the outside world is under constant scrutiny. Non-compliance with established rules can result in further restrictions, including confinement to one's cell. Solitary confinement (The Hole) may be employed for various reasons, such as altercations between prisoners, assaults on staff, violations of prison regulations, or concerns for an inmate's well-being (Probationinfo). In addition, there exists the potential for the abuse of power by prison authorities, potentially jeopardizing the rights of those under their supervision.

Personal space also represents a significant concern for prisoners, particularly in overcrowded facilities. As of June 2023, the UK's total prison population stood at approximately 95,526. Between 1900 and 2018, the prison population in England and Wales increased fourfold, with roughly half of this growth occurring after 1990 (*UK prison population statistics*). Overcrowding not only exacerbates the already limited freedoms of the incarcerated but also poses significant health risks. These include inadequate nutrition, limited access to physical activity and fresh air, higher rates of infection, and an increased likelihood of mental health challenges, including self-harm and psychological distress (University of Law). Therefore, the substandard living conditions and infringements on fundamental human rights in correctional facilities have fueled arguments supporting the abolition of prisons altogether.

Arguments Against Prison Abolitionism

I.Retribution

Retribution, often represented by the phrase "an eye for an eye, a tooth for a tooth," centers on the notion of giving individuals their just deserts – a punishment equal in force to the harm inflicted (*Vice, crime, and American law*). Lextalionis, similarly rooted in retributive

justice, calls for commensurate retaliation for offenses (Laik et al.). This principle emphasizes a direct correlation between the severity of the crime and the following punishment (Jura). Therefore, some maintain that prisons, as instruments of retribution, should remain in place.

Offenders against society, according to this perspective, should face consequences aligned with the law of retaliation, leading to their confinement. The act of committing a crime positions the individual as an antagonist to societal norms, thereby necessitating punishment for violating established laws and regulations. For such individuals, imprisonment represents both retaliation and retribution. Advocates for this view argue that retribution in the prison system is crucial to guarantee punishment for the guilty, protect the innocent, and finally restore equilibrium to a society disrupted by criminal behavior (*Argument for abolishing capital punishment*).

II. Deterrence and Rehabilitation

Both deterrence and rehabilitation act as preventative measures against criminal behavior. While the former instills a fear of repercussions, thereby discouraging individuals from engaging in unlawful activities, the latter aims to transform individuals, eliminating their desire to commit crimes. These processes, implemented in correctional facilities, guide offenders toward a law-abiding path.

Human behavior is often guided by a consideration of consequences. The likelihood of criminal activity reduces when potential repercussions are widely understood. This principle of deterrence effectively reduces crime rates, often through the application of minimal penalties (*Punishment—retribution, rehabilitation, and deterrence*). The prospect of reincarceration can also represent a deterrent, motivating former prisoners to refrain from future criminal behavior. This logic underpins the argument that prolonged incarceration for a larger number of criminals contributes to a lower overall crime rate. Indeed, this reasoning forms the basis of "3 strikes" laws enacted in various states. California's "3 Strikes" law, for instance, mandates significantly harsher sentences for individuals convicted of a felony who have prior convictions for "serious" or "violent" felonies (*Punishment—retribution, rehabilitation, and deterrence*). This approach aims to deter crime through the threat of amplified penalties.

Rehabilitation, in contrast, focuses on shaping the future conduct of criminals. By offering opportunities for personal growth and transformation, this approach aims to prevent individuals from adopting a life of crime and instead guides them toward becoming productive members of society who respect the law. Rehabilitative efforts offer an approach to benefiting society while reducing the likelihood of re-offending. Such programs may include drug and alcohol treatment, educational opportunities, and counseling services (*Prison rehabilitation*). Broadly speaking, rehabilitation comprises two primary categories. Educational and vocational training programs equip offenders with skills applicable beyond prison walls, while psychological rehabilitation addresses mental health concerns (*Do prisons make us safer?*). Research analyzing various rehabilitation strategies has presented that cognitive-behavioral

programs implemented in correctional settings consistently reduce recidivism rates by at least 15 percent, with some programs demonstrating reductions approaching 30 percent (Santa Cruz).

III. Protection of the Society

Imprisonment represents a means of incapacitating offenders, thereby protecting the public. By segregating criminals and dangerous individuals from society, prisons prevent them from committing further crimes. This separation is essential for maintaining social order.

While imprisonment may not constitute a suitable long-term solution for effectively reducing crime rates, it represents the most direct method for temporarily protecting society from threats. Confinement prevents further victimization by those who pose a potential danger. Moreover, separating offenders from society can reduce their negative influence on younger generations.

Imprisonment for public protection (IPP) exemplifies the use of incarceration to protect society. IPP targets individuals considered 'dangerous' whose offenses, however, do not warrant a life sentence (*Imprisonment for public protection (IPP)*). Offenders receiving an IPP sentence are assigned a minimum term of imprisonment. Release is contingent upon the determination that continued confinement is no longer necessary to ensure public safety (*The IPP factsheet*). Numerous actions are taken to protect the public from offenders serving IPP sentences, including: daily communication between approved premises (AP) and law enforcement, collaboration with Integrated Offender Management (IOM) to support joint efforts and information sharing, regular inspection of mobile devices, utilization of polygraph testing, and communication with the victim liaison unit (*Sentences of imprisonment for public protection thematic*).

Conclusion

The abolition of prisons remains an unresolved issue, with well-founded arguments presented by proponents and detractors. While John Locke famously argued that "The end of law is not to abolish or restrain, but to preserve and enlarge freedom. For in all the states of created beings capable of law, where there is no law, there is no freedom." (*Two treatises of government and the revolution of 1688*), the practicality of prison abolition remains questionable. While prison reform is a possible feasibility, no viable substitute currently exists to address the challenges in the contemporary criminal justice system. The United Nations Office on Drugs and Crime (UNODC) recommends that prison reform consist of areas such as pre-trial detention, prison administration, alternative sanctions and measures, and societal reintegration (*Prison reform and alternatives to imprisonment*). However, many correctional facilities have already implemented such reforms. Moreover, prison reform itself can generate further complications, including increased administrative and assessment expenses, and the potential for the misuse of authority.

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Evaluating the Potential of Magnetohydrodynamics Drives in Watercrafts
By Magnus Andreas Simmons

Abstract

This review article aims to evaluate the potential of Magnetohydrodynamic drives (MHD drives) for powering watercrafts, such as container ships. With climate change and greenhouse gas emissions becoming an increasingly pressing issue, the review also compares MHD drives to traditional combustion engines and assesses their viability as environmentally friendly alternatives. It does this by analysing past research papers and reports on the topic and closely related fields.

The review reveals that the potential of MHD drives for powering watercraft is significant, in particular, due to modern technological developments, such as the achievable strengths of magnetic fields, which have allowed for improvement over past prototypes. Additionally, the article discusses ongoing programs implementing MHD drives in watercraft and shows the implications for the corresponding commercial industries, if these were to succeed.

1. Introduction

The global transportation sector alone is responsible for roughly 20.2% of the world's total yearly greenhouse gas emissions, with an estimated 11% of these emissions attributed solely to the international commercial shipping industry ("shipping emissions" 2023). Moreover, emissions in this sector have been growing consistently and significantly in recent years due to increasing global trade and rising demand for the transport of goods (Olmer et al. 2017). Consequently, there is a pressing need for alternative, green technologies to help reduce these emissions and provide more environmentally friendly options. Such innovations could not only significantly contribute to mitigating climate change but also encourage other large and well established industries to pursue similar advancements.

With over 20 trillion US dollars allocated annually in the public sector to meet global and local sustainability goals (Kharas et al. 2019), developing these alternative technologies can help address this issue at its root and allow for reduced spending on other climate initiatives in the future.

This review article aims to evaluate the potential of Magnetohydrodynamic drives (MHD drives) to power watercrafts and serve as a sustainable alternative for shipping. Magnetohydrodynamics being the study of electrically conductive fluids in a magnetic field (Zonouzi et al. 2019).

1.1 Fundamental principles of Magnetohydrodynamics

Fundamentally, when moving ions or other charged particles enter a magnetic field, a force acts upon them, known as the Lorentz force. The force occurs, due to the close relation and interaction between the crossing electric fields of the ions, and the magnetic field, as defined by

Maxwell's equations (Stoker 2009). As a result, the ions are spatially moved. Electrically conductive fluids contain many of these ions. Consequently, ions are continuously propelled, resulting in the formation of a stream and generating thrust.

The direction of the Lorentz force is dependent on the direction of motion of the particles relative to the magnetic field lines. The direction of the force can be determined with the Right- or Left Hand Rule depending on the respective charges of the particles. It simply and concisely describes the effects of interactions between electric and magnetic fields (Figure 1) (Lincoln 2018).
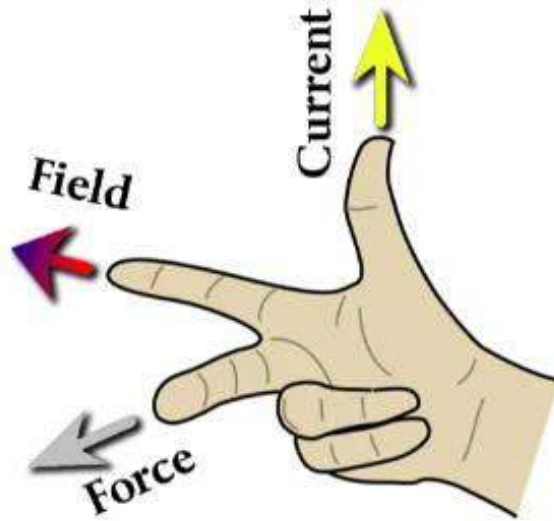
Fig.1 Left Hand Rule showing the formation of the three fingers and the physical quantity they represent (Lincoln 2018).

The figure illustrates the function of each finger in the Right and Left Hand Rules: the thumb represents the direction of ion movement, the middle finger shows the direction the Lorentz force is acting in, and the index finger represents the orientation of the magnetic field lines.

The strength of the Lorentz force (in Newtons, N) is dependent on three physical quantities (Gregersen et al. n.d.): the electric charge of individual ions passing through the magnetic field (measured in Coulombs, C), the velocity v of these ions relative to the magnetic field lines (measured in metres per second, m/s), and the magnetic flux density B (the strength of the magnetic field, measured in Tesla, T). Additionally, the strength of the Lorentz force is influenced by the angle of contact α of the ions and the magnetic field lines. The force is maximised when this angle is directly perpendicular (90°). This relationship between the physical quantities and the resulting Lorentz force, can be expressed using the following formula (Figure 2) (Gregersen et al. n.d.):

$$F_L = Q * v * B * sin(\alpha)$$

Fig. 2 Formula for the calculation of the Lorentz force in Newtons N (Gregersen et al. n.d.).

The electrically conductive properties of the fluid also have an effect on the magnitude of the resulting propulsion and force of thrust. A better electrically conductive medium contains a higher concentration of ions, which leads to an overall larger amount of ions being propelled in a given time (Suganuma et al. 1997).

This propulsion of ions, however, is not only possible in fluids. MHD's counterpart known as Magneto-aerodynamics being the equivalent in ionised gases, and generating thrust through propulsion thereof (Shang 2001).

1.2 Fundamentals of Magnetohydrodynamics drives

A Magnetohydrodynamic drive (MHD drive) is a device that uses charged particles, like ions, to generate thrust in a fluid. Its design is quite simple, consisting of just a magnet and two plate electrodes, which means it has no moving parts and runs solely on electricity (Schmelzer 2019).

The magnet creates the required homogeneous magnetic field, while the electrodes create an electric field that allows an electric current to pass through the fluid, ionising it. This ionisation increases the number of ions present. Additionally, the electrodes can attract these ions and redirect them towards themselves, ensuring the Lorentz force acts in the appropriate direction, as shown by the Right- and Left Hand Rules. The electrodes also facilitate the movement of stationary ions by accelerating them through this attraction (Suganuma et al. 1997).
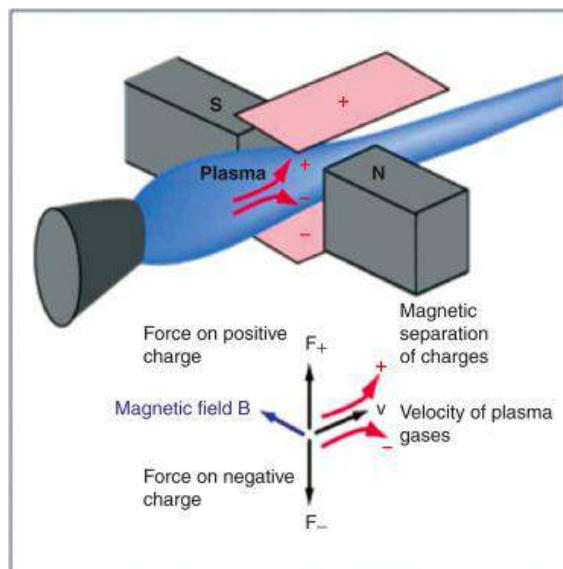
Fig.3 Schematics of a Basic MHD drive showing arrangement of parts (Sheikholeslami et al. 2016).

There are two types of MHD drives: internal and external. Internal MHD drives are located within the confines of the given device, whilst external drives would, for example, be attached to the outside (Suganuma et al. 1997). The differences and significant characteristics of these types will be discussed further in this review article.

2. Magnetohydrodynamics

2.1 Theoretical potential and applications

Magnetohydrodynamic technologies and MHD drives have a wide array of applications, for instance in medicine to control blood flow and redirect it to a particular part of the body or help control flow velocities during surgeries (Rashidi et al. 2017). Alternatively, they can be used as generators, converting thermal and kinetic energy directly into electrical energy. This is achieved through Electromagnetic Induction and the underlying principles of Magnetohydrodynamics (Sarkar 2017). Nevertheless, one of the most pertinent day to day applications of Magnetohydrodynamics and its correlating principles, would be the use of MHD drives to power watercrafts. The potential for Magnetohydrodynamic drives for powering watercrafts is particularly significant. This is due to MHD drives using fully electrically powered jets to thrust themselves forward, making them a cleaner and eco-friendlier alternative to traditional gas-powered combustion engines; these power the vast majority of today's watercrafts and emit large amounts of CO2. This is exemplified by the shipping industries aforementioned yearly greenhouse gas emissions. One major advantage of MHD drives is that they have no moving mechanical parts and therefore are virtually maintenance free. By contrast, combustion engines rely on complex mechanical systems, such as sequentially firing pistons and rotating crankshafts, to push themselves forwards. These require continuous maintenance, care and replacement and can lead to mechanical failures. MHD drives reduce the risk of such failures considerably (Suganuma et al. 1997).

Another major advantage is their considerably reduced impact on wildlife. On account of MHD drives lacking external moving parts like propellers, they are less likely to physically harm or damage the surrounding environment and wildlife (Arcangeli et al. 2022). Moreover, their lack of moving parts makes them nearly silent, which is particularly beneficial for marine life, such as whales, that can often be disoriented by traditional watercrafts (Arcangeli et al. 2022). These features once again enhance the eco-friendly characteristics of MHD drives for powering aquatic vehicles.

Furthermore, this trait of near total silence also has great military potential, as it could make submarines more silent and considerably less detectable. Consequently, the submarine's stealth capabilities could be significantly improved by using MHD drives for propulsion ("MHD submarine" 2023). This aspect of military interest and significance for the field will be explored further in this review article.

A theoretical aspect of the sustainable potential of MHD drive-powered watercrafts is that, if paired with eco-friendly energy sources like solar panels or wind turbines, energy could

be generated locally, while the vehicle is in motion. Additionally, batteries could store any excess energy produced in order to be used at a later time. As a result, the net greenhouse gas emissions from vessels using this technology could be significantly reduced to nearly zero.

Lastly, MHD's aforementioned counterpart Magneto-aerodynamics, which as described above generates thrust through the propulsion of ions in ionised air or other ionised gases, could be used similarly in the future, to power sustainable flight and aeroplanes (Shang 2001).

2.2 Real world limitations

Although MHD technologies hold considerable promise, there are still several pressing challenges and limitations that currently hinder their practical usage. The main issue associated with MHD drives is their possible levels of performance and speed capabilities. These limitations stem primarily from the achievable strength of the Lorentz force.

The achievable strength of the Lorentz force, and therefore the corresponding propulsion, is relatively weak, making it difficult to justify the high costs associated with powering MHD drives and producing their individual components, especially when compared to combustion engines in this regard (Suganuma 1997). This limitation is largely due to the historically attainable strengths of magnetic fields, which have greatly restricted the resulting propulsion and consequently overall performance of such vessels (Suganuma 1997). Additionally, the electrical conductivity of seawater further weakens the Lorentz force acting on the ions. Although seawater initially appears to be a good electrical conductor, its relatively low concentration of ions limits the propulsion's power. Consequently, the achievable speeds and performance of vessels using MHD drives are also negatively impacted (Suganuma 1997). Moreover, the concentration of ions in the water cannot be directly influenced under realistic conditions. Hence, this is especially impactful for Magneto-Aerodynamics, as the concentration in ionised gases is particularly low.

A further drawback of MHD drives is the magnetic leakage from their magnets (Suganuma 1997). Magnetic leakage - the loss of magnetic flux along a circuit (Bubenik et al. 2014) - has the potential to harm the surrounding wildlife and environment. For example, it could disorient migratory fish species, subsequently making their migration longer and more energy-consuming (Pophof et al. 2023).

Lastly, electrolysis is another limitation. When electric current is run through water, it causes a chemical reaction called electrolysis (Dobó et al. 2016). This chemical reaction produces chlorine gas, which is a toxic substance. If released in large quantities, chlorine can harm the surrounding environment and wildlife.

The following table summarises the advantages and disadvantages associated with MHD drives (Figure 4):

Advantages / Potential	Disadvantages / Limitations

1. Replace Combustion Engines:
   a. Reduce Mechanical failures
   b. Wear and Tear of components
   c. Sustainable alternative
	1. Limited Performance:
	   a. Propulsing Lorentz Force
	      i. Weak magnetic fields
	      ii. Electrical conductivity of seawater

2. Produce no noise:
   a. Protect surrounding wildlife
   b. Military application in submarines
	2. Magnetic Leakage:
	   a. Harm surrounding wildlife and environment
	      i. Migratory fish species affected

3. On the go clean energy generation
   a. Theoretical implementation
	3. Electrolysis:
	   a. Production of toxic Chlorine gas
	   b. Harmful to surroundings

2.3 Methods to overcome these limitations

Despite these limitations, there are certain methods to enhance the performance of MHD drive powered vessels and, to some degree, mitigate their drawbacks in real-world settings, thereby improving their usability. Essentially, performance can be improved by amplifying the strength of the Lorentz force acting on individual ions, which would in turn boost the resulting propulsion and thrust. To amplify the strength of the Lorentz force, the physical quantities that it is dependent on and that can be directly influenced on must be increased, as indicated by the corresponding formula mentioned above.

The first physical quantities that can be influenced are the velocity *v* and the angle of contact α of the ions in the fluid. The velocity can be increased by raising the voltage V, which strengthens the electric field between the two electrodes ("Dielectrics" n.d.). A stronger electric field allows ions entering the crossing fields to be deflected more forcefully towards one of the electrodes, resulting in a perpendicular motion of ions relative to the magnetic field lines and also an amplified Lorentz force. Additionally, this deflection can accelerate the entering ions boosting their velocity. However, by increasing the voltage the rate of energy consumption also increases leading to further challenges with energy efficiency. Moreover, by increasing the voltage the rate of electrolysis is also accelerated, leading to the production of a greater amount of harmful chlorine gas (Dobó et al. 2016). Therefore, it is essential to strike a balance between performance, energy efficiency and environmental protection when determining a suitable voltage between the electrodes of an MHD drive.

The second and final physical quantity that can be influenced is the historically limiting magnetic flux density, B. This can be done by using an electromagnet, which is typically stronger and more adaptable than traditional permanent magnets ("Electromagnets" 2024). An electromagnet consists solely of a conductive wire wound into a coil, with electricity flowing through it. The strength of an electromagnet's field is dependent, among other physical quantities, on the amperage I in the circuit (Pendry et al. 2006). By increasing the amperage, we can easily and rapidly boost the magnetic flux density of the generated magnetic field (Pendry et

al. 2006). In addition, we could use a superconductor for the electromagnet's wiring and cool it. A superconductor, such as mercury, is a substance that provides no resistance to flowing electricity when cooled below a certain temperature, allowing for much higher than typically achievable amperage (Qin et al. 2005).
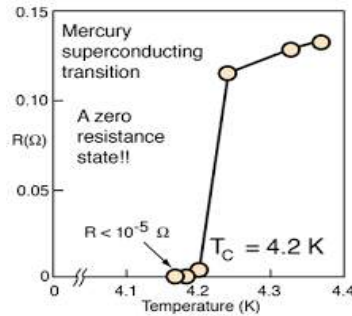
Fig.5 Electrical Resistance of the superconductive substance Mercury at different temperatures, in an experiment conducted originally by H. K. Onnes (Kumbahr 2019).

These methods both lead to a greatly increased magnetic flux density of the magnetic field, which in turn leads to a significantly amplified Lorentz force acting upon the ions. However, a stronger magnetic field can also cause a greater amount of magnetic leakage. This problem can be addressed by designing the watercraft around the appropriate type of MHD drive. External MHD drives tend to allow for significant magnetic leakage, as they are directly exposed to their surroundings. By contrast, internal MHD drives paired with magnetic shields can dampen this leakage and limit exposure to safe and acceptable levels. However, the added magnetic shielding may also increase the weight and cost of the vehicles (Suganuma 1997).

The Lorentz force is also dependent on the individual charges q of entering ions. However, this factor can not be directly controlled in realistic conditions.

Even though the implementation of these methods would improve the performance and the efficiency of MHD drives, there would still be large costs associated with the production of such high end parts, in particular the powerful, superconductive magnets. Moreover, the weight and size of components, such as the cooling system for the superconductor, could lead to difficulty with fitting high amounts passengers or cargo. This could lead to difficulties in making these watercrafts a commercially viable alternative.

3. Past examples and modern technological developments

3.1 Past Examples

In the past, there have been prototypes of MHD drive-powered watercrafts, the most notable being the Yamato-1, developed by Mitsubishi Heavy Industries LTD. Created in 1991, the Yamato-1 underwent its first test drive on open water in 1992. It reached a maximum speed of 15 kilometres per hour (about 8 knots), with a length of 30 metres and a weight of around 185 tons. The MHD drives themselves were primarily powered by a superconductive electromagnet

cooled with helium gas to generate the necessary magnetic field for propulsion. However, the project was eventually shut down due to limited performance (Suganuma et al. 1997).

A publication regarding the Yamato-1, published by Suganuma and colleagues, discussed various developments and challenges faced during the ship's design phase (Suganuma et al. 1997). Even though it implemented many of the aforementioned methods to overcome performance limitations, it noted that the vessel's performance was greatly constrained by the technology of its time, particularly, the limited strength of the then achievable magnetic fields. The superconductive electromagnet used, was only able to maintain a continuous and uniform magnetic field of four Tesla throughout the drive. The publication goes on to state that, in order to achieve performance comparable to combustion engine-powered watercrafts, the magnetic flux density of the field would need to be at least twenty to thirty Tesla (Suganuma et al. 1997). It also mentions that while there were reports of superconductive electromagnets capable of reaching these strengths at the time of production, they could not operate uniformly, continuously, or over a large enough area to be suitable for implementation in the Yamato-1 prototype. Hence, the project did not secure further funding and was shut down in the early 90s.

This past project has left somewhat of a negative sentiment toward MHD-powered watercrafts among manufacturers, leading to scepticism about their potential and future commercial viability. Consequently, there has been a lack of further research conducted into MHD drive technology as alternatives for powering watercrafts.

3.2 Modern Technological Developments

However, since the Yamato-1 project was shut down, technology and innovation on a global scale have advanced significantly. Academic institutions and universities, such as MIT, have developed electromagnets capable of generating magnetic fields with flux densities of around 20 Tesla continuously, uniformly and on a larger scale than necessary (Chandler 2021). These advances far exceed what is required for implementation in watercrafts like the Yamato - 1. These electromagnets are currently used in prototype atomic fusion reactors (Chandler 2021). The advances in achievable strength are largely due to rare earth barium copper oxide (ReBCO) superconductors, which can sustain higher magnetic flux densities than previously possible (Selvamanickam 2023). Additionally, ReBCO superconductors have a relatively high critical temperature, allowing them to remain superconducting at more accessible temperatures (Selvamanickam 2023), and therefore improving the energy efficiency of the MHD drives they are used in, from as low as 30%, in the Yamato-1, to potentially as high as 90% ("MHD submarine" 2023). These developments also greatly address the energy efficiency limitations of MHD drives.

These advancements have reignited some interest in the development of MHD drive-powered watercrafts. Recently, military research organisations have taken notice of these developments, citing both the technological advancements as the reason for these technologies becoming worth pursuing ("caterpillar drive" 2024). The Defense Advanced Research Projects Agency (DARPA) has launched a 42-month program referred to as the Principles of Underwater

Magnetohydrodynamics Pump (PUMP). This program, led by Dr. Susan Swithenbank, is intended to develop an MHD drive-powered submarine ("caterpillar drive" 2024). Military spending once again demonstrates the potential of these technologies. DARPA plans to attach one of these drives to the Virginia-class submarine USS Montana in the coming months to test its performance and manoeuvrability in real-world settings ("caterpillar drive" 2024).

If DARPA were to succeed in developing a capable and well performing MHD drive-powered vessel, it could shift sentiment and promote the adoption of these more sustainable alternatives in sectors like the shipping industry and private boating. Consequently, it may be beneficial to relevant parties to commence researching the implementation of MHD technologies for their own commercial applications. This would possibly provide them with an edge over their competition and allow them to meet environmental compliance quotas. While these developments show considerable promise, DARPA has raised concerns about the options for materials used for the electrodes, specifically their inability to withstand corrosion and last throughout the vessel's lifetime ("MHD submarine" 2023). The PUMP program aims to address these concerns and explore options, such as the production of new and more capable materials. Therefore, the program and its future results need to be examined closely.

Conclusion

All in all, the potential of Magnetohydrodynamic drives in watercrafts, as shown in this review article, is significant. They not only offer a more sustainable and green alternative to traditional fossil fuel powered combustion engines, but can also reduce the amount of mechanical failures. Additionally, their silent operation and lack of moving parts, actively shield and protect the surrounding environment and wildlife. In the past, limitations such as achievable forces of propulsion and energy efficiency raised concerns and have contributed to negative commercial sentiment toward the implementation of MHD drives in watercrafts. This situation has led to limited developments. However, modern technological breakthroughs - particularly in magnetic field strength, due to the use of ReBCO superconductors - have opened up new possibilities for achieving the methods to overcoming these limitations and improving upon the drawbacks of earlier prototypes. These advancements have led to an increase in the launching of programs aimed at addressing the remaining issues and demonstrating the capability of MHD drive-powered watercrafts in real-world applications. If these projects were to succeed in their objectives, it could lead to the historic sentiment towards these technologies changing, and result in an increase in their commercial usage in industries, such as shipping.

In the future, research on MHD technologies and drives should focus on further enhancing performance and resolving the materials challenges currently being addressed. Additionally, exploring new fields of application should be a priority, as this could lead to the implementation of these sustainable alternatives in other sectors.

Constraints

Some constraints in the data collection for the review article included the lack of officially published financial figures regarding the production of these vessels and their individual components in past research papers, reports and articles. These would have facilitated a better and more precise analysis of MHD and MHD drives as a commercially viable option and realistic alternative.

Methods

The methodology of gathering information and data for this review article, included reading and evaluating a wide array of articles and past Research Papers. This was done by entering keywords, such as Magnetohydrodynamics, MHD drives and Yamato-1, into different academic journals, for instance, ScienceDirect. Additionally, these keywords were entered into search engines in order to find fitting articles and evaluate the gathered data and information. Papers that had been published more recently, specifically regarding magnetic flux densities of uniform, continuous and sizable magnetic fields reaching around 20 Tesla, were valued more significantly. The selected sources were compared with others in the field, in order to ensure the gathered information and data was as unbiased, factual and objective as possible. Lastly, certain basic fundamentals and core principles of the relation and interactions between electric and magnetic fields were taught in High School Physics classes.

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AI-Based Car Scratch Detection Framework Using CNN and Recursive Wheel Detection System by Chinar Deshpande

Abstract

This paper analyzes how techniques in deep learning can help car dealerships improve the efficiency and quality of their services offered to customers on a day-to-day basis[1]. This study is necessary to work on an overlooked part of the business-to-customer industry. Although, for most consumers, the efficiency of most saturated service providers is not of concern, in the landscape of newer innovations like the electric car and autonomous vehicles, the car repair industry is one that needs to be revamped.

To answer this question, a detailed literature review was conducted, and a deep learning-based solution to effectively scan the surface of cars from images and identify the areas with scratches, chipped paint, and other damage indicators was conceived. The study proposes the construction of a CNN framework, along with a recursive wheel detection system, to automate the scanning process. Since at present, considerable manual effort is involved in services offered by dealerships that are in charge of car damage analysis, there is an error margin that can be eliminated using our method.

Our results showed that the framework has a 94% accuracy rate with successful complete detection of damage on cars. Additionally, it has multiple applications such as detecting damage on other vehicles. All moving vehicles could potentially use the methods discussed in this study to deploy a self-repairing algorithm to fix basic scratches on the body of the vessel.

Introduction

Since its invention in the early 19th century, photography became an achievement of the human mind and hands, a means of capturing moments of real life, in a completely different way to a painting or a description with words[2]. Since then, images and videos have expanded exponentially, being used for scientific, social, political, and personal causes today[3] .

Under computer vision, image processing is a particularly interesting topic. Encompassing applications in defense, biomedical engineering, multimedia computing, remote sensing, pattern recognition, and more, image processing includes powerful techniques experienced programmers can use to solve complex problems. This paper focuses on computer vision's application in enhancing efficiency within the automotive industry.

In the modern world, the automotive industry has observed huge advancements in the areas of safety, comfort and performance. Enhanced safety features such as Advanced Driver Assistance Systems(ADAS)[4], which provide real-time feedback and assistance to drivers, are already being implemented in autonomous cars manufactured by leading automobile companies. The ability to learn almost instantaneously is incredibly powerful, with the notable aspect of potentially improving humans' quality of life.

However, one overlooked aspect of common automobiles is the maintenance. A frequent problem experienced by regular consumers is the appearance of scratches on the body of the car.

Even while the car is stationary, parked safely in a garage or a parking lot, more than 60% of Americans' cars have been damaged[5]. This is a time-taking problem to solve as it has been observed that in most countries, simple car repairs take at least a day or two to complete, even for the smallest scratches or dents. This is due to manual inspection that delays the resolution. There's still scope for gaps after manual processing as due to human error there may be small dents and scratches that might get missed out. This, in turn, puts pressure on both owner of the vehicles as well as the dealership.

For the purposes of this paper, to combat this issue, an algorithm based on edge detection and computer vision transform techniques is used to achieve a suitable output. Edge detection is beneficial to reduce background noise, unwanted features, and focus the main force of the algorithm/ neural network on the main aspects of the image. Along with edge detection, the impact of an allied CNN network was investigated to enforce inferences of the research further. The findings contribute to the development of reliable and practical solutions for automating car scratch detection in real-world scenarios. The paper also introduced the CNN architecture employed, explaining its design choices and highlighting its suitability for scratch detection. Furthermore, the training procedure, including the optimization algorithm, hyperparameter settings, and model evaluation metrics were evaluated. To enhance the performance of the scratch detection system, various data augmentation techniques such as random rotations, flips, and translations were investigated. Additionally, transfer learning strategies by fine-tuning pre-trained CNN models on related tasks were further explored.

The general methodology used to conduct background research for the study involved several rounds of a detailed literature review. This analyzed multiple different papers and evaluated their impact on the topic, which helped the study to focus on a less discovered area of Car Scratch Detection. Multiple datasets were used to train the CNN several times. They were compared to each other based on accuracy, image size, features, number of images, and other factors. This eliminated most shallow datasets and alienated the best dataset, which was used for the final result.

Results

After training the CNN model on the dataset, it achieved an accuracy of 81% on the test set. This accuracy indicated the model's capability to correctly classify the types and severity of damage present in the car images. Moreover, the obtained accuracy is comparable to state-of-the-art methods for similar tasks, demonstrating the effectiveness of the proposed approach.

Furthermore, the incorporation of the preprocessing step to remove wheels significantly enhanced the algorithm's performance. By focusing exclusively on the car's body, the framework is able to reduce background noise and false positives, increasing the effectiveness of the algorithm . This refinement contributed to the overall accuracy and effectiveness of the algorithm in identifying and categorizing car damages.
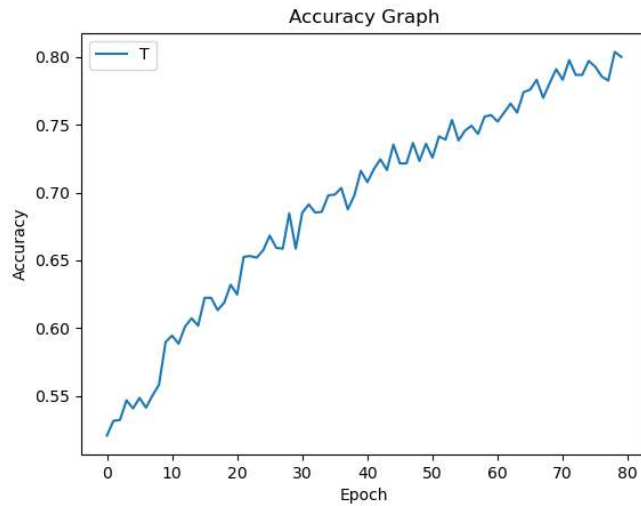
Fig 1: Accuracy Graph of the Model

As seen in Figure 1 above, the accuracy was steadily increasing, and did not stop even at 80 epochs. Although the model could have performed better with more epochs, the risk of overfitting the model was too high. With more images, the current accuracy of the model would increase, and the model can be trained with more demanding parameters as well. The final accuracy is a little above 81%, but the graph is steadily increasing.

Discussion

Car Scratch Detection is one application of this type of algorithm/ research, out of many possible paths. Attempting to remove noise and unnecessary features from the image is a crucial factor in image processing applications. For example, when detecting a specific object in a setting, like a blackboard in a classroom, objects like desks, doors, and cupboards can always be filtered out since the algorithm can be sure that these background objects are not relevant to the success of the algorithm.

The recursive wheel detection algorithm proposed in this study is a specific use case of this concept. It focuses on increasing the accuracy of the algorithm by working on the problem in an organized and dependable framework, instead of relying on a higher percentage of accuracy from a Machine Learning model.

Name	Training Accuracy (%)	Built-in Model (Y/N)
VGG16 (Proposed)	**94**	**Y**
ResNet34	99.4	Y
YOLOv3	77.4	Y

Table 1: Accuracies of Models Compared

The final accuracy turned out to be 94% using the recursive wheel detection algorithm, the VGG16 model, and training it on the dataset mentioned. It outperforms YOLO by quite a bit, but falls short of ResNet[6] due to a lack of images. Currently, the framework has been built based on a 3000-image dataset. To extend its range to greater heights, at least 20-30,000 images are needed to train the model further. Also, the framework does not function well in areas of lower light quality as of now.

Methods

As mentioned earlier, the proposed methodology illustrated the use of a novel computer vision framework to detect scratches or dents on car images. The foundational motivation behind this approach found its roots in the interpretation of these requisite scratches/dents/instances on cars as distinct noise with respect to the images being studied. Thus, these scratches were considered as undulations affected by sharp changes in pixel intensity in an otherwise 'smooth' image. This interpretation was supported by the kind of images within the dataset viz. zoomed-in images of car bodies from a variety of angles and positions with negligible distraction in terms of background content.

Another important aspect considered before proposing an innovative method was existing research on the topic. Within the sub-field of quality control using machine learning and CNNs, there have been some important contributions.

Bruni et. al. (2004) present a generalization of Kokaram's model for scratch lines detection on digital film materials[7]. In the 2010s, these models became more sophisticated and Hyundai Motors' researchers wrote the research paper "Deep Learning-based Car Scratch Detection". Next, the important innovations made were of Jayaseeli et. al who propose employing convolution neural networks to build a Mask R-CNN model that can detect the area of damage on a car[8]. Leveraging these advancements, researchers and engineers have started exploring CNN-based approaches for car scratch detection, aiming to develop accurate and efficient systems that can automate the inspection and assessment process.

A method is conceived that could essentially be thought of as an 'unveiling technique'. i.e., removing all other forms of noise and intensity disparities of the image to leave us with a perfect residue of scratches or dents. The images are converted to grayscale since the ulterior motive is to represent the scratches with maximum clarity against a completely uniform background and then localize it on the original input image, or rather, detecting the scratches on a binarized image.

The dataset used[9] comprised over 3000 images of damaged cars, spanning a wide range of damage types including fine scratches, dents, and major damages. These images are sourced from various sources to ensure diversity in terms of car models, damage severity, lighting conditions, and viewing angles. Additionally, the dataset contains images captured at different zoom levels, encompassing both zoomed-in and zoomed-out perspectives. This diversity ensures that the trained model is robust and capable of accurately detecting and classifying car damages under varying conditions.

Fig 2: Images from the Car Scratch Dataset

Figure 2 consists of sample images from the Samyuktha Mobile Car Scratch Detection Dataset. The four on the left are whole images (without any scratches/ damage) and the ones on the right are damaged/ scratched cars.

Fig 3: Output of a Laplace Transform

A 'LoG' (Laplacian of Gaussian) transformation is what follows[10]. Once the originally colored image is converted to a grayscale one, a level of Gaussian smoothing blur is applied to denoise the holistic image so that minimally sharp and normal structural variations across the make or outer-body design of cars have no long-lasting impact in terms of contributing to false positives being detected later. The Laplacian filter applied next helps in effective and semantic edge demarcation on the car-image, while also representing the intensity disparity or noise elements within each such bounding area defined by the resultant edges. Having applied the Gaussian filter earlier eradicates amplified and redundant instances of noise, and thus the LoG-transformed image leaves us with what could be called an initial set of *'competing candidates'* for the set of scratches to be identified, localized in every mini-region marked by boundaries in the image.

A subsequent morphological opening operation helps us to reduce the set of noise candidates obtained from the LoG output further and effectively filters out the specks of low intensity as can be seen in Fig.

Binary thresholding is then done to promote the 'brightest white' of these noises, the most intense ones with pixel values closest to pure white (255) are found in patches and highlighted in the output mask image, as a resultant detection of the scratched or dented area on the car. To boost the accuracy of scratch detection in terms of definite lines, which are often statistically dense in most real-life scenarios (datasets), a Houghlines detector module is also included so that stray yet significant solitary lines are equally confidently ascertained as scratches by the algorithm((N. Aggarwal and W. C. Karl, "Line detection in images through regularized hough transform," in *IEEE Transactions on Image Processing*, vol. 15, no. 3, pp. 582-591, March 2006, doi: 10.1109/TIP.2005.863021)).

Additionally, utmost precautions, procedures, and efforts were taken to ensure that the data was not biased. The images were taken from a number of different car owners from various socioeconomic backgrounds. The lighting was also diverse throughout the dataset, from extremely bright images (in peak sunlight during the day) to darkly lit images (at night, or with dim/ poor lighting). Also, the quality of the images also differed to make sure that any mobile phone camera worked well with the framework. Finally, the color of the cars was also variant, changing from bright colors like white and yellow, to dark colors such as brown and black. All of these precautions ensured that the model was trained on a diverse dataset, and would not present major biases when confronted with new images.
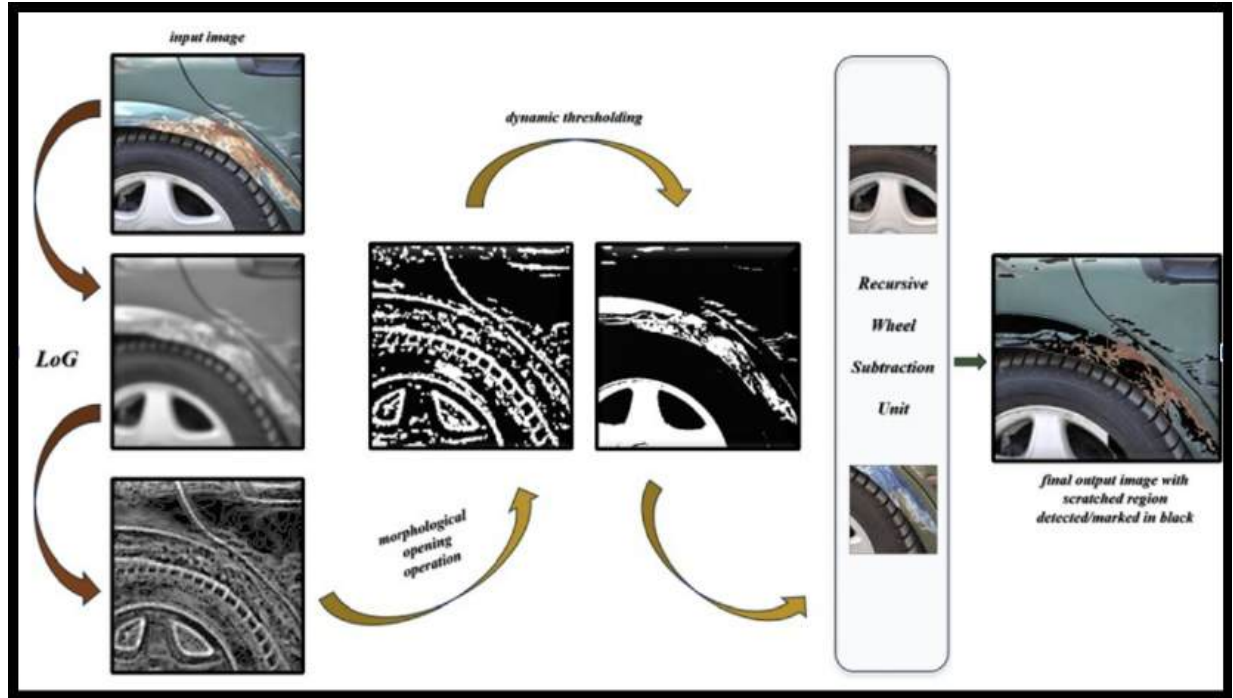
Fig 4: Complete Car Scratch Detection Process

Acknowledgments

Conclusions

In conclusion, this study primarily aimed to create and utilize an efficient computer vision framework to accurately detect scratches, dents, chipped paint, and other forms of damage on the body of a car.

In this study, images with too much light reflected off of them were disregarded from the dataset. This was because of multiple factors, mainly because in a dealership setting, the light environment will be in control. Additionally, since light makes it difficult for even humans to spot scratches on cars, disregarding images with extreme lighting was the right way to go. However, it is suggested that future research be conducted with more diverse datasets as well (in terms of lighting) to ensure that car scans may be conducted in broad daylight as well.

The experimental results showcased the efficacy of the CNN-based approach for detecting and classifying damaged areas on cars. The diversity of the dataset, along with the incorporation of preprocessing techniques, ensured the robustness and generalization ability of the trained model. Additionally, achieving competitive accuracy without pretraining underscored the effectiveness of the proposed methodology.

It will help dealerships make their services more efficient, leading to more customer satisfaction and efficiency. It will be an integral part of the dealerships' system, perhaps even changing the process in such a way that multiple vehicles can be serviced at the same time. Additionally, the recursive car wheel detection system also sets a precedent for other object filtering methods in different areas, not just car scratch detection. Any prediction algorithm can be made more accurate by filtering out unwanted noise and objects, and this study captures this idea perfectly.

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Prewar Inflationary Forces in the Hyperinflation of Weimar Germany
By Dahyun Oh

Abstract

This paper attempted to shed attention to the often ignored early-on contributors to Weimar inflation. Even though the Treaty of Versailles is widely perceived as the determining factor, the wartime factors such as a lack of workforce and low tax rates established an inflationary atmosphere that contributed to the later hyperinflation. This paper explained the buildup by examining the demand-pull inflation, cost-push inflation, and expectations inflation as well as the war effort policies, such as funding military expenditure with loans or introducing conscription in detail in respect to the economic situation of Germany during the war, which led to the conclusion that the inflation, while its extent would differ, would have been inevitable. Nevertheless, this paper also acknowledged the impact of the Treaty of Versailles and the excessive printing of money that took place. In conclusion, this paper emphasized the significance of the pre-existing factors and that the Treaty of Versailles may not be the sole factor that led to hyperinflation of 1921-1923.

Introduction

Following World War 1, hyperinflation consumed Weimar Germany from 1921 to 1923. Many scholars such as Adam Fergusson put emphasis on the Treaty of Versailles, arguing that the high reparations demanded by the victorious parties brought about the over-printing and eventual depreciation of the German Papiermark (Fergusson 4-5). Indeed, the Treaty of Versailles, whose prime objective was to settle peace without triggering the German sentiments for revenge, had been the subject of dispute at the time of implementation (Myerson 195). For example, the renowned British economist J. M. Keynes criticized the treaty for its unrealistic reparations bill and described it as "a Peace which, if it is carried into effect, must impair yet further…the delicate, complicated organization, already shaken and broken by war." However, while it is true that the Treaty of Versailles was burdensome to the Germans, the peace treaty was not the sole cause of the hyperinflation. Rather, inflation in Germany had been heralded before the end of the First World War; with long-term causes of low unemployment rates, reliance on loans, commodity price shocks, and hoarding, inflation to some degree would have occurred in postwar Germany even without the Treaty of Versailles. This paper thus attempts to shed attention to the often ignored early-on contributors to Weimar inflation by examining the demand-pull inflation, cost-push inflation, and expectations inflation.

The German Economy Before and After the First World War

Before the First World War, the German Reich maintained a strong economy. Germany had "a gold-backed currency, expanding industry, and world leadership in optics, chemicals, and machinery" (Goodman). Notably, between 1870 and 1900, its population rose from 41 million to

56 million, coal production from 34 million to 149 million tons, and steel production from 0.3 million to 6.7 million tons (Baumgart 151). Its share of world manufacturing output increased from 8.5% in 1880 to 13.2% in 1900 to 14.8% in 1913, surpassing that of Britain, which was reduced from 22.9% in 1880 to 13.6% in 1913 (Dailey and Webb 13). It was a prime global exporter, ranking second, just behind Britain, exporting textile fabric and yam, coal and coke, and iron and steel. Despite the persistent overall trade deficit, Germany showed increasing trade surplus with its European trade partners (Hungerland and Wolf). The German GDP per capita in 1913, with 3,648 international dollars, was on a par with France with 3,485 international dollars and slightly lower than Britain with 4,921 international dollars (Maddison 382). From the macroeconomic indices presented above, it can be assumed that Germany rivaled European neighbors in economy and international relations. Even in August 1914, one month after the start of the war, Germany had the most powerful and well-equipped military force in the world and could outnumber its enemies in a war; Germany was unmatched by its neighboring powers such as Russia and France, since Russia lacked the industry or transportation system to match that of the Germans and the French military size was only about two thirds that of Germany (Zeller 3-4). When given this information, assuming that Germany was formidable would be tempting.

Expecting its victory, Germany funded its military expenditures with loans during the First World War. Germany planned to recuperate its wartime debts by annexing lucrative industrial regions from defeated nations, collecting financial reparations, and by establishing German hegemony in post-war Europe (Evans 103). Consequently, aggregate debt of the German Reich rose from 5,202 million in 1914 to 104,944 million marks in 1918 (Balderston 227). Yet, contrary to its anticipations, Germany came out of the war defeated and saw no hopes of economic recovery. Eventually, German marks rapidly devalued, with the exchange rate of German marks against the US dollar increasing from 4 marks before the war to 12 marks in April 1919 per dollar (Evans 103). The Treaty of Versailles, whose Article 231 (War Guilt Clause) attributed the cause of the war to Germany, added on to this inflationary energy (Evans 65). Through this treaty, vindictive nations, especially France, demanded territorial confiscation and heavy reparations from defeated Germany. Indeed, the treaty returned Alsace-Lorraine to France, demilitarized the Rhineland, and granted coal mining controls in Saar to France (Fergusson 15). With the loss of these valuable industrial areas, German industrial production decreased by 58% from 1913 to 1919, hindering Germany's ability to stimulate its economy and thus pay its debt (Evans 104). Also, the Reparations Commission set Germany's final liability at 132 billion gold marks in 1921, threatening Germany with the occupation of Ruhr if Germany did not comply (Fergusson 36). Despite these financial crises, the politically vulnerable German government continued printing the marks, because it wanted to avoid criticisms for raising taxes (Evans 104). Any governments who sought to raise taxes were accused of submitting to the Allied reparations demands by their political opponents in the nationalist right (Evans 104). Consequently, the dollar rate leaped to 7,000 marks per dollar by December 1922 (Evans 104). With this unbridled inflation rate, the German government could no longer meet its reparation requirements, thereby leading to the French and Belgian troops' occupation of the Ruhr in January 1923 (Evans 105).

In response to the Ruhr crisis, the German government encouraged passive resistance against the French and the Belgians. The resultant stoppage of workers and factories deprived Germany of its massive earnings from the region and required government subsidy for its 6 million residents (Fergusson 122). While the general strike ended in September 1923, the inflation continued, with 4.2 trillion marks needed for one US dollar by December 1923 (Evans 105). Many scholars such as Adam Fergusson and Carl-Ludwig Holtfrerich argue that, despite the postwar inflationary pressures, the hyperinflationary pressures only started after the Treaty of Versailles and the Invasion of the Ruhr. Nevertheless, such claims seem to neglect the impact of the long-term wartime inflationary energy that amplified the short-term causes which eventually triggered the hyperinflation in the Weimar Republic; the high inflation rates that prevailed in wartime Germany accumulated the stress on the German economy to hinder it from performing normal economic activities after the Treaty of Versailles. Thus, this paper seeks to demonstrate how the pre-existing factors created a condition in which the later hyperinflation could prosper.

Wartime Inflationary Pressures

Inflation is a multicausal economic phenomena in which the general price of goods and services increases throughout the economy—or, in other words, when the general value of money falls (Labonte and Weinstock 2). Inflation can be classified into three types based on their causes: demand-pull inflation, cost-push inflation, and expectations inflation. These three types of inflation were observed in Germany with the outbreak of World War One, after which the German economy rapidly fell into a downward spiral, especially due to macroeconomic mismanagement by the government. Consequently, the German economy was already devastated by the Great War before the Treaty of Versailles, entailing symptoms for the postwar hyperinflation.

Demand-Pull Inflation

Demand-pull inflation happens when aggregate demand increases without a proportional increase in aggregate supply (Labonte and Weinstock 6). Some contributors to demand-pull inflation are low unemployment rates and low tax rates.

Unemployment rates in the German Reich in the final years of the First World War were unparalleled to that before the war. Germany's unemployment rate, which had ranged from 2.7% to 4.7% between 1903 and 1913, plummeted to 1.0% in 1917 and 1.2% in 1918, being the third from lowest and the lowest, respectively, among seven other Western powers (i.e. Australia, Canada, Denmark, Netherlands, Norway, Sweden, and the United Kingdom) (Galenson et al. 455). This low unemployment rate—in addition to reduction in labor force due to over 2 million military casualties and 7 hundred thousand civilian deaths by the end of the war as well as to the sweeping pandemic of the Spanish flu that killed over 260,000 Germans in 1918—would have increased labor scarcity (Hirschfeld, et al; Förtsch and Rösel 1). In addition, although female employment increased by 45.6%—which could be observed as firms attempted to offset the shortage of labor—it could not compensate for the lost male workforce who could not return

from the war, eventually leading to a 10.4% drop in the total workforce between 1913 and 1918 (Ritschl 34). The reduction in the working population would have thus accelerated the competition between firms to attract workers, leading them to compete by offering higher wages. Indeed, the wages of German workers increased significantly during the war. For example, between June 1914 to October 1918, the average hourly earnings of Bavarian workers increased by 225.5% in the war industry (i.e. metals, machinery, instruments, and chemicals), 215% in the intermediate industry (i.e. mining, stone and clay, wood, leather, paper, and building), and by 198% in the civilian industry (i.e. food, brewing, textiles, clothing, shoes, printing, glass, pottery, gas and electric, transportation, and trade) (Bry, *Wages during* 199). It is important to note that the firms' competition for workers through the increase in wages was not limited to the skilled male workforce, but was extended to unskilled male, female, and youth workers. Indeed, in the Magdeburgian metalworking and machinery industry, the average hourly earnings of skilled male workers increased by 147%, unskilled male workers by 121%, female workers by 111%, and youths by 132% (Bry, *Wages during* 198). The Magdeburgian chemicals industry also exhibited a similar trend, but the average hourly wage of female workers increased more extensively than that of skilled male workers, with a difference of 76% points (Bry, *Wages during* 198). This increased demand for skilled and unskilled workforce alike would have further stimulated the competition for labor among firms, which would have attracted the workers through even higher wages. Increased wages would then stimulate the consumers to purchase more, increasing the aggregate demand in the society. Under the law of demand, this increase in aggregate demand will lead to the increase in the price level, thereby resulting in inflation. Therefore, the low wartime unemployment rates generated potential for a postwar inflation in Germany. The decreasing unemployment rates and increasing inflation rates in this case is also outlined by the Phillips curve, which suggests an inverse relationship between the two factors (Hoover). The inverse relations hence denote that the low unemployment rate due to the enlistment of military-aged men is indicative of inflationary pressure.

Furthermore, tax rates in the German Empire during the First World War were very low, despite its status as a combatant nation. German top marginal income tax rate was merely 4% in 1914, at the start of the war when that of Britain was 17% (Piketty 1). Nearing the end of the war in 1918, Germany still exhibited a top marginal income tax rate of 20%, when that of Britain and the US reached 53% and 77%, respectively (Piketty 1). The low tax rate was because Germany, unlike other nations, relied on its loans to finance its war efforts, rather than government revenue from high taxation. The avoidance of high tax rates was both due to the belief that the war would be short and to German central federal government's inability to impose high tax rates to its states. Indeed, in 1914-1919, German tax revenues as a percentage of total government revenue only amounted to 16.7%, while that of Britain reached 26.2% (Balderston 229). In addition, the wartime German monetary base rose more rapidly than the British monetary base, especially due to greater governmental pressure on borrowing from the domestic capital market; from December 31, 1913 to December 31, 1918, the average percentage change per annum for German monetary base recorded 44.8%, compared to 20.2% of Britain (Balderston 237). This

difference is attributable to the British naval blockade of Germany, which cut off German trade with the US and made the German Papiermark seem high-risk to foreign consumers. The vulnerability of the Papiermark hindered Germany from international trade and servicing dollar debts, rendering Germany an unfavorable trade partner (Brown 39). Thus, with insufficient foreign currency financing that came from Switzerland and the Netherlands, wartime Germany was deprived of other options but to print money, especially after they had abandoned their gold-backed currency in 1914 (Brown 39). This increase in money stock, which entailed depreciation of the Papiermark, indubitably brought inflation during the war, with the GDP price inflation rate advancing to 25.2% in 1915, 30.3% in 1916, and 49.0% in 1917 (Zucman and Piketty 1). Although these rates are relatively insignificant when compared against postwar values of 1703% in 1922 and 300,000,000% in 1923, they are huge when compared against the prewar value of 0.6% in 1913 and the modern target inflation rate of 2-3% (Zucman and Piketty 1; *Why Does the*). Hence, it can be concluded that the reliance on loan augured Weimar's postwar hyperinflation.

Cost-Push Inflation

In addition to the demand-pull inflation, cost-push inflation also contributed to the postwar hyperinflation that Germany faced. Cost-push inflation occurs when the cost of production increases without the proportional increase in aggregate demand (Labonte and Weinstock 7). Some causes of cost-push inflations include commodity price shock and shortage of labor, both of which reduce the supply of firms by increasing the cost of production.

Commodity price shock occurred in wartime Germany, particularly due to the British maritime blockade. In 1913, Germany imported the most from the US, Russia, and Britain (Hungerland and Wolf). However, as those nations turned against Germany or as their trade was reduced by the naval blockade, German imports rapidly reduced, dropping by 55% from its prewar levels (*The Blockade of*). In particular, with the intensified British blockade on maritime supply of goods in 1916, German import of foodstuffs and war material collapsed between 1916 and 1918. During the period, German imports of grain dropped from 20063 tons to 7333 tons, flour from 682 tons to 279 tons, and meat from 5778 tons to 260 tons (Ritschl 17). It is unlikely that the situation could have changed, since German-British relations were significantly fractured during the First World War. Truly, Britain had been Germany's biggest export partner in 1913, but their mediatory conference proposals to diplomatically resolve the war in July 1914, shortly before the outbreak of the war, had all been ignored by Germany. Consequently, due to the relentless British naval blockade, Germany experienced severe food shortages during the war despite government efforts to regulate food production and distribution, through means such as price ceilings on foodstuffs and food rationing (Hungerland and Wolf; Ritschl 17-18). At the same time, German imports of copper, tin, rubber, nickel, and cotton were also cut off by the blockade (Zeller 12). Nearing the end of the war, only 4% of the 1,700 prewar spinning and weaving mills, a quarter of oil mills, and 15% of soap production plants remained (Zeller 16). Thus, it is clear that the import shortage radically reduced commodity supplies of all sectors in

Germany. This scarcity would have brought a decrease in quantity supplied when the quantity demanded remained constant, under the premise of *ceteris paribus*, causing the increase in price according to the law of demand; as the products were made more scarce, consumers competed more for it by offering higher prices for the goods and services, thereby uplifting the price of the products. Indeed, the yearly averages of wholesale index numbers in Papiermark in comparison to 1913 levels rose by 5% in 1914, 42% in 1915, 52% in 1916, and 79% in 1917 (*ZAHLEN ZUR* 16). The increase in commodity prices indicates the increase in the cost of production, since the commodities are used as factors of production for firms. The raised cost of production would again engender an increase in the price of manufactured goods, since firms will seek to raise the price of their goods and services to compensate for increased cost of production to maintain their profit. The shortage of labor, which increased the wages, as explained above, would also have added the burden to the cost of production. The increased cost of production would have decreased the aggregate supply, but the unchanged demand would have shifted the price upwards, as consumers who were willing and able to buy the product competed to purchase it. The increasing prices of rye bread (with the addition of wheat flour) exemplifies the situation, since the prices of 1kg of rye bread in Berlin skyrocketed during the war, with annual averages rising by 50% in 1915, 39% in 1916, 43% in 1917, and 75% in 1918, in comparison against 1913 levels (*ZAHLEN ZUR* 34). The consequences of increasing prices, especially of necessities such as food, eventually manifested as the Turnip Winter in 1916-1917, during which female mortality rose by 11.5% in 1916 and 30.4% in 1917 above prewar rates (Keegan 495). In turn, the increase in aggregate price would have contributed to the postwar inflation in Germany.

Commodity price shock in wartime Germany can also be attributed to Germany's mandatory conscription that took place during the First World War, which resulted in reduction of skilled workforce from the German industry. During the war years, government spending on the military skyrocketed, with its share of GDP increasing from 3.20% in 1913 to 15.43% in 1914 and reaching the apex with 59.35% in 1918 (*Military expenditure*). At the same time, military personnel as a share of total population steeply escalated from 1.28% in 1913 to 11.97% in 1918, as a result of conscription of young men, which withdrew about 40% of male labor workforce (Herre and Arriagada; BLUM 1065-1066). This military conscription came from the labor force from other sectors, eventually decreasing the skilled male workforce from industries and replacing it with unskilled male, female, or youth laborers. Consequently, labor productivity dropped, with the employment-weighted estimate of total labor productivity from 1913 to 1918 plunging by 22.3% per employee and by 35.2% per hour (Ritschl 7). Due to this phenomenon, German industrial production further declined. The decrease in industrial output would have increased the scarcity of commodities, thus encouraging consumers' competition for them by offering higher prices. The increase in necessities are manifested through the upsurge in cost of living, which increased by 204% from 1914 to 1918 (Bry, *Wages in* 308). Hence, it is clear that Germany's conscription of males was conducive to hyperinflation.

Expectations

Inflation from expectations, which contributes to the preexisting inflationary pressures, is not to be neglected when discussing the preliminary causes. This phenomenon occurs when individuals change their consumption habits based on their predictions on the economy and can be exemplified by the hoarding of commodities (Labonte and Weinstock 8).

Indeed, with the outbreak of World War One, speculation of price increases by the German civilians rose, consequently upbringing panic purchases and hoarding of staple foods (BLUM 1068). To restrict uncontrolled food prices from those behaviors, the German government introduced food rationing in 1916 and price ceilings. However, these measures proved to be ineffective as they were poorly coordinated. For example, meat and staple food prices were inaccurately calculated, with relatively higher estimation of meat prices than that of staples, resulting in the government's prohibition of grain fodder to livestock to save grain for human consumption, after mere two weeks since the start of rationing (BLUM 1069). Consequently, daily ration shrank to 1,000 calories per person in 1916-17, only nourishing 50-60% of the nutritional needs of an average person (BLUM 1069). The discrepancy between official prices and natural prices created by these means brought in illegal trade of food in black markets, enabling the rich to hoard food and further exacerbating price inflations. Indeed, the respective official prices of rye flour and beef in 1917-18 were 1.85 and 2.80 marks per pound, which had increased from 1914 levels of 0.15 and 1.00 marks; yet, they were relatively insignificant compared to their unofficial counterparts that recorded 4.00 and 4.75 marks (BLUM 1070). These inflated values reflect the limited efficiency of government efforts to prevent inflation and manifest the price expectations' contribution to the postwar hyperinflation in Germany.

The Treaty of Versailles

Despite the contributions of pre-Versailles Treaty factors that occurred during the First World War, it is nevertheless true that the Treaty was the determining factor to the German hyperinflation. The Treaty of Versailles's impact is vividly illustrated by the change in the cost of living, which astoundingly increased by 3730.52% in Germany between 1919 and 1923, belittling the 303% wartime increase between 1914 to 1919 (Bry, *Wages in* 308). Similarly, the comprehensive index of wages per week or per day increased by 101% in Germany from 1914 to 1918, but is also trivialized by the bewildering surge by 33701.8% between 1920 and 1923 (Bry, *Wages in* 307). Hence, despite the preexisting wartime inflationary pressures, the extent of the inflation was far exacerbated by the signing of the Treaty of Versailles and the Invasion of the Ruhr. Nonetheless, the aforementioned long-term wartime inflationary energy amplified the short-term causes which eventually triggered the hyperinflation in the Weimar Republic. The high inflation rates that prevailed in wartime Germany accumulated the stress on the German economy to hinder it from performing normal economic activities after the Treaty of Versailles. For instance, the reduced labor force due to high casualties would have continued to contribute to inflationary pressures after the Treaty of Versailles, since labor scarcity increased. For another

instance, decreased productivity would have also led to shortage in goods and services, increaseing the already high demand due to hoarding. As such, as wartime inflationtary factors perpetuated in the German economy even after the Treaty, it is important to acknowledge their roles in upbringing the later hyperinflation of 1921-23.

Conclusion

From the discussion above, it can be concluded that demand-pull, cost-push, and expectations inflation were long-term causes that contributed to the postwar Weimar hyperinflation to a large extent. Inflation would have been unavoidable due to wartime efforts to uphold the military, regardless of the economic punishment by the Treaty of Versailles or the insensible printing of money to make reparations. Indeed, wartime inflationary trends in victorious nations as well as defeated nations support this thesis, as France, UK, Austria, and Poland saw similar increases in inflation rates from 1914 to 1918 by 30.0%, 20.6%, 13.5% and 66.4%, respectively, when Germany had inflation rates of 17.9% (Lopez and Mitchener 38). They, too, experienced inflation to some extent after the First World War, as the cost of living rose by 69% in Great Britain and 70% in the US from 1914 to 1923; this data further substantiates the counterfactual existence of inflation in Germany without the Treaty of Versailles (Bry, *Wages in* 308). The national concentration on the military for the total war, which characterized the First World War, would have contributed to the prevailing global shift towards inflation that was not limited to Germany. In the final analysis, this paper claims that while the Treaty of Versailles decisively contributed to the Weimar Hyperinflation, the early-on contributors to the inflation should not be neglected.

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Implications of Corporate Philanthropy on Consumers By Ria Patibandla

Abstract

The following research paper attempts to indulge and explore the world of corporate philanthropy and the implications on its consumers. This research is intended to highlight the possible ethical gaps in corporate philanthropy and dissect the possible ways corporate philanthropy is taking a turn away from its true purpose of philanthropy. The research method utilized was second nature including extensive content analysis based on past academic journals integrated with a qualitative analysis from participants of corporate philanthropy.The analysis hints at the reasoning behind the ethical gaps in corporate philanthropy. Our research uses a mixed method approach to understand and analyze the perspective of corporate philanthropy from both local and global corporations. Then we analyze this by understanding consumers' opinions on corporate philanthropy. We combine both to provide an analysis from both sides that represents the current notion of corporate philanthropy in the status quo. We use perspectives from two different types of consumers. We use data set points from both consumers under the age of 18 and consumers over the age of 18 to provide a strategic and thorough analysis of data from different viewpoints. We then utilize data from a different set of corporations to understand the different mentalities of corporations and their perspectives. We notice the differences between corporations who are local and corporations which are global. We then combine both these data sets along with the implications of corporations to understand the perspectives of both sides and combine both together along with some external sources to provide a proper and detailed analysis and result. By combining these different perspectives and sets of data were able to provide a well thought out and developed analysis and results.

Literature review

"With great power comes great responsibility," an oft-quoted phrase, has found resonance in the corporate world. As corporate entities rise in stature and influence, there's an unwritten mandate to contribute positively to society. Enter the realm of corporate philanthropy. Unlike previous eras where charitable acts by companies were occasional, today, philanthropy has become a cornerstone of corporate strategy, inextricably linked with brand identities. Moreover, the ripples of these actions traverse far, influencing societal perceptions and consumer behavior. Drawing insights from numerous scholarly articles, this literature review aims to unearth the intricacies of corporate philanthropy and its overarching implications. As corporate philanthropy develops, the more society notices the benefits that each side is obtaining and the distinction between both is very prevalent. The issue of corporate philanthropy being moral is growing day by day due to numerous reasons. Corporate philanthropy is the act of a company contributing to improving the well-fare of their community usually through donations or funding (Cuypers 2) The very essence of corporate philanthropy has seen a transformation. No longer limited to monetary contributions to select charitable causes, it's been redefined to align with corporate visions, missions, and even business goals. (Cuypers 1) offer an insightful perspective,

presenting corporate philanthropy as a strategic initiative, laced with genuine intentions to foster societal good. However, in this mesh of business and charity, (Hemphill 1) uncover an inherent tension — a constant tussle between the profit motives of a corporation and its societal obligations. Often corporate philanthropy is seen as a benefit to the community, however as the activity develops it is posed as a benefit to the corporate companies and often seen as a method to gain social compassion from its consumers.

The 21st-century consumer is complex. Beyond the quality and price points of products, there's an increasing emphasis on the values a brand represents. (Hemphill 3) dives deep into this evolution, highlighting a scenario where consumers expect corporate entities to be flag bearers of societal change. In parallel, there's a rise of the discerning consumer, as outlined by Carroll and (Lee 5). This consumer segment, while appreciating genuine philanthropic efforts, is quick to call out actions that reek of opportunism, further complicating the philanthropic landscape. 39% of corporate companies on the fortune 500 have participated in corporate philanthropy. This is almost half of America's highest grossing corporations participating in this activity (Lee 5). The motive behind the act of philanthropy should be to promote the welfare of a companies community, however with corporate philanthropy growing many consumers feel it becoming more monetized (Lee 2). This makes consumers question what is the motive behind these companies and their reason for contributing in these acts.

Philanthropic initiatives, while immediately benefiting charitable causes, cast wider societal nets. Delving into the macro implications, (Galaskiewicz 2) illustrates a scenario where corporate-driven community projects ignite civic participation, and in some cases, even shape policy narratives. Such expansive influence, however, isn't without its critics. Figures like (Galaskiewicz 1) caution against an overwhelming corporate influence, arguing for a delineation between profit-driven strategies and democratically decided societal directions. The fact that companies put on through corporate philanthropy can be very beneficial to them and can be a loophole through many ways (Powell 2) States how in 2014 when Tesla was caught being harmful to the environment. They were excused by society only for participating in corporate philanthropy. Another example can be companies using the act of corporate philanthropy as a marketing strategy to attract more consumers to their products by painting a vivid image of them following the "moral code" (Powell 2)

A significant offshoot of corporate philanthropy is its direct impact on brand perception. As elucidated, when consumers identify a brand with positive societal contributions, it often leads to a 'halo effect' — an overall positive brand perception influencing purchasing decisions. But this halo can quickly tarnish. (Muller 1) highlight scenarios where perceived insincere initiatives have led to backlashes, consumer distrust, and even brand boycotts. Whenever a corporation is utilizing the act of corporate philanthropy for their own good it feels as if their consumers are being used which raises the question of morality in the consumers eyes as they feel "used for a capitalist purpose" (Marx 1).

In the epoch of climate change and environmental consciousness, corporate philanthropy has found a new playground — sustainability. (Szocs 2) elaborates on this trend, noting a

convergence of digital consumerism and a palpable tilt toward sustainable, eco-friendly products. In this dynamic setting, corporate philanthropy is not merely an act but an assertion of a brand's commitment to a sustainable future. The downturn on this argument is very contradicting as often companies who advocate on climate change and participate in actions to reduce are the ones who are contributing the most to climate change or contribute a substantial amount (Szocs 2). Depicts how companies can often be very contradicting through their acts of philanthropy and how at least 60% of companies who participate in corporate philanthropy have been accused of contributing to the act which they are "advocating for" (Shaw 1).

  The digital revolution hasn't spared any sector, philanthropy included. Icons of traditional publishing, like The Encyclopedia Britannica, have had to recalibrate their strategies, leaning heavily digital, as highlighted by Cauz (qtd. in "Encyclopedia Britannica"). In such a backdrop, corporate philanthropy too is experiencing a transformation, leveraging digital platforms to amplify reach, engage with younger demographics, and redefine societal impact.
A fascinating sub-segment of corporate philanthropy is 'green publishing.' With the world veering toward eco-friendly alternatives, (Shaw 1) throws light on the challenges within. While digital seems the apparent green alternative, the infrastructure — servers, energy consumption, and e-waste — poses environmental challenges.

  In the commercial cacophony, libraries stand as pillars of knowledge dissemination. Norrick-Ruhl and Vogel shine a light on these repositories of knowledge, showcasing them as models of sustainable knowledge sharing, emphasizing access over ownership, and underlining the essence of genuine philanthropy.

  Corporate philanthropy, in its multifaceted avatars, has become a force majeure, influencing societal trajectories and molding consumer perceptions. Its vast potential is matched by equally significant challenges. The dance between corporate interests, societal welfare, and consumer perceptions continues to evolve, mandating continuous exploration, understanding, and adaptation.

Methods

  This study on corporate philanthropy employed a multifaceted approach to comprehensively investigate the implications of integrating technology. Leveraging a hybrid methodology, surveys were conducted to gather real-time insights from corporate entities actively engaged in philanthropic endeavors. This direct interaction provided invaluable data on the nuances of implementation and its impact on corporate practices. Additionally, a thorough review of existing research papers in the domain of corporate philanthropy and technology was undertaken. By synthesizing insights from both primary survey data and established literature, this study aimed to construct a holistic understanding of the efficiency, scalability, and security effects arising from the incorporation of data into corporate philanthropy. This combination of empirical data and theoretical foundations not only enriched the analysis but also facilitated a nuanced exploration of the complexities inherent in this intersection of technology and corporate social responsibility. We focus on the intercomplexity between corporate philanthropy and their

consumers. To bring this to light through corporations of corporate philanthropy, the best result and analysis stems from a mixed method approach of A qualitative and quantitative analysis. We do this by providing a series of questions to understand how the consumers feel based on their perspectives and experiences with corporate philanthropy. We then analyze this data by comparing it to the corporations responses and their opinions on corporate philanthropy. We use a data set from local and larger corporations to see their motivations regarding corporate philanthropy. We then utilize data sets that are provided from larger corporations online to see the benefit that larger corporations receive from contributing such as increasing reputation, tax exemptions and marketing strategies. We then combine these findings to analyze the perspectives of consumers along with the intrinsic motivations of these corporations both local and larger corporations.

Results & findings

Findings:The overall survey and results of this conducted research depicts the differences of corporate philanthropy between different general groups and different perceptions of their employees. Along with this we have different perceptions from corporations and are also available from corporations who have participated in corporate philanthropy. The overall findings are all significant as they would be utilized to create a combined analysis of all the findings together. We provide a few different layers of our findings. We begin constructing this through consumers' perspective to understand what employees and consumers below think of corporate philanthropy. We then focus on the audience and consumers above the age of 18 which is where we find and have received most of our significant data from our consumers. After this we move onto finding data from corporations. We focus on both local and global corporations. We understand from this process that local corporations are more interested in contributing to their community and how global corporations might have a bigger reach but not a more significant impact. We also understand the different types of corporate philanthropy that most corporations contribute to, by doing so we can understand how these corporations are able to contribute to their communities. We also understand the certain loopholes corporations find that result in them contributing to insignificant work in an overall standpoint. There are multiple ways that corporations can use that result in them providing this work which in turn benefits the corporations as they are able to use the tax receipts and use the idea of corporate philanthropy to gain a moral basis on their ground which is why even though local corporations have a smaller reach their impact is more thorough and significant. By utilizing these sets of data we are able to collectively provide the significant part of our research paper as it offers us the evidence to back up and analyze our hypothesis. We overall find the youth under the age of 18 are less passionate and motivated to contribute to corporate philanthropy and are less likely to be desperate consumers of this act as they have less responsibilities in total. When we look towards consumers and employees above the age of 18 they have more contribution towards corporate philanthropy as they have more responsibilities and are more compassionate towards the cause. The same comparison is present when looking at the corporations itself. We notice how local

corporations have a greater motivation to contribute to and give back to the community. We notice how although local corporations may not have as big of a reach they certainly have a more significant impact as there are limited alternative motives. The notion however alters whenever we focus on larger and global corporations. This is due to the fact that corporations' philanthropy may be compromised by ulterior motives that are not present for local corporations. This results in the idea that although larger corporations may have a larger branch their impact however lacks as they are not thorough with their impact and their activity that they are contributing. When you are looking at overall comparison we notice that the niche we are trying to research lies specifically at the hands of larger corporations.

Figure 1: Under 18 Perception Responses

QUESTION	RESPONSE 4	RESPONSE 5	RESPONSE 6	RESPONSE 7
1.Perception of corporation	Very good and good maintenance.	Good for local corporation status.	Yes, however it could be better to maintain.	Could be better with a better reputation.
2.How could they do better?	Contributing to more meaningful causes.	Not one way in particular.	Consistency would be better overall.	Finding more ways to donate/contribute meaningfully.
3.One thing that they do well in corporate philanthropy.	Consistency with corporate philanthropy.	Creating meaningful contributions even as a local company.	The cause they choose to donate is good.	They donate once a while but could do better.
4. How engaged are you employees in philanthropy	Moderate.	Pretty decent.	Very rare.	Sometimes.
5.How effective is their impact.	Very effective as they are consistent.	Pretty good.	Minimal.	Pretty effective for the amount of contribution.

Figure 1 is a significant factor that contributes to my research as it reveals a multifaceted perception of corporate philanthropy from employees under the age of 18. This chart serves as a powerful statement of the youth's perception and engagement of corporate philanthropy in their workplaces. This chart shows a significant part of my research which shows how a younger audience has less contribution towards corporate philanthropy. We believe this to be because people under 18 have less input of philanthropy as they start to tend to gain a moral basis as they get older. Majority of people who have contributed to or who have experienced the act of

corporate philanthropy are typically over the age of 18 as they have more passion and responsibility when contributing and may also face and find a greater need when being in the position of the consumer.

Figure 2: Over 18 Perception Responses

QUESTION	RESPONSE 8	RESPONSE 9	RESPONSE 10	RESPONSE 11
1.Perception of corporation	Minimal contribution to corporate philanthropy.	Decent contribution to corporate philanthropy.	There is a good amount of contribution to corporate philanthropy.	Only sometimes there is philanthropy.
2.How could they do better?	Contribution to more causes and finding better ways to donate.	Contribute more to places that need help.	Donate to better causes and engage more people.	Do more corporate philanthropy.
3.One thing that they do well in corporate philanthropy.	They engage their employees in philanthropy.	Donate to a good place sometimes.	Get a lot of people to help and contribute.	They do minimal but they donate sometimes.
4. How engaged are you employees in philanthropy	good.	Not much.	Required to participate.	Sometimes I participate.
5.How effective is their impact.	Very good and they are consistent.	Sometimes it can be effective.	It is effective.	They have a good impact.

The chart listed for Figure 2 is very significant to the overall outcome of the research project. The significance behind this figure is the idea that it voices the notion behind the drastic difference in employee perception from a younger generation and an older generation. The above 18 general public has a greater and better perception of corporate philanthropy however the younger generation has a lower engagement. Through this greater engagement we are able to provide a greater data set point and understanding of corporate philanthropy as we would be able to get a perspective from a better viewpoint as these people have had more detailed and significant responses and ideals.

Figure 3: Corporation Perspective

QUESTION	RESPONSE 12	RESPONSE 13	RESPONSE 14	RESPONSE 15
How often do you contribute to corporate philanthropy?	Not often but once a while.	We contribute often.	I contribute a significant amount.	Once a while.
How engaged are your employees?	About half of them.	25-40% will usually contribute.	Usually main employees will help out.	Not very engaged in it.
How significant is your impact?	Our impact varies.	We believe it helps, it is often monetary.	We contribute through acts not monetary.	It helps out sometimes.
Did you increase your brand perception through this?	Yes, we believe more people are interested in our corporation.	Sometimes it increases.	Yes we feel it helps.	I think so.
How interested are you in CP?	Very interested and we hope to repeat.	We are interested.	Very interested.	We help out and are interested.

For this part of the research we gained data from local companies who have participated in corporate philanthropy. Figure 3 has a significant contribution to this research as it provides a perception from the other side of the research question as well. These multiple companies who have participated in this survey have shown their perceptions and have shown that local companies are interested in supporting their community. This provides an analysis to combine with both forms of perceptions through the research question. We understand from this data set point that corporations who are local may not have as great of a reach on their community, however they most certainly have a greater and more significant impact as they are more thorough and hands-on with their work in comparison to global corporations.

Figure 4:Types of Corporate Philanthropy

Figure 5: Types of Corporate Philanthropy

Corporate philanthropy can be different for different corporations. Figure 5 portrays the different types of corporate philanthropy that corporations typically participate in. The graph above is a poignant part of our research as it shows how companies can participate and the different levels of their contribution. It is shown that matching programs are typically the most popular. These programs help us understand the most and the different types of corporate philanthropy as we are able to understand the different layers and contributions that consumers receive.

Conclusion

The importance of research on corporate philanthropy has a significant implication on the overall act. Corporate philanthropy, an act of philanthropy where corporations give back to their community and their consumers, has been on the rise for the past decade. Corporate philanthropy has shown to be beneficial to certain groups of consumers. In this study the researcher aimed to understand the implications of corporate philanthropy through the eyes of the consumer and understand the true motivation behind the corporations acts. From the beginning it was evident that corporate philanthropy has been beneficial however there has been concern regarding corporations' motive behind their contributions.

Corporations have reported that they try their best to contribute to the act of philanthropy. Corporations that have a smaller background often have more local and small scale impact however their impact is more thorough and significant as it is more meaningful and hands on. Bigger corporations have had more monetary contributions however the impact is less significant as there is not a proper system in the distribution of money and after the donation/contribution has been made there is a lack of accountability as it is not as hand on in comparison to local businesses making a more significant impact. The act of corporate philanthropy has also been discussed as a forefront for corporations to increase their reputation. Many large corporations have been in the spotlight for trying to use corporate philanthropy as a tactic to increase their reputation or use as a marketing strategy to attract more consumers. This is especially common with larger corporations as multiple corporations have been shown that they strategically make contributions to philanthropy after a scandal or a loss of attention in the media. This has also raised the question of ethicality when participating in corporate philanthropy as many companies have used it instead of contributing to the act while remembering the cause. Due to this there can be a lack in the actual contribution that the act makes and how much it truly benefits people of the community.

Corporate philanthropy can be shown and displayed in multiple forms. Although the most common form is shown to be through monetary donations various companies have different sectors and ways they contribute to this act. This is a brighter side for corporate philanthropy as for larger corporations acts such as volunteering make a more significant impact as it is more throughout and more significant. In the future this topic will allow us to contribute more to our community and make a stronger shift away from a capitalist community. Throughout the rise of corporate philanthropy as the topic of ethicality has been brought up there has also been significant concerns on the question of capitalistic ideals. Often capitalistic ideals have been shown to be unethical and create a divide between the true purpose of philanthropy. A mutual benefit is not considered an act of true philanthropy as corporations have been seen trying to use this as a ploy to increase their benefits substantially.

The act of philanthropy is meant to be pure with no alternative motive however this is a very significant issue that we deal with. Along with a rise in capitalistic ideals and questionable acts on unethical motives there has also been issues with employee engagement. Often a common form of corporate philanthropy can be shown as volunteering or helping with deeds. Corporations can sometimes require or highly encourage their employees to participate in this act as it is a good form of contributing to the needs of their community. However, sometimes there has been shown to be a lack of interest from employees. We understand that corporations have many different ways in which they can benefit from contributing to corporate philanthropy. Our fear is that their true and intrinsic motivation behind corporate philanthropy is to gain benefits rather than making an impact on their community. Corporations have multiple popular ways in which they can gain benefit, some entailing tax receipts and gaining tax exemptions or to increase their market ground or using this act to increase their moral compass and standing. We see this as whenever corporations contribute to corporate philanthropy they are able to use this as

a tax write off, we have seen multiple corporations use this notion to increase their benefits. Along with this we have also seen corporations use corporate philanthropy as a way to increase their moral compass as whenever corporations are on hot feet they are able to revise their perception by using corporate philanthropy. The acts previously mentioned of volunteering are more significant as they can have a less of a gateway to creating unethical gaps for contributions but when there's a lack of interest and motivation from employees contributing to corporate philanthropy then this act also becomes insignificant as it is not truly beneficial to the consumers or beneficiaries receiving this treatment. These differences can however vary depending on the corporation that is contributing to the act. We notice how local corporations have a great impact on their acts of philanthropy. We also notice how local corporations focus more on service based acts while larger corporations focus heavily on monetary benefits when contributing.

In a conclusive way the true benefits of corporate philanthropy are supposed to lie with the consumers of this act. However as it becomes more popular the philanthropic portion tends to become unmeaningful making it harder for the act to be truly philanthropic. We notice how ulterior motives presenting themselves to larger corporations results in them compromising the true act of philanthropy using it for their own benefit as well. We notice how more local corporations participate in corporate philanthropy in an ethical way without compromising their true motive in this act. The overall impact of corporate philanthropy is aimed to assist and benefit the community that has supported the corporations, when the corporation is acting on philanthropy their acts are hoped to be in a significant way with a true motive of helping and supporting their community and support system.

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Analyzing the Effect of Higher Spending on Research and Development Prior to FDA Approval on the Likelihood of Financial Success for Antineoplastic Drugs
By Prahalad Srinivasan

Abstract

      The drug industry has demonstrated significant growth since the beginning of the 21st century, a lot of which due to the increased development of anticancer (also called antineoplastic or oncologic) drugs. As these drugs can be life-saving, people are willing to pay significant money for chemotherapy or other cancer treatments, making the market for anticancer drugs especially profitable. While existing research discusses the cost of these drugs to the customer, there are major gaps in current scholarly conversation on the research and development (R&D) costs, which we will aim to address. Our study will analyze the effects of increased spending on research and development for antineoplastic drugs on the market with financial success of these drugs, in an attempt to find an association between these 2 variables. Ultimately, the research found that a moderate to strong positive correlation does not exist between R&D costs for antineoplastic drugs and financial success, while also highlighting the necessity for increased transparency within the pharmaceutical industry in order to continue similar research and potentially make predictive models.

Introduction

      With the consistent need for new drugs and treatments, the pharmaceutical industry is undoubtedly one of the fastest growing and most profitable industries in the world. According to a study conducted by Abel Womack in 2016, Generic Pharma companies lead global industries in terms of profit margin with a 30.0% margin, while Major Pharma as well as Biotechnology are close behind with margins of 25.5% and 24.6% respectively (Boczenowski, 2024). Since then, the pharmaceutical market has demonstrated significant overall growth, with a report from IQVIA indicating that the revenue of the global pharmaceutical market has increased from 1.116 trillion USD in 2016 to 1.607 trillion USD in 2023, a 44% increase (Statistica, 2024). These statistics show significant industry growth accounting for the inflation rate of approximately 22% during this time period.

      However, entering the pharmaceutical industry by putting a drug on the market can be a lengthy process, often taking companies 10-15 years to complete while requiring an investment of 100 millions or even billions of US Dollars (Doroshenko, 2024). Prior to putting a drug on the market in the United States, it must be approved by the Food and Drug Administration (FDA). A majority of the costs incurred during drug development is with the final goal of receiving FDA approval to distribute the drug publicly, with these spendings known as research and development costs. The process begins once a molecule of therapeutic potential is identified. At this point in time, no knowledge exists about how it would work as a drug within the human

body. Companies then invest in a molecule by conducting research to understand how it would work as a drug within the human body, a process that involves determining dosages, mechanism of action, comparing it with other already existing drugs, and completing basic testing on animals. Once this stage is complete and the company is sure that the drug they have developed has a place in the market, they are eligible to apply for investigational new drug status with the FDA. After their application is reviewed and approved, they can proceed with clinical trials. The FDA mandates 4 stages of clinical trials, but some developers may choose to conduct more to ensure safety. After the clinical trials are completed and are successful, the developers must then apply for New Drug Approval with the FDA, which allows them to formally put the drug on the market (Lukaszewicz, 2023). A majority of drugs are turned down prior to reaching this stage either because there already exists a very similar drug or because the drug could be potentially unsafe. However, the 10% that do make it to public distribution are already facing a significant loss due to R&D costs, meaning they must first break even before beginning to make profits.

This especially holds true for antineoplastic drugs, or drugs used to control cancer, including chemotherapy drugs, as well as other miscellaneous oncologic drugs which are used to supplement chemotherapy. Due to the severity of all forms of cancer, cancer drug research and development is happening frequently, with developers' capital cost per drug expected to be approximately 1.2 billion USD, according to a study published in 2024 (Sertkaya et al., 2024). The 1.2 billion USD is a higher cost compared to other therapeutic areas, with oncologic drugs estimated to have the 2nd greatest estimated capital cost out of the 14 areas investigated in the study. However, this does not mean that R&D spending is consistent across antineoplastics. A study investigating research and development costs for 10 such oncologic drugs include R&D costs that range from 178.2 million USD to 1.950 billion USD, a difference of over 1.7 billion USD (Prasad & Mailankody, 2017). The significant difference between R&D costs represents unique approaches to the R&D phase by different antineoplastic drug developers, with some choosing to budget spending on R&D to limit potential losses, while others opt to increase R&D spending hoping it will lead to a better drug and hence increased profits. Varying approaches raise the question: Does Higher Spending on Research and Development Prior to FDA Approval Increase the Likelihood of Financial Success for Antineoplastic Drugs?

Literature Review

Search Strategies

Sources for this section were found by searching multiple databases of peer-reviewed published research in order to ensure credibility. The databases searched were academic journals with all published sources undergoing a thorough review process in order to ensure reliability and validity. The key phrases used for the search include: "drug research and development", "cancer drug costs", and "cancer drug revenue".

Overview

Current discussion on the research and development costs and revenue associated with drug development for oncologic drugs as well as for other therapeutic areas exists but only to a certain extent. Researchers have comprehensively studied R&D costs using mathematical models to predict values, while detailed studies also exist with a focus on revenue and sales trends within the pharmaceutical industry. While these both have been studied individually, research published with the aim of connecting both contains certain limitations, making it impossible to draw reasonable conclusions about the effect of increased R&D spending on financial success. Our study aims to fill that gap in existing literature by analyzing an existing dataset to understand if such a connection exists. Prior to compiling and analyzing data, a thorough literature review was conducted, examining the 3 types of existing research on the topic: those focusing on R&D costs, those focusing on drug sales and revenue, and those attempting to connect both within a single study.

Research Focusing on R&D Costs

Existing research with a focus on R&D costs typically aims to predict the costs of the process by compiling data based on previous estimates and studies. The standard baseline definition of research and development costs is considered as the amount of capital invested in the process prior to being granted FDA approval to place the drug on the market, including labor costs, capital to purchase technology and other tools to aid the drug development stage, as well as costs incurred during the clinical testing stage. In this literature review, 2 studies with the sole focus of R&D costs will be examined: "Research and Development in the Pharmaceutical Industry", a review published by Austin & Hayford for the Congressional Budget Office, and "How Much Does It Cost to Research and Develop a New Drug? A Systematic Review and Assessment", published by Schlander et al. in 2021.

The first of the 2 sources, published by Austin & Hayford for the Congressional Budget Office (CBO) of the United States to be used as nonpartisan insight regarding drug research and development costs within the country (Austin & Hayford, 2021). While this study does not focus on answering a specific research question, it describes and analyzes various historical trends regarding research and development costs, which is insightful for our study. Towards the beginning of the analysis, multiple short-term trends regarding the number of drugs approved by the FDA and the amount of money spent on research and development are analyzed. The author found that annual R&D spending is increasing substantially, with total spending across PhaRMA firms going from under 60 billion USD in 2012 to over 90 billion USD in 2019. However, since the number of drugs approved by the FDA has not increased as significantly in recent years, the study determined that increased overall spending on R&D does not necessarily lead to an increase in approved drugs, which could be attributed to drug developers' willingness to spend more money on R&D per project in order to develop a more effective drug. The study also claims that the 3 factors considered when deciding R&D budgets are "anticipated lifetime global revenues from a new drug, expected costs to develop a new drug, and policies and programs that influence the supply of and demand for prescription drugs". Based on this, it is reasonable to

conclude that developers are willing to spend more on R&D due to the exponential increase in drug revenue since the start of the 21st century.

Another finding made by Austin & Hayford's study which remains relevant to our study is through their analysis of retail spending across various therapeutic areas. Based on federally collected data from 2009-2019, oncologic drugs have increased the most in retail spending and as of 2019 have the greatest retail spending out of the 19 therapeutic areas examined, encouraging developers to invest more resources into developing such drugs.

The second R&D based study we will examine in this literature review was also published in 2019 and attempts to answer the broad question "How Much Does It Cost to Research and Develop a New Drug?" (Schlander et al., 2021). The primary research methods used by the authors was literature review, as they used a systematic literature review to gather a database of 22 articles and 45 unique R&D cost estimates for drugs. They then considered various factors to calculate a suitability score which is an individual score for each cost estimate, meant to rate the accuracy of the estimate. Some of the variables they examined for each study include the role of public investment, post authorization R&D costs, variations in regulation and approval time, and variations in the complexity of clinical trials or drug discovery. Each article was given a score for each variable based on the extent to which they considered them, and scores were then compared to determine which studies account too much or too little for a certain factor in R&D costs. While the main findings and conclusions from this study are limited to the understanding that specific estimates over-consider or under-consider factors affecting research and development costs, it is one of the first studies that evaluates the reliability of estimates, and hence is pioneering research to developing a standardized system to estimate drug R&D costs. Such research, while remaining significant, is mostly hypothetical, because many of the actual R&D costs are unknown, making it impossible to understand whether the estimation methods are accurate.

Research Focusing on Drug Revenue

Existing research on drug revenue examines trends and patterns within the pharmaceutical industry including variance in revenue across therapeutic areas and changes over time. Because financial reports of drug development firms can be readily accessed online and often have revenue from individual drugs for each year, studies on drug revenue are conducted often to discover new trends and offer valuable insight to the industry as a whole. The following literature review will analyze one such study, "Trends in drug revenue among major pharmaceutical companies: A 2010-2019 cohort study by Meyers et al.", to understand if any insight can be gained towards this research by examining drug revenue trends.

Meyers and his team examined data from 2010-2019 for the 10 highest revenue generating companies within the pharmaceutical industry in 2010 (Meyers et al., 2022). The data points they gathered included annual revenue for each year for each company and percentage of revenue from oncologic drugs, in order to investigate the trend of cancer drugs becoming a larger part of the pharmaceutical industry. The conclusion they drew about oncologic drugs is

consistent with that of other studies: the revenue generated from these drugs have increased in the 2010s, and will continue increasing. From the 10 companies examined, the cumulative annual revenue from oncologic drugs increased over 70%, while that for all other drugs decreased by 18%, highlighting the growing significance of cancer-curing drugs in comparison to others. The second significant finding of this study is the disapproval of a common hypothesis that "the fall of blockbuster medications would lead to an erosion in global sales". While there were time periods where revenue went slightly downwards or stayed the same, the overall trend in the industry is an increase, due to the profitability of oncologic drugs. The conclusions drawn from this study add significantly to the scholarly conversation about drug revenue by making multiple broad but accurate claims about the industry as a whole, something which we hope to build off of in our study by connecting drug revenue to R&D investments.

Research Connecting R&D Costs with Revenue

The final type of research examined in this review includes those that choose to study both R&D costs and drug revenues together or attempt to find a connection between them. We hope to complete a study similar to this with the goal of drawing an association between both the variables discussed. In this literature review, two such papers will be analyzed: "Research and Development Spending to Bring a Single Cancer Drug to Market and Revenues After Approval" by Vinay Prasad and Sham Mailankody, and "Comparison of Sales Income and Research and Development Costs for FDA-Approved Cancer Drugs Sold by Originator Drug Companies" by Kiu Tay-Teo, André Ilbawi, and Suzanne R. Hill.

The first of the two papers, co-authored by Prasad and Mailankody, is one of the pioneering studies for understanding and estimating exact research and development costs for cancer drugs (Prasad & Mailankody, 2017). Through reaching out to companies, gathering online data, and completing statistical analysis, they were able to determine the most accurate prediction to date of the individual research and development costs required for each of 10 oncologic drugs. While they did not conduct further research on the 10 R&D and revenue values other than basic statistics for central tendency, the data they gathered has served as a valuable dataset for other research papers, with the 10 data points also a part of our data analysis.

The second and final paper discussed in this literature review, "Comparison of Sales Income and Research and Development Costs for FDA-Approved Cancer Drugs Sold by Originator Drug Companies" authored by Tay-Teo et al., is also equally significant to our research, as it aims to answer the same question, but makes large assumptions (Tay-Teo, et al., 2019). They compiled a dataset of revenue and sales values for over 100 oncologic drugs developed and placed on the market in recent years, in order to determine if there is a positive return on investment for these drugs. However, instead of using individual R&D costs for each drug, they chose to assume that the R&D cost for every drug is $648 million, based on the findings of Prasad and Mailankody. While this led them to conclude that there is a positive ROI for oncologic drugs on the market, the results are not necessarily accurate as each drug likely had different research and development costs. Still, the conclusions are of significance as the graph

of revenue over time for each drug showed a logarithmic progression for nearly every drug studied, meaning oncologic drugs have an initial rise in sales and then eventually level up. We hope to replicate this study in a way, while filling the gap in current literature, as we will analyze each R&D value individually in an attempt to find association with the sales revenue of the drug.

Materials & Methods

Study Design

Our study was conducted to determine if there is any association between research and development costs incurred by oncologic drug developers and the amount of revenue they earned from drug sales. The time period for our study is the start of the 21st century, with all drugs discussed being put on the market in the 21st century, even if research and development for some drugs began in the 1990s.

Data Sources

The method used for our study is purely observational and analytical, as no experiments were conducted and all data was already existent. Online searches through databases, published journals, and previous research allowed for a dataset of 14 oncologic drugs to be gathered and analyzed. The data collected for each drug includes the following: research and development costs, total revenue (latest measure), and time spent on R&D. Using these values, Revenue-R&D costs and return on investment per dollar spent on R&D were also calculated. Out of the 14 drugs, data for 10 of them was collected from the study conducted in 2017 by Prasad and Mailankody, which was discussed in the literature review. These drugs were chosen by Prasad and Mailankody because they were the only drugs on the market from the developing company, and hence financial data for research and development was easier to calculate. The data for the other 4 drugs came from multiple data sources. Research and development estimates for 3 drugs (Unituxin, Imfinzi, and Sarclisa) came from an article published by the King's College in London, while similar cost estimates for Keytruda was pulled from an article by pharmaceutical news website fiercepharma. The revenue and time taken for R&D were both collected from yearly financial reports published by the drug development companies of each drug. All revenue costs are accurate to the most recently published financial report on the drug, with missing data filled in using a linear growth estimate (Unituxin). The revenues for the 10 drugs pulled from the study conducted by Prasad and Mailankody were copied over from their study which contained data accurate to 2017 financial reports. After this, more recent financial reports were collected and used to update the revenue for drugs which had not been on the market for a significant amount of time until 2017 (less than 4 years). Some of these drugs became obsolete or were withdrawn during this time, and hence complete data was unavailable.

Statistical Analysis

After R&D costs and revenues were updated for all 14 oncologic drugs based on the system described in the previous section, inflation was accounted for. All monetary values not already updated to 2023 were adjusted for inflation based on the value of the USD in 2023 to increase accuracy. After this, all graphical and statistical analysis to find association between R&D costs and revenue or time spent on R&D and revenue were conducted through Google Sheets and CODAP.

Uncertainty and Assumptions

As the R&D cost data are not mandated to be made public by drug developers, most choose to keep it hidden. Hence, the values published online are all estimates and are by no means fully accurate. However, for the purpose of our study, it was required to assume that these values are accurate. Also, revenue data for some drugs became unavailable after the 2017 measurement done by Prasad and Mailankody, either due to change in ownership of the drug or discontinuation. In this situation, we assumed that the value for revenue measured in 2017 remained accurate, after adjusting for inflation. Another assumption we made is that the drug revenue tapers off after 4-5 years of being on the market. While this does not remain true in all cases, drug revenue almost always follows a logarithmic scale, where growth eventually stops. Hence, we assumed that as long as each drug inspected in the study was on the market for a minimum of 4 years, their revenues can be compared on the same scale, ignoring discrepancies in market time after 4 years. For example, Eculizumab was on the market for 8.8 years at the time of revenue calculation but several other drugs were only on the market for 4.1 years. However, for the purpose of the study, this discrepancy was ignored under the assumption that drug revenue follows a logarithmic scale and the majority of revenue is accumulated over the first 4 years on the market.

Results

Dataset

The dataset used for analysis consists of 13 data points with each of the following variables: Drug Name, Drug Development Company, Research and Development Costs (millions of USD), Revenue, Time Spent on R&D, and year of revenue last updated. All monetary values are adjusted to 2023 inflation rates. From this data, the following were calculated: Revenue - R&D (millions of USD) and return per $ spent on R&D. While the purpose of the study is to focus on an association between R&D costs and financial success, time spent on R&D was later added because data was readily available and could be used to make additional findings. All data values examined can be found in the appendix section, while a consolidated graphical representation of the data comparing research and development costs with revenue is shown in Figure 1.

Figure 1:

Comparison of R&D costs with Revenue for the 13 oncologic drugs examined
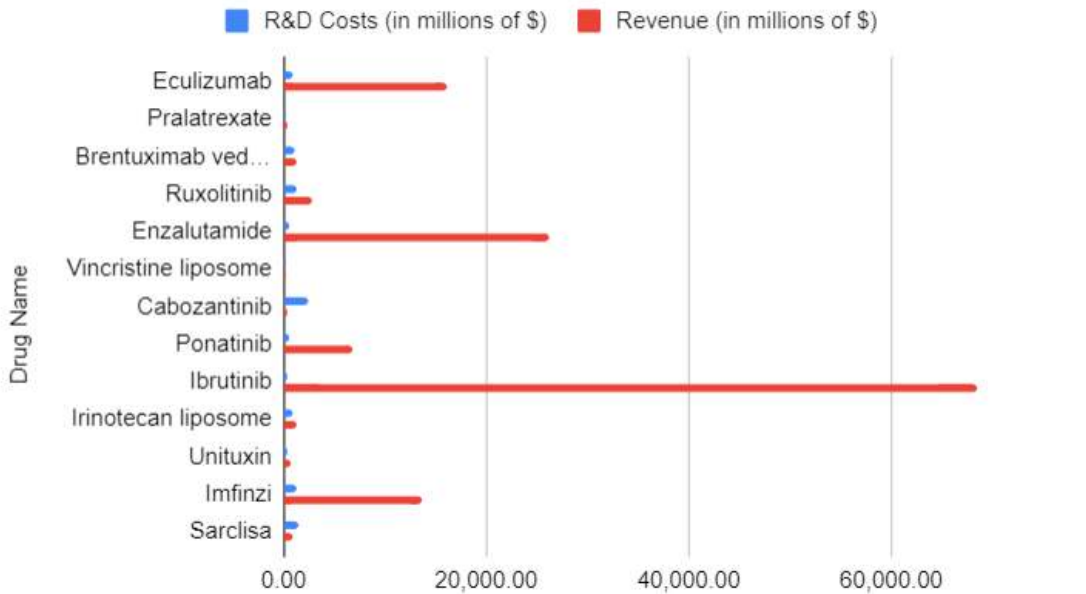
Out of the 14 drugs on which data was collected, Keytruda was excluded due to it being a severe outlier for revenue and R&D costs. Significantly more money was spent on R&D for the drug also leading to a much higher payout. Keytruda was also the most recent drug on the list and Merck is currently one of the most highly valued companies in the industry, likely accounting for the increased values. Removing Keytruda from the data set left 13 values which were then analyzed for central tendencies, variability, and association to determine if increased spending on R&D leads to increased financial success (measured in return per dollar invested in R&D and Revenue-R&D costs).

Central Tendencies and Variability
R&D Costs

Since the data for Research and Development costs for all 13 oncologic drugs under investigation has a coefficient of skewness of 0.8824, indicating a moderate positive skewness, the best measure of central tendency would be median and the best measure for variability would be interquartile range.

From this dataset, the median R&D cost is 1014.1 million USD, higher than the value calculated by Prasad and Mailankody, which is due to the addition of 4 drugs which were manufactured and put on the market at a later date than the first 10 examined in the original study. The median value is a reasonable estimate of the research and development cost to manufacture and put on the market an oncologic drug in 2023. The IQR for R&D costs from the

13 values measured is 1029.855 million USD, the spread between the middle 50% of values in the dataset.

Revenue

Since the data for revenue for all 13 oncologic drugs under investigation has a coefficient of skewness of 2.663, indicating a strong positive skewness, the best measure of central tendency would be median and the best measure for variability would be interquartile range.

From the dataset under study, the median revenue calculated was 1324.12 million USD, a reasonable estimate of the amount of revenue an oncologic drug earned in a time period of 4-8 years before 2023. Assuming a drug spent the median R&D costs and earned the median revenue calculated, the R&D-Revenue would be 310.02 million USD, which is likely on the lower end as multiple drugs took significant losses which skewed the dataset. The IQR for revenue from the 13 values measured is 14327.14 million USD, the spread between the middle 50% of values in the dataset, suggesting extremely high variability in the dataset, 75th percentile-25th percentile has a difference of over 1 billion USD, even though the median is only 1324 million USD.

Time Spent on R&D

Since the data for R&D time for all 13 oncologic drugs under investigation has a coefficient of skewness of 1.823, indicating a strong positive skewness, the best measure of central tendency would be median and the best measure for variability would be interquartile range.

From the dataset of 13 oncologic drugs, the median time spent on R&D is 7 years, with the IQR for the values being 2.8 years.

Return per $ Spent on R&D

Since the data for return/$ for all 13 oncologic drugs under investigation has a coefficient of skewness of 3.283, indicating a strong positive skewness, the best measure of central tendency would be median and the best measure for variability would be interquartile range.

From the dataset of the 13 oncologic drugs, the final value calculated was return per dollar spent on R&D, by dividing the revenue by the cost of Research and Development, allowing all values to be on the same scale for better comparison. The median value from this dataset is $2.05/dollar spent on R&D, indicating that companies approximately double their R&D costs through revenue in their first 4-8 years on the market. The IQR for return/$ spent on R&D from the 13 values measured is 12.4028667155 USD, the spread between the middle 50% of values in the dataset.

Association

The CODAP platform was used to test for association between variables. The primary variables for which association was tested for were R&D costs and Revenue, R&D costs and Revenue- R&D Costs, as well as R&D costs with return/$ spent on R&D, because these would

allow for the primary research question to be answered. Association was also tested for time spent on R&D with revenue in an attempt to understand the effect of a different variable. For each LinReg estimate, the equation, r value, and r^2 values are noted in order to understand the strength of each relationship. Then, a 2-tailed linear regression GOF test was conducted to determine if the slope is of statistical significance.

R&D Costs vs Revenue

Figure 2:
The Line of Best Fit for R&D Costs vs Revenue
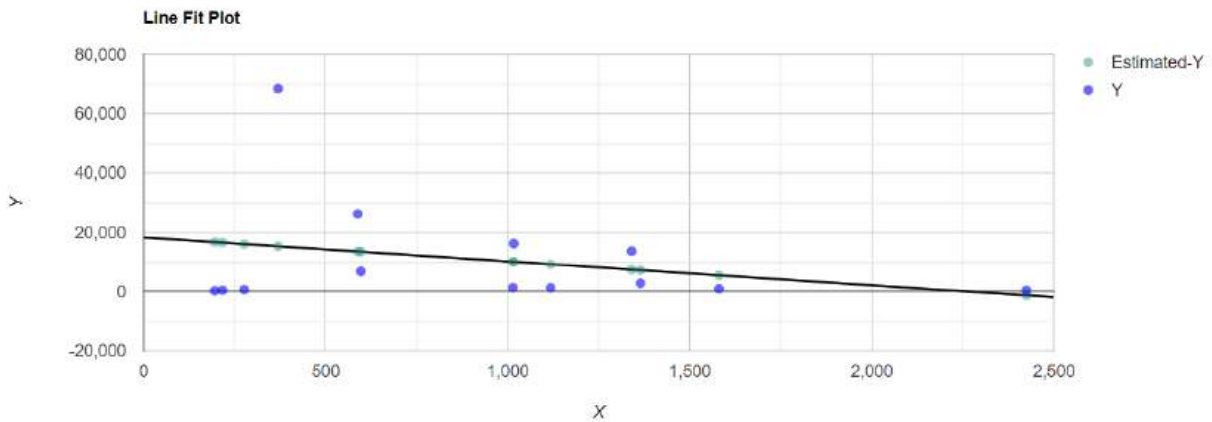
$\hat{Y}$ = 18191.3335 - 8.0399X
r^2 = 0.075
r = -0.2739
The r value of -0.2739 indicates a weak negative correlation between R&D Costs and Revenue for the 13 drugs studied, with the r^2 value of 0.075 indicating that 7.5% of the variability in revenue can be explained by R&D costs.
H0: β_1=0; no linear relationship between x and y
Ha: $\beta_1 \neq 0$; significant linear relationship between x and y
α = 0.05
p = 0.3653 for 2 tailed test
Since p > 0.05, we fail to reject the null hypothesis that there is no linear correlation between R&D Costs and Revenue.
R&D Costs vs Revenue - R&D Costs

Figure 3:
The Line of Best Fit for R&D Costs vs Revenue - R&D Costs
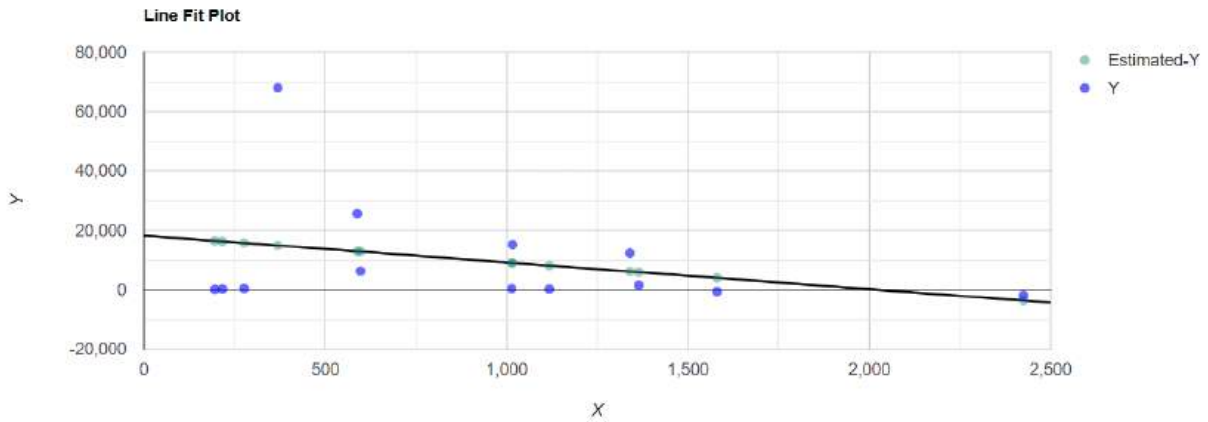
$\hat{Y}$ = 18191.3335 - 9.0399X

r^2 = 0.09297

r = -0.3049

The r value of -0.3049 indicates a weak negative correlation between R&D Costs and Revenue - R&D Costs for the 13 drugs studied, with the r^2 value of 0.09297 indicating that 9.297% of the variability in Revenue - R&D Costs can be explained by R&D costs.

H0: $\beta1$=0; no linear relationship between x and y

Ha: $\beta1 \neq 0$; significant linear relationship between x and y

α = 0.05

p = 0.3111 for 2 tailed test

Since p > 0.05, we fail to reject the null hypothesis that there is no linear correlation between R&D Costs and Revenue - R&D Costs.

R&D Costs vs Return/$ spent on R&D

Figure 4:
The Line of Best Fit for R&D Costs vs Return/$ spent on R&D
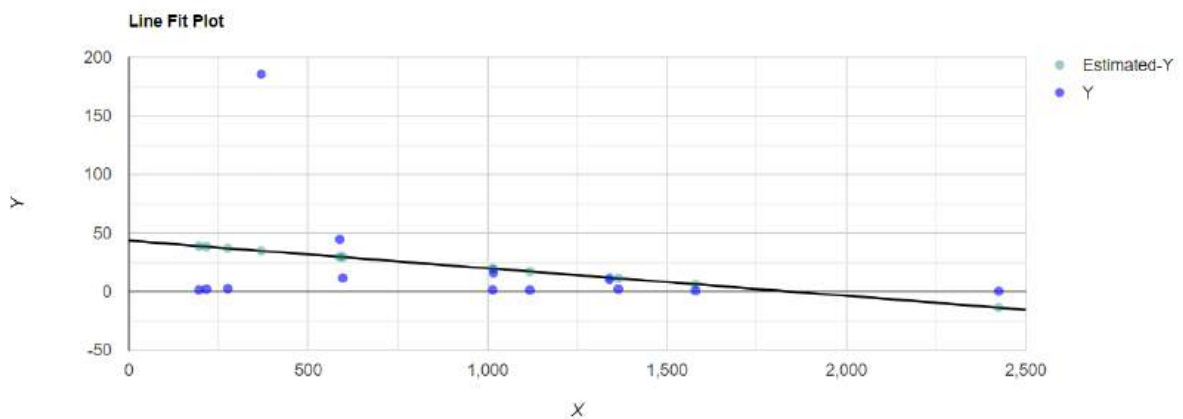
Ŷ = 43.3422 - 0.02357X

r^2 = 0.09131

r = -0.3022

The r value of -0.3022 indicates a weak negative correlation between R&D Costs and Return/$ spent on R&D for the 13 drugs studied, with the r^2 value of 0.09131 indicating that 9.131% of the variability in Return/$ spent on R&D can be explained by R&D costs.

H0: β1=0; no linear relationship between x and y

Ha: β1≠0; significant linear relationship between x and y

α = 0.05

p = 0.3156 for 2 tailed test

Since p > 0.05, we fail to reject the null hypothesis that there is no linear correlation between R&D Costs and Return/$ spent on R&D.

Time spent on R&D vs Revenue
Figure 5:
The Line of Best Fit for Time spent on R&D vs Revenue
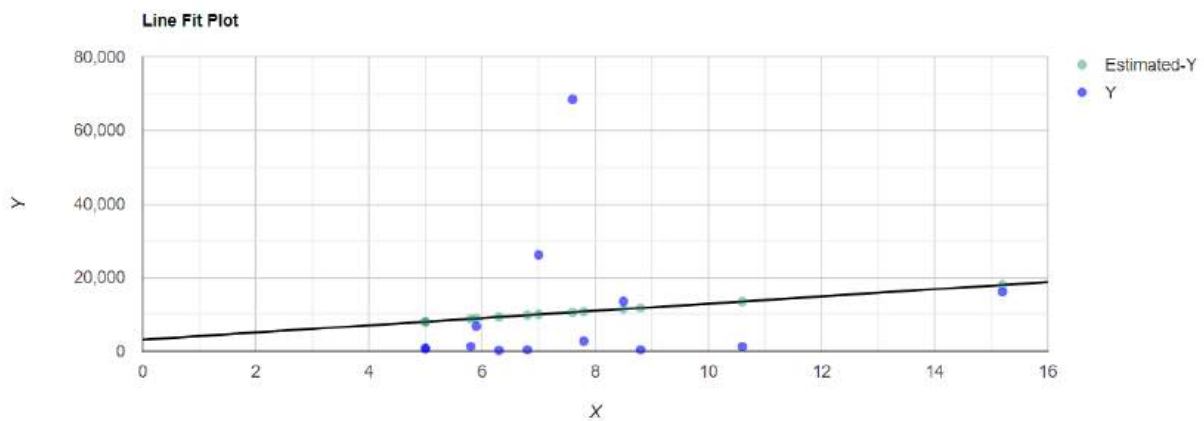
Ŷ = 3141.2455 + 980.7605X

r^2 = 0.02003

r = -0.1415

The r value of 0.1415 indicates a very weak positive correlation between Time spent on R&D and Revenue for the 13 drugs studied, with the r^2 value of 0.02003 indicating that 0.02003% of the variability in Revenue can be explained by Time spent on R&D.

H0: β1=0; no linear relationship between x and y

Ha: β1≠0; significant linear relationship between x and y

α = 0.05

p = 0.6447 for 2 tailed test

Since p > 0.05, we fail to reject the null hypothesis that there is no linear correlation between Time spent on R&D and Revenue.

Summary

After analyzing linear regression lines for each of the 4 associations discussed above, each of them failed to reject the null hypothesis that there is no association between the 2 values observed. All 3 associations between R&D costs and a measure of financial success indicated a weak negative correlation with each having a p-value of approximately 0.3, meaning there is not enough convincing evidence to prove that there is a correlation between R&D spendings by oncologic drug developers and and financial success (Revenue, Revenue - R&D Costs, and Return/$ spent on R&D). The same conclusion was drawn when Time Spent on R&D was compared to Revenue, as a very weak positive correlation was observed with a p value of over 0.6, failing to reject the null hypothesis that there is no association between Time Spent on R&D and Revenue.

Discussion & Conclusion

Our study seeks to determine whether increased spending on research and development for oncologic drugs correlates with greater financial success for the drug on the market. After examining previously published studies on the topic, it is to our knowledge that no current research examines an association between R&D Costs and Revenue statistics for any group of drugs. By analyzing a diverse dataset with the R&D costs ranging from as low as 195.54 million USD to as high as 2424.99 million USD, various approaches to research and development spending were accounted for. The drugs examined also experienced varying amounts of financial success, with the revenue values examined including values from 253.71 million USD to 68423.86 million USD. Finally, the data was collected from drugs put on the market as early as 2009 (Eculizumab) to as recent as 2021 (Sarclisa) while being adjusted for inflation, meaning the data accounts for various time periods and market trends while also being comparable on the same scale. These characteristics of the dataset allow for broader generalizations to be made that could accurately reflect all oncologic drugs on the market

Our analysis, while being the first to examine the specific relationship between R&D costs for oncologic drugs and financial success, builds off prior scholarly conversation. Previously published studies aim to predict R&D costs for cancer drugs individually or aim to connect R&D costs and financial success by making broad generalizations that do not accurately reflect R&D costs of individual drugs (see literature review). Our study aims to address this existing gap in current literature and inform the ongoing scholarly conversation about oncologic drug research and development costs.

Findings

Conducting data analysis for central tendencies and association allowed for several valuable findings to be made. The median R&D cost for the dataset of 13 oncologic drugs is 1014.1 million USD, while the median revenue was calculated as 1324.12 million USD. Given this dataset has been updated to include more recent values and was adjusted for inflation, these are reasonable estimates for how much it costs to develop a new oncologic drug as of 2023 and how much revenue one can expect from the drug during its first 4-8 years on the market.

However, these estimates are likely on the lower end for both values, as the oncologic drug industry is constantly growing, meaning more money will be required for R&D in the future, but a higher revenue can also be anticipated.

Linear correlation tests were also conducted for 4 pairs of variables as discussed in the results section. Weak, negative correlation was found for all 3 pairs of variables that compared R&D costs with a measure of financial success. While the p-values for each of these 3 linear regression tests were above the alpha value, failing to reject the null hypothesis, the analysis from our paper contrasts common belief that increased spending on R&D yields higher financial success for oncologic drugs, as there is strong evidence that there does not exist a moderate to strong positive correlation between any of the 3 associations examined. The lack of association could be attributed to a myriad of reasons, including quality of researchers, therapeutic potential of the molecule being studied, and type of cancer for which the treatment is intended for.

Implications and Future Directions

The findings made in our study allow for a major gap in current scholarly conversation about R&D costs to be filled and can be used as a backbone for future research. In the short term, the finding that a strong positive correlation likely does not exist between R&D costs of oncologic drugs and financial success could inform drug development companies to take a more controlled and analytical approach to spending during the R&D phase. Our study could also be a driving point for smaller drug development companies with limited resources to enter the market should they believe they have a drug with significant oncologic potential, knowing that larger companies with significantly more resources are not necessarily at an advantage. In the long term, this is the first step to potentially predicting the financial success of an oncologic drug, something which could be done with more time and resources by examining a myriad of variables along with implementation of a machine learning model. Creating such a model would also require significantly more data points for R&D costs to be made public by drug development companies.

Future research to be considered in the short term involves further analysis of the 13 data points examined, which could be done by sorting the data through a categorical variable such as development country or number of other drugs developed by manufacturer.

Limitations

The most significant limitation of our study is undoubtedly the small dataset used for analysis. The small dataset was one of the contributing factors to a large p-value, with less than 10% of all oncologic drugs available on the market being accounted for. Unfortunately, R&D costs are not readily made available by drug development companies, the primary factor leading to a small dataset being examined, highlighting the need for further transparency within the drug development field, specifically on R&D costs. These costs are accurately recorded for internal use, but making it accessible to researchers would allow for significant findings within the field,

including improvement of our study as well as the creation of a predictive machine learning model for the financial success of drugs.

Conclusions

   Overall, the findings in our study allow for multiple significant conclusions to be made. First, it is clear that based on the data points observed that there is not a moderate to strong positive correlation between R&D costs and financial success, valuable information with potentially significant implications to the drug development industry. Secondly, it is clear that more transparency is imperative for future studies regarding R&D costs and financial success. While this analysis was conducted with a small dataset, access to a more thorough dataset could be used to test existent theories while opening up a myriad of possibilities for future research.

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Appendix

Table 1

Detailed Statistics for all 14 drugs for which data was collected

Drug Name	Pharma Company	R&D Costs (in millions of $)	Revenue (in millions of $)	Revenue - R&D ((in millions of $)	Time spent on R&D	return per $ R&D	year till revenue	Additional Notes
Eculizumab	Alexion Pharmaceuticals	1,016.34	16,144.78	15,128.44	15.2	15.88521558	2017	>4 years on market
Pralatrexate	Allos Therapeutics	216.23	428.1	211.87	6.8	1.979836285	2018	updated with 2018
Brentuximab vedotin	Seattle Genetics	1,117.77	1,285.71	167.94	10.6	1.150245578	2017	>4 years on market
Ruxolitinib	Incyte Corporation	1,364.65	2,798.78	1,434.13	7.8	2.050914154	2017	>4 years on market
Enzalutamide	Medivation	588.35	26,189.43	25,601.08	7	44.5133509	2017	>4 years on market
Vincristine liposome	Talon Therapeutics	195.54	253.71	58.17	6.3	1.297483891	2017	no additional data
Cabozantinib	Exelixis	2,424.99	425.01	-1,999.98	8.8	0.1752625784	2017	>4 years on market
Ponatinib	Ariad Pharmaceuticals	596.8	6,784.57	6,187.77	5.9	11.36824732	2017	>4 years on market
Ibrutinib	Pharmacyclics	368.94	68,423.86	68,054.92	7.6	185.4606711	2021	updated to 2021
Irinotecan liposome	Merrimack Pharmaceuticals	1,014.10	1,324.12	310.02	5.8	1.305709496	2017	approval withdrawn by FDA
Unituxin	United Therapeutics	276	658.4	382.4	5	2.385507246	2023	
Imfinzi	AstraZeneca	1340	13596	12256	8.5	10.14626866	2023	
Sarclisa	Sanofi	1580	894	-686	5	0.5658227848	2023	
Keytruda	Merck	46000	101601	55601	9	2.208717391	2023	

Note. Keytruda was excluded from the study for analysis purposes as it was a strong outlier

A Review of The Man Awakened from Dreams: One Man's Life in a North China Village 1857-1942 by Henrietta Harrison By Sophia Peng

The Man Awakened From Dreams by Henrietta Harrison documents the life of Liu Dapeng from his early years as a student studying for the provincial examinations to his death eventually as a farmer. Liu is far from your "generic" biographical material; he never came to national power, his ideology was never circulated antemortem, and the trajectory of his life was not unlike the majority population of China during his time. However, it is precisely these that Harrison takes advantage of to show readers, in complexity, the average life during an extraordinary era. Harrison writes the biography referring to Liu's fifty years' worth of diary entries through which we see the collapse of the Qing dynasty, the Boxer Rebellion, the subsequent rise of the Kuomintang and the Chinese Communist Party, the tensions between the two parties, and eventually Japanese occupation. All the while, we see Chinese government and society detach from Confucian ideology and eventually turn to modernization through the eyes of a man who stays loyal to his Confucian ideas. I highly recommend this book - Harrison's holistic but extremely helpful rendition of biography; not only did I feel somewhat emotionally attached to Liu Dapeng and was able to read the book for pleasure, I was also able to analyze uncurated aspects of China during the country's most transformative, and possibly most controversial era. On the observation deck of Liu's life, readers see and get to weigh out how far Liu's unyielding Confucianism takes him, and how much it drags him behind. In China's modernization, corruption becomes commonplace. The tension between morality and corruption in relation to commerce and personal wealth is an apparent throughline of the achronological biography. Mirroring Harrison's holism, I will indicate deficiencies I see in the book to divulge also the positive attributes that the book possesses which delineate my recommendation.

Harrison does not narrate the life of Liu in chronological order. Rather than following a fluid progression of Liu's life, Harrison jumps back and forth between certain experiences to highlight different themes including education, filial piety, local politics, business, and farming, causing a narration lined with periodic repetition. There are times where Harrison retells experiences with no additional information or input. With this said, if repetition is a compulsory coupling with the achronological structure of the biography, it is imperative that the latter is not to be forfeited. It is the very structure of the biography that allows readers to perceive Liu's life from an "observation deck." Readers observe Liu's life from afar and not from within; we are able to view Liu's life in full before actually finishing the book. In this way, Harrison sets readers up for analysis throughout the book instead of after it. For example, Harrison does not point out explicitly the tension between morality and money until the fifth chapter. But because one is constantly brought back to earlier and later points of Liu's life where that tension played a role, they are able to identify immediately that the theme of "morality versus money" would be a booklong, or rather, "lifelong" throughline. The achronology can also serve emotional purposes.

In moments where Harrison explains Liu's desire for influence and power, or his deep trust that his reputation will be able to sustain his family, readers follow already aware of Liu's failure for governmental position and eventual inability to sustain his family through business which he originally gained through his Confucian credit. We read Liu's last diary entry knowing he dies five days later, a man ruthlessly left behind by the world around him. The awareness that this biography's shuffled structure brings to readers carries a sort of melancholy so raw and therefore unprecedented in portrayal of modern Chinese history.

At different points in the biography, Harrison introduces and elaborates on "credit" and "corruption" in separate instances, but she does not go in depth on the comparison of the two in terms of the financial benefits. "The Confucian self-presentation of businessmen continued well after such morals had become irrelevant to local government… Trust was essential to commerce… most exchanges relied on credit." (122) Liu was the "businessman" in this instance. Harrison reveals that Liu's trustworthy reputation, which he earns in the village by being a dedicated Confucian, brings Liu financial benefit. In fact, Liu benefits enough from his "credit" to support, though scarcely and for a limited time, his entire family. On the other hand, Harrison does not conceal the benefits of corruption. Harrison also briefly mentions some of the absurd taxation put in place by Chinese warlords. "Ge Rui made a fortune… using registration taxes [and]... accepting bribes… Such behavior was typical of those who came to power in rural areas." (134) After Liu resigns from the coal office after learning about "impossible" tax demands, Ge Rui takes his position. Utilizing the limited authority this position provided, Ge Rui takes advantage of corrupt taxation laws and creates a local monopoly in coal mining. Ge Rui is corrupt, but one can assume that he is able to put more on the table for his family than "the coarsest and cheapest kind of grain," (153) unlike Liu. Harrison never definitively weighs out the financial benefits of credit in comparison to corruption but she gives plenty of suggestive detail. Ge Rui most likely ends up leading a much more comfortable life, until the cultural revolution at least, than Liu who barely scrapes by and is unable to provide his younger son education due to lack of funding. Liu is punished for being "moral" and not circulating corruption. However, the question arises of what *is* truly "moral?" In Confucian China, "benevolence," "duty," and "filial piety" define "moral." Modernizing China is almost completely detached from Confucianism and does not allow for these Confucian principles to coexist. Liu serves as evidence. Refusing corruption leads Liu to poverty and inability to support his family, failing his duty and filial piety. "[Liu] was aware that life as a farmer was not what his parents had hoped for him" (143) With this said, are Liu's actions truly "moral?" On the contrary, is Ge Rui completely "immoral" for utilizing corruption in order to support himself and his family in a time where there is virtually no other way to obtain wealth? Is the comparison between Liu and Ge Rui still a matter of good or bad, or is it simply the difference between traditional morality and new society?

Although hardly a criticism, Liu's life through Harrison sparks more questions than it answers. In addition to the questions of what morality truly is, other questions of morality strike me in relation to Lu Xun's writing. There is an unmistakable resemblance between Liu Dapeng and Lu Xun's Kong Yiji. An undying aspiration to gentry status via examinations, a Confucian

commitment to education, which fails indefinitely. Reduced to poverty, left behind. Lu Xun's writing, for a century, has been curated to circulate Mao's ideology: the idea of erasing the old, in this case Confucian China, and embracing the new. The story of Kong Yiji is taught to criticize the foolish obstinacy of a Confucian scholar who instead of becoming a helpful member of society, does nothing but read all day aspiring to an opportunity which has already passed him by. Transplanting Liu Dapeng in Kong Yiji's place brings questions as to what or who Lu Xun truly meant to criticize. Could Lu Xun have meant to criticize the feigned Confucianism, like that performed by Liu's classmates at the Academy instead of the actual Confucian principles? Perhaps Lu Xun never meant to criticize Confucianism but rather the modernizing society - through the mocking laughter and bullying directed at Kong Yiji, Lu Xun illustrates the sad reality of modern disrespect for education. Liu Dapeng's story gives power to see vastly differing interpretations of the very loudspeaker of Mao's ideology.

At times, Harrison mentions extreme circumstances of others but does not go further in depth and give readers insight on how these circumstances affect the psyches of the people affected. For example, Harrison briefly mentions profound gender inequality and the correlated high death rates of women due to factors such as feet bounding, eating customs, etc. As Harrison bases the biography off of one life, deeper understanding of other groups of people is not as accessible.

It is important to note that elaborating on each critique does not signify and rebuttal, instead it is to highlight what I believe to be evidence of complex decision making by the author and to appreciate the questions that Harrison's language brings up for readers and leaves unanswered; which is powerful and drives curiosity. Liu's entries provide a completely uncurated version of modernizing China, providing unseen details of popular life and opinion, and even provoking doubt in the curated history we've read and giving power to see certain sources in a novel light.

Ebola Zaire: A Literature Review and Suggestions for An Effective Treatment
By Venkata Siddharth Pendyala, Pranav Kokati, and Srijan Cherupally

Abstract

Ebola Zaire, a virulent filovirus, and member of the *Ebolavirus* genus, poses significant public health risk given its high lethality and severe clinical presentation. Ebola Zaire was identified in 1976 in the Democratic Republic of Congo and has undergone multiple outbreaks, including a devastating outbreak in 2018. Ebola Zaire transmission occurs most frequently through direct contact with infected body fluids and is associated with unsafe healthcare practices and animal reservoirs, particularly bat species. The clinical presentation of Ebola Zaire transitions from initial non-specific phase symptoms to severe hemorrhagic fever, dehydration, and multiple organ failure. The infection causes immune dysfunction by infecting dendritic cells and macrophages, which reduces antigen presentation and phagocytic function, allowing a wider spread of the virus. Surviving infected patients may experience long-lasting sequelae including musculoskeletal pain and vision problems; mere naked examination shows the virus may remain in body fluids for months. We review the present understanding of the transmission, clinical representation, and pathophysiology of the Ebola Zaire virus along with suggesting the urgent need for treatment and preventable response. The paper further demonstrates the possibilities of treating Ebola Zaire, including interventions such as CRISPR CAS9.

Introduction

Ebola Zaire, a very contagious and deadly filovirus, always risks outbreaks across West Africa. Part of the genus *Ebolavirus*, it is the most brutal of all its relatives, including Ebola Sudan (*Sudan ebolavirus*), the Taï Forest virus (*Taï Forest ebolavirus*), and Bundibugyo virus (*Bundibugyo ebolavirus*) (Al-Tammemi et al.). With advanced antivirals and supportive treatment, the mortality rate is about 50%, yet in certain cases, the case fatality rate can be a staggering 90% (Izudi and Bazunirwe).

Ebola Zaire first appeared in 1976 near a village in Yambuku, Democratic Republic of Congo. According to a World Health Organization bulletin, 318 cases of viral hemorrhagic fever were recorded between September 1st and October 24th, with 280 deaths. In 1995, the virus struck again, this time infecting a 36-year-old male laboratory worker in Kikwit 2 Hospital, Zaire. Laparotomy revealed an abnormally large intra-abdominal hemorrhage, causing the patient to die five days later. Medical personnel caring for the deceased patient reported becoming ill with fevers, headaches, muscle, joint and back pains, and hemorrhages (Muyembe and Kipasa). The virus has since slowly claimed lives in an irregular, unpredictable pattern, with notable outbreaks in years such as 2018 in which DR Congo was hit with 3317 confirmed and 153 probable cases of Ebola, with 2287 deaths (a mortality rate of 66%) (Wadoum et al.).

Transmission and Clinical Manifestations

Ebola is transmitted via blood and bodily fluids such as urine, feces, vomit, saliva, and sweat (Kourtis et al.). Exposure can occur through mucous membranes such as the mouth, inner eyelids, genitals, or open wounds. Transmission of Ebola is also in part due to unsafe medical practices in rural areas, such as reusing needles or not properly sterilizing medical equipment. (Gimm and Nichols). Healthcare workers are exposed to Ebola by entering direct contact with infected patients or handling their contaminated fluids. Several papers have found Ebola antibodies in fruit and insectivorous bat species such as *Eidolon helvum*, *Epomophorus gambianus*, *Rousettus aegyptiacus*, *Micropteropus pusillus*, *Epomops franquetti*, and *H. monstrosus* (Ogawa et al.), suggesting these to be potential natural hosts. The complete collection of natural Ebola hosts and their circulation is still unknown (Leendertz et al.). Within one to four days of initial general symptoms, patients tend to experience high fever and its corresponding symptoms, extreme asthenia, and aching muscles. In certain cases, asthenia can be so severe that it interferes with the ability of the patient to perform even the most basic tasks necessary to maintain their bodies. During this time, white blood cells begin to multiply due to bodily signals from the immune system (Qureshi). A problem with these nonspecific symptoms is that they could easily be diagnosed for a similar ailment, such as malaria, leading to the patient receiving improper or insufficient care. In children, initial symptoms are strikingly like those of measles and meningococcemia (Qureshi), making an accurate diagnosis difficult. The patient will eventually get diarrhea, vomiting (in some cases they may expel black vomit, which is a vile concoction of partially digested blood), abdominal pain, bloodshot eyes, severe bleeding, and rash. Due to the excessive expulsion of fluids from vomiting and diarrhea, the patient will become extremely dehydrated (Qureshi). Natural means of hydration become difficult due to nausea and loss of the ability to swallow. Electrolytes such as sodium, chloride, and potassium are lost in the loss of fluid (Qureshi). Pregnant women are likely to have a miscarriage and are at a higher risk of death and more illnesses.

Survivors of Ebola usually have a controlled cytokine response, as opposed to those who are so unfortunate as to experience a cytokine storm and the responding inflammation and blood vessel damage (Jain and Khaiboullina). Early activation of T-cells (especially cytotoxic cells) has been recorded in some surviving cases (Runa et al.). This is then followed by maintaining an active CD3 T-cell population. Many survivors report a type of post-Ebola syndrome, in which they experience symptoms such as musculoskeletal pain (problems with walking or moving), headaches, eye pain, clear ocular discharge, red eyes, blurred vision, abdominal and chest pain, itching, insomnia, anorexia, flaky skin, nasal congestion, fever, and blisters (Scott et al.). For survivors, Ebola may remain in bodily fluids for up to ninety-one days.

Physiology, Genome & Immune Response

The Ebola virus is composed of a 19-kilobyte negative-sense RNA genome, which encodes seven genes transcribed by the viral RNA polymerase. This RNA genome is encapsulated by nucleoproteins NP and VP30. These nucleoproteins, in conjunction with

proteins VP24 and VP4, contribute to the formation of a lipid bilayer that surrounds and protects the virus particle (Beeching et al.).

The Ebola virus's preferred replication sites are dendritic cells and macrophages. Dendritic cells work as a leadership system for the immune system by detecting antigens and migrating to lymphoid organs to stimulate cellular T-cells and B-cells. By targeting dendritic cells, Ebola disrupts the immune system's ability to retaliate. Ebola targets macrophages for a remarkably similar reason – macrophages are primarily responsible for phagocytosing, which is the process of engulfing and digesting pathogens, dead cells, and debris; by removing the body's ability to obliterate clutter, Ebola effectively creates a clear path to spread through the body (Beeching et al.).

During a viral infection, Ebola can cause a dysregulated immune response consisting of both pro-inflammatory and anti-inflammatory cytokines (Banadyga et al.). Inflammatory responses are key elements especially in asymptomatic patients, as the response might be used to control viral replication and the induction of specific immunity. In survivors, there were significant levels of IL-1β, TNFα, IL-6, MIP-1α and MIP-1β in plasma with proinflammatory cytokines appearing 4-7 days after the infection. Proinflammatory cytokines can sometimes tend to directly inhibit the replication of many viruses, activating the cytotoxic functions of macrophages while initiating different immune responses (Baize et al.).

Novel Applications of Genetic Modification

Ebola virus infects macrophages and dendritic cells via receptors such as NPC1 and TIM-1. There is little current research on the impacts of removing such receptors, but techniques such as RNA-i (RNA interference) or CRISPR cas9 could be used to knock them out, disabling Ebola's entry into the cell. However, this may directly impact the cellular function of dendritic cells and macrophages for antigen presentation and stimulation of T and B-cells.

Instead, we propose to use the dendritic cell as a template for a new, immune cell that has both NPC1 and TIM-1 knocked out (so that Ebola cannot infect it), and a mechanism to release TLRs (toll-like receptors) (Yamaoka and Ebihara), C-type lectin receptors (Jain and Khaiboullina), RIG-I-like receptors (Chang and Kubota), DAMPs (damage-associated molecular patterns) (Ning et al.) and PAMPs (pathogen-associated molecular patterns) (Ning et al.), so that normal dendritic cells may recognize an infection. Creating a new cell allows the immune system to retain all natural abilities, as well as obtain a new warner cell that could identify an infection earlier on and cause T-cell populations to rise significantly. This new cell can be combined with treatments such as corticosteroids, which are anti-inflammatory drugs that are chemically like cortisol (Hogdens and Sharman), a natural anti-inflammatory hormone in the human adrenal gland. This reduces collateral damage left by cytokine storms or pro-inflammatory cytokines, keeping blood arteries intact and preventing excessive hemorrhages. Monopotassium phosphate can be used for replenishing lost electrolytes (Jain and Khaiboullina), and supportive treatments like IV fluids may be implemented for dehydration. Together, this is a complete treatment therapy that may significantly increase a patient's chances of recovery and reduce the side effects

found in post-Ebola syndrome. With this therapy, a computer program that uses anatomograms, machine learning, and Monte-Carlo simulations can be used for a simple predictive modeling of the virus's progression in the body, as well as determining optimal insertion points for multiple drugs. RLHF (reinforcement learning from human feedback) techniques can be used to fine-tune the model and lead to agreement with data points from non-human experiments.

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Sleep Disorders, Symptoms, Causes, Treatment : A Systematic Review
By Satya Chaudhary

Abstract

Sleep disorders develop as a result of interference in the body's sleep-wake cycle. They are pervasive and substantially impair patient's health and well-being. In this research paper, we present a comprehensive review of the taxonomy of sleep disorders, crucial for differentiating between conditions and elucidating symptoms, causative factors, and pathophysiological mechanisms to facilitate appropriate treatment, all to assist medical practitioners in diagnosing and treating sleep disorders within clinical practice. Common sleep disorders exhibit symptoms such as difficulty initiating or maintaining sleep, snoring, or restless legs, and can lead to excessive daytime sleepiness, mood disturbances, and impaired cognitive function. Diagnosis relies on a thorough assessment of the clinical history and an extensive physical examination. In particular cases, referral to a sleep laboratory for further investigation with polysomnography is advised. Treatment for sleep disorders involves implementing a consistent sleep schedule, cognitive behavioural therapy, medications or supplements, and using devices like CPAP. Effective treatment requires targeting underlying co-morbid conditions. Sleep disorders are prevalent and significantly impact an individual's health and well-being. By understanding the taxonomy, symptoms, causes, and pathophysiology of these disorders, healthcare providers can effectively diagnose and manage sleep disorders, improving patient outcomes.

Key Words: Sleep disorders, Neurological disorders, treatment, Stress, Sleep apnea, Anxiety, Restless leg syndrome

Introduction

In the current period, sleep disorders have become increasingly recognized as a critical public health issue, affecting millions of individuals worldwide. The modern lifestyle, characterized by high levels of stress, extensive use of digital devices, and disrupted daily routines, has significantly contributed to the rise in sleep disturbances. Conditions such as insomnia, sleep apnea, and restless legs syndrome are not only common but also have profound impacts on physical, mental, and neurological health. The COVID-19 pandemic has further exacerbated these issues, with many individuals experiencing heightened stress and anxiety, leading to widespread sleep problems.

Sleep disorders affect a significant portion of the US population, with about one third experiencing trouble sleeping annually, totalling approximately 50 million adults. Around 10 million seek medical help each year, with over half receiving prescriptions for sleeping pills (Hauri et al.).

Recent studies have highlighted the complex interplay between stress, anxiety, and sleep, and their collective impact on neurological disorders (Paliwal et al.).Stress and anxiety are known to exacerbate sleep disturbances, which in turn can worsen neurological conditions,

creating a vicious cycle that impairs overall health and well-being. Furthermore, sleep disorders such as insomnia, excessive daytime sleepiness, and parasomnias, including nightmares, are commonly observed in patients with neurological diseases (Garza-Ulloa) (Shah et al.).

Sleep deprivation significantly impacts human health, contributing to neurological disorders like dementia, Alzheimer's, and Parkinson's disease. It impairs brain functions, disrupts the immune system, and could lead to substantial healthcare and economic burdens if not addressed (Bishir et al). The regulation of sleep and wakefulness involves intricate autonomic processes that are often disrupted in neurological disorders, leading to significant sleep disturbances (Pavlova et al.). This disruption can have profound implications for the pathophysiology of various neurological conditions, further underscoring the need for comprehensive research in this area.

Furthermore, Sleep is crucial for brain health, supporting recovery, memory consolidation, and overall well-being. Allowing neurocritical patients to sleep is essential for their recovery, as sleep supports brain healing and memory formation. Noise reduction techniques can improve sleep quality, but sleep disturbances often remain overlooked, potentially contributing to higher morbidity and mortality (Siclari et al.).

This review aims to synthesize current research on the interconnections between sleep disorders and neurological health, exploring the underlying mechanisms, clinical manifestations, and potential therapeutic interventions. By examining a diverse array of studies, we seek to provide a comprehensive understanding of the role of sleep in neurological disorders and offer insights into future research directions and clinical practice improvements.

Year	Author	Title	Merits	De-merits
2020	Bishir et al.	Sleep Deprivation and Neurological Disorders	Comprehensive review on sleep deprivation impacts, Addresses neurodegenerative disease links, Highlights molecular and biochemical alterations	Needs for more empirical data, Generalizability of finding, Complex explanations of biochemical pathways
2020	Siclari et al.	Dreams and nightmares in healthy adults and in patients with sleep & neurological disorders	Provides insights into dream physiology, Research has diagnostic value	Complex explanation provided for dream mechanism; Limited generalizability provided
2020	Maestri et al.	Excessive daytime sleepiness and fatigue in neurological disorders	Comprehensive coverage of topic, Recommendations for individualized treatment, Integration of lifestyle interventions	Varied treatment efficacy, Need for more specific data, Complexity in diagnostic approach
2024	Paliwal et al.	Consciousness, Intensive Care, and Sleep: An overview	Promotion of noise reduction techniques, Focuses on sleep's role in recovery,	Lacks immediate outcome evidence, Complexity in

		of neurological disorders	Advocacy for sleep in neurocritical care	defining sleep, Unclear impact on mortality
2021	Mayer et al.	Insomnia in neurological diseases	Detailed information about insomnia, Clinical recommendations mentioned	Recommendation is very general and can affect varied outcome, Limited detail on treatment options
2018	Fink et al.	Autonomic regulation during sleep and wakefulness: a review	Focuses on neurological disorders, Large scope related to sleep disorders	Provides limited clinical applications, Review is complex and meant for specialized people
2021	Yin et al.	Sleep Disturbances in autoimmune Neurologic Diseases	Coverage of sleep disorder concept is wide, Has clinical relevancies, Focuses on emerging topic	Does not provide backing data/ insights, Not practically implemented
2020	Tiseo et al.	Migraine and sleep disorders: a systematic review	Provides recent biochemical insights, Informs combined treatment strategies, Detailed systematic review	Needs more empirical data, Provides limited understanding of proposed mechanism
2018	McDermott et al.	Sleep disorder and risk of stroke	Addresses the major health concern well, Provides detailed classification of sleep disorders, Identifies novel risk factors	Limited conclusive evidence, Uncertainty on non-apnea disorders

What are sleep disorder?

Sleep disorders encompass difficulties related to the quality, timing, and duration of sleep, leading to daytime distress and functional impairment. These disorders often coincide with medical ailments or psychological issues like depression, anxiety, or cognitive disorders. Various types of sleep disorders exist, with insomnia being the most prevalent. Additional examples include obstructive sleep apnea, parasomnias, narcolepsy, and restless leg syndrome.

Challenges with sleep are associated with both physical and emotional issues. They can either contribute to or worsen mental health conditions and may serve as indicators of other psychological disorders.

Types of Sleep disorder:
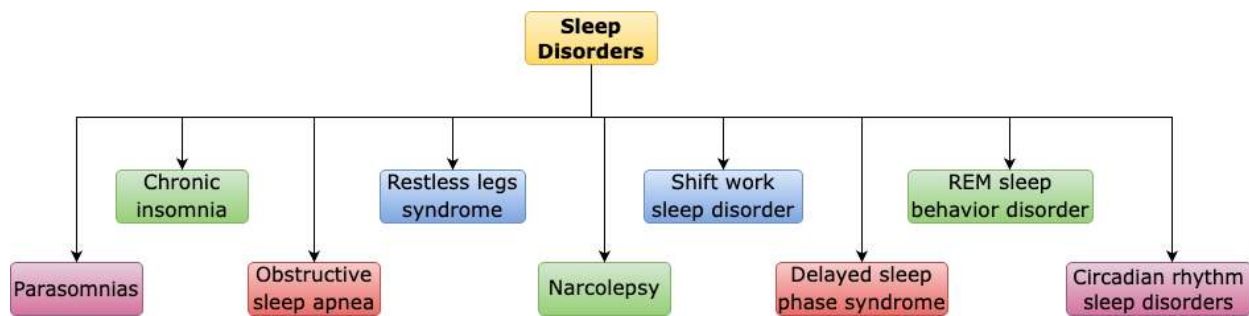
Fig 1: Common types of sleep disorders

There are several types of sleep disorders, common disorders are represented in Fig. 1, each characterized by distinct symptoms and impacts on sleep patterns and overall well-being. The most common sleep disorders are:

Chronic insomnia is marked by persistent difficulty falling asleep or staying asleep, typically occurring at least three nights per week for a minimum of three months. This can lead to feelings of fatigue, irritability, and impaired daytime functioning.

Obstructive sleep apnea involves episodes during sleep where breathing stops momentarily due to the relaxation of throat muscles, often accompanied by loud snoring. These interruptions can disrupt sleep and lead to daytime sleepiness and other health issues if untreated.

Restless legs syndrome is characterized by an irresistible urge to move the legs, often accompanied by uncomfortable sensations, particularly when resting or lying down. This can significantly disrupt sleep quality and contribute to daytime fatigue.

Narcolepsy is a neurological disorder where individuals experience uncontrollable episodes of sleep during the day, regardless of circumstances. This can lead to sudden and unpredictable bouts of sleepiness, potentially affecting daily activities and safety.

Shift work sleep disorder occurs in individuals whose work schedules require them to be awake and active during hours that are typically reserved for sleep. This can result in difficulty falling asleep, staying asleep, and experiencing excessive daytime sleepiness when they need to be awake.

Delayed sleep phase syndrome involves a persistent inability to fall asleep at a desired bedtime, often leading to staying awake for several hours beyond when sleep is desired. This can cause

difficulty waking up at the required time for work or school, impacting daily routines and responsibilities.

(Rapid Eye Movement) REM sleep behavior disorder is characterized by physically acting out vivid and often intense dreams during the REM stage of sleep. This can involve movements such as talking, shouting, or even violent actions, posing potential risks to the individual and their sleep partner.

Each of these sleep disorders presents unique challenges and requires specific approaches for diagnosis and management to improve sleep quality and overall health.

Symptoms of sleep disorder:

Signs of common sleep disorders can vary depending on the type, but may include:
- Difficulty initiating sleep, taking longer than 30 minutes to fall asleep regularly.
- Difficulty maintaining sleep, waking up frequently during the night and struggling to return to sleep.
- Occurrences of snoring, gasping, or choking during sleep.
- An urge to move legs when at rest, with relief upon movement.

During the day, additional symptoms may arise due to insufficient sleep, such as:
- Excessive daytime sleepiness, frequent daytime napping, or falling asleep during routine activities.
- Changes in behavior, such as difficulty concentrating or paying attention.
- Mood swings, including irritability and difficulty managing emotions.
- Challenges meeting deadlines or fulfilling performance expectations at school or work.
- Increased likelihood of accidents or falls.

Causes of sleep disorder:

Sleep disorders arise due to disruptions in the body's natural rhythm of sleep and wakefulness. Various factors can contribute to this disturbance depending on the specific type of sleep disorder one experiences. These factors may include:
- Underlying medical conditions such as heart disease, asthma, chronic pain, or neurological disorders.
- Mental health issues like depression or anxiety disorders.
- Genetic predispositions.
- Medications that have sleep-related side effects.
- Night shift work schedules.
- Consumption of substances like caffeine or alcohol close to bedtime.
- Imbalances in brain chemicals or deficiencies in certain minerals.
- Snoring, which is most commonly associated with being overweight and having anatomical alterations in the upper airway, worsens with age. Loud snoring can be a symptom of obstructive sleep apnoea, a condition in which breathing stops for as long as

10–60 s. A drop in oxygen in the blood during this period alerts the brain, causing a brief arousal (awakening) and breathing resumes. Repeated stoppages of breathing cause multiple sleep disruptions at night and can result in daytime sleepiness.

These diverse factors can all play a role in causing disruptions to normal sleep patterns, leading to sleep disorders.

Diagnosis of Sleep Disorder:

A healthcare provider will diagnose a sleep disorder after conducting a physical examination to evaluate your symptoms and perform appropriate tests. These tests, which may include blood tests or imaging, help the healthcare provider understand the underlying causes of your symptoms.

People may also be requested to maintain a sleep diary, documenting their sleeping habits. This includes recording their bedtime, the time they fall asleep, and when they wake up each day. It's important to note any daytime naps and how they felt before and after sleeping. Estimating sleep onset time is acceptable due to the difficulty in pinpointing the exact moment they fall asleep. Alternatively, some individuals choose to utilize devices like smartwatches or actigraphs to track their sleep cycles accurately, providing insights into their sleep patterns. Brain wave changes, eye movements, breathing rate, blood pressure, and the electrical activity of the heart and other muscles can be used to diagnose sleep disorders.

Polysomnography should be performed in cases suspicious for underlying organic sleep disorders (e.g., periodic leg movements, sleep related breathing disorders). Polysomnography is recommended in therapy-refractory insomnia. (Ophoff, et al.).

Upon consultation, the primary care provider may refer to a sleep specialist for a polysomnogram, commonly known as a sleep study. This test monitors and records specific body and brain activities during sleep to aid in diagnosing potential sleep disorders. The results of the sleep study will be analyzed by a healthcare provider to confirm the presence of a sleep disorder and guide further treatment recommendations.

Treatment for Sleep Disorder:

Treatment options for various sleep disorders encompass a range of approaches, such as:
- Establishing a consistent sleep schedule and adopting good sleep hygiene practices.
- Engaging in cognitive behavioral therapy.
- Using medications (such as sleep aids or stimulants) or supplements (like melatonin).
- Adjusting medications or doses that contribute to excessive drowsiness (always consult with your healthcare provider before discontinuing any medication).
- Employing a CPAP (continuous positive airway pressure) device or undergoing neurostimulation to manage sleep apnea.
- Exploring light therapy. ((Sleep Disorders, Diseases and conditions, Cleveland Clinic)

- According to (Gulia et al.) report, cardiovascular diseases were least prevalent among the subjects who slept for 7–8 h per night.
- Both behavioural therapies and prescription medications are considered effective means to treat insomnia. Reports have suggested that addressing the conditions of depression and cognitive impairment in the elderly population may help improve not only their quality of life but also reduce insomnia. ((Gulia et al.) (Dou et al.).
  - Treating with or switching to extended-release dopaminergic, either as transdermal application or extended-release levodopa, is recommended to improve subjective sleep quality.
  - Eszopiclone, dioxepine, zolpidem, trazodone, ramelteon and melatonin can be used for the treatment of insomnia in PD patients. However, evidence for the efficacy is insufficient (Mayer et al.).

Conclusion

Sleep disorders encompass a spectrum of conditions characterized by disrupted sleep patterns, manifesting in various symptoms including insomnia, excessive daytime sleepiness, and abnormal sleep behaviours. While underlying causes range from neurological factors to lifestyle influences, accurate diagnosis often remains challenging due to the complexity of sleep architecture. Current treatment modalities, though beneficial for many, exhibit limitations, necessitating further research. By delving into the intricate relationship between sleep and neurological function, as highlighted by recent studies, we can anticipate advancements in diagnostic tools and therapeutic interventions, ultimately enhancing the quality of life for individuals affected by sleep disorders.

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Diagnosing Mental Health Based On Text Data By Rishab Jain Kamalesh

Abstract

Many people live their lives, not understanding the severity of their mental health problems. An estimated two-thirds of people with serious mental illness symptoms go unnoticed. Mental health illnesses have many symptoms and one way people identify them is through the patient's language. Language is a key part of diagnosing mental health; this method can allow anyone to diagnose others in a normal way. However, diagnosing oneself is difficult. So rather than needing another person, the puzzling question is if machine learning is a way that people could diagnose themselves or their close ones, based on their language on social media posts or texts. The approach we chose to tackle this question was to create a neural network, based on large data samples. After the creation and testing of the model, the model outputted various performance results. The model results were pretty evenly split between true positive and false positive, without around a 51% split between our outputs. We gained around a 90% accuracy rate for our model. We found out that the network was spot-on in terms of its testing and could provide real-life results. Our results were an indication that there is a method such that machine learning could help diagnose an individual's mental health issues. Mental health is quite a complex web of strands and we have addressed how to identify one strand.

Introduction

Mental health is an aspect of people's well-being that is often overlooked, despite efforts across the world to improve awareness. Over two-thirds of people experience the struggles of mental health illnesses without proper notice or diagnosis. (WHO 2001) Stigmas revolving around mental health and their issues often cause patients to not open up about themselves and their feelings. (WHO 2001) People suffering from mental health disorders tend to neglect themselves as they are looked down upon socially and are viewed in a negative light. (Psychiatry) A lack of care for these individuals imposes serious health issues and costs the US economy around $193 billion annually. (NAMI 2023) These issues go beyond just the patient and affect their loved ones as well as their general society. One analysis that may bridge the gap between diagnosed and undiagnosed mental health cases is the emphasis on a person's language. The words one chooses affect how one looks at the world and generally define one's actions and beliefs. (Hogg Foundation 2023) Most traditional ways of diagnosis implement a trained professional analyzing a patient's language and tone, but this often requires someone or the patient themself to see changes in the person's mental health to get professional help. During a time when people express themselves online by posting on social media or texting others, the situation presents itself with an uncommon method to leverage language usage to diagnose mental health. Could machine learning detect if a person has mental health issues based on their language online?

Over recent years, there have been many attempts to combine the machine-learning world with the medical field in order to help doctors in their journey of diagnosing and treating patients. In this case, some people have tried to use machine learning to help and diagnose mental health patients. One approach that has been used to solve this issue is a study, by Ameer, Iqra, et al, prioritizing the use of deep learning and transfer learning. The study investigated how effective the models of machine learning, transfer learning, and deep learning were in classifying five of the most common mental illnesses, depression, anxiety, bipolar disorder, ADHD, and PTSD, based on user data from Reddit. The study found that the pre-trained RoBERTa transfer model achieved the best performance with an accuracy score and f1-score of around 0.83. The highest-performing mental illness classification tasks were ADHD and PTSD while the poorest-performing classes were depression and anxiety; this disparity is due to shorter posts for depression and anxiety and these illnesses were often hard to tell apart from others. However, the study does have some limitations in the way it works. The data is all from a single platform, Reddit, which could make it flawed since Reddit is one of the more undercover social media platforms. Adding on, the models, which were described in the study, weren't always as accurate as they could have been. This study developed the prior work by bridging the gaps with the usage of a dataset made up of texts rather than data from just one specific platform. To build upon prior research, we chose our models to be more accurate and pinpoint rather than decently accurate, which wouldn't allow an appropriate real-life medical case scenario.

Our study aimed to develop a machine learning model to predict mental health status using a collection of text data, which would be the basis of all model training and testing. With the research and technology available, the plan is to develop and train a neural network, which can diagnose mental health issues while minimizing the number of incorrect diagnoses to get an accessible tool that can detect the early stages of mental health cases. Considering the situation, the network will have to be a supervised classification model.

Methods

Dataset

Pointing towards a specific dataset for the project came down to many differing situations and factors. A dataset needs to contain real-life data in this context for the model to be accurate. Not only that, the dataset itself had to be large, since a bigger dataset meant the model could learn more about the situation and the task itself. A larger dataset would provide a better balance between the testing and training data, allowing the model to learn more and be tested on more. The dataset that was chosen for this research project was the Mental Health Corpus dataset (Kaggle), consisting of real texts from people with anxiety, depression, and other mental illnesses. The collection of texts contained two separate columns: one containing the actual texts and the other containing a number.

Figure 1. This bar graph illustrates the balance of mental stability and instability in the dataset, showing a close balance of the two values.
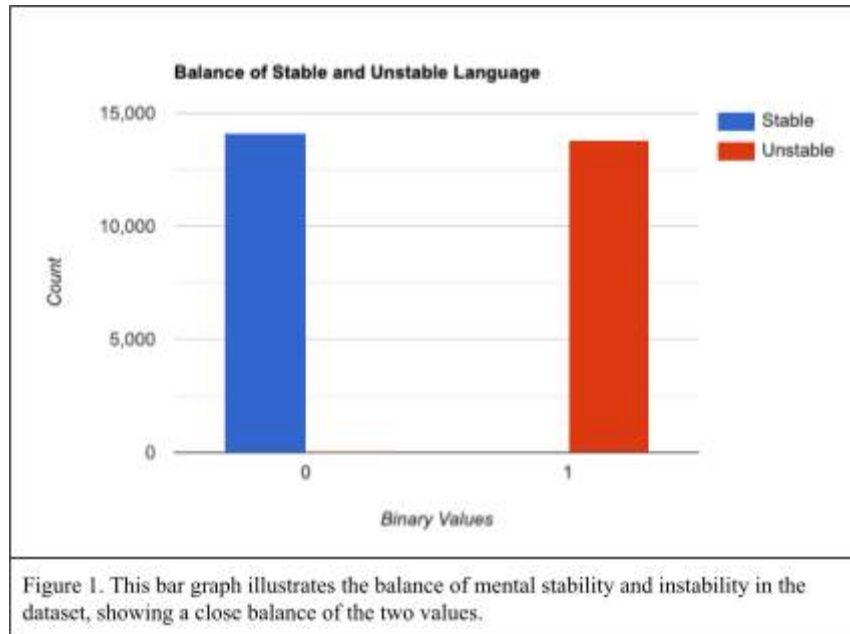
The number was a binary value, representing the mental stability of the text: a zero for a comment from a mentally stable person and a one for a text from a mentally unstable person. Between the two binary classes, there was close to a fifty percent split: about 14,139 of the 27,972 values were given the binary value of zero, while the remaining 13,838 were given the binary value of one *(Figure 1)*. This balance in labels allowed for the model not gain any bias of one side over the other.

With this data, the problem was a classification one as the machine learning approach was to train the model to identify if some text is coming from a potentially mentally unstable person or not, based on the data given. The model would classify inputs into different outputs. Since the goal of the project was to classify whether or not the data contained a comment from a mentally unstable person, the problem that needed to be answered was a supervised learning problem. The column of binary integers was the output the model strove for and the actual text data is the input the model got.

Dataset Preprocessing

For the project, we needed to preprocess and analyze the dataset several times so the model could try to understand the language data appropriately. The problem of potential missing data needed to be addressed, which we just dropped before moving on. To clarify, for some rows in the data, there was some information missing, and due to this, we dropped those rows. We then transformed the dataset file into an embeddings file so the model could be tuned fairly easily by extracting those embeddings from the file. For this task, the best tool was the BERT tokenizer, which we implemented to try and tokenize the language data; it involved breaking down the raw text data into small "tokens" and these tokens were processed by the BERT model much quicker. The output from the tokenizer returned two things: an input ID and an attention

mask. The input ID was an ID that corresponded to the data sample itself and the attention mask would tell the model whether the data sample was from a mentally stable person or not. Through this approach, the data was preprocessed to be used to train and test the model.

Models

Solving the problem of whether machine learning techniques could correctly diagnose patients with mental stability or instability based on language data in social media or texts, involved a lot of different processes. The model had to be able to take texts and labels from a .csv dataset and use that to create a diagnosis based on a person's language. It had to be trained, tested, and able to output the results based on the datasets and the input provided to the model.

When creating the model, there was a decision to be made about what to focus on and what didn't matter. For this project, the focus was always on accuracy since incorrect diagnoses about a person and their health, specifically their mental health, would lead to someone mishandling a situation based on an incorrect result. Still, keeping the model as optimized as possible would need to be key since the model shouldn't take hours for one diagnosis and that would be a waste of time. The model needs to be efficient so it can run multiple diagnoses back to back and diagnose lots of people's mental health stabilities.

While using a pre-built structure for the neural network might have been easier, it would not provide as high of an accuracy as we would have liked for our purpose of the model. Rather, the neural network was made up of many custom layers that were fully connected and could process complex embeddings. The neural network was made of several dense layers, using the ReLU activation function for text analysis. The use of the neural network had hidden layers of varying dimensions, which were optimized to be 256, 512, or 1024 units. The ReLU activation function was used to introduce non-linear patterns, enhancing the model's capability to capture complex patterns in the embeddings. The network simplified the layers to two outputs: the binary value zero for a comment from a mentally stable person and the value one for a text from a mentally unstable person.

Lots of problems were prevented during the creation of the network through built-in features. One such problem was the situation of overfitting, which occurs when the model learns too much from the training data and can't make any new real predictions. Dropout regularization was one of the many solutions that was implemented for this complex problem. (DataCamp: Dropout Regularization 2024) This technique involved us randomly removing the neurons during the training of the network so the network wouldn't just memorize the training data. The rate of dropout was something that we had to play around with and tweak in order to find the optimal range of values.

Model Training

Dynamic conclusions allowed us to adjust the training and testing data split ratio to see which ratio would yield the most accurate results for the model. After lots of testing and playing around with values, the ratio we chose was 75% to 25% training-testing ratio. Due to a

combination of accurate results and still wanting the model to learn from a large data sample, we chose our final ratio of seventy-five to twenty-five for training to testing. (*Figure 2*)

During the training phase of the model, a cross-entropy function was used as the loss function, which is common in classification problems. A cross-entropy function encourages the model to output more accurate results. (DataCamp: Cross-Entropy 2024) During the usage of this in the project, the cross entropy function punishes incorrect results but even more so when the

Figure 2. This pie chart shows the split of the training and testing data of the dataset, clearly showing a three to four split.
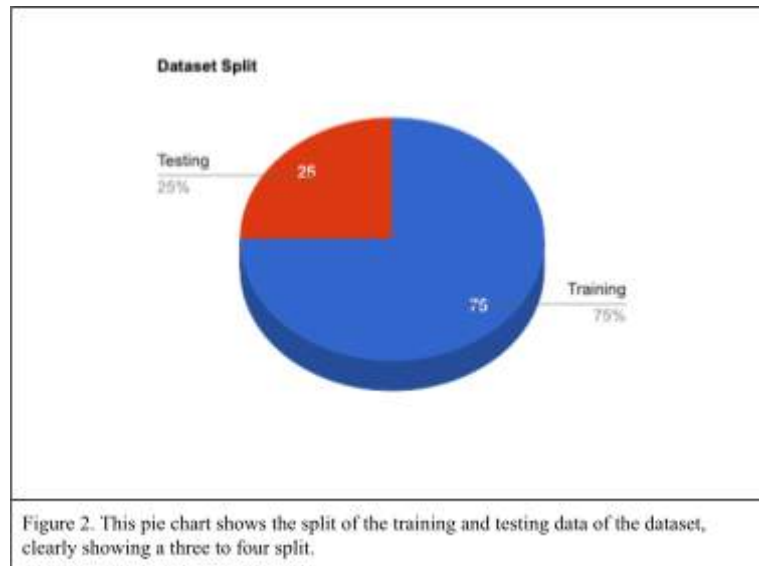
model is confident.

In order to optimize the model, we used an Adam optimizer. An Adam optimizer automatically makes the model more effective on bigger datasets and helps the model learn faster. (Analytics Vidya 2024) In the code, the Adam optimizer helps the model conclude its results quicker and makes the model more stable.

To automatically adjust any extra factors, hyperparameter tuning made sure the model worked as efficiently as possible. For the hyperparameter tuning in our exploration, we used a flexible framework known as RayTune. The factors that were adjusted in particular were layers, learning rate, dropout rate, and batch size. Mostly random search operations were used to find the most accurate value for the factors. Another tool that was part of the expansive framework was the ASHAScheduler tool. This algorithm optimizes the computer's resources by automatically discarding training tasks that don't seem promising to the more promising tasks, which helps the model's performance by forcing it to focus on the best possible ones. (Ray 2021)

After the training of the data, the model was tested on the checking portion of the data that was set aside at the very beginning of the data split. Several key metrics were tested and recorded to see the actual accuracy of the model itself, mostly consisting of key metrics used for classification problems, such as accuracy, precision, recall, and f1-score. Additionally, a confusion matrix was also generated to help complement the metrics for a bigger picture of the model. For the project, these metrics provided a good insight into how the model performs and how close it is to the intended purpose.

Results

       Based on the Mental Corpus Dataset, the model returned a vast variety of results based on the task of separating text on its mental stability using text analysis. The first result the model returned was validation accuracy, the number of correct predictions divided by all predictions. The next result from the model was a report of classification metrics, which were accuracy, precision, recall, and f1-score. The equation for accuracy is the number of correct predictions divided by all predictions while precision involves all of the correct positive predictions divided by the total amount of positive predictions. Recall's formula is the number of correct positive predictions divided by the total number of correct positives and incorrect negative predictions. F1-score is measured by two times precision and recall divided by precision plus recall.

Validation Accuracy: 0.9029306769371033

Figure 3. The image shows the validation accuracy.

Table of Classification Metrics: This is an indicator to how well the model performed in regard to its numbers.

Figure 4	precision	recall	f1-score	support
Class: 0	0.93	0.87	0.90	3535
Class: 1	0.88	0.93	0.90	3460
accuracy			0.90	6995
macro avg	0.90	0.90	0.90	6995
weighted avg	0.90	0.90	0.90	6995

Figure 5. Image Courtesy of Wikimedia Commons

In *Figure 4*, the f1-score metric shows that the model was pretty good with its outputs and predictions and usually gave out a good result. The overall accuracy of the f1-score in the model was 0.90, and this value would make sense since the two classes' (0 and 1) scores are the same. In this case, the classes' sample size is extremely similar, meaning that both values for all three metrics should be similar and that is indeed the case.

Discussion

Figure 6. The labels "Not Dangerous" and "Dangerous" correspond to the texts "Mentally Stable" and "Mentally Unstable", respectively.
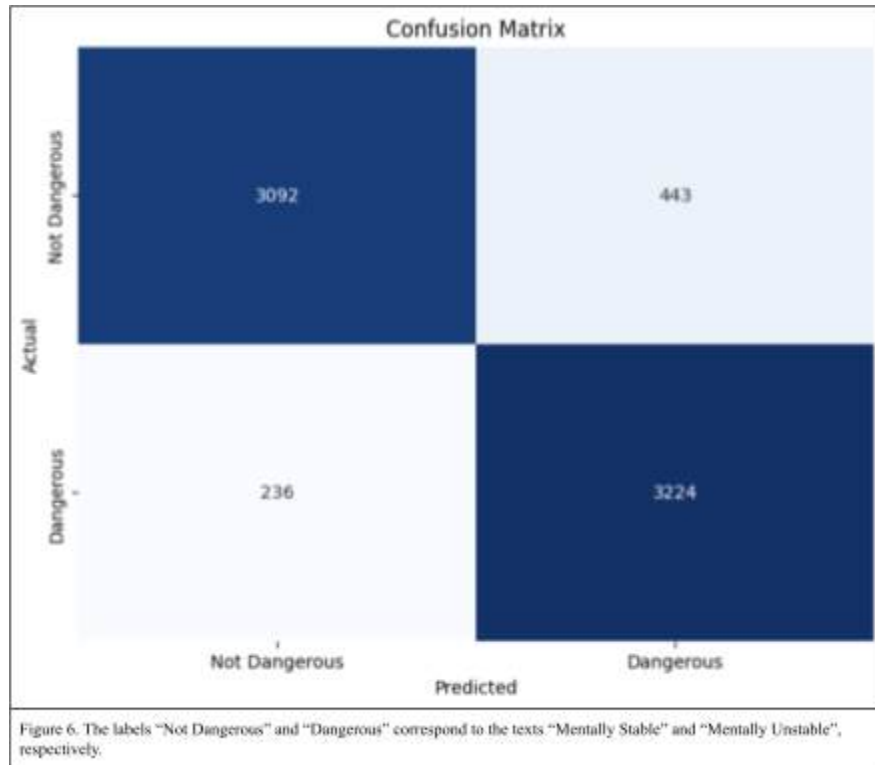
During our operation with the classification model, the model was able to get a good performance out and displayed an interesting confusion matrix. (Figure 6) As you can see the values of TP and TN in the confusion matrix are relatively high compared to the rest of the matrix. When you calculate the ratio of TP + TN over all of the values, you get 90.29%, which is the exact same number as the validation accuracy. The similarity indicates that the metrics are linked to the classification table of metrics. Our confusion matrix also shows a low rate of FP and FN, displaying the limited amount of errors and misclassifications the model makes. The confusion matrix along with the metrics table proves the model's well-suitedness to classify texts as mentally stable or unstable based on the analysis of the text.

The results indicate that the raw neural network has a lot of potential to be further developed into a useful tool for others. The model's strong performance shows that the network can diagnose texts as mentally stable or unstable with a relatively high level of success. These results point towards the idea that machine learning can successfully diagnose patients' mental health based on language analysis. Improvements can still be made, however, as can be seen in the decently moderate level of FP and FN values in the confusion matrix.

Many factors could contribute to these levels of false predictions for the model. Some texts could be severely misleading in their word choices so much so that it throws off the model. In these situations, the language is never going to be straightforward and will rather be more ambiguous than normal texts. Strong emotional language may sometimes also be perceived as mentally unstable even though the language may not be related to anything mental. The appropriate strides to make would be to use multiple datasets and try to create multi-layers of neural networks to separate emotion from mental concern.

Even though the model was successful in its task, the approach we took does, unfortunately, have some limitations. One limitation is the data collection since even though the dataset was diverse, it only encompassed a single modality approach. A multimodal dataset would allow the model to learn a lot more about human behavior and mental health while keeping itself focused on the task at hand. Moving on, the model was not as nuanced as it might have needed to be for an expansive and important topic such as mental health diagnosis. The model can be applied to predict multiple mental health states.

Conclusion

With mental health issues on the rise across the globe, a tool could help the interested try to diagnose themselves and understand where they stand on the spectrum of mental health. With such a complicated task, the attempted solution itself encompassed a lot of complex steps and information to function appropriately. It explored the potential of using machine learning as a tool to diagnose mental health using texts from social media. The methodology in this case started with the preprocessing of the data, where the BERT tokenizer broke the data down into small packets and passed it into an embedding file. Creating a custom neural network was also necessary as a pre-built one might not get the appropriate accuracy for a medical procedure such as this. The neural network, using a hyperparameter framework such as Ray Tune, was able to optimize itself and create a highly efficient model, which was accurate. Having a high validation accuracy of around ninety percent, the model was able to diagnose dangerous and not dangerous texts accurately. The accuracy, precision, recall, and f1-score were all around 90%, showing that the model performed well. Another medium of performance was the confusion matrix of the model. The matrix showed a high number of TP and TN counts while trying to limit the amount of FP and FN counts to zero. The significance of the research lies in the fact of its real-world application. According to this, the model was true in most of its predictions during the testing phase and its false predictions were quite low. Despite the overall success, the model could still be improved in its approach. It could incorporate data from other modalities so the model would get more context about mental health and be able to make better decisions as a result of that. New neural networks may also need to be incorporated into the process since a nuanced approach will be needed to tackle such a diverse concept of mental health. New preprocessing techniques could also be added to help the model work better against ambiguous language such as sentiment analysis. While the current model does lots of tasks well, it also shows lots of promise in the future to be built upon.

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The Neurological Underpinnings of Long-Term Learning: A Review
By Peter Yoon

Abstract

Long-term learning is essential because it enables humans and other animals to develop long-term memory that helps overcome any problematic conditions in the future. The present review summarizes the state of knowledge of the neural substrates of long-term learning and memory in humans. The systems involved are the various subdivisions of long-term memory, including the system that explicitly supports long-term memory, the hippocampus. The system that implicitly supports long-term memory is the basal ganglia cerebellar circuit. Processing of long-term memory involves procedural memories. This paper briefly discusses the central long-term memory storage and consolidation theories, including systems coordination and multiple trace theories. The review also outlines the function of the medial temporal lobe, the amygdala, and other structures of encoding and retrieval of different forms of memories. Last, two patient cases, including H. M. and C. W., are discussed to show how damage to memory systems interferes with long-term learning behaviors.

Introduction

With the birth of intelligence, the biology of life granted organisms the most crucial ability for their survival: learning. Learning is the process by which we acquire knowledge and skills that help organisms survive and help us thrive in our diverse environments. Of all types of learning, long-term learning is the most important for our adaptations and cognitive growth. From procedural to explicit learning, long-term learning allows us to retain essential knowledge and skills that help us grow through our ever-challenging environments. We have adapted specific brain structures that function as memory keepers to allow us to retain and build upon memories. For the most part, the Hippocampus is considered the anatomical structure that is crucial for explicit memories. Modern advancements in science still do not allow for a quantifiable measure of "memory" or level of "learning." However, behavior is indicative that learning has taken place.

On the other hand, the absence of those behaviors indicative of learning can be tied to brain lesions. There have been a few cases in which lesions in specific brain structures led to changes in behavior. This review aims to synthesize those findings and tie them together with the current understanding of long-term learning to explore the current landscape of this subfield in Neuroscience.

Long-term learning can be defined as an organism's ability to demonstrate experience-dependent changes in behavior. This differs from short-term learning, which can be defined as the acquisition of new information or skills that is relatively quick and transient. Sensory and working memory falls under this umbrella, as both forms are temporary. In the case of visuospatial sketchpad memory, a form of sensory memory, non-verbal visual storage, and rehearsal occur, in which simplistic sensory details can be retained for a few hours. For example,

the grid number of a parked car would be a visuospatial sketchpad memory for a shopper at Walmart. Thus, short-term learning involves temporarily acquiring information or skills that can be easily forgotten. In contrast, long-term learning leads to more durable, experience-dependent changes in behavior and knowledge that are stored and retrieved more permanently. The key distinctions lie in the duration of the learning effects, the depth of information processing, and the underlying neurological changes involved in each type of learning.

Long-term learning can be split into two parts: implicit and explicit memory. Explicit memories refer to facts or events that can be elucidated, such as semantic and episodic memories. Research points to the fact that explicit memories are primarily stored and processed within the medial temporal lobe, particularly the hippocampus and surrounding structures (Squire & Zola-Morgan, 1991). Episodic memories, for example, are directly related to the entorhinal cortex, a component of the medial temporal lobe (Van Strien et al., 2009). Implicit learning, on the other hand, involves unconscious memory, with minimal thought required. Implicit memory does not start unconsciously; instead, it begins as explicit memories as we go through the motions of what eventually becomes an unspoken memory. Take shooting in basketball, for example. When we start learning, the procedure for learning how to shoot is quite explicit; we can verbalize each step, from foot placement to power distribution, and this intricate process becomes a smooth, unexplainable motion. Examining the brain's gross anatomy, as we learn, memories get shifted from one area to another. This demonstrates the shift from explicit to implicit memory. Explicit memory relies on medial temporal lobe structures, such as the hippocampus. Implicit memory, on the other hand, is learned through habit formation and repeated practice, recruiting basal ganglia-thalamic circuits (Packard & Knowlton, 2002).

Implicit Memory:

Practice makes habits, and habits are permanent. Procedural learning is the process of acquiring implicit memory that can help aid several actions and skills (Shmuelof & Krakauer, 2011). In procedural memories, minimal thought is required to retrieve and act upon information. At first, all memories are encoded through explicit learning. We must be able to explain the processes of what we learn, and eventually, with much repetition and practice, explicit memories become implicit (Anderson, 1982). Repetition is crucial in creating procedural memories, as seen through forming habits in our daily lives. The routines, rituals, and behaviors we repeat over and over become things we do not have to think about when doing them constantly or consciously. Indeed, it seems that implicit learning occurs quite naturally, as opposed to the formation of declarative memories, which require persistent study (Squire & Dede, 2015). To us, learning to step on a car's brakes while steering the wheel is much easier than learning the meaning of all the signs ahead of a driver's license exam. After all, procedural learning encompasses the essential activities constituting our lives as organisms. As great as this sounds, it is a double-edged sword; on the one hand, we do not need to study how to tie a shoelace for a lengthy period. We observe, act, and practice this until memories are formed (Ashby et al., 2010). Implicit memories are pretty stable but relatively inflexible, making erroneous encoding a common occurrence. When

we learn something the wrong way, for example, how to play a piece for a marching band, it is pretty difficult for us to mold what we have learned into what is fact-correct.

The basal ganglia and cerebellum are most commonly associated with procedural memory. The basal ganglia lie beneath the Hippocampus in the forebrain and are associated with habit formation (Graybiel, 2008). Furthermore, the Cerebellum is located between the cerebrum and the brainstem and is associated with movements (Manto et al., 2012). Scientists have found that both structures related to implicit learning, habit formation, and motor learning fall under procedural learning (Doyon et al., 2009). Studies of non-human primates have yielded results that tie deficiencies in the basal ganglia to Parkinsonian symptoms (Emborg, 2007). Indeed, an anatomical structure related to implicit habit formation, including walking and basic movements, could be the primary determinant of Parkinsonian symptoms (Parent & Hazrati, 1995). Although Parkinson's disease itself has generally been tied to issues in the substantia nigra, a structure near the brainstem, it is pretty clear to see why issues with the centers of motor habits would yield similar symptoms. The cerebellum, on the other hand, is often referred to as the "mini-brain" (Sokolov et al., 2017). It is a structure related to motor and thought coordination and an essential anatomical structure mediating multiple functions in the broader brain. Consequently, if the cerebellar connection to the rest of the brain is interrupted, this damage can disrupt the brain's ability to work (Bastian, 2006).

Perceptual learning is also a type of learning that falls under the implicit category. This type of learning involves the concept of working memory, as it involves the experience-dependent enhancement of our comprehension (Seitz & Dinse, 2007). We draw upon what we have previously learned to help us perceive new experiences. This type of learning is generally more challenging to study and define, as there is an immeasurable array of unique situations and individual differences that shape perception, thus, this type of learning. Emotional learning is another type of implicit learning. This type of learning is sometimes called classical conditioning and was first discovered by Ivan Pavlov in his famous experiment with his salivating dogs (Pavlov, 1927). This type of learning involves the heavy involvement of the limbic system, the center of emotion in our brain (LeDoux, 2000). The amygdala, in particular, underlies emotional learning as it regulates associative learning and instinctive behaviors (Maren, 2001). Classical conditioning, in which one neutral stimulus is paired with a favorable stimulus, is likely to trigger a release of positive emotions through hormones and neurotransmitters. Indeed, our amygdala works with the hypothalamus when receiving these stimuli and deems them favorable (McGaugh, 2004). Thus, emotions are deeply rooted in these associations that we remember through emotional learning.

Explicit Memory

Explicit learning is a kind of learning that tends to involve purposeful understanding, which is not passive. Episodic and semantic learning are classified under this category, as each is a type of learning that can be effortfully controlled, and that is revealed during verbal reporting of the information that has been learned. Typically, episodic learning is the kind of learning

whereby specific, individual, personal, and stressful life events are encoded and easily remembered or consolidated (Tulving, 1983). Episodic is virtually similar to detailed biographical accounts destined for narration and includes many contextual factors, such as the areas where the events occurred, the sequences of action or behavior that took place, and feelings or sentiments that accompanied these events. These flashes make up the memories that enable a person to recall and rehearse, virtually 'reimagine' concrete episodes of his or her past, and present them to experience them again in principles, as it were, and with great detail. Episodic memory is based on integrating different types of information into a single entity, representing the experienced event/episode (Baddeley et al., 2009). Specifically, the visual information regarding the surroundings, the auditory stimuli including people's conversations and other sounds, as well as feelings, thoughts, and contextual information regarding the specific event all become integrated into the episodic memory trace, thus being part of the overall picture. Singly, most explications of episodic memories are broad in that they contain not just the facts of what happened but also the feeling tone and the current viewpoint at the time of the event. It is this capacity to be able to detach and go back in time and immerse one's self back again in the verbal, olfactory, visual, tactile, and affective aspects of prior events that are considered to be very distinctive of human beings and is reputed to be central in the construction of personal identity. Episodic memory is thought to involve the encoding and retrieval of particular events. It is considered to be mainly located in the hippocampus and several other neighboring structures within the medial temporal lobe (Squire & Zola-Morgan, 1991). The hippocampus expressly assumes a central role in linking various components of an episode to form a distinct episodic memory and in the recall and repeat of a concept known as retrieval-induced reinstatement.

Semantic learning, however, is the ability to learn and retrieve such facts, concepts, and specific out-of-context information. Semantic memories are part of the fundamental structure of an individual's crystallized intelligence – a set of acquired knowledge, figures, definitions, and shared understanding of the environment accumulating during a person's existence (Tulving, 1972). Compared to episodic memory, which is vivid and personal, semantic memory is a more general and public-domain sort of knowledge. They include all the prior acquired knowledge, all categories interrelations between them, and all lexical, grammatical, and logic patterns governing particular spheres of information. Semantic learning mainly occurs when some material is learned directly and formally, for example, when reading, studying, or being told something by someone else. However, it can also be a form of constructive processing arising from the gradual distillation of patterns taken from experience and extracted into different levels of abstraction, where they constitute the elements of conceptual knowledge and general, reusable representations (Baddeley et al., 2009). About the richness of an individual's semantic knowledge, one can say that it correlates with a person's level of education, information domains to which a person is exposed, and his or her life experiences. Semantic memories are all-inclusive because they enable us to communicate well, solve problems, and maneuver our social and cultural world competently. Episodic memory is primarily tied to the medial temporal lobe and hippocampus. However, semantic memory is widely assumed to be extensive

throughout many parts of the cortex, especially regarding areas most involved in higher cognitive functions and language (Binder & Desai, 2011). For semantic memory, the middle and inferior temporal gyri and the part of the frontal cortex should be involved. Anticipating, semantic memories can be divided into several subtypes: general knowledge of the world, semantically significant individual knowledge (for example, one's job or place of living), and exceptional knowledge in a particular sphere (for example, a specialist's knowledge of the field). Another significant interaction is between the semantic and episodic memory networks because they are responsible for the efficient storage and retrieval of information. Therefore, semantic knowledge can be viewed as the primary or organizing structure on which new episodic memories are built. In contrast, episodic experiences can be seen as enhancing and elaborating on existing semantic knowledge about subjects.

Indeed, there is constant crosstalk between these two types of learning, as semantic memories aid in recollecting episodic memories and vice versa (Tulving, 1972). For example, when remembering Seoul, the city where I was born, I simultaneously recall the semantic facts I know about Seoul and the core episodic memories I associate with it. Explicit memory, in contrast to implicit memory, is unstable but flexible. In this way, explicit memories are prone to be tampered with, which we see in misinformation and wording effects (Baddeley et al., 2009). Furthermore, explicit memories are easily forgotten and retrieved incorrectly, resulting in embarrassing moments when we blurt out the wrong day when asked about our friend's birthday. However, they are also quite flexible. We may encode an event or fact incorrectly, yet the flexible instability of explicit memory makes it malleable; thus, we can relearn and fix incorrect information that we may have learned.

Explicit learning takes place mainly in the hippocampus. The hippocampus is a seemingly elongated tube-like structure in the limbic system, but a coil is folded into this shape. Each length of the hippocampus serves a different purpose, from the dentate gyrus to CA1 and CA3; each coil segment contributes to the formation and consolidation of explicit learning (Squire, 2009). Indeed, the hippocampus is far more complex than meets the eye. Emotion contributes to explicit memory, as seen through flashbulb memories. Once again, the amygdala plays an essential regulatory role in managing memory, which also applies to explicit memory. Intense emotional experiences, such as trauma, excitement, or fear, back up flashbulb memories. These experiences are usually incredibly noteworthy, emotionally charged situations that linger in the memory. The amygdala's involvement extends to aiding the hippocampus in encoding memories more cleanly and precisely, creating a more vivid and memorable memory (Phelps, 2004). For example, many people remember where they were during 9-11 with great precision. The trauma of witnessing such a shocking event facilitated the amygdala's involvement, which aided in strengthening the learning process of these episodic memories.

On the other hand, the amygdala can also prevent encoding and divert access to explicit memories. For example, let us say that we have recently moved houses. Our hippocampus has not fully learned the route to our new home, yet our striatum remembers the location of our old

home. In a moment of great stress on the road, our amygdala is an inhibitor of our explicit learning. It diverts our actions to the responsibility of our striatal motor movements.

On the other hand, the amygdala can also inhibit striatal learning and enhance hippocampal learning. We see this again in the 9-11 incidents, in which the amygdala inhibited the implicit memory of those experiencing it but made the event a vivid episodic memory. The amygdala does balancing and puppeteering between these two systems, enhancing and inhibiting each over the other in appropriate situations.

Theories of Long-Term Memory

There are multiple theories surrounding long-term learning and its encoding process. The first of these theories is the Systems Coordination Theory. This theory states that the hippocampus is initially very much involved in consolidating a memory until it strengthens it to a point where it is no longer involved (Squire, 2009). The Systems Coordination Theory, this theory supports the idea of anterograde amnesia, as hippocampal damage may inhibit the ability to form new memories but would not affect the learning that had already occurred and had separated from the hippocampus; following the SCT, the Multiple Trace Theory came to fruition. This theory suggested that the hippocampus acted as an index of portal activation, activated when encoding memories and bringing in association areas (Moscovitch et al., 2005). According to this theory, whenever one visits a memory, another index from the hippocampus is established, making memories easier to find over time. This theory explained why older memories could be more resistant while acknowledging how incomplete hippocampal lesioning could result in some long-term memory being retained. This theory would thus predict both anterograde and retrograde amnesia, as a damaged hippocampus would mean that fewer indexes could be formed, limiting the ability to create new memories. Conversely, similar to the damaged index of a book, a damaged hippocampus could cause retrograde amnesia by making it harder to find the pages in which each memory was stored.

Case Studies

Henry Molaison, known by his initials H. M., is undoubtedly one of the most widely-known patients in neuroscience. The best information they could ever have wished for regarding the human brain, with special emphasis on memory, came from this man's case. H. M. is a man whose life was filled with a severe condition in his childhood and the groundbreaking operation that turned the world of neurology upside down. Henry Molaison was born on February 26, 1926, and suffered from very severe and often occurring epileptic seizures that affected his life to the maximum measure. Since the epileptic tone of H. M.'s seizures grew uncontrollable by the age of 27, the doctors decided that in 1953, neurosurgeon Dr. William Beecher Scoville performed an experimental procedure to alleviate H. M.'s epilepsy. This surgery involved the bilateral removal of the medial temporal lobes, including significant portions of the hippocampus, amygdala, and adjacent cortical areas. The surgery successfully reduced H. M.'s seizures but had an unexpected and profound side effect: The operation disrupted the

hippocampus, and it led to a major side effect: anterograde amnesia. H. M. was unable to create new superordinate long-term memories. Despite the postoperative apparent ability to learn new things and memorize information briefly, the man could not store this information in his long-term memory. This outcome gave a definite and perhaps shocking reminder of the contribution of the medial temporal lobes in storing new memories. The gross anatomical level involves the hippocampus that was severely removed from H. M., and this component provides efficient structures for the creation of declarative memory. These are the following: semantic memories, of facts and semantic memories and episodic memories, encompass a person's experiences. The locus of the hippocampus processes formation in coordination with other neighboring regions of the medial temporal lobe for storage in short-term memory so that information is transferred to long-term memory (Squire, 2009). Removing these areas in H. M.'s brain caused a breakdown of this process, offering empirical evidence of these zones' involvement in memory formation. In addition to observing the immediate effects of the surgery on H. M., Milner conducted a series of tests on him to assess the scope and severity of his amnesia. She found that H. M. had completely lost the capacity to create new declarative memories, but he could develop new procedural memories (Milner et al., 1968). Procedural memory is a subtype of implicit memory, which entails learning skills and tasks executed through practice in other areas of the brain besides the medial temporal lobe through the basal ganglia and the cerebellum. A classic example in this regard is H. M. learning to trace a star with his right hand while looking at his reflected image in the mirror. Even though H. M. could not recall having done the task before, but he got better with practice, evidence that his secondary or procedural memory was functional (Milner et al., 1968). This separation of the two types of memory paved the way for understanding more components of memory processing in the brain and called attention to different functions of the brain structure. Indeed, the importance of the case involving H. M. cannot be overemphasized. In effect, for the first time, it offered concrete evidence that memory is not a singular entity but is made up of several components supported by different brain structures. This realization was key in changing the direction of memory research from investigating just the distinction between systems to identifying the various systems and how they worked in conjunction. His case also led to further explorations of the parts of the brain like the hippocampus and the medial temporal lobe in the formation, storage, and recall of memories, a gradual unfolding of H. M.'s condition through research. Originally, the decrease in the frequency of seizures was categorized as a beneficial result of the treatment, yet the side effect of amnesia was at the center of attention. Individual analyses revealed that, although H. M. could interact with others and perform everyday tasks, he failed to retain newly acquired information during the examination to any measurable extent. Despite having verbal abilities and social competence in longitudinal studies done over decades, valuable data about the stability of the condition and the restrictions of the mnemonic reserve were obtained. Regarding his other memory, retrograde amnesia was present but again not as severe as the anterograde one; H. M. regained the ability to remember events and information before the surgery. Different aspects of his and her life were recallable, though there was a loss of time-sequenced and episodic

information and some generalization. This pattern of forgetting assisted the researchers in identifying the temporal gradient of retrograde amnesia and implied that older memories are stored differently from new ones (Squire, 2009). The final summarization of the case of Henry Molaison allows for the conclusion that the latter can be viewed as the key to understanding numerous principles in the field of neuroscience. It also sheds the required light on the medial temporal lobes in encoding LTM, especially the hippocampus, which is part of declarative memory. H. M.'s case, therefore, provided the much-needed gateway to testing the dichotomy of explicit and implicit memory systems in subsequent neuropsychological studies. Nonetheless, his discoveries have, in one way or another, helped to shape a scientific thought that endures and propels further neuroscientific research. Besides H. M.'s historic role in enhancing the knowledge of memory systems, his case held much more for the neuroscience and medical science fields. This case depicted physicians' and surgeons' ethical concerns and accountability as they performed experimental surgeries. The physical consequences of his surgery led to a reconsideration of the possible dangers attached to invasive medical operations of the brain, and in particular, ones that seek to address the medial temporal lobes. Moreover, research on H. M.'s case has been carried out at multiple phases throughout his life, which makes him a subject of valuable longitudinal studies in neuroscience. For years, he agreed to submit to testing that offered investigators an extended look at the result of various cortical injuries on memory and other cognitive processes. Such large and integrated data acquisition was particularly instrumental in constructing new theoretical concepts and paradigms of memory processing. These include the directions, the generations, the methodologies, and the technologies of neuroscience research: where H. M.'s case was influential, too. The need to comprehend his condition contributed to neurological breakthroughs, including the MRI and PET scans that enable differentiating structures and functions of the brain. They have since then played a crucial role in diagnosing various neural disorders and treating them accordingly, thus enhancing the existing research tools in the clinical practice environment. Additionally, it may be noted that the findings derived from the investigation of H. M.'s case have been useful in formulating the approaches to cognitive rehabilitation. Knowledge of factors underlying various kinds of memory has contributed to developing strategies for working with patients with impaired memory to restore at least some of them to perform daily activities independently. Spaced repetition, memory prompts, and skill practice interventions are now routinely applied to patients with amnesia and other cognitive disorders.

Clive Wearing's story is one of the most unique and tragic documented accounts in neuroscience, bearing witness to the mechanism of memory and the consequences of its absence. Musician and conductor Clive Wearing fell ill in 1985. He was left with amnesia due to herpes simplex encephalitis, which damaged a chunk of his brain, including the hippocampus and the surrounding areas. See Man Without A Memory on BBC for an exciting synopsis of Clive Wearing's story. This made him powerless to form new memories as he was diagnosed with anterograde amnesia and also suffered from critical retrograde amnesia, which made him unable to recall most of the events from his past (Squire, 2009).

Wearing's case is well documented, with essential knowledge of the brain, particularly of memory gained from it. Various viral diseases may sometimes cause harm to the nerves, for example, herpes simplex, which usually causes cold sores. However, they may occasionally lead to encephalitis, where the virus goes to the brain. Evaluating the effects of the virus in Wearing's case, it would affect his medial temporal lobes, making radical alterations to his hippocampus, an area of the brain that contributes to the development of new memories with consciousness (Scoville & Milner, 1957). It damaged the concentration of short-term memory, which can no longer be transferred to long-term storage, and his memory span is about 3 seconds. At the gross anatomical level, the hippocampus is known to be involved in storing information from the short-term to the long-term memory. This area of the brain in the structure of Wearing is in a condition where he was subjected to a life with no past or future.

He possesses procedural memory – the capability to complete activities he was trained to do before his disease, such as playing the piano. However, he does not remember being taught these skills or events that occurred a few minutes earlier. This division of the procedural and declarative memory systems, brought out by Wearing's case, correlates with the studies done on the case of Henry Molaison, although with an even deeper and fuller loss of memories (Milner et al., 1968). Clive Wearing's condition has changed his life significantly since he suffers from the affliction called prosopagnosia, a type of amnesia. He is disoriented all the time and equally wakes up with this feeling that he just emerged from unconsciousness. His diary contains how he wakes up from the bed and then crosses them out as he forgets to record it since the last time he woke up. This cycle of amnesia shows how severe this condition is and gives a brief look into the life of a man who cannot form new memories or, for the most part, remember anything at all.

Clive Wearing is one of the more famous cases for understanding memory and the brain's capacity to encode and retrieve information. His condition has also made the hippocampus necessary for memory formation. In contrast to H. M., Wearing remembers something from his previous life, but this memory was affected by retrograde amnesia that affected him beginning from an early age. Thus, he only has a few recollections from his past life. Consequently, based on this extensive memory loss, it can be concluded that the medial temporal lobes are not only involved in creating new memories but also in recalling older memories (Squire, 2009).

Deborah Wearing, wife to Clive Wearing, has been a central figure in revealing and comprehending his state. Her stories reveal the struggles and disappointments of Clive's amnesia. Contrastingly, Clive remains cognisant of Deborah's existence as a significant woman in his life but cannot recall pertinent exchanges or occurrences about which she has spoken. This phenomenon indicates much more to be learned about emotional memory and the brain areas involved in organizing and storing the emotional importance of events, including parts of the brain different from the medial temporal lobes, like the amygdala (Milner et al., 1968). Wearing's case provided one of the most significant revelations, namely, that it is possible to distinguish between different types of memory in terms of functionality. His ability to recall specific events in his day-to-day life and general knowledge is affected; however, his ability to do tasks that are

patterned or require practice is still functional. This allows him to continue playing the piano and conducting music, actions that are thoroughly familiar to him in terms of practice.

The fact that procedural memory is preserved in the case of brain damage, which involves the basal ganglia and cerebellum, proves that different memory systems exist in the brain. Evaluating Clive Wearing's case means transposing the findings of the theoretical and practical neuroscience study. They have applied his condition in the clinical management and care for people who suffer from severe memory disabilities. Evidence-based interventions embrace the idea of providing structure in patients' lives and preventing further deterioration. Methods like environmental prompts and the upkeep of schedules are used to make the patients' everyday activities possible regardless of their conditions. Moreover, knowledge of the neural substrates of Clive's condition has contributed to the expansion of neurorehabilitation, intended to capitalize on normally functioning memory networks to enhance the quality of life (Squire, 2009).

The case of Henry Molaison (H. M.) and Clive Wearing also gives deep insights into the details of human memory. It opens a new horizon of the comprehension of the human brain's mechanisms of encoding, storing, and recalling knowledge. Such case studies also stress the importance of some of the specific structures of the brain, like the hippocampus and other related medial temporal lobe regions, in the determination of both the STMM and the LTM. H.M.'s case helped define where implicit and explicit memory differs; H.M. had most of the medial temporal lobes, including substantial parts of the hippocampus, removed bilaterally and was incapable of creating new explicit memories. However, his capacity to obtain new P-Ms signified that he or she potentially obtained standard high implied memory systems, which involve the basal ganglia and cerebellum. This division was critical in transforming a singular memory concept into a multiple-process system making up the human brain. These realizations were further supported and elaborated by Clive Wearing's case. This herpes simplex encephalitis affected his hippocampus and other surrounding areas, which eventually impaired his ability to recall events that occurred before the attack and in the period after the attack; hence, anterograde and retrograde amnesia were evident.

Nevertheless, he could still perform procedural memory, which enabled him to play the piano, an activity he had done beforehand while severely ill. The case of Wearing suffering from retrograde amnesia that prevented the recall of immediate and remote memories strengthened the idea in the Multiple Trace Theory of the hippocampus's importance in retrieving older memories. According to this theory, the hippocampus aids in searching for information in the cortex, enhancing the memory trace.

Future Implications/Research

Further research can be focused on the following points derived from the cases of H. M. and Wearing. First, elucidating the exact neural basis by which the procedural memories are preserved when the hippocampus is significantly compromised could give some idea on the rewiring of the brain and the possibility of rewiring for treating different memory diseases.

Further studying the application of basal ganglia and cerebellum and its contribution to procedural learning and habit formation would also help understand other strategies of these systems to cover hippocampal impairments. Moreover, the relationship between emotions and episodic memories, evident in both cases, should be examined in the future. The present study that reveals the amygdala's contribution to enriching first-person perspective with details and effects on episodic memories also points to multiple connections between structures involved in memory integration. It could help in designing better therapies for diseases like PTSD, where the memories of the trauma are very vivid and have intrusive effects on people's lives. However, similar to all case studies, the cases of H. M. and Wearing have limitations due to the nature of the case study research. Thus, the specificities of acquired brain injury might limit the applicability of results to participants with memory dysfunction. Both brains are alike yet different; thus, the impact of a similar injury may be entirely different for different people.

In the same way, the therapist's interest in the most severe types of amnesia could be a source of bias and prevent the identification of details regarding the less severe forms of memory loss. The method of each of these case studies is also longitudinal, which provides large amounts of data over time, although at the same time, poses some questions regarding sustainability and validity due to the possible impact of external factors on the results. For example, the caregiving role that Wearing's wife, Deborah, played involved looking after him in addition to being a source of psychological support; this may, in some ways, have suppressed the effects of his memory loss, thus making his case a complex one to understand.

The ensuing questions have yet to be answered in memory research. An important one is the identification of the specific procedures and time of memory strengthening and transformations of various types of memories into long-term ones. While the Systems Consolidation Theory provides the framework, the Multiple Trace Theory details the patterns, but the mechanism still needs to be present. Another exciting area is memory retraining or, in other words, memory reparation. Methods like neurofeedback, cognitive methods, or the administration of drugs could improve the memory performance of a person with hippocampal damage. How can neuroplasticity help when the memory systems are damaged, and what can be done to utilize it for therapeutic purposes?

Moreover, investigating memory's genetic and molecular mechanisms might explain why some people stay more protected from memory loss than others. Knowledge of the genetic memory component could help implement personalized preventive techniques and remedies. The cases of H. M. and Clive Wearing have played a significant role in developing theoretical advances regarding memory and its neural basis. These cases show the importance of the hippocampus and other related cortical regions in generating, storing, and recalling memories. Lastly, these case studies illustrate abundant information, which is also a testimony to the further complications of memory processes and a plea for further research. Thus, unraveling the mechanisms of memory further is crucial since it will pave the way for more effective treatment of memory degradation or disorders and increase appreciation of the brain's potential.

Conclusion

Learning is a core component of animal behavior that shapes personality, intelligence, and evolution. Scientists have yet to find a way to measure learning and memory directly, as the relationship between our relatively simple behaviors and the complex cortical processes is simply too hazy for modern technology to unmask. However, researchers have begun to map learning to a certain extent through inference by observing behavior. Additionally, the few cases available for study, such as that of patient HM and CW, and breakthroughs in neuroscience have contributed to a greater understanding of the neurological underpinnings of learning. The theories and postulates that have emerged from this renaissance of neuroscience promise a more informed future. One in which we may understand the reasons for deficits in learning. One in which we may understand how exactly we can learn the best. One in which we may understand the reason for neurodegenerative diseases that inhibit memory formation. Learning remains an elusive measurement unit that constantly shifts away from contemporary understanding. Nevertheless, neuroscience is paving the way for a more informed future, leading to a more informed humanity.

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The Theoretical Side of International Relations By Anish Gopala

I. Introduction

There are a plethora of ways to view the actions of nations toward each other in a modern, ever-developing world. States can often act unpredictably, but there are some important patterns that researchers and theorists have recognized throughout the years. Beyond this, there are many ways to interpret the roles that international organizations play in the global system and their relationship to the states that comprise them. The four most cited international relations theories are realism, liberalism, constructivism, and marxism. Realism posits that states act purely based on self-interest and survival, are inherently enemies, and are constantly working to gain military power. Another important theory in international relations is liberalism, which looks at the world on a more optimistic note. Liberals posit that international organizations foster communication and peaceful solutions between states. Additionally, liberals believe that states are not inherently enemies of one another and would prefer to diplomatically resolve conflicts rather than resort to violence. The third idea of constructivism emphasizes the importance of ideas and social beliefs in the behavior of states toward one another. Lastly, Marxism is based on human materialism and how social class differences within a capitalist economy will ultimately lead to a communist economy. The differences between the attitudes of these four theories can be shown by what they focus on in different states and how they view international organizations such as the UN; realism views international organizations as a resource for member states, liberals view them as an actor in global politics, constructivists view them as a forum for different states with conflicting norms to settle disputes, and marxists view them as instruments of capitalism, materialism, and social class distances.

II. Realism

Although it entirely ignores the sociocultural differences between states, realism is much more complex than a depressingly pessimistic view of states' behavior as a "mad grab" for power, measured in troops and guns. Taken as a whole, realism assumes that the global order is anarchic, all states have military capabilities, states are not certain of other states' intentions, states are in a constant bid for survival, and states act rationally. The first idea of realism, now called "classical realism", maintains that states' behavior can be explained by human behavior; that is, humans are thought by many to be simply motivated by self-interest with no kindness at heart. This behavior can be applied to states as well. Classical realism emerged as a "response to the idealist perspective that dominated international relations scholarship in the aftermath of the First World War" (Korab-Karpowicz & Julian 2023). Championed by thinkers such as Hans Morgenthau, this idea posits that peace is best achieved through multipolarity, or the distribution of great military power across multiple different global "superpowers", as it makes deterrence of a hostile power easier if there are many other actors ready and willing to retaliate against their aggression. One example of multipolarity was the time period before WWI, when the German, British, French, Austro-Hungarian, and Russian empires had power over much of the world.

However, another school of thought emerged from thinkers such as Kenneth Waltz, now known as neorealism, or structural realism. Just like classical realism, neorealism posits that states act in self-interest to survive; however, it does not explain this phenomenon with human behavior. It instead claims that the world exists without a central global government with control over all nations, meaning the world is anarchic. For this reason, states are in a constant struggle to gain power so they can defend themselves in case of an attack. Additionally, neorealists claim "bipolarity [is] more stable than multipolarity" (Walt 1998). That is, two great world powers lead to a stable global order instead. Neorealists believe bipolarity leads to peace because of the equality of two great powers, unable to attack each other because it will surely mean their own demise. Beyond this, there exist two subcategories within neorealism: defensive and offensive realism. Defensive realism posits that smaller nations ally to stop a nation that has gained too much power and is considered a more optimistic view of states' interactions, even within the negative boundaries of realism. On the contrary, offensive realism claims that states are uncertain about other states' intentions, and so they must work toward gaining as much power as possible for security. Realism is a theory about the interactions between states, and state cooperation is most greatly shown in the formation of international organizations, such as the UN. Due to the pessimistic nature of realism, realists mainly discredit the effectiveness of international organizations in maintaining global peace. They believe that the selfish nature of states will always prevail over such agreements, and conflict will eventually break out. Additionally, realists believe that international organizations themselves have little power; it is the states that come together to create them that wield the most influence. In realist thinking, a state builds a coalition to make an international organization, and the international organization in turn does the work of that state. This shows how realists view international organizations as a resource for states to use to do their bidding and meet their own agenda, which differs from the more optimistic outlook of liberalism, which will be discussed later. However, in order to build an international organization, all the actors involved must have something to gain. While relative gains are how a state benefits from an international organization in comparison to the other states involved, absolute gains are how a state benefits regardless of how others are affected. Due to the pessimistic nature of realism, realists mainly concern themselves with the "relative" gains that a state receives from an international organization, instead of the "absolute" gains.

III. Liberalism

Whereas realism promotes a "self-help" view of the world with limitless pessimism, liberalism looks at international relations with more optimism. It holds that states do not inherently want to attack each other because it is much easier to diplomatically resolve conflicts and gain economic power than to go to war. One of the major thinkers of liberalism was Immanuel Kant, who famously invented the "Kantian Triangle", or a triangle depicting the three main sources of peace between states. The first is economic interdependence, which provides an incentive to diplomatically resolve issues: economic gains. Simply put, "states in highly interdependent economic relationships tend to refrain from fighting with their commercial

partners" (Russett & O'Neal 2001). If two countries go to war, it could harm the economic exchanges of those nations, making it unreasonable to go to war unless absolutely necessary. The next element of the Kantian triangle is the democratic peace theory. This posits that democratic countries are less likely to go to war with each other. Beyond a shared belief in democracy which unites democratic countries and discourages armed conflict between them, this idea originated because democratic leaders are under pressure to satisfy their electorate's wishes to stay in power. Oftentimes, the population of a country will criticize leaders who go to war, seeing the burden placed upon the common people. Due to leaders' desire for reelection and popular support, they are inherently discouraged. The third element of the Kantian triangle is international organizations, which liberals view as a necessary contribution to global peace and prosperity. Unlike realists, liberals view international organizations as having moderate control over the states that comprise them. In this way, liberals view international organizations as "actors", or entities with some measure of control over their own actions. This is different from realists, who view them as simply a resource to be used by states for selfish gains. Additionally, unlike realists, liberals believe that the absolute gains of a state from an international organization are more important than relative gains. Liberals believe that intergovernmental or international organizations such as the UN provide a forum for states to resolve their disagreements with each other. Additionally, liberals posit a number of reasons that actors are discouraged from "cheating" in an agreement. One of the main reasons is that if many allies share security or economic interests in an agreement, they risk not only losing those potential gains, but also the risk of other former allies turning on them if they cheat. In this way, liberals believe that states have tangible reasons to obey the commitments they make to international organizations, and these organizations can help establish global peace.

IV. Constructivism

The third, variant strain of thinking in international relations is called constructivism. Constructivism is different from realism and liberalism in that it places major emphasis on ideas and societies of different states. Put simply, the international system "is constituted by ideas, not material forces" (Jackson & Sorenson 2007). Whereas realism views countries in the military power they have, contructivism views how different governments think differently about certain issues, and how different states have different sociocultural norms. One of the constructivist criticisms of realism is how it views states only on how many guns and tanks they have, not the beliefs present in their respective societies. Liberalism and realism view international relations at the level of states, but constructivism views it at the level of individuals. Constructivism is more optimistic about global affairs than realism and posits that states are not enemies by default. This means that constructivists focus on how norms affect the behavior of people in societies. Constructivism views the world in shared understanding between states, even if those states have different norms and ideals. In this lens, constructivists view the UN as promoting and enforcing new global norms with the ultimate goal of global peace. They see the UN as a forum of different states with different ideas who can resolve their differences. In this way, constructivists differ

from realists, who view international organizations as a resource for states to selfishly use under their control, and liberals, who view them as independent entities with measurable control over the states they are comprised of. Some of the norms the UN has sought to normalize in all countries are human rights advocacy and economic equality for all people. One example of this was the 2011 Libyan civil war and humanitarian crisis, which led to the UN intervening to indirectly help topple Muammar Gaddafi's tyrannical government and restore political order in the region. While these may conflict with the local norms of certain world regions, the UN has sought to safeguard these sacred tenets across the world through diplomatic discussions with deviant governments and, when necessary, peacekeeping missions.

V. Marxism

Marxism, the last international relations theory, developed by Karl Marx, goes back to basics and prioritizes the wellness of the Earth and those that inhabit it. Marxism is a direct condemnation of capitalism and the materialism that breeds it. Unlike the other theories discussed, Marxism is grounded in Marx's philosophical ideals and is not directly related to international relations. Rather, its ideals influence international relations, especially when it comes to the desire to limit capitalism. According to *International Relations Theory* by Maïa Pal, "A Marxist would stress that IR is not just about states' foreign policy or the behavior of politicians, but more about survival (or more broadly, life), reproduction, technologies and labour" (Pal, 2018). This statement emphasizes that capitalism and sovereign states exist as a result of past societal circumstances and class struggles - primarily between the upper class and the working class. In a single society, Marxism emphasizes the importance of viewing it as a whole rather than an entity separated by class. This thought process also translates into international relations, where Marxists dislike the concept of territorial borders and the migration issues that arise because of it. Pal connects this concept back to capitalism by explaining that, "movement of peoples occurred long before capitalism, but capitalism shapes those movements in conjunction with the creation of borders and economic productivity" (Pal). In addition to this, Marxism in terms of international relations condemns democracy because it serves the rich, leading to more societal divisions, and therefore more capitalism. According to article "Relevance of the Marxist International Relations Theory" by Hammad Khan, Marxism "accepts the participation of the international organizations in the form of MNCs and other organizations" but doesn't believe that they will uplift the lower class in any way and only believes they will primarily benefit the upper class.

VI. Conclusion

Overall, realism, liberalism, constructivism, and marxism vary greatly in how they view states and international organizations like the UN. While realists view states as barbarically working for their own survival through military aims, liberals claim that it is in states' self-interest to cooperate with one another. Beyond this, realists view international organizations as simply vessels of member states to fulfill their own interests while having no real power,

while liberals view international organizations as actors with power over the member states and the ability to encourage peace between them. Additionally, constructivism looks most deeply at the different norms between states and views international organizations as forums to communicate between nations with differing norms and ways to enforce global norms. Lastly, Marxism emphasizes how human materialism has bred capitalism throughout history and has increasingly divided the rich from the poor, a situation unfortunately exacerbated by international organizations. Realists view international organizations as resources, liberals view them as actors, constructivists view them as forums, and marxists view them as instruments of capitalism. All of these different theories have been influenced by different times in history. As time goes on, humanity is being faced with different challenges and conflicts. New international organizations are being formed every day between governments to help humanity from these threats. So the question remains: will humanity unite for the betterment of all people, or will we continue to divide ourselves into oblivion?

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How Increasing Sucrose Concentration in Dialysis Tubes Leads to an Increase in Water Intake By Angelina Loh

Abstract

The purpose of the osmosis lab is to use the change in mass of dialysis tubing to determine the relationship between solute concentration and the movement of water through a selectively permeable membrane. Different concentrations of sucrose (M) are placed in six different dialysis tubings and the mass was taken. The tubings are later placed in the same concentration, in different beakers, of tap water for the same time. The different masses of the final dialysis tubings compared to the beginning dialysis tubings shows that as the concentration of sucrose increased, the water diffused into the dialysis tubing increased as well. This is because water moves from the side that has more free water concentration to the side that has less free water concentration. In conclusion, the increase of solute concentration in dialysis tubings led to an increase in mass, due to the increase of water intake into the tubing.

Introduction

Osmosis is the diffusion of free water across a selectively permeable membrane. Solutions with higher solute concentrations have lower free water concentration because the clustering of water molecules around solutes causes the water to be unavailable to cross the membrane. Water tends to diffuse from higher free water concentration to lower free water concentration, or from lower solute conc ex entration to higher solute concentration. This continues until both concentrations of either side of the membrane are equal.

Osmosis is driven by tonicity, which is the ability of a surrounding solution to cause a cell to gain or lose water. There are three types of solution that determines tonicity: isotonic solution, hypertonic solution, and hypotonic solution. An isotonic solution results in no net movement of water across the membrane, which means water diffuses at the same rate from both sides of the membrane. In this case, the volume of a cell will be stable, or barely have a difference. In a hypertonic solution, there are more solutes outside of the cell than inside. This means the cell will lose water, and decrease in volume. In a hypotonic solution, the solute concentration inside the cell is more than outside the cell. This results in the cell bursting or overflowing.

The goal of this osmosis lab is to demonstrate how the tonicity of a cell determines osmosis across a selectively permeable membrane. The selectively permeable membrane is represented by the pores in dialysis tubing. The solution outside of the tubing will be isotonic when the solution inside the tubing is distilled water. The solution outside of the tubing will be hypotonic when the solution inside the cell contains different amounts of sucrose. Water has less free water concentration when the dialysis tubes are concentrated with solutes compared to the solution outside that has no solutes, which has more free water concentrationo. Based on the knowledge of osmosis and tonicity, the increase in solute concentration in the tubings will lead to

an increase in water molecules into the tubings as well. This means there will be a change of mass in the dialysis tubings.

Research Question
What is the effect of different contractions of sugar solutions on the percent change of mass of dialysis bags?

Experimental Hypothesis
Hypothesis: As the concentration of sucrose solution increases, there will be an increase in mass in dialysis bags.
Null Hypothesis: There will be no change in mass of dialysis bags in the different concentrations of sugar solution.
Alternate Hypothesis: There will be a change in mass of dialysis bags in different sugar solution concentrations.

Variables
The independent variable is the different concentration of sucrose solutions placed into the dialysis tubings.
The dependent variable is the change in mass in dialysis tubings.
Some of the variables that need to be controlled include the time the dialysis bags are placed into the water. This is controlled by using a timer that is set to 30 minutes. Another variable is the amount of sucrose solution that is placed into each of the bags. This is controlled by using a 10 mL syringe that is filled two times, so 20 mL of solution is placed in each of the bags. Another variable that needs to be controlled is the temperature of the experiment. This is controlled by conducting all of the experiments in the same room, so the temperature is unchanging. An important control variable is the slight changes in the amount of solution or time the dialysis bags are placed into the water. For example, it cannot be guaranteed that all the bags contain exactly 20mL of solution. This is taken into account by calculating the percent change in mass at the end of the trials. By calculating the percent change in mass, you are able to determine the difference in mass of dialysis tubings regardless of the slight differences in mass.

Materials
1. Six 30 cm strips of presoaked dialysis tubings
2. Six beakers, each ⅔ full with tap water
3. 10 mL plastic syringe
4. <u>20 mL each of</u>
    a. Distilled water
    b. 0.2 M sucrose solution
    c. 0.4 M sucrose solution
    d. 0.6 M sucrose solution

e. 0.8 M sucrose solution
f. 1.0 M sucrose solution
5. Electronic balance
6. Timer
7. Paper napkins to dry

Method/Procedure
1. Obtain six 30 cm strips of presoaked dialysis tubing. Fill six beakers ⅔ full with tap water, which should be set to the side.
2. Tie off one end of each of the dialysis tubings, allowing one side to be open to put in sucrose solution.
3. Pour 20 mL of each of the following solution with a 10 mL plastic syringe into separate bags:
   a. Distilled water
   b. 0.2 M sucrose solution
   c. 0.4 M sucrose solution
   d. 0.6 M sucrose solution
   e. 0.8 M sucrose solution
   f. 1.0 M sucrose solution
4. Tie off each bag leaving some air space
5. With a paper napkin, gently blot the bags and place each separate one on the electronic balance.
6. Record the mass of each of the six dialysis tubes for the initial mass (g).
7. Place the dialysis bags at the same time into the separate beakers ⅔ full with tap water you prepared at the start. Make sure to start your 30 minute timer once the bags are placed in.
8. Once the timer is up, remove each bag and carefully blot the bags to make sure there is no excess water on the outside.
9. Re-mass the bag on the electronic balance and record the data for the final mass (g).
10. Calculate the percentage change in mass for each of the dialysis tubings.
    a. % change=(final mass-initial mass / initial mass) x 100
11. Record the percentage change in mass of each of the tubings into your data table.
12. To gather three trials of this experiment, record the data collected from two other groups.

Data Collection

Table 1-Trial 1 of Initial Mass, Final Mass, and Percentage Change of Dialysis Tubes

	Initial mass (g) ± 0.01g	Final mass (g) ± 0.01g	Percent change (%) ± 0.01%
Distilled water	20.46	20.38	0.39
0.2 M	20.98	22.18	5.72
0.4 M	21.46	23.68	10.34
0.6 M	21.65	25.13	16.07
0.8 M	23.05	27.17	17.87
1.0 M	23.06	28.07	21.73

Table 2-Trial 2 of Initial Mass, Final Mass, and Percentage Change of Dialysis Tubes

	Initial mass (g) ± 0.01g	Final mass (g) ± 0.01g	Percent change (%) ± 0.01%
Distilled water	19.64	22.38	13.95
0.2 M	19.14	20.49	7.05
0.4 M	18.52	21.14	14.14
0.6 M	22.10	25.89	17.15
0.8 M	23.29	28.35	21.73
1.0 M	22.64	27.89	23.19

Table 3-Trial 3 of Initial Mass, Final Mass, and Percentage Change of Dialysis Tubes

	Initial mass (g) ± 0.01g	Final mass (g) ± 0.01g	Percent change (%) ± 0.01%
Distilled water	20.85	21.40	2.21
0.2 M	21.72	23.38	7.64
0.4 M	22.90	24.55	7.21
0.6 M	15.30	21.46	17.27
0.8 M	23.17	27.05	16.75
1.0 M	23.12	27.83	20.37

Processing the data

      The mean of the percentage change of mass was calculated, which was used to calculate the standard deviation of the values. The standard deviation was then used to calculate the SEM (standard error of the mean). The error bars were then represented on each of the points on the graph. A line graph to process this data because it takes into account the increasing percentage change of the mass in relation to increasing solute concentration. A line graph allows all three of the trials to be compared with each other.

Sample Calculation: Mean of Mass Percentage Change of three trials (1.0 M Sucrose)

(21.73% + 23.19% + 20.37%)/3 = 21.76%

Measures of Confidence - Standard Error of the Mean and Confidence Interval:

Table 4-Mean Percentage Change of the Different Sucrose Concentrations

	Distalled Water	0.2 M	0.4 M	0.6 M	0.8 M	1.0 M
Mean Percentage Change (%)	5.52	6.80	10.56	16.83	18.78	21.76
Standard Deviation	7.36	0.98	3.47	0.66	2.61	1.41

Table 5-Standard Deviation of the Mean and Confidence Intervals of the Different Sucrose Concentrations

	Distalled Water	0.2 M	0.4 M	0.6 M	0.8 M	1.0 M
Standard Error of the Mean	4.25	0.57	2.00	0.38	1.51	0.81
68% Confidence Interval	1.27-9.77	6.23-7.37	1.47-5.47	16.45-17.21	17.27-20.29	20.95-22.57
95% Confidence Interval	-2.98-14.02	5.66-7.94	6.56-14.56	16.07-17.59	15.76-21.8	20.14-23.38

Presentation of Results

Mean of Mass Percentage Change of Dialysis Tubes Containing Different Concentrations of Sucrose
(Error bars represent 95% confidence interval)
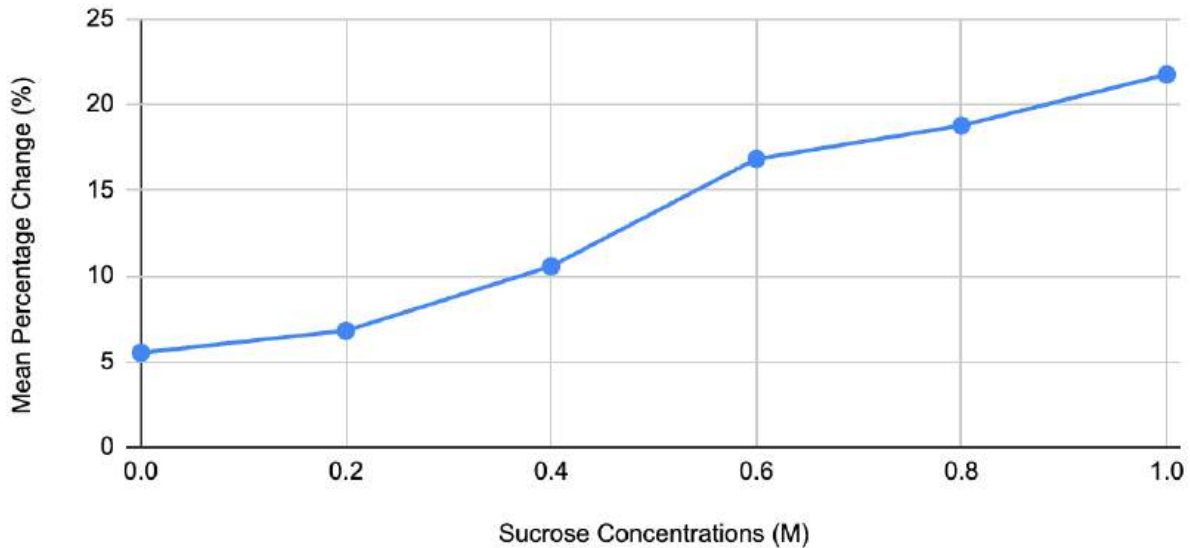
Limitations of Experimental Design

While the data is highly reliable because the percentage change took into account the small differences in the dialysis tubing masses at the start of the experiment, a factor that was not as reliable was the consistency of duration of the experiment. Since it was impossible to place all the bags into the solution at the same time and take them out at the exact same time, the duration that the dialysis bags were placed into the beakers differed slightly by a few seconds. This would have slightly affected the final masses of the dialysis tubes. Although the results are still accurate, there may have been a very slight difference in the final masses (±0.01).

Suggestions for Improvement

Some modifications that could have been made include using a more accurate electronic balance that could measure more significant figures. This would have given us more accurate data that we could process. Also, more trials (larger sample size) could have been conducted to give more accurate representation of the data.

Conclusion and Evaluation

The experimental results confirm the hypothesis: as the concentration of sucrose solution increases, there will be an increase in mass in dialysis bags. What is the effect of different contractions of sugar solutions on the percent change of mass of dialysis bags? As the sugar solution concentration increases, the percent change of mass increases in the dialysis bags as

well. In trial one, as the sucrose concentration increased from distilled water (0 M) to 1.0 M, the percent change in mass increased from 0.39% to 21.73%. In trial two, as the sucrose concentration increased from distilled water (0 M) to 1.0 M, the percent change in mass increased from 13.95% to 23.19%. In trial three, as the sucrose concentration increased from distilled water (0 M) to 1.0 M, the percent change in mass increased from 2.21% to 20.37%. The results confirmed my hypothesis because there was an increase in percent change of mass as the sucrose solution concentration increased. This confirms that tonicity does affect osmosis because when dialysis tubes contain a hypertonic solution, the movement of water goes into the bags. Water moves from an area of greater free water concentration to lower free water concentration. As the water molecules pass through the membrane, or the pores in the dialysis tubings, the mass of the dialysis tubings increase.

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An Overview of Ethical Concerns and Questions of CRISPR-Cas9 Medical Technology
By Nicholas Ellis

Introduction

Scientists have been looking for ways to alter and change the human genome for many years, and many methods have come about for manipulating DNA. However, by far the most intricate and precise method for doing just this is a technology known as CRISPR-Cas9. CRISPR-Cas9 makes use of RNA technology as well as DNA splicing proteins in order to precisely and effectively edit the DNA of a cell in whatever way a scientist chooses. This level of genetic alteration, though, brings ethical concerns with it. Many have likened this kind of genetic alteration to disturbing the code of life or even "playing God." There have also been concerns for the technology's future use, what it will be used against, and so on. Many of these concerns are well founded, and should be carefully considered by any researchers and scientists.

Background

CRISPR is an acronym that stands for 'clustered regularly interspaced short palindromic repeats' [1]. Before it was used as a technology, it was a natural system present in archaea that was theorized to be used as a sort of immune system. Palindromic sections of DNA were intermixed with spacers, which are sections of the DNA from a bacteriophage or other virus. Once the viral DNA was embedded within the CRISPR system, the cell would transcribe the DNA into RNA that CRISPR associated proteins, called Cas proteins, would use to locate the incoming virus of the same type, and eliminate it [2]. This system was key to discovering how CRISPR can work in human beings. The main way this occurs is through the Cas proteins. Essentially, if scientists can design personalized guide RNA, then they could attach this RNA to a Cas protein. If this protein were to enter a human cell, it would function as it would in bacteria, and it would destroy the DNA associated with the RNA. This is how Cas technology can target specific genes that code for specific genetic diseases, allowing scientists to replace the gene with a non-mutated version [3].

This technology is revolutionary in the way that it is currently the most advanced and precise way for genes to be directly edited, switched, and destroyed. This has obviously opened up many new opportunities and prospects for altering the human genome to eliminate genetic diseases such as sickle cell disease or muscular dystrophy. However, it seems as though CRISPR-Cas9 technology in humans is still very much in its infancy, and it will take much more time and research before its potential is truly realized. However, the potential of CRISPR does not merely extend to human medicine. It can extend to other fields such as agriculture, where CRISPR is beginning to be used to make crops and fruit that can be heat resistant or slower to ripe [4]. All in all, CRISPR has an astounding number of potential uses for the future of humanity. However, this great technology also comes with heavy considerations about the ethics of altering the human genome.

Ethical Questions and Concerns

Many people are concerned about the advent of CRISPR-Cas9 technology in medicine due to the possibility of errors in the technology, producing potentially harmful mutations or potentially eliminating the wrong segments of genes. Off-target effects such as these have been tracked in a 2021 study by the Proceedings of the National Academy of Sciences of the United States of America have shown off-target effects to be present in about 16% of their subject cells in a [5] study that underlines the importance of ensuring a basic standard of safety for all CRISPR related treatments. However, this aspect of CRISPR could be smoothed out and solved over time with more research. And indeed, scientists have been creating safer CRISPR technologies. In December 2023, the first CRISPR based treatment for sickle-cell anemia was FDA approved [6]. This shows that the methods and results of CRISPR based treatments are becoming safer and more effective, which is necessary if they are to become the future of tackling genetic diseases.

However, others are concerned about germline CRISPR treatments affecting any offspring the person receiving the treatment may have. Some have brought up questions of consent. If someone plans to get pregnant and receives CRISPR treatment, then the child of that person would also be affected by the parent's treatment without the child's consent. However, many have argued against this being a legitimate concern, as parents already make many decisions that affect their children before they are born. This issue also brings up a larger question of if germline editing should be legal at all. Some have argued that germline editing is not something to be entirely scared of, as it may allow parents to give birth to a healthy child if there is a significant chance of a child having a genetic disease. Some believe this to be unethical, however, as the child would have their genetics altered through treatment. However, many believe that just as consent is often implied when resuscitating someone, consent can be similarly implied when saving a future child from a disease.

There have also been ethical questions concerning the economics of CRISPR treatments. Many people wonder how expensive CRISPR treatment options will be and if this will have a serious effect on the pre-existing healthcare disparity between the upper and lower classes. This is already a concern with other medical treatments, but considering the possibilities for germline editing, disparities in treatment could not only advantage those with the means to afford it, but it could put their children at a biological advantage. Casgevy, a CRISPR treatment for sickle-cell disease, currently sits at a wholesale acquisition cost of around 2.2 million US dollars [7]. While the price point for patients may decrease in the future as further research allows for cheaper and more effective manufacturing, it may be many years until the treatment is affordable for the average patient. This trend of extremely expensive treatments using CRISPR makes sense given the precision and complexity behind the treatment, but it may become a serious problem as new CRISPR treatments for highly common issues continue to be put into action, only for the wealthy to be able to afford them. This is not necessarily an issue with the treatment itself, but rather something researchers and manufacturers should keep in mind when developing treatments.

Some have concerns with how CRISPR will be used. Specifically, there are concerns that CRISPR will not be used for treating diseases, but rather for genetic "enhancements," as some have called them [8]. When considering the possibilities for CRISPR in the future, these changes could range from changes in one's appearance to far more serious changes. Changes like these, in a best case scenario, could remove genetic predispositions to cancer, cardiac diseases, and more. However, many would propose this falls under the category of "prevention" rather than "enhancement." Many agree that CRISPR treatment, when not in response to medical concerns, should be highly regulated.

Furthermore, public opinion on CRISPR may present another obstacle and point of consideration for researchers. A survey from CivicScience [9] presented information on a survey taken on public opinion on CRISPR treatment being used in a variety of circumstances. A wide majority of people familiar with CRISPR, about 70%, felt either neutral or positively about CRISPR as a whole. Among US adults who held opinions on CRISPR, 27% believed the treatment of diseases with CRISPR was unethical. However, 68% of those surveyed believed the editing of an embryo's DNA to be unethical, and 58% of people believed altering the genetic makeup of animals to be unethical. Additionally, these results are among adults already familiar with CRISPR technology. Those who are unfamiliar with the technology may be even more apprehensive about its uses. These apprehensions are well founded in many cases, and will undoubtedly present an obstacle for some areas of CRISPR, as certain areas will remain unresearched due to scorn from the public and the scientific community.

Conclusion

CRISPR-Cas9 technology has very high potential in human medicine. Its development could lead to a far better future in the world of medicine, but it is important to remember the ethical concerns that can come along with treatments as potent and modern as CRISPR. Some of these concerns include the potential for unintended effects of the CRISPR treatment, the morality of germline treatment, the potential for economic difficulties, and the problem of public perception. CRISPR researchers should take these concerns into consideration during their research and development of new treatments.

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Dance Movement Therapy Mitigating Physical, Mental, and Cognitive Conditions
By Swapna Ramachandran

Abstract
      Dance Movement Therapy (DMT) is a therapeutic practice which uses emotional, physical, and verbal movements to mitigate various health conditions. This literature review examines the impact of DMT on conditions such as chronic pain, cancer, depression, schizophrenia, PTSD, dementia, and communication disorders, based on research papers identified through a Google Scholar search. Findings suggest that DMT is a valuable type of therapy that can alleviate symptoms and improve quality of life. Nonetheless, more research is needed to compare different types of DMT methods and more studies should be conducted to improve DMT methods. This paper concludes that DMT is considered as a supplemental treatment for numerous health conditions, and requires further research to engage its use in clinical settings.

Keywords Dance Movement Therapy, Post-Traumatic Stress Disorder, Cancer, Chronic Pain, Communication.

Introduction
      Dance movement therapy (DMT) can be effective and purposeful for therapeutic improvement, however, much research still has yet to be done (Koch, Sabine, et al., 2019).
      DMT has been used for thousands of years in a therapeutic manner. It has been proven to heal through its use of emotional and physical movement (Ritter, Meredith, et al., 1996). It creates a balance between health and a sense of presence as the therapy focuses on movements specific to an issue (J, Shilpa, et al., 2015). DMT has been acknowledged as a profession since the 1940s when pioneers created dance therapy conceptions. There is less statistical research on the efficacy of DMT as most of the research is interpretation-based and descriptive (Koch, Sabine, et al., 2019).
      Dance movement therapy can be used to further help physical issues such as cancer, chronic pain, and child obesity alongside existing treatments (Good Therapy, 2018). It also helps soothe mental issues like anxiety, depression, and disordered eating, as well as cognitive issues, in particular, dementia and communication problems (Good Therapy, 2018). The American Dance Association talks about DMT as a use of movement in therapy as a method for improving a person's emotional, social, cognitive, and physical unity (Kiepe, Marie-Sophie, et al., 2012).
      Dance movement therapy can be used in numerous ways depending on a person's issue. For example, if someone is suffering from personality disorders, dance movement therapists will use a technique called mirroring which involves matching an individual's movements and steps with another individual (Honey Lake, 2019). Another technique that might be used by a dance movement therapist is called jumping rhythms. This technique is known to help by having patients do vertical movements which mitigates depression (Honey Lake, 2019). Lastly, a very

common technique used for patients that need help expressing their challenges is called movement metaphors. An example of using this method is by giving a patient a white flag in order to help them celebrate emotional surrender (Honey Lake, 2019).

This paper sets forth on how DMT helps physical, mental, and cognitive health by referencing many authors with a similar idea. Every author mentioned in this paper has a different approach on DMT, but each relates to the broad idea of it. DMT is not only used in research but also used in other settings such as rehabilitation, social groups for older adults.

Methods

Search Strategy

The search engine used was Google Scholar.

The search terms used to identify relevant research papers were: "dance movement therapy + dementia," "dance movement therapy + autism spectrum disorder," "dance movement therapy + cancer," "dance movement therapy effects on cognitive issues," "dance movement therapy effects on physical issues," "dance movement therapy effects on mental issues," "dance movement therapy effects on social issues," "What is dance movement therapy?" "What are different types of dance movement therapy?" "When was dance movement therapy created?"

Inclusion Criteria

Many studies have shown that dance movement therapy works better on adolescents, however it is still relevant towards older individuals. This study focuses on people of all ages with different physical, mental, and cognitive issues that can possibly benefit from DMT.

Studies ranging from any year which were written in English were reflected in this paper. Studies using a clear methodology and results section were also greatly considered.

Exclusion Criteria

Research in papers which focused on training or experiences of professional/experienced dancers were not included in this paper.

Author & Year of Publication	Number of Participants	Type of DMT	Type of Disease or Condition	Summary
Cohen et al., 1999	4	Rhythmic patterns, use of expressions, verbal language	Leukemia	DMT used to help children's mobility and increase activity levels.
Meekums et al., 2015	147	Interactive dance movement	Depression	Majority of participants felt depression symptom relief following DMT intervention.
Zilius, 2010	1	Movement-based	Chronic pain and fibromyalgia	DMT intervention helped the participant feel relief from chronic pain and fibromyalgia.
Bendel-Rozow, 2021	98	Recovery-oriented dance movement therapy	Schizophrenia	Participants felt relief of symptoms of schizophrenia after using RODMT for treatment.

Levine et al., 2015	1	Visualization, metaphoric imagery, repeated movements	Post-Traumatic Stress Disorder (PTSD)	The participant felt less pain and controlled trauma after using DMT as a treatment.
Karkou et al., 2023	204	Use of movement and music	Dementia	Dance Movement Therapy reduced the depression felt as a side effect to dementia, lessening the participants' dementia.
Corteville, 2024	3	Touch, deep breathing, improvisation, mirroring	Self-esteem and communication	Participants felt relief from low self-esteem and improved communication skills through DMT intervention.
Sengupta et al., 2020	1	Mirroring	Communication	Participant improved communication skills after dance movement therapy intervention.

Discussion

Why people should be interested

Dance movement therapy, compared to other therapies, is still being explored and studied as an alternate or additional treatment for many conditions (Koch, Sabine, et al., 2019). DMT provides many benefits such as mitigation to symptoms and effects of physical, mental, and cognitive conditions (Ritter, Meredith, et al., 1996). While DMT is not expected to cure illnesses, it can help alleviate social effects of these conditions improving feelings of loneliness felt by individuals with physical, cognitive, and mental conditions (J, Shilpa, et al., 2015).

DMT helping physical issues:

Dance movement therapy has a relevance to physical issues as it can help mitigate different levels of chronic pain in conditions such as headaches and movement disorders that affect body-image (Zilius, Marie Newsom, 2010). DMT can have the ability to relieve many types of pain patients experience (Zilius, Marie Newsom, 2010). Zilius described that chronic pain, which seems like an issue that mainly affects older individuals, can actually occur at a young age (Zilius, Marie Newsom, 2010). Zilius describes a case, originally presented by Goodill, of a nine-year-old girl who was diagnosed with fibromyalgia and chronic migraines. The child's pain was so severe that it was close to paralysis. A dance movement therapist was able to work with the girl and give her a movement based treatment that reduced the migraines and lessened the fibromyalgia . There were no unexpected results or side-effects in this study, emphasizing DMT's relevance in alleviating physical issues (Zilius, Marie Newsom, 2010).

Another physical issue that can be mitigated by DMT after the use of other treatments is cancer (Cohen, Susan O et al., 1999). A paper written by Cohen and colleagues discusses how a baby was diagnosed with leukemia at just four weeks old. The baby's eyes were constantly closed, body stiff like a rock, and abdomen was swollen. Doctors suggested treating him with dance movement therapy so therapists stroked, used stretching movements, and rhythmic patterns along his spine, upper/lower connections, and side/side connections. These movements helped the baby regain a sense of his body. The baby could feel various connections in different regions in his body, helping him to move around (Cohen, Susan O et al., 1999). The structure and

creativity used by the dance therapist helped the baby overcome the challenges it faced throughout its cancer journey, supporting the conclusion that DMT can be used to treat physical issues (Cohen, Susan O et al., 1999).

A similar study was done by Cohen and colleagues with participants slightly older than the baby with leukemia (Cohen, Susan O et al., 1999). Three preschoolers, age four, were also diagnosed with a type of leukemia called lymphoblastic leukemia. Dance movement therapists spent 8 weeks working with them, and used various methods of dance movement therapy such as the use of expressions in dance movement, verbal language, and balancing postures. These strategies were used to get the children to adapt to the way that they would normally use their bodies (Cohen, Susan O et al., 1999). The DMT affected the children positively and helped their bodies to respond to their inner thoughts (Cohen, Susan O et al., 1999).

DMT helping mental issues

Dance movement therapy can not only ease physical issues but also diminish pain felt mentally (Meekums B et al., 2015). Mental health conditions such as depression and anxiety can be treated through DMT (Meekums B et al., 2015-16). A paper written by Meekums and colleagues presents a research study with 147 participants who were being evaluated for effects of DMT on depression. The result of this work suggests that the therapy had positive effects on a portion of the study participants. The majority of participants felt relief from their depression symptoms following the DMT intervention, hence highlighting that individuals with mental health conditions can also benefit from DMT (Meekums B et al., 2015-16).

Another type of mental issue that can be treated through dance movement therapy is schizophrenia (Bendel-Rozow, Talia, 2021). Schizophrenia affects an individual's ability to think, act, and feel. A study done by Bendel-Rozow discussed how a group of adults with schizophrenia were taken to a 13-week recovery session, where DMT would be the main source of treatment (Bendel-Rozow, Talia, 2021). Ninety-eight participants were told to take a survey of their abilities before their sessions began to compare to the results. However, throughout the duration of the sessions, participants did drop out. The data of participants who dropped out halfway through the sessions is not recorded in the results of this study (Bendel-Rozow, Talia, 2021). Results of participants using DMT as a treatment were compared to results of participants using illness management and recovery (IMR) treatments (Bendel-Rozow, Talia, 2021). Interventions in IMR include behavioral training, psychoeducation, coping skills, etc. Outcome of this comparison was that DMT is as effective as IMR treatments, proving that DMT for mental issues is a suitable recovery program (Bendel-Rozow, Talia, 2021).

Post-traumatic stress disorder, known as PTSD, is another major mental issue that many individuals undergo (Levine, Brooklyn et al., 2015). A study done by Levine and colleagues talks about a trauma victim, who is experiencing grief, that has sudden tension points in her body. A dance movement therapist started the patient off with a scan of their body to help visualize where the pain was located. They then used a dance technique where they had the patient imagine the movement before actually doing it. This created a connection between the

patient's mind, body, and brain and also helped the patient move around more (Levine, Brooklyn et al., 2015). This study has a positive outcome as the patient was able to lessen the pain she felt and improve her control over the frightening memory she held with her (Levine, Brooklyn et al., 2015). Dance movement therapy develops an awareness of the body and how it responds to a specific type of PTSD. This helps dance movement therapists locate the pain and helps the patient recover (Levine, Brooklyn et al., 2015).

DMT helping cognitive issues

Dementia, which is considered as a cognitive condition, is when an individual's daily life is disrupted due to lack of thinking and social abilities. Individuals with dementia can experience memory loss and depression (Karkou et al., 2023). In a study done by Karkou and colleagues, a group of 204 adults with dementia were placed in a 12 week dance movement therapy program. Many of the adults faced a side effect of depression due to low social abilities, so experts used dance movements and different music to stimulate the brain and mind (Karkou et al., 2023). This 12-week dance intervention had a positive outcome on the dementia patients, such that they were able to recover from the depression, suggesting that DMT can mitigate cognitive conditions (Karkou et al., 2023).

Cognitive conditions like low self-esteem and communication can also be managed through dance movement therapy (Corteville, 2024). In a study done by Corteville, two out of the three highschool girls were noted to be unhappy with the relationships they had with their fathers and all of them had low self-esteem about their body image which resulted in less communication with peers (Corteville, 2024). The DMT sessions lasted 8 weeks, where numerous dance movement techniques like, mirroring, improvisation, touch, and deep breathing were used. All three participants felt better about their bodies, and their self-esteem improved. Most importantly, throughout the dance movement therapy sessions, the participants were able to open up to others and enhance their communication skills (Corteville, 2024). The DMT sessions also helped the two girls who had a rough relationship with their fathers to talk about it with them and improve their relationships. This study demonstrates another way that dance movement therapy can help improve cognitive conditions (Corteville, 2024).

Communication skills are a key factor in daily life, so excelling in them is imperative. Unfortunately, some individuals are unable to improve their communications, but this can be helped through the intervention of dance movement therapy (Sengupta et al., 2024). A study done by Sengupta and colleagues, discusses an individual who was diagnosed with severe autism. This led to challenges in communication for the individual, as well as high sensitivity to touch and impulsiveness (Sengupta et al., 2024). Dance movement therapists used a dance movement therapy technique called mirroring over a period of nine months. Results of the DMT were immediate and increased hormonal changes, and brain, mind, and body stimulation. It also increased the activity level of the individual, further improving their communication skills (Sengupta et al., 2024). This again shows how DMT can alleviate cognitive conditions.

Explanation of hypothesis

Throughout this paper, the idea of dance movement therapy benefitting physical, mental, and cognitive conditions has been discussed. This paper accurately shows that DMT can be used not only to heal emotional pain, but also to stimulate body movements that an individual might have trouble with. It also shows that dance movement therapy takes a natural approach in alleviating conditions through the use of rhythmic movements, verbal language, use of expressions, and more. It is much healthier than using a prescribed drug, that can have many side effects, to cure a painful condition.

Implications of this work

Physicians and other medical staff treating patients with mental, physical, and cognitive conditions should consider prescribing dance movement therapy as a supplemental treatment. Very rigorous styles of dance or various bodily movements are not recommended for people with conditions of chronic pain, cancer, etc, as they might aggravate the condition. Rhythmic movements, use of expressions, and verbal language can improve physical movements (Cohen, et al., 1999). Whereas, movement and music based dance movement therapy may alleviate mental and cognitive conditions (Meekums B, et al., 2015-16).

Limitations

Dance movement therapy is an upcoming ideology. There is very little research currently published comparing different types of DMT. Research on adults and children have outweighed the research taken of older individuals in this paper. Some research taken has shown bias in male over female and female over male participants due to the diagnosis. This paper purely focuses on participants that have completed a specific DMT program.

Future directions

Doctors and other medical specialists can further the understanding and utility of dance movement therapy by prescribing it to eligible patients. Dance movement therapy is effective in alleviating pain both mentally and physically. It increases brain, mind, and body stimulation, hence proving why it should be researched further. More specialists can conduct research on DMT and it can be incorporated into normal treatments. The use of prescription drugs could be lessened and a more natural approach through dance movement therapy can and should be taken.

Conclusion

This paper aimed to determine the effects of physical, mental, and cognitive conditions after the use of dance movement therapy. It also proved that dance movement therapy has a positive effect on physical, mental, and cognitive conditions as most participants felt relief of pain after their DMT sessions. This paper also gives a clear view on how DMT is being used and how it can be used in the future. The use of DMT will benefit many individuals as it uses natural body movements, language, and visualization.

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The Truth About America's Wilderness Programs By Olivia Basshart

Context

The last thing someone struggling with their mental health would want is to be woken up in the middle of the night by a pair of strange adults, saying something along the lines of "this could go one of two ways." So many questions, so few answers, and a forced journey half-way across the country to a facility in the middle of the woods. In a world where youth mental illness is on the rise, enrollment in these kinds of treatment programs is a reality for many teenagers whose parents long for a reliable solution. The facilities in question can be classified as being a part of the *troubled teen industry*- an umbrella term that, according to the American Bar Association, is comprised of "private youth programs, therapeutic boarding schools, residential treatment centers, religious academies, wilderness programs, and drug rehabilitation centers" (Krebs, 2021). As of 2024, more than 1500 of these facilities are said to be currently running in America, with the number constantly increasing. People get admitted for a variety of reasons- mental illness, suicidal thoughts/actions, family conflict, substance abuse- and the underregulated industry is not planning on simmering down anytime soon with the average profit being $1.2 billion a year (Jenkins & Mohammadi, 2023).

Literature Review

Through comprehensive research, the researcher found three significant themes of the troubled teen industry. To start, there is not one established view on this network of treatment centers. Many sources proclaim the negative aspects and standings of these institutions. One that was of extreme significance being undergraduate researcher, Jamie Mater's report, *The Troubled Teen Industry and its Effects: An Oral History.* This researcher interviewed nineteen adults who had been a part of a specific institution in southwestern United States through the video call platform Zoom (Mater, 2022). Mater used a *grounded theory approach* (used "to produce or construct an explanatory theory that uncovers a process inherent to the substantive area of inquiry") to code and denote similar responses in the collected interview transcripts (Singh & Estefan, 2018). Mater asked a series of questions to the participants that analyzed their experiences before, during, and after treatment. She reported many similarities between respondents of instances of abuse, medical mistreatment, discrimination, cult tactics, and exacerbation of previous mental health conditions. Many participants reported being degraded/punished in severe and inhumane ways by staff, being forced to conform to unhealthy coping mechanisms such as self-harm and disordered eating, and experiencing a severe loss of identity due to the isolation and extreme mistreatment they were subjected to. One the other hand, multiple sources stated the positive potential these organizations have/could create. One study investigated specifically *wilderness therapy programs*, which are defined by the Washington State Institute of Public Policy as programs that "combine therapeutic elements with outdoor activities in a natural setting to help treat individuals with a range of needs (WSIPP, 2022)." The author analyzed the effects of contained 3-week programs and continuous 8-week

systems, finding that the structure of these systems could lead to a wide range of positive social and emotional benefits, with a large emphasis on increased responsibility and personal growth (Russell & Hendee, 1999). The second finding declares a general lack of intervention and quality of treatment in the TTI, embodied by a St. Louis University Law Journal. This work goes into detail about how many facilities continue to thrive today despite increasing lawsuits and reports of abuse. It introduces two major "legal loopholes" that allow for this continuation: the signing over of parental rights to the organizations and inadequate state regulation. Many parents do not realize the implication treatment will have on their children, as it is common to fall victim to deceptive marketing. Wanting to do whatever is best for their children, admitting them to a treatment center requires parental rights to be signed over, severely limiting the parents' influence on medical care, education, and visitation rights. In addition to this, there are limitations regarding how much state governments can interfere. It is common for these facilities to be privately owned and with this lack of public government funding comes a lack of governmental authority in the way things are run. Any visits that do happen have been seen to be usually pre-planned. This allows for the facilities to prepare ahead of time and appease the inspections of government officials, which is not necessarily representative of the usual standards by which they operate. Some programs are also religiously affiliated, which makes it difficult for government intervention for fear of violating religious freedom rights. This lack of oversight and parental rights have been strong contributors to unchecked abuse (Younis, 2021). The third finding is from a researcher at the State University of New York and gives insight into the high-profit nature of the TTI. It acknowledges how there has been a rising rate of mental illness as well as an increase in profitable healthcare. Wanting effective treatment, parents desperately turn to these programs in hopes of eradicating their children's mental illness. This demand has resulted in a modern shift from a previously small network of treatment options to a now large, multimillion-dollar industry that continues to expand. As previously stated, there is a significant lack of federal regulation that allows these facilities to remain open, even though administration standards and ethics may not be met 100% of the time. The unchecked authority, high costs, and growing need for treatment allow for these organizations to prosper and keep making profit (Gotbaum, 2023).

Based on these foundational studies, the researcher identified a gap in existing knowledge of the troubled teen industry. There was not enough research on individual branches of treatment and their effects, specifically for wilderness therapy programs. The little research that was available was outdated and conflicting, not going in-depth enough about the effects it had on attendees and what this means for the future of these programs. This need for reliable and specific data influenced the researcher's question: How do wilderness therapy programs affect attendees' emotional well-being overtime, relationship with/openness to future treatment, and willingness to speak about mental health related matters? Based on previous research, the researcher hypothesized that when analyzing from before to after treatment, there would be three main findings. The first is a mainly negative emotional impact. This was theorized because while there were mixed viewpoints and experiences about the TTI, in the grand scheme of things, the

negative aspects seemed to outweigh the positive aspects and potential for growth. Secondly, it was estimated that there will be a decrease in willingness to receive treatment because of the original experience. If the first part of the hypothesis proved to be true for the sample, then it is logically sound to believe that those who emotionally declined from treatment would not want to engage in any similar future endeavors. Thirdly, it was predicted that there would be an increase in desire to advocate for mental health. This was speculated because regardless of the overall effect- positive or negative- people would likely want to speak out about their experiences if given an opportunity, just for different reasons. It can be thought of in a similar manner to leaving a review about a restaurant- people typically leave reviews if they have a spectacular dining experience, or a very negative one with the purpose of advising others. In terms of wilderness programs, if one's experiences were positive, there is a high chance of a client wanting to share the benefits they garnered with others. On the other hand, if one's experiences were negative, it is valid to predict that they would want to speak out to inform others of this obstructive experience to prevent someone from being subjected to similar practices.

Method

The researcher used a mixed-method approach surveying wilderness therapy program attendees. The selected population was anyone who has attended a wilderness therapy program in the United States. These parameters were constructed because selectively looking at wilderness programs aligns with the research gap and primary focus of that branch, and keeping the scope of participants within the United States allows for enough variability in data across fifty states while still being controlled to one country. Examining responses from non-wilderness therapy programs and/or participants outside of the United States could lead to potential confounding variables, which the researcher tried to eliminate to get the most accurate and specific data.

A survey was chosen as the means of collecting data for various reasons. Surveys are consistent, organized, and allow for efficient and meaningful data analysis. The researcher was considering utilizing interviews as well but decided against it for various reasons. As the population was very specific and hard to contact at times, time constraints were one barrier that would not allow for the collection of surveys and thorough interviews. With how in-depth the survey was and the elaborate nature of responses, interviews were seen as too repetitive and unnecessary. Lastly, interviews were disregarded to avoid the ethical breach of emotional sensitivity/damage, as reminiscing on mental health related topics is personal and potentially traumatizing for some participants. This structured survey approach allowed for significantly efficient and clear data analysis, as the researcher is comparing answers to the same questions across a plane of all respondents.

When constructing the survey, the mixed method approach allowed for quantitative and qualitative questions and responses. Questions that inquired about participants' ages, program durations, and scale responses were categorized within the quantitative section. This kind of data is effective as it provides a numerical depiction of answers that can easily be translated and

interpreted. Questions that inquired about participants' experiences, opinions, elaborations, and detailed emotional effects were categorized within the qualitative section. Qualitative questions were included for more personal, specific responses that cannot be answered by a set list of choices. A variety of open and closed ended questions were also used- open ended questions usually falling under the qualitative section to allow for respondents' elaboration and closed ended questions falling mostly under the quantitative section as they were typically numerical.

Since this topic has not been widely researched, there is little the researcher could base survey questions off. The overall structure and specific questions were original, but influence can still be accredited for multiple question types. As mentioned earlier, the University of New Hampshire research project inspired the ideas of continuity in the questions. Mater asked her participants questions that draw on experiences before, during, and after treatment. Analyzing the experiences before and after, not just during, creates a window to investigate change and continuity overtime which is why the researcher adopted this question style/focus. This structure allowed for a clearer, big picture understanding of the people and events being studied (Mater, 2022). In addition to this, some questions where the participant is supposed to quantitatively record their emotions or opinions were influenced by American social psychologist Rensis Likert's Likert scale. This form of ranking usually has five-seven answer choices and measures "attitudes, perception, knowledge, values, and behavioral changes." Reading from left to right, choices range from a strong emotion or statement such as *Strongly Disagree t*o the opposite emotion, such as *Strongly Agree*, with the middle option usually being *Neutral (*MWCC, 1999*)*. This range of answer choices allows for flexible answers where participants have more freedom in responding compared to a limited question that is simply answered with "yes" or "no." Utilizing this scale allows answer choices to align closer to how the respondent truly feels.

The first section of the survey consisted of mostly qualitative, open-ended questions to gather general information about the respondent and the program they will be referring to throughout the rest of the survey. Name, preferred communication form, age, gender, facility name/location, and treatment duration were asked. This provided a foundation for more specific, personal questions that will follow them. It also provided a demographic basis that could be analyzed to see its potential independent role in treatment outcomes. The second section of the survey contained mostly closed-ended qualitative questions that precede open ended questions prompting respondents to expand on their answer if they are comfortable. These questions asked the background/reasons for admission, change in relationship with the person who sent them there, and overall experience on a Likert scale. Another set of questions inquired about the involuntary or voluntary nature of the admission process, transportation process, and program itself. This could be used to later analyze a possible connection between these answers and how participants rated their overall experiences. In addition to this, multiple questions followed the Likert scale to grasp an idea of participants' mental state and outlook before and after their treatment. To get an extensive picture of the effects of treatment and investigate the three points of the researcher's hypothesis, participants were asked to compare the changes or presence in

anxiety, depression, and PTSD as well as their willingness to try new things, raise mental health awareness and try other mental health treatment experiences if needed.

To distribute the survey and construct a sample of participants, the researcher greatly benefited from the use of social media. Using platforms such as TikTok, Facebook, and Instagram, they started the process by joining support and connection groups of people who had received treatment in facilities classified under the troubled teen industry. Most of the respondents were derived from these groups as they enabled the researcher to efficiently reach a large quantity of people through a singular post. These posts, comments, and direct messages all informed the recipient of the researcher's purpose of inquiry and the potential role they could play by completing the survey. Once participation was agreed to, ethical standards were met by including the informed consent document before participants took the survey, using their survey submission as a form of consent (See Appendix A). The document outlined the personal privacy precautions taken such as using pseudonyms if needed when analyzing and publishing data, using a password encrypted computer, and keeping all responses confidential. Participants were not required to answer every survey question and were explicitly informed of the survey's voluntary nature. This ensured emotional comfort and security protection that would hopefully produce genuine, accurate responses.

Once data was collected, *thematic analysis* was used to interpret the findings. This was selected as the best means of examination as it is used for "identifying, analyzing, and interpreting patterns of meaning" within a set of data (Clarke and Braun, 2015). The self-created and exploratory nature of the questions required a method of interpretation that analyzed general trends to depict new ideas, which is exactly what thematic analysis aims to accomplish. This general analysis of patterns will be used to answer the three original parts of the research question- emotional effects, openness to treatment, and willingness for advocacy.

Limitations

While the researcher tried to minimize interference, there were still limitations that affected the research process. As the troubled teen industry and the issues revolving around it are underrepresented and specific, the population was difficult to reach, especially since the parameters were narrowed to just wilderness therapy programs. Many of the people the researcher reached out to didn't respond, and the sample the researcher did obtain was smaller than they had hoped, leading to a limited sample size. In addition to this, there was a lack of resources, time, and outreach capabilities as the researcher is a student. No funding could be received to incentivize participants which would have likely increased response rate, and the researcher had to gather their sample in a smaller time than desired. While the sample is still greatly representative, these limitations hinder it from being fully representative of all wilderness therapy attendees in the United States.

Results

The survey yielded results from 27 individuals; each having undergone treatment at a wilderness therapy program in the United States.

Chart 1: Gender
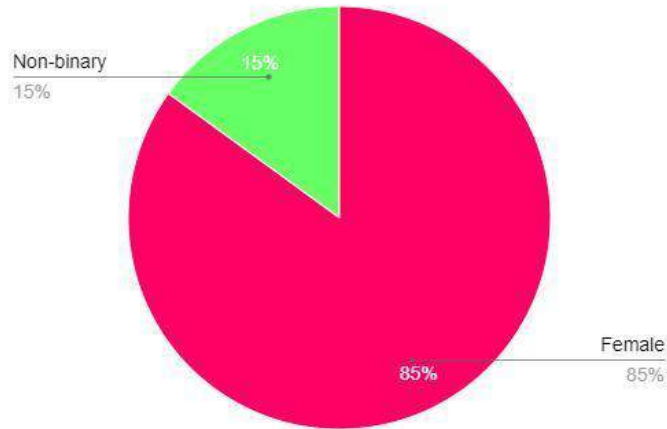
In chart 1, when inquired about gender, 85% identified as female, 0% identified as male, and 15% identified as non-binary.

Chart 2: Admittance Age
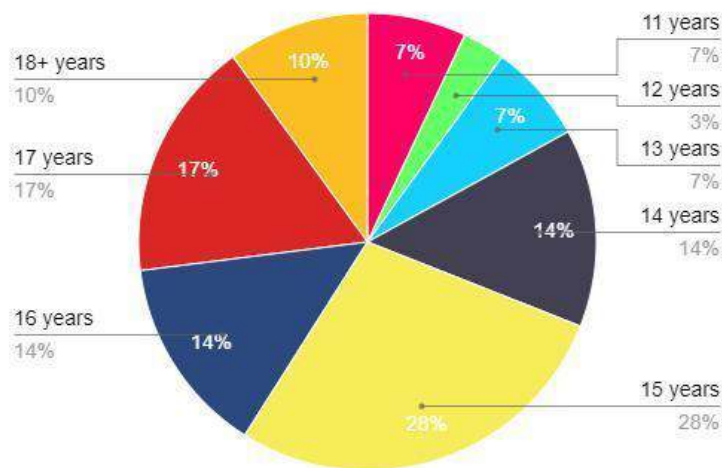
In chart 2, people's age when admitted varied from 11-65 years old. 7% of people were 11 years old, 3% of people were 12 years old, 7% of people were 13 years old, 14%

of people were 14 years old, 28% of people were 15 years old, 14% of people were 16 years old, 17% of people were 17 years old, and 10% of people were 18 years or older. The most prevalent age group was 15 years, and the least common age was 12 years.

Chart 3: Facility location by U.S. region
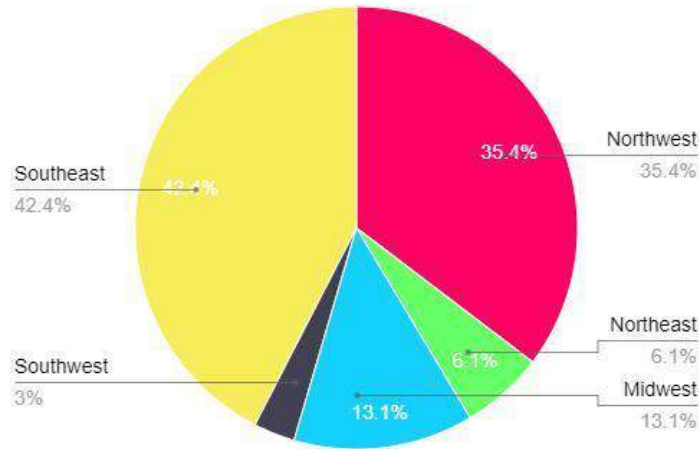
The locations of respondents' facilities came from all over the United States, as seen in Chart 3, with 35.4% of people having received treatment in the Northwestern region, 6.1% in Northeastern region, 13.1% in the Midwest, 3% in the Southwestern region, and majority of people in the Southeast region at 42.4%. The most common treatment length was 0-1 years at 41% of people, 33% of people were treated for 1-2 years, 11% of people were treated for 2-3 years, and 15% of people selected "other."

The most common reasons for being admitted were depression, anxiety, suicidal thoughts/actions, running away from home, substance abuse, and rebellion against authoritarian parents. When asked to rate their overall experience on a Likert scale, 74% of people selected "extremely negative" and 26% answered "moderately negative." When asked to elaborate on this, some of the most representative/common responses written were "I experienced all forms of abuse," "prison is better than this place," and the "staff did not have qualifications." Participants placed emphasis on the methods of punishment and isolation used, saying they were "forced to eat spoiled food," "expected to turn on each other," "not allowed to talk to our parents," and "not allowed to speak for months."

When the researcher inquired about the voluntary or involuntary nature of the experience, responses followed a similar pattern. Participants were asked to reflect on their admission, transportation, and experience.

Chart 4: Admission
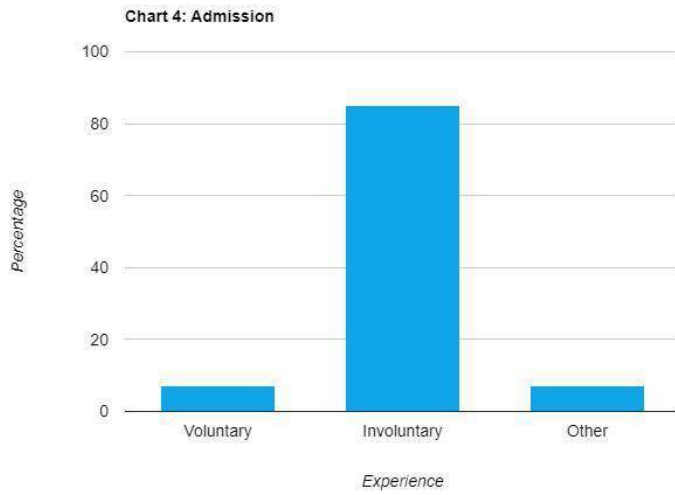
Regarding admission, 7% answered "voluntary," 85% answered "involuntary," and 7% answered "other."

Chart 5: Transportation
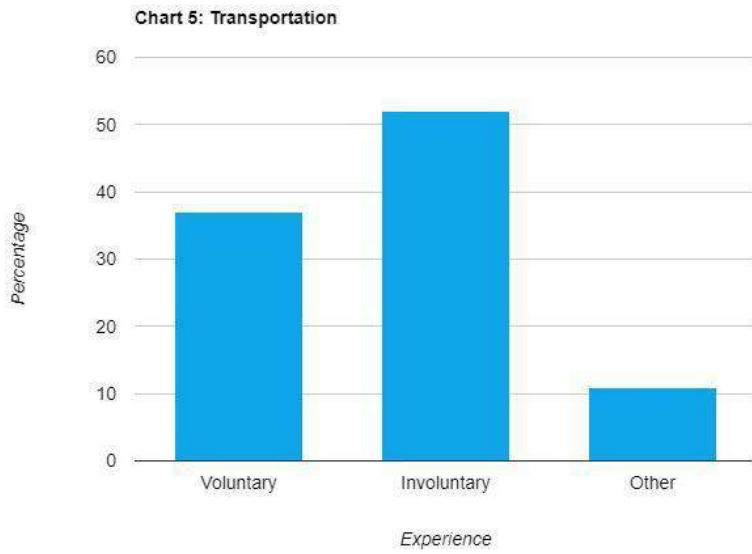
Regarding transportation, 37% of people answered "voluntary," 52% of people answered "involuntary," and 11% of people answered "other.

Chart 6: General Experience
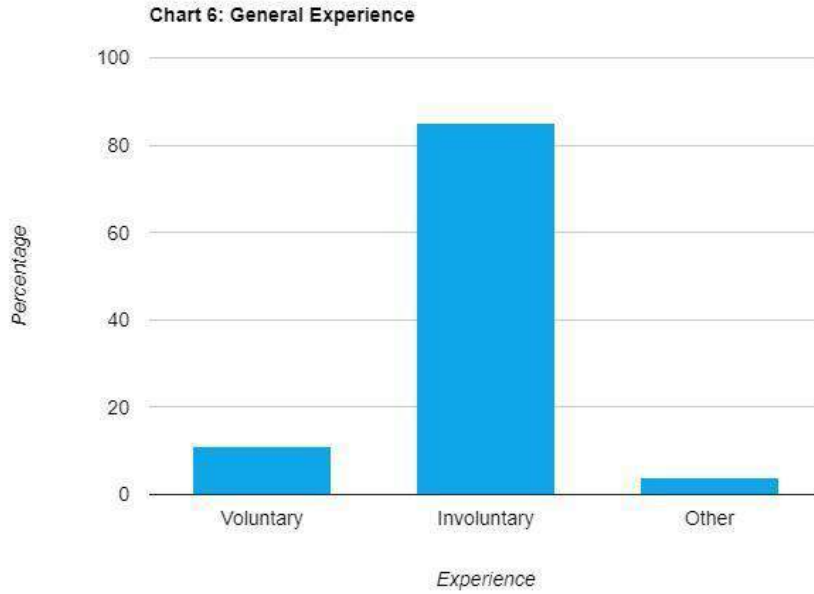
Regarding general experience, 11% answered "voluntary," 85% answered "involuntary," and 4% answered "other." In addition to this, when asked to choose "yes," "no," or "other" to answer if the treatment experience was the same as it was advertised, 0% of people said "yes," 85% of people said "no," and 15% of people chose "other."

Chart 7: General Mental Health Change Overtime
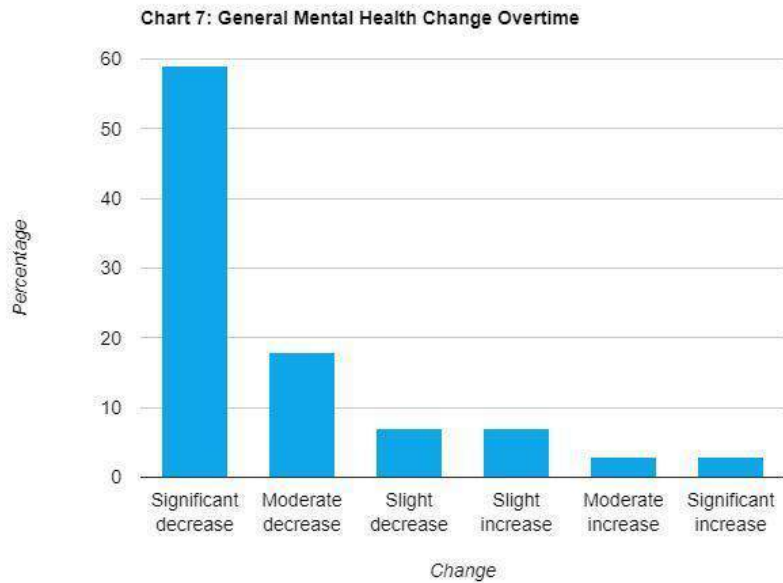
When investigating change overtime, participants were asked to rate their change in mental health over the course of treatment on a Likert scale ranging from "significant decrease' to "significant increase." Most respondents selected "significant decrease" at 59.2%, 18.5% selected "moderate decrease," 7.4% selected "slight decrease," 0% selected "no change," 7.4% selected "slight increase," 3.7% selected "moderate increase," and 3.7% also selected "significant increase."

Participants were asked to answer a Likert scale of 1-5 with "1" signifying no connection and "5" representing a strong connection to an inquired condition. For each topic, the respondent would input a response about before and after treatment to analyze the change overtime. The topics inquired about were the presence of anxiety, depression, PTSD, desire to speak out about mental health, willingness to try new things, and willingness to pursue treatment. An increase was found in anxiety, depression, PTSD, and the desire to speak out about mental health, while a decrease was found in willingness to try new things and willingness to pursue treatment.

Analysis and Limitations of Results

From Chart 1, it is gathered that most respondents (85%) were female, a small amount (15%) were non-binary, and no respondents were male. This raises questions and concerns about *sampling bias*, which is "when a sample does not accurately represent the population being studied." Sampling bias can occur from errors in data collection and lead to the under or over representation of groups within a population (Simkus, 2023). This introduces the limitation of participant gender to have potentially influenced survey responses. As seen in Chart 2, the most common participant age was 15 years old with a mostly even distribution of admission ages being observed, not leading the researcher to believe that any one age group had a specific outcome on treatment experience. While facility location varied as recorded in Chart 3, the most popular location of treatment was in the Southeastern United States at 42.4% and the second most popular location was Northwestern United States at 35.4%. Participants from both locations reported overwhelmingly negative responses to open and closed ended questions, not leading the researcher to observe any significant role that location plays besides differences in descriptions of climate. When asked about treatment length, most respondents (41%) selected their treatment lasted 0-1 years, with a positive correlation being observed between increased treatment length and negative answers on later questions. This implies that longer treatment periods may have more of a potential for creating a decline in mental health than shorter treatment periods. The most popular responses of reason for admission were "depression," "anxiety," "suicidal thoughts/actions," "running away," "substance abuse," and "rebellion." With 74% of respondents reporting an "extremely negative" experience and 59.2% of respondents reporting a "significant decrease" in mental health as a result of their program, it is logically sound to infer that the reasons clients were admitted for not only did not receive proper treatment, but were likely

exacerbated; having the opposite effect of the facilities purpose and raising concerns of overall effectiveness. In Charts 4-6, when participants were asked if the admission, transportation, and general treatment processes were voluntary or involuntary, an overwhelming majority reported it being involuntary in nature. As depicted, 85% stated their admission was involuntary, 52% said their transportation was involuntary, and 85% said the general treatment experience was involuntary. 85% of people also answered that their treatment was not the same as was advertised. A strong correlation was found between involuntary treatment and a negative trend of responses, highlighting that voluntary treatment and proper depiction of services could enhance the mental health treatment experience.

Implications

Given the profoundly negative nature of responses, it is evident that a reform of wilderness therapy programs and the troubled teen industry in general needs to occur. The two most impactful ways to positively change the outlook of these facilities are to inform the public about this inhumane trend and advocate for stronger government regulation. Educating society can increase awareness of not only the general public, but also the fraction of those considering these facilities as treatment options. Studies such as the one performed in this paper, more attendees speaking out, and an increased media presence are all ways to bring this issue into the public eye. One example of a non-profit industry making strides against the troubled teen industry is Breaking Code Silence. Through research, advocacy, and legislation, they strive to "uplift, organize, and inspire present and future generations, while promoting youth rights and evidence-based alternatives to the troubled teen industry" (BCS, 2024).When public issues such as this become a widely talked about phenomenon, it allows people to finally see the previously suppressed flaws in the system and advocate for needed change. This is vital as it is a highly underrepresented issue. Attention also needs to be drawn to the troubled teen industry for those who are considering admission of themselves or someone else into treatment. As previously stated, in addition to the inhumane nature of these organizations, false program advertising was also a significant issue. People need to be aware of the statistics and traumatizing events reported at these facilities that commonly get brushed under the rug. Physical abuse, mental abuse, sexual abuse, starvation, isolation, limited and censored communication, dehumanizing punishments, and unqualified medical/emotional treatment are just some of the tragedies hidden from the public eye, especially to those considering admission. Organizations typically only describe the supposed positive or desired outcomes, leading many uninformed, desperate people to fall victim to deceptive marketing and advertising. Therefore, if there was increased societal awareness, the issue could not only be suppressed, but those seeking treatment could be well-informed and see the truth about the troubled teen industry. A second solution to reform the troubled teen industry would be to increase government regulation. As of now there is little

intervention in the practices, structure, and quality of care, and practically no intervention if these institutions are privately owned and funded. Harsher/more regulatory laws that would allow frequent administrative check-ins and stricter monitoring of practices would transform these programs into safe, beneficial ones that genuinely contribute to the well-being of clients.

Future Research

Future research could follow a variety of different directions. To start, in an explanatory manner, closer investigation and/or more studies replicating the procedures of this researcher's experiment could be performed to analyze the presence of a link between the demographics collected and participants' experiences and answers. Something specific to further analyze would be the potential effects of gender on responses, as this sample had no male representation. Exploratory research could also be performed stemming from the findings of this study. As research was confined to data collected solely from wilderness therapy program attendees, it would be interesting to research another branch of treatment such as religious based institutions, especially given the background of limited government interference due to potential 1st amendment violations of religious freedoms in existing programs. Researching the same question regarding another branch would allow for comparison between responses, allowing future researchers to further study the continuities and change of mental health, openness to future treatment, and willingness to advocate.

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"I am not religious, but I am spiritual." What Could the Speaker Mean by "spiritual"?
By Wangwang Ma

When we hear the word "spiritual," we imagine a person breathing at the top of a hill under the sunshine, believing sunshine and fresh air can bring them energy and inner peace. Doing yoga and an aromatherapy massage could also be a stereotype of being spiritual—like the character Pheobe in Friends. When someone says "I am not religious, but I am spiritual," it is clear that this person holds that being spiritual is fundamentally different from being religious. This difference, according to Niekerk, is "notoriously hard to define" (8). In an attempt to clarify this distinction, this essay will first lay out the definitions of spirituality and religion, then explore the reason for this distinction by examining the development of spirituality.

From the etymological perspective, the word "spirituality" originates from the Latin word "spiritualitas," which originates from the Latin word "spiritus," a noun, and the Latin word "spiritualis," an adjective (King 7). According to the online Latin dictionary, both words contain meanings of breathing, air, and spirit ("Online Latin Dictionary Olivetti"). Since spirit has the connotation of air and breathing, it could be concluded that it is untouchable, invisible, and essential. According to King, the words "spirits" and "spiritual" can be traced back to the translation of the Greek biblical terms "pneuma" and "pneumatikos." It is notable that in St. Paul's definition, spirit ("pneuma") is not the opposite of body ("soma" or "corpus,"), but the opposite of flesh ("sarx") (King 7). In St. Paul's definition, a distinction was made between the spiritual and the soul ("psyche") which is closely associated with animal life (Beck para.2). The spiritual is wholly other from animal life in the way that it is associated more with the Spirit of God than nature (Beck para.5).

The Merriam-Webster dictionary records the definition of spirituality as the quality or state of being spiritual; it could therefore be inferred that "spirituality" shares the same disconnection from the flesh, or the animalness, and association with what is higher than the natural order. The contemporary understanding of spirituality, specifically in the context of Western culture, means "a sense of connection to something bigger than ourselves" which would allow us to seek the meaning of our lives beyond mere existing (Delagran "What is spirituality? Taking Charge of Your Wellbeing"). Being connected with this higher existence means being "released from the burden of ego, and discharged into a larger world that enables us to focus less on our ego and more on our larger cosmic identity" (Van Niekerk). For this reason, spirituality is also often related to a variety of ideas advocating for environmental sustainability and other social responsibilities (Leal Filho).

Religion, on the other hand, consists of "narrow, dogmatic, and strictly rationalistic views" of "worldviews and life goals" (Forman 2). Unlike spirituality's direct dissociation with flesh and nature, religion offers guidance to people's lives in this world through a set of moral teachings and disciplines (Forman 177). According to the Merriam-Webster dictionary, religion is "a personal set or institutionalized system of religious attitudes, beliefs, and practices". Being religious therefore requires some form of personal or institutionalized system that gives a certain set of rules or teachings that regulate people's lives in terms of ethics, with the prospect of attaining a higher status

when the current life ends — such as Nirvana in Buddhism or Heaven in Christianity. Religion is by nature systematic, and therefore lacks spirituality's emphasis on being shapeless and intangible like air. Under a close examination of the definition of one's being spiritual and being religious, it could be observed that interestingly, the distinction lies not in the belief in the existence of something higher than the animal or natural world, but in the way one practices this belief. Not only so, spirituality also has its roots in the Bible. Why, then, would the speaker in question, who isn't strictly atheist, strongly deny the word "religious" and embrace spirituality instead?

It is necessary to examine this question in a historical light. Forman, in his book Grassroots Spirituality: What It Is, Why It Is Here, Where It Is Going, provides an overview of the development of spirituality as a rebellion against religion. In his analysis, the Renaissance and the Enlightenment created an age of reason that made people value rationality. Although the Renaissance and Enlightenment did not destroy the authority of religion, they gave people a solid foundation of critical thinking and a sense of people orientation. As capitalism, humanism, and liberalism started to emerge, people started to pay more attention to themselves and their current lives in the material world. Things changed drastically in the 1960s. According to Woodhead (2016), people are tired of "living in a particular way in order to prepare for the next (true-higher) life" (428) . They began to doubt precisely the systematic nature of religion that taught them to prepare for heaven rigorously, just like during medieval, although times have changed, "as constituted and regulated by the roles, duties, and obligations of the institutional order, the 'given' or 'traditional'" (Woodhead 429). People's "frustration with organizations and institutions now shows itself as distrust of religious dogma and other capricious rules that perpetuate institutional power" (Nielsen para. 5). This frustration brought about the possibility of the emergence of spirituality, which frees people from rigid moral rules and allows them to explore their personal connection with the higher being. Under this context, spirituality emerges. It is something that opens up the potential of "'feeling alive'; of self-exploration and growth; of getting in touch with as much as possible of what life has to offer; of experiencing 'the quality of life'" (Woodhead 429) in people's current life.

The process of modernization also pushed spirituality forward. According to Nielsen , "Demographic trends have moved people toward a faceless suburbia where it is difficult to feel a sense of community and deep connection with others" (para. 5). One of the most important advantages of being a member of a religion, the unity of the community, was removed due to modernity. Meanwhile, the need to think beyond materialism and consumerism drove people to seek deep connections with something that could connect to their own value. According to Woodhead, spirituality catered to "what people are most interested in: their own intimate and personal (and their relational) lives" (428). In addition, the emergence of feminism also caused people to abandon religion. Forman states that "changing gender roles, family structures, and feminism also contribute to spirituality" as feminists started to reject the traditional gender roles and family structures constrained by religion. In this context, spirituality became a substitute for religion as it does not contain systematic teaching and, therefore, could be interpreted on a personal level and catered according to individual needs.

With a thorough examination of spirituality and religion, it is now safe to conclude that spirituality could be seen as a rebellion against traditional religious values, specifically religion's nature of being rigid and systematic. It emerges with the development of modernity and appeals to people's renewed need to connect with some higher being not after but during their current life. Therefore, when a person says "I am not religious, but I am spiritual," it is best to interpret the word "spiritual" as a personalized relationship with something higher than the animal, material world, a belief of individual's potential to attain meaning and value in life, and a positive life philosophy that values social responsibility stemming from transcending one's own ego.

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Identification of Screw Parameters for Affordances using Vision Language Models

By Niu R[1], Panthi J[2]

Abstract

　　To advance robot autonomy within versatile frameworks that utilize Screw Theory to model affordances, automating the identification of screw parameters defining these affordances is crucial. Current state-of-the-art approaches utilize data-heavy machine learning algorithms to identify these parameters for a limited set of objects and are unable to consider task context while doing so. In this paper, we use a Visual Language Model (VLM) and leverage the plethora of internet data it has already been trained on to extract screw parameters from a passed-in image and prompt. Because of the VLM's ability to interpret natural language, it also seamlessly takes task context into account. We assess our approach through experiments showcasing its success across various affordance types, including objects with potential multiple affordances contingent on the application context. By defining success rate as the correct identification of affordance type and affordance location, we observe that our method has an average success rate of 91.43% for tested single and multiple affordance cases.

Keywords: Screw Theory, Affordances, Screw Parameters, Visual Language Model, Natural Language, Task Context, Affordance Type, Affordance Location

Introduction

　　Real-world deployment of robots requires them to be able to perform a diversity of tasks. A general-purpose robot could perform tasks that could vary from moving a stack of books across a table surface, to turning a wheel valve, or opening a door. These movements are very different from each other, so it would be very inefficient to have a different program for every single task. There is a need for a versatile framework that is able to handle different tasks in a template-like manner. A recent promising approach by Pettinger et al, *A Versatile Affordance Modeling Framework Using Screw Primitives to Increase Autonomy During Manipulation Contact Tasks,* utilizes the concept of screw-based affordances to solve this problem (1). The framework is also made robust by incorporating compliance to tackle runtime task uncertainties. However, an important limitation of their work is that the screw parameters needed to define task affordances are hard-coded. For an efficient and autonomous real-world deployment, it is vital for robots to be able to identify these parameters during runtime. We present an innovative solution involving the usage of a Vision Language Model (VLM) to identify screw parameters.

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Affordances

  The term "affordance" comes from the 1977 book *The Theory of Affordances* by JJ Gibson. It was initially used in psychology and defined as what an environment "offers [an] animal, what it provides or furnishes, either good or ill" (Gibson 56) (2). For example, a paper affords writing, a ladder affords climbing, and a knife affords cutting. In robotics, the property of an object that allows it to be manipulated is the object's affordance. For example, a microwave door's affordance is the rotational motion that allows it to open or close. An object could have multiple affordances as well, for instance, a water bottle can afford opening its lid for drinking. However, one could also grab it and move it across a table.

Screw Theory

  Screw Theory was formalized by Sir Robert Ball in his book *A Treatise on the Theory of Screws* in the context of mechanics to describe rigid body displacement (3). The idea is that any rigid body displacement can be described as a motion about some screw, and this method provides a compact way to describe 3D motion as a normalized 6x1 vector consisting of angular and linear velocities (4). An intuitive example is a mechanical screw whose motion can be described by identifying its location from some frame of interest, screw axis, rate of rotation, and its pitch (the ratio between the amount of translation and rotation), as shown in Figure 1. If its pitch is zero, the screw performs pure rotational motion, and if it is infinite, its motion is purely translational. For a non-zero finite pitch, the screw exhibits "screw" motion. One can use this model to describe task affordances in terms of elementary motions. For instance, when moving the book across the table, the axis of movement can be thought of as through the center of the book, and the movement as translational motion along that axis. When opening a door, the axis is through the hinge of the door, and the movement is a rotational movement about the axis.
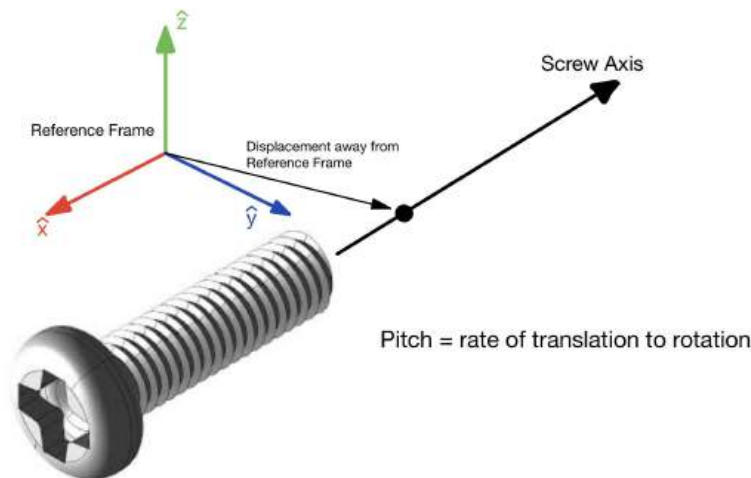

Figure 1. Depiction Of Screw Parameters (5)

Related Works

Early works such as *Affordance Templates for Shared Robot Control* by Stephen Hart and other researchers used Affordance templates to semi-automate complex tasks (6). In their work, affordance templates provide the details of how a robot can perform tasks by describing its affordance through a series of end-effector (EE) pose waypoints along the affordance path. For instance, when turning a valve, the EE waypoints would be along the circumference of the valve. Also, the object affordance has to be known prior to runtime, as the robot is ultimately just following a template. Any change in the environment would cause the task execution to fail. This was fixed by keeping a human operator in the "operational" loop by allowing them to control the affordance template parameters during runtime. However, this method still requires the operator to define affordances for every object that the robot is tasked to manipulate.

Adam Pettinger and other researchers tried to solve the problem of having to manually define task-dependent affordances in *A Versatile Affordance Modeling Framework Using Screw Primitives to Increase Autonomy During Manipulation Contact Tasks* (1). A promising method which uses Screw Theory to model affordances was introduced in order to describe any task affordance in terms of elementary pure rotational, translational, or screw motions. This method of modeling object affordance lowered task duration and the amount of force and torque applied to the object, and ultimately provided a "flexible [model] to represent many manipulation objects" (Pettinger et al. 8). However, in their work, they manually identify screw parameters prior to runtime, and thus, there is a need for automatic identification of these parameters for autonomous real-world deployment. Moreover, there is the possibility of the change in screw parameters due to environmental uncertainties. Even though Pettinger et al. address this issue with admittance control – up to 10 centimeters for translational tasks and 0.35 radians for rotational, exact identification of screw parameters during runtime would improve this error window.

There are efforts to detect parameters describing object affordances using vision systems. Early methods, as described in Ben Abbatematteo et al.'s *Learning to Generalize Kinematic Models to Novel Objects*, used a single photo of an object and a machine learning algorithm with a ResNet-18 backbone to deduce kinematic models of unseen articulated objects (7). However, their method is only able to identify objects from a limited set of object classes that their model was trained on. Another method by Scott Niekum and other researchers, presented in *Online Bayesian Changepoint Detection for Articulated Motion Models*, used easily identifiable fiducial markers on the object in conjunction with demonstration learning to identify object articulation motion parameters (8). A major limitation of their approach is that it is not practical to collect the plethora of demonstration data along with the cumbersome usage of fiducial markers to represent the diversity of real-world manipulation tasks. A novel approach, proposed by Ajinkya Jain and other researchers in the paper *ScrewNet: Category-Independent Articulation Model Estimation From Depth Images Using Screw Theory*, known as ScrewNet, aimed to solve some of these issues by using multiple raw depth images to identify screw parameters (9). ScrewNet is able to identify screw parameters without prior knowledge of the object description, essentially making

a generalized model for many objects. ScrewNet is able to do this because it "uses screw theory to unify the representation of different articulation models and performs category-independent articulation model estimation from depth images" (Jain et al. 6). Because Screw Theory provides a general model to capture various object articulation motion, ScrewNet just needs to identify an object's screw parameters to describe its motion. Although its method is promising, it requires a lot of data for training, as do many data-driven approaches, and only works for 1 degree-of-freedom articulated objects. Furthermore, their method is unable to consider the context for the affordance for objects that could have multiple affordances.

Our Method

We address these limitations by leveraging a VLM powered by GPT-4V, specifically Copilot, to predict screw parameters. VLMs leverage a cornucopia of internet data for training and have the crucial benefit of inferring context from natural language. They can be utilized to identify screw parameters from passed-in images and, more importantly, identify them contextually. For instance, the task affordance could be different for manipulating a book depending on the application. If the task is to push the book across a table, the screw axis could be thought of as through the center of mass of the book in the direction of motion, and the movement is purely translational along that screw axis. However, if the task is to turn a page in an open book, the screw axis is through the spine of the book, and the movement is purely rotational around that axis. By passing context along with an image, we can query a VLM to identify the task affordance that is relevant to that context. In summary, our method aims to improve two aspects of current screw parameter identification methods: lack of generalization to a broader category of objects and an inability to take task context into account, as one object can have multiple affordances, depending on the task at hand.

Experimental Setup

We split the experiment into two parts, but both queried Copilot to identify the screw parameters from a passed-in image. For each object that we passed into Copilot, we prompted the VLM five times and used the "New topic" button each time. Prompting the VLM multiple times for each object through a new topic ensures the VLM does not have a memory of the previous interactions and provides a fresh stochastic output (10). We engineered the prompt in a way to ensure that Copilot responded with a text string that we could easily evaluate (or in future work, implement in automated programs). This included explicitly telling the VLM that we are in the scope of Screw/Affordance theory and robotic object manipulation, what each affordance type means, and the exact format of the desired response.
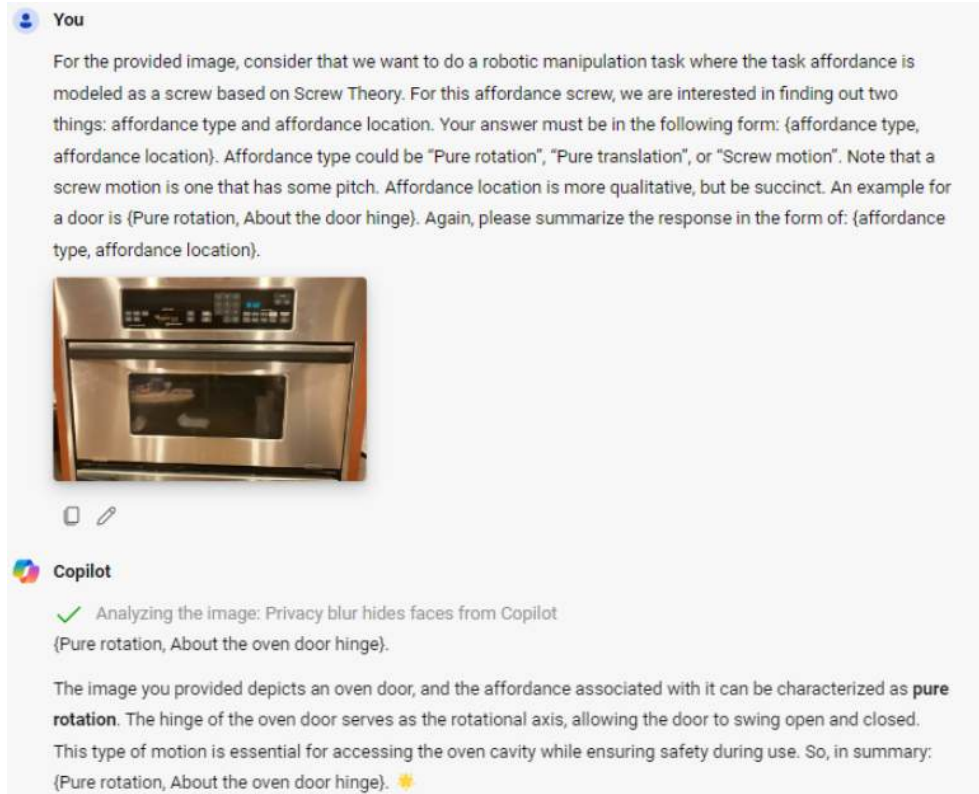
Figure 2. Example Prompt And Output For Single Affordance Screw Parameter Identification

The first part was regarding objects which have only one affordance where we do not give the VLM the task context. The prompt we fed Copilot was in the form: "[image] For the provided image, consider that we want to do a robotic manipulation task where the task affordance is modeled as a screw based on Screw Theory. For this affordance screw, we are interested in finding out two things: affordance type and affordance location. Your answer must be in the following form: {affordance type, affordance location}. Affordance type could be "Pure rotation", "Pure translation", or "Screw motion". Note that a screw motion is one that has some pitch. Affordance location is more qualitative, but be succinct. An example for a door is {Pure rotation, About the door hinge}. Again, please summarize the response in the form of: {affordance type, affordance location}." Refer to Figure 2 for an example of the prompt and output for a single affordance test case.
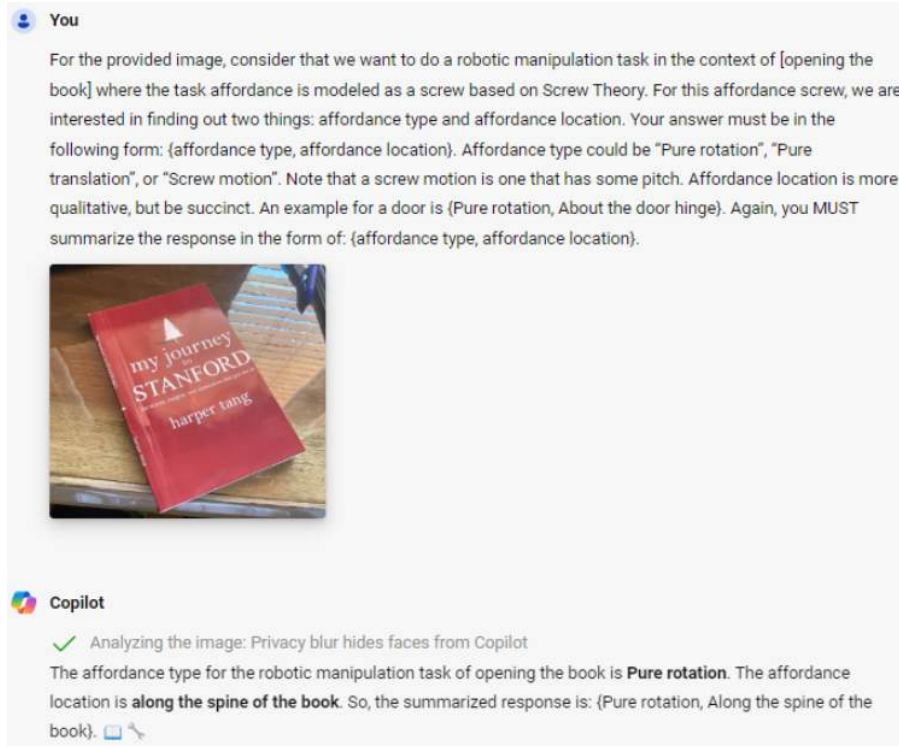
Figure 3. Example Prompt And Output For Multiple Affordance Screw Parameter Identification

The second part was regarding objects with multiple relevant affordances depending on the task context. The prompt we fed Copilot was in the form: [image] "For the provided image, consider that we want to do a robotic manipulation task in the context of [context] where the task affordance is modeled as a screw based on Screw Theory. For this affordance screw, we are interested in finding out two things: affordance type and affordance location. Your answer must be in the following form: {affordance type, affordance location}. Affordance type could be "Pure rotation", "Pure translation", or "Screw motion". Note that a screw motion is one that has some pitch. Affordance location is more qualitative, but be succinct. An example for a door is {Pure rotation, About the door hinge}. Again, you MUST summarize the response in the form of: {affordance type, affordance location}." Refer to Figure 3 for an example of the prompt and output for a multiple affordance test case.

In the expected output, affordance type is the type of motion required to manipulate the object at hand (translational, rotational, or a combination of both, i.e. screw motion). The affordance location is a qualitative description of where the screw axis is in relation to the passed-in object. An output in this form gives us a quantitative way to evaluate the response from the VLM.

Results and Discussion

Single Affordance Case

In the first part, we studied objects that have only one relevant and clear affordance. We tried the task of opening a drawer, opening a microwave door, fastening a screw and a bolt, pulling out a tissue from a tissue box, and rotating a mini fan, to evaluate our method to correctly identify screw parameters. We selected these objects as they are common in everyday lives and represent purely translational motion (opening a drawer, pulling out a tissue), purely rotational motion (opening a microwave door, rotating a mini fan), and a combination of both translational and rotational motion (fastening a screw and a bolt).

We define overall success as the correct identification of both the affordance type as well as the location. Additionally, we also evaluated the success for correct identification of just the affordance type or the affordance location. The results of the first part of the study showed great success in Copilot's ability to identify screw parameters of objects with one main affordance. It was able to correctly identify the affordance type for every object task for every trial. However, for the case of affordance location identification, it failed one time for the mini fan trial, resulting in the affordance location total success rate of 96.67% (29 successes out of 30 trials). (Refer to table for summary statistics). Therefore, the overall success rate for the single affordance experiment was 96.67%. The comprehensive results are summarized in Table 1.

It is interesting to note that although Copilot was able to give the screw parameters in the correct output format every time for both purely translational and purely rotational task affordances, it struggled to do the same for screw motion affordance objects. Instead of giving affordance parameters in curly brackets in the form of {affordance type, affordance location}, Copilot would always just put them in bold. Furthermore, we observed that the overall success rates for translational and screw tasks were 100%, while it was 90% for rotation tasks. The details of these trails are available in the attached appendix at
https://drive.google.com/drive/folders/1v55yTKy2nY3ovfBHZx6lU8J1JjebNpAr?usp=sharing.

Table 1. Summary Statistics for Single Affordance Detection

VLM Task	Expected Affordance Type	Expected Affordance Location	Affordance Type Success Rate	Affordance Location Success Rate	Overall Success Rate
Drawer	Translation	Top edge of drawer	5/5	5/5	5/5
Microwave Door	Rotation	Handle of microwave door	5/5	5/5	5/5
Screw	Screw Motion	Along axis of screw	5/5	5/5	5/5
Mini Fan	Rotation	Center of fan head rotation axis	5/5	4/5	4/5
Tissue Box	Translation	Out of opening in tissue box	5/5	5/5	5/5
Bolt	Screw Motion	Along axis of bolt	5/5	5/5	5/5

Multiple Affordance Case

In the second part, we studied objects with multiple affordances. This means that the object could have different screw parameters based on the application at hand. For this case, we

also opted to select objects representing everyday manipulation scenarios. Specifically, we chose to use a book, water bottle, computer mouse, and laptop. For the book, one application is that we could move the book across a table (rotational or translational), and in another context, we could open the book (rotational). For the water bottle, we could both pick up the water bottle directly upwards (translational) or drink from it by opening the lid (screw motion). For the mouse, we could move it across a table (rotational or translational) or use the mouse by clicking the left or right mouse buttons (translational) or turning the scroll wheel (rotational). For the laptop, we could close the laptop lid (rotational), or type on the laptop's keyboard (translational). We supplied text in bold in the previous sentences as context to Copilot for these trials.

The results showed Copilot is also proficient at identifying screw parameters with task context in mind. It had an overall average success rate of 87.5% (35 successes out of 40 trials). It was able to correctly identify the screw parameters of the book, water bottle, and mouse for both task contexts with a 100% average success rate. However, although it was able to correctly identify the screw parameters for all trials of closing the laptop lid, it failed to identify the affordance type for all trials of pressing a key on the keyboard. Instead of pure translation, it identified rotation or screw motion for the affordance type. We hypothesize that this could be due to the nuanced mechanics of typing on a keyboard. The comprehensive results of these studies are summarized in Table 2.

We also observed that similar to the single affordance case, Copilot would not always give the output in the form of {affordance type, affordance location}. However, when this happened, it would always put the screw parameters in bold text, which we counted as a valid output. The details of these trails are available in the attached appendix at https://drive.google.com/drive/folders/1v55yTKy2nY3ovfBHZx6lU8J1JjebNpAr?usp=sharing.

Table 2. Summary Statistics for Multiple Affordance Detection

VLM Task	Expected Affordance Type	Expected Affordance Location	Affordance Type Success Rate	Affordance Location Success Rate	Overall Success Rate
Move book across table	Translation	Horizontal surface of book	5/5	5/5	5/5
Open Book	Rotation	Spine of book	5/5	5/5	5/5
Pick up water bottle	Translation	Vertical axis of water bottle	5/5	5/5	5/5
Opening water bottle lid	Screw Motion	Lid of water bottle	5/5	5/5	5/5
Move mouse across table	Translation	Table surface	5/5	5/5	5/5
Using mouse	Translation OR Rotation	L/R Mouse Button OR scroll wheel	5/5	5/5	5/5
Close laptop	Rotation	Hinge of laptop	5/5	5/5	5/5
Type on laptop	Translation	Through vertical axis of keycap	0/5	5/5	0/5

To encapsulate the efficacy of our method, we noted that when looking at both single and multiple affordance cases, the overall success rate of this framework was 91.43% (64 successes out of 70 trials).

Conclusion

In this paper, we explored a method to advance the automation of screw-modeled affordance frameworks for real-world robot deployments by proposing and evaluating a method to autonomously identify the screw parameters describing various tasks. Our method using Copilot, a visual language model, improved upon current methods of automatic screw parameter identification by leveraging the massive amount of internet data that language models are trained on and supplying context from natural language processing. From our experiments, we discovered that Copilot can identify affordance types and affordance locations for objects with one main relevant affordance with a near-perfect success rate of 96.7%. For the case of multiple affordances, our method also resulted in a remarkable success rate of 87.5%.

For future work, we would like to implement this framework on a program that directly interfaces with the robot so that we are able to have an end-to-end framework that can identify screw parameters from images and execute the related affordance. In this work, we looked at cases that had a single affordance at a time. In the future, it would be interesting to study object affordances that are sequential, for instance, opening a fridge door and then retrieving an object from inside.

A limitation to this work is the response turnaround from Copilot, which was in the tune of 5 seconds. This limitation could hinder real-time implementation of this approach to identify screw parameters during runtime. This is something that could be improved upon with local visual language models or future advancements with Copilot upgrades. Additionally, for multiple affordance detection, the contexts we supplied were detailed. For high-level task planning, we would hope for the VLM to be able to identify screw parameters from very broad context descriptions.

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Feminism, Commercialization, and the Male Gaze in K-pop: Idol and Fan-effect Analysis
By Zihan Luo

Abstract

With the global rise of the K-pop industry, the shaping and commercialization of female idols have led to critical discussions about feminism and the male gaze. This article explores the complex dynamic between the empowerment of female K-pop idols and their submission to social and commercial pressures, focusing on the representation of femininity in K-pop videos and performances. Through an analysis of fan perceptions, industry practices, and an online survey of K-pop fans, this paper explores how the commodification of feminism in K-pop both challenges and reinforces traditional gender norms. The study suggests that while feminist themes such as female autonomy and empowerment are increasingly visible in K-pop, they are often presented through a male perspective, undermining their authenticity. We believe that the commercialization of feminism in K-pop has perpetuated narrow standards of beauty and objectification of female idols, even though it has also provided moments of genuine empowerment.

Feminism, Commercialization and the Male Gaze in K-pop: Idol and Fan-effect Analysis

Since the debut of BTS and PSY's Gangnam style in 2012, K-pop has evolved from a domestic entertainment model to a global cultural phenomenon. BTS, for example, has amassed over 78.7 million YouTube subscribers. Their song *Fake Love* (2018) reached No. 10 on the billboard chart and remained there for six weeks. *Boy With Luv* (2019) debuted at No.8 and stayed for eight weeks, while *Dynamite*, released in 2020, reached No.1 and stayed on the charts for 32 weeks, debuting as a stream 7,778,950 on Spotify, and BTS Jungkook's *Seven* (2023) topped Spotify charts with 15,995,378 streams on its release day. Similarly, Blackpink's *Pink Venom* (2022) debuted at No.1 on Spotify, and Stray Kids' s *God's Menu* has garnered over 400 million views and Spotify has had more than 7 billion streams. K-pop's influence extends beyond music charts, as it has become a staple at international events like the Olympic Games and major sports events. This global impact necessitates a deeper study of K-pop's role in shaping contemporary culture.

The study of girl groups and female performances in K-pop is particularly important. While boy bands such as Bigbang and BTS dominated the scene from 2012 to 2016, recent years have seen a significant rise in popularity and recognition of girl groups. Notably, fourth-generation girl groups like Blackpink and Twice have been active for over seven years, such as Blackpink BORN PINK WORLD TOUR earned more than 100 billion won, over 73,172,000 dollars, while newer groups like ITZY, IVE, and NewJeans have rapidly gained international acclaim. These girl groups have introduced a variety of styles, from Blackpink's street style to Twice's energetic pop hits like *Cheer Up* and *Talk That Talk*. ITZY's girl crush anthem *Wannabe* and NewJeans' urban style exemplified in *Supernatural* have also made significant inroads into the American market. As a result, girl groups are attracting increasingly

diverse and global fanbase. Lesserafim even made it to the Coachella Music Festival, being the second new generation girl group to make it to the Coachella after BLACKPINK, showing its global influence.

Songs featuring energy, sexiness, self-expression, and love have become particularly prominent in girl group songs and music videos, a trend expected to continue through 2023-2024. In 2019, when the girl crush trend was on the rise, ITZY's debut song *Dalla Dalla* had the idea "I am unique," and their 2020 song *Not Shy* had the lyrics "let just be who we are, do what we do." wanted to show female power. Similarly, (G)I-DLE's 2022 release *Tomboy*, which has garnered over 330 million views on YouTube, continues to showcase assertive female perspectives. However, the quality of follow-up songs featuring feminist themes varied, often relying on repetitive motifs.

While these girl group themes and concepts have encouraged discussion on women's autonomy and self-confidence, they sometimes express strength through defiance rather than showcasing genuine feminine power, which may lead to another framework of expressing that one must show a girl's power through strong revenge. " The majority of mainstream K-pop idols are actively encouraged to indulge feminine stereotypes, cultivating demure, cutesy, and nurturing personas (Lin & Rudolf, 2017; Yoon, 2019). While the creation of the 'fuckable fantasy woman' has long been a preoccupation of music moguls worldwide, strategies to boost listenership in Korea are especially reliant on the objection "cation of the female body (O'Brian 2002)."(Venters, L., Rothenberg, A., & Bonn Center for Dependency and Slavery Studies, Universität Bonn. (2022).

Beyond musical styles, K-pop girl groups' stage costumes have become increasingly revealing, with short skirts and exposed midriffs becoming standard stage attire. This trend raises questions about whether these choices reflect female autonomy or cater to the male gaze. The choreography of many girl groups, including elements like twerking, and the expression of Blackpink member Jennie on the American reality show *the Idol* express too hot in her expression management.

While there is undeniable diversity in musical styles, the prevalent use of sexual representation needs scrutiny. As a form of artistic expression and commercial enterprise, K-pop should consider its impact on fans of different ages. According to my research, the majority of K-pop idol fans range from minors to 22 years old. These fans often emulate their idols' actions, fashion, body shapes, and expressions, which subtly influence their perceptions and behaviors. It would affect the progress of feminism if content centered on misogyny is promoted under the guise of feminist expression.

This paper examines the existing feminist research and literature on the development of K-pop idols and analyzes K-pop's portrayal of female images and standards to answer the question whether commercialization in K-pop benefits female idols' career condition, and how do fans perceive its impact on themselves. It explores the application of K-pop's body and male gaze in daily life, its impact on women's lives, and the factors that cause controversy over K-pop's sex in music videos.

Literature Review

The image of female K-pop idols has always adhered to strict standards, with both early and recent girl groups expected to maintain photogenic, thin bodies. Choi Yujin, a former member of CLC and current member of KEP1ER, highlighted this in the height and weight measurement section of CLC's variety show *It's Real - Women's Army Special* - special forces challenge. Her height of 164

centimeters and weight of only 42 kilograms exemplify the stringent body management standards expected of female idols.

The role of patriarchy in the production and promotion of Korean girl groups cannot be overlooked. Many mainstream female idols are encouraged to embody traditional feminine stereotypes, cultivating demure, cutesy, and nurturing personas (Lin & Rudolf, 2017; Yoon, 2019). Globally, the creation of the 'fantasy woman' for male consumption has long been a focus of music executives, but in Korea, strategies to boost listenership heavily rely on the objectification of the female body (O'Brian, 2002).

Moreover, female idols are typically held to narrower beauty standards than their male counterparts, which increases the vulnerability of young women and girls to the demands of middle-aged male managers and agency executives. Pipher (1994) likens adolescent girls to "saplings in a hurricane," suggesting that women exposed to power imbalances are at greater risk of abuse. (Venters, L., Rothenberg, A., & Bonn Center for Dependency and Slavery Studies, Universität Bonn, 2022).

The aesthetic ideal of thinness in K-pop, as in many other cultures, is largely shaped by social discipline. In the context of Chinese history, the preference for slimness became idealized after the Tang Dynasty, which had previously embraced more inclusive and diverse beauty standards. Similarly, the K-pop industry enforces narrow beauty standards, particularly for female idols. They are often expected to maintain a particular facial and bodily "perfection," which usually involves rigorous dieting, regular skincare routines, and even plastic or cosmetic surgery. It is an open secret among Koreans and K-pop fans that many idols undergo plastic surgery before their debut, and they continue to maintain very slim figures. (Fuhr, 2016). For example, during a recent tour, members of TWICE, who have been active for nine years, appeared noticeably thin in fan-filmed dance videos. Fans observed that "Mina looks fine on camera, but in person, she looks noticeably thin..., " highlighting the ongoing pressure for body management. (Red: 千茶君, 2023). On the other hand, when NMIXX's Choi Jiwoo, who is less thin, faced criticism for her appearance during a debut performance, comments about her body, such as "Female idols must maintain good body management," underscored the societal expectations placed on female idols. (Weibo: 开心果拿铁无糖版, 2022).

The health impacts of these extreme standards are often overlooked, despite the physical demands of idol performances. Plastic surgery is also a common practice among idols. For instance, DAY6 drummer Dowoon once mentioned on Bubble, JYP Entertainment's paid communication platform, "I got Botox today... the jawline..." indicating the normalization of cosmetic enhancements in the industry.

K-pop's pervasive sexualization content and emphasis on appearance have become increasingly overt to many audiences. Revealing costumes, suggestive choreography, and sexual innuendo are common in music videos and live performances of mainstream K-pop girl groups. Moreover, much of the lyrical content in these groups' music illustrates how K-pop manipulates young female idol's femininity to meet socially prescribed roles, either reinforcing Western stereotypes of Asian women as exotic sexual objects or perpetuating the Korean patriarchal ideal of women as submissive, fragile, and innocent. This practice in tun reinforces sexist attitudes and traditional gender roles (Xi Lin & Robert Rudolf, 2017).

Distinguishing between the expression of female beauty and autonomy and the male gaze's influence on sexual temptation is a complex issue. For example, in the K-pop girl group Kiss of Life's latest song, "Sticky," the music video uses summer beach visuals to showcase the members' bodies. While some sexy movements, such as the dance move where they remove their jackets, do not make viewers uncomfortable, a specific shot from behind, showing a girl riding a bicycle with an emphasis on her top hips, made many viewers uneasy. One viewer commented, "The angle focusing on the hips is not how women look at women… This is how some men view girls, and the photographer wants us to adopt this male gaze."

Throughout her work, Mulvey follows Freud in associating activity, subjectivity, and agency with masculinity, and passivity and objectification with femininity. She argues that, unlike photography or other art forms, film is in uniquely positioned to create identity and desire through the opposition of activity and passivity, subjects, and agents versus objects. The movement in film, particularly the movement of the camera, generates the male gaze by panning up and down a woman's body, often fragmenting it into parts and focusing on specific features, such as the face. This process turns the woman into an object. (Oliver, 2017) This male gaze is also used in videos with pedophilic undertones. The debut track "Magnetic" by Illit sparked significant controversy for both its arrangement and the video. After the vocals end at 02:03, a bed squeak sound is prominently featured, which, in the context of a girl group with a juvenile theme, directly reflects a disturbing male gaze and pedophilic tendencies. The video contains numerous allusions to pedophilia. The opening scene, showing the girls walking barefoot in white lace socks in an under-lit hotel, sets a tone of innocence juxtaposed with unsettling sexualization. The video's imagery also prominently features the unicorn, a symbol steeped in medieval lore, representing purity and virginity. According to legend, the unicorn is a kind of creature like a horse or goat. Its longhorn can heal wounds and purify water. It is a symbol of healing and purifying spirit. Ancient versions of unicorns, especially the medieval tapestry "The Hunt of the Unicorn," one of which is In the Unicorn In Captivity, where the unicorn comes back to life and is kept in captivity. The unicorn is tied to a tree and restrained by Wallander, but the chain is weak, and the fence is low enough that the unicorn can easily cross and escape if he wants to. Then it became clear that his imprisonment was voluntary. At the same time, the red stains on the unicorn's body are not blood; these red stains represent the underground juice from the pomegranate that burst from above. Many of the plants in the picture echo themes of marriage and fertility and were hailed as fertility AIDS for men and women in the Middle Ages. (Douban: ellenbuch_coda, 2021) At a pivotal moment in the video, just before the song reaches its climax, the five girls are shown trapped in a V-shaped wall from a top-down perspective, an image that evokes disturbing sexual connotations. As the song crescendos, the unicorn, along with the girls' toys, falls to the ground, symbolizing the loss of innocence and purity. This visual narrative suggests the girls' transition from innocence to a corrupted state, reinforcing the problematic elements of the male gaze and its implications in the media.

Research Method

To explore fans' perceptions of the current K-pop idol industry, as well as their understanding of idol autonomy versus passive expression (e.g., in music videos where companies determine the tone), I

conducted an online survey. Given the niche nature of K-pop entertainment and the subjective expression nature of the questionnaire questions, an online survey was chosen over other methods such as street interviews or live interviews. The anonymity of the online format encouraged respondents to express their true thoughts without fear of judgment, leading to more authentic and comprehensive responses.

The survey was distributed across various online platforms such as Weibo and Douban, resulting in 102 valid responses. The questionnaire included a range of questions designed to gather insights into " fans' impression of female idols, their expectations of how female idols "should" be presented, the perceived evolution of different K-pop music videos over the past five years, the reasons behind the rise of girl crush style, and whether certain camera angle, outfits of K-pop choreography, and movements evoke discomfort. Additional questions explored the difference between sexy and male gaze-driven imagery, as well as the impact of idol behavior on fans, such as purchasing the same clothing or experiencing body anxiety due to idol influence.

The demographic breakdown of respondents included 35.29% minors under 18, 58.82% aged 18 to 22 (mainly college students), 4.9% aged 22 to 30, and 0.98% aged 30 and above. The gender distribution was 98.04% female and 1.96% male, with 99.02% of the respondents living in China, and 0.98% living abroad, mostly in Canada. These demographics reflect the typical characteristics of K-pop fan groups, primarily young women. However, the inclusion of respondents across various age groups and both genders, as well as those living in different countries, contributes to a more diversified set of viewpoints.

In addition to analyzing the 102 responses received from the survey on Weibo, I also searched for keywords and discussions on known K-pop topics across other platforms such as Douban. This broader search allowed me to gather a wider range of opinions. By observing the comments on specific topics, I not only collected the opinions of those who posted but also observed the general sentiment expressed by others in the discussion threads. This approach revealed that most fans approach women's issues with seriousness and without bias. When fans noticed that idols released songs or music videos with negative portrayals of women, such as illit's *Magnetic*, their first reaction was often to critically analyze the anti-feminist elements rather than blindly defend the idol. This indicates a growing awareness and progress in feminist consciousness among K-pop fans.

Research Finding

Female Image

Based on the questions posed in the questionnaire, this section analyzes the image of K-pop female idols as perceived and appreciated by fans, as well as how the image has evolved over time. It is crucial to understand the form and public perception of female idols in order to analyze their influence on fans.

Reasons For Admiring Female Idols In response to the question "Why do you like your idol? Do you have a favorite style?" 59% of the respondents mentioned female idols, indicating the broad appeal of these idols. The reasons for their admiration can be categorized into several themes: the energy derived from idols, idols' impressive talents, outstanding appearance, the appeal of the concepts

expressed by the idol groups, and their admirable personalities.

Many respondents noted that they draw energy from idols' performances, describing them as infectious, fun, and confident. Idols provide emotional support and inspire fans, helping them to feel more positive and motivated in their own lives. The general audience in their posts, work, or school, in the face of difficulties if the stage itself transmitted the energy, then the state of the audience will be better, this is also the meaning of idol and other entertainment industry practitioners are needed. Needless to say, idols as singing and dancing performers, dancing and singing strength is their basic job. The concept of "Mu Qiang"(admiration for strength and ability) was frequently mentioned in the answer, which idols embody through their hard work and stage performance. When we look at those who have achieved great achievements in life, we can't help but feel admiration and longing. This desire inspires us to take action, pursue our goals, and make progress. (Douban: laviedeshan, 2023) Many fans from the behavior of idols generated the pursuit of dancing or singing or some hobbies, this kind of seeing the excellent performance of others to stimulate their own potential is a positive "Mu Qiang" joint effect, that is, from paying attention to others to improve themselves.

The idea of liking idols because of their outstanding appearance is very simple and universal, that is, the human pursuit of beauty. Appearance, whether it is looks or body, is also part of the overall strength of idols.

Influence of Conceptual and Cultural Themes Another large group of fans is attracted to idols' song concepts. One respondent mentioned, "I really like the unique and unconventional concepts of Aespa and Red Velvet, and I also like TripleS 'works about East Asian girls."

The rise of East Asian aesthetics in K-pop has resonated deeply with female audiences. Examples of this style include *Ditto* by NewJeans and *Girls Never Die* by tripleS. This style is known for portraying a realistic picture of women's existence in East Asia, resonating deeply with K-pop's predominantly female audience. The feminist discussions and expressions stimulated by this style are appreciated for exposing the real female living environment in East Asia. The collectivism reflected in the East Asian style often portrays themes like groupism and blurred personal boundaries. For example, in the music video of Girls Never Die, the recurring raven imagery symbolizes the tragic perspectives of women. The music video depicts girls being pulled back from the brink of death, which is a kind of self-salvation. the reason why they escape from death is that other women accompany them, making women in deep pain realize that women themselves are not individuals, but ones to gain hope. Most respondents who mentioned the concept of "appreciation" said that the reason they like such concepts is to look in the mirror, find themselves, and heal themselves.

John Berger's quote, "If we accept that we can see that hill over there, we propose that from that hill we can be seen." (Berger, 2008) reflects the mutual recognition of beauty and identity. This resonates with fans who see themselves reflected in the East Asian aesthetics of these music videos.

The Human Side of Idols A frequently mentioned keyword in the responses was "character." Beyond their professional attributes, many fans appreciate the human side of idols. Aside from the characteristics that an this job brings, the common side of idols, such as their personality and characteristics, also attracts many people. This connection between fans and idols represents a departure from the conventional star-chasing mentality, emphasizing a more personal and human relationship.

Some fans particularly enjoy the ordinary aspects of their idols, while others are drawn to the special interactions(fansight) idols offer through fan communication platforms like Bubble and Weverse, as well as during concerts and fan meetings. This kind of interaction represents fans' expectation of reciprocity and highlights the commercial nature of K-pop, where fan engagement is often driven by the expectation of some return. The structure of the entertainment companies further deepens this commercial dynamic, which will be elaborated on in the following sections.

Perception Of Female Idols and Male Gaze In response to the question "How should female idols be perceived?" many participants emphasized attributes like strength, good looks, and vitality. Some respondents argued that idols should not conform to any specific mold but should simply be themselves. In contrast, opinions varied widely in response to the question," How do women idols show you most of their feelings?"

Keywords that were repeatedly mentioned included "good-looking," "like a packaged image," and "no opinion." One respondent noted, "It felt gorgeous during the fourth generation and before...... in short, a hundred flowers bloomed. But now, the fifth generation gives me a strange feeling. They have their style, makeup, and everything, but it is wrong. In addition, too much interpretation and marketing now affect perception." (The fourth generation refers to groups that debuted between 2014 and 2017, and the fifth generation relates to groups that debuted between 2018 and 2023.) Most respondents point to a "beautiful empty shell" concept.

It was also mentioned that "female idols' skirts are getting shorter, and they are wearing less and less." "On the stage, exposing legs, arms, and even waist has become a must for female idols." Women's aesthetics are diverse, and not everyone appreciates bare limbs. However, the homogeneity of aesthetic expression makes us reflect on which audience groups favor such sexualized portrayals. The answer seems evident: the mass influence of the male gaze.

This influence is evident in the changing portrayal of female idols in K-pop music videos. In response to the question, "What do you think has changed about the image of women in music videos over the last two years compared to before?" 13 respondents mentioned the male gaze and similar expressions, while 20 mentioned the enormous output of girl crush concepts, often masquerading as female empowerment. One respondent remarked, "There was a significant decrease in sensuality but no decrease in masculinity." Another noted, "Just under the guise of 'showing their bodies'… I have no issue if female idols genuinely want to wear certain outfits. Still, in many cases, female idols express discomfort with the clothes, saying they're uncomfortable or cold, etc." To conform to the market's mainstream feminist awakening, there's also a push to market these choices as "confidence." However, some respondents felt that idols are sometimes too focused on looking beautiful, neglecting the quality of their stage performances.

Commercialization of Feminism in K-pop The commercialization of K-pop makes it easy to see how feminism has been commodified. The essence of K-pop can be summarized as "dream making," where idols serve as carriers for a larger purpose rather than being the purpose itself. Since K-pop's global expansion in 2016,expressions of "gratitude" and love for fans have become a standardized part of the industry. This has led to formulaic and commercialized performances, with many idols' actions confined to a small framework, leaving little room for personal expression.

As the fanbase has expanded, the reasons people admire idols have diversified. However, few fans are drawn to idols purely for their association with K-pop. Instead, idols often lose their true selves under the industry's transformation and discipline. This is why homogeneity has become so pervasive among K-pop idols—they all fit the stereotype of being "beautiful, thin, and female."

The industry has become more assimilative, focusing on showcasing the feminine beauty or cuteness" There is also the image of a female warrior, though it often lacks authenticity. The emphasis on assimilation highlights the fungibility of female idols, where the design and manufacture of the concepts suppress their artistic expressiveness. Many respondents noted that many realistic factors are ignored as companies pursue "exquisite beauty" and AI-enhanced aesthetics. Most music videos are filled with special effects and glamorous makeup, but anything too fake and empty leaves audiences feeling insecure.

Moreover, companies are trying to present changes in women's rights, confidence, thought, and depth. However, the core has not changed over the past decade, and diversity has decreased. For example, (G) I-DLE has gone viral since the release of Tomboy in 2022 and won second place on Melon (a popular streaming platform in Korea). However, they've returned to the same concept in subsequent releases. "Nude," released in October 2022, touched on male coagulative behavior, and *Queencard*, released in May 2023, continued the girl crush theme. *Superlady*, released in January 2024, was another feminist expression of girl crush. While the concepts that (G)I-DLE attempted to convey were commendable and got some viewers thinking, the overly repetitive content didn't seem necessary. The repeated refrain in *Superlady* "I am a superlady" contrasts with the playful expression in Tomboy," "I don't want to play this ping pong, I would rather film a Tik Tok, your mom raised you as a prince, but this is queendom, right?" The difference is stark. Rather than being an indictment or expression of feminism, "maintaining the heat" seems to be a more fitting explanation.

With girl groups like (G) I-DLE and Blackpink gaining significant attention and fans for their feminism themes, entertainment companies appear to have found a way to market this trend." Initially, girl groups focused more on metaphorical feminism, creating music videos that constituted a complex drama-filled storyline that would be praised in later years. However, recent girl groups have shifted towards chanting slogans, which some respondents feel represents a regression compared to earlier feminist music videos.

In addition, despite the increasing number of these feminist songs, the rights of women themselves are not guaranteed. Famous female idol Sulli was abused, rumored, and harassed by the audience because she did not wear a bra in public. More teams are using feminist slogans or images as marketing tools but not endorsing sovereigns. Many idols, such as ITZY Chaeyoung, have clarified that the top is very short, and they should be careful to walk out during the performance.

Audiences' Opinion of Feminism In K-pop Respondents noted that the increase in female independence, changes in the audience demographic, and increased number of female fans correlated with the rise in girl crush songs. While it's difficult to determine whether this is due to the ideological evolution of female audiences or the appeal of the girl crush style itself, both explanations suggest that societal progress—notably the improvement in women's education and a deeper understanding of equality-- has led women to demand gender equality and safeguard their rights and interests.

Regardless of which came first, this development has led women to reflect on their situations and attempt to break free from traditional roles. Although more women are choosing to live independently, there is still a strong undercurrent of male chauvinism, prompting women to develop various strategies to resist it. The girl crush style of the music aligns with this resistance and has therefore gained popularity. To a certain extent, Girl Crush focuses on female power and encourages female audiences to engage more deeply.

However, K-pop culture itself puts women who become idols as commodities." It is also unclear whether girl crush will be able to transcend the impact of its slogan and flashlights."

Girl Crush Is Not the Only Way For Women To Express Themselves However, if we give the crushing style the only accepted form of female expression, it risks suppressing other styles and limiting women's freedom to explore diverse modes of self-expression. For example, unlike the plethora of girl crush songs and concepts that emerged in 2023, the girl group Twice seems to have taken a different path. Their songs are sweet, the members transmit energy with smiles on the stage, and the lyrics describe the growth of women, mostly drawn from ordinary lives. However, with the rise of feminism and the girl crush trend, many viewers have questioned whether this emphasis on vitality has impacted the development of female independence and self-improvement, potentially hindering the growth of the "strong female protagonist" concept. When asked, "Is girl crush the only way for women to show their power?" and whether other styles, such as vitality, should be considered merely ways to please men, all respondents answered negatively.

Respondents emphasized that "There are more and more styles prevalent in K-pop girl groups today. Neither the sci-fi futuristic style of XG and Aespa, the teenage girl style of NewJeans, nor the sophisticated style of Twice should be considered cuties. It just proves that girls have unlimited possibilities." Respondents to the questionnaire repeatedly mentioned that women are diverse and can express themselves in many ways. "Women can also show self-power through tenderness. G crush is a strong expression of self-power, but it's not unique. "The vitality style, for instance, highlights a girl's sunny and cheerful nature, and its audience should not be limited to men. No matter what style is chosen, it simply reflects the diversity of women. "No matter the form of expression, each has its audience. People can feel energized when they listen to vitality songs; gentle and firm songs can soothe them when they need comfort. However, everything must be based on respecting the female idol.

Girl Crush Style's Dilemma The definition of girl crush has changed from expressing a woman's power to a fixed style: cool makeup, indifference to men, and sometimes a mean girl persona. The rise of the girl crush style can be traced back to girl group 2NE1, which is representative of a bold, hip-hop-influenced aesthetic that included elements of metal and rock, contrasting sharply with the style of earlier girl groups like Girl's Generation. The novelty attracted many t female fans, and as a business-driven industry, K-pop naturally sought to replicate and reproduce these successful models.

However, the commercialization of the girl crush style has led to contradictions. The makeup and expressions of female groups wearing miniskirts and imitating orgasms in performances are essentially at odds with the original definition of a girl crush, creating a disconnect in the presentation of the stage. By understanding the expression of girl crush, we can see that it was never meant to be a rigid style, but rather a courageous and firm expression of itself. Feminism in K-pop should allow women to

return to a broader standard of female expression, embracing diversity rather than conforming to a fixed style.

Some respondents also point out that "the company is exploiting the women's rights market from a male perspective, but in fact, their control over women's rights in these groups does not show any genuine support for women's rights." In planning a comeback, whether the company respects the will of female idols, whether decisions are made based on gender equality, and whether the choices are acceptable to female idols are crucial. Any style can show the strength of women, even one focused on heartbreak. Many styles can show a female idol's (or woman's) experiences and inner thoughts, and facing the self is also a way to show female power. Girl power is not about cool makeup and lyrics in a music video, but about respecting the human rights of female artists and their own musical opinions or aspirations behind a comeback. This respect is what embodies girl crush, while many girl crush videos feel inauthentic.

Discomfort With Sexualization in Choreography and Music Video Regarding the question, "Do you feel uncomfortable with certain movements in K-pop choreography or the shooting Angle and dress of a music video?" 74.5 percent of the respondents reported feeling some discomfort. Examples include Illit's debut music video "Magnetic" and Kiss of Life's "Sticky," which contain sexual innuendo and ambiguous scenes. Other controversial examples include Nayeon's solo music video "ABCD," Lesserafim's "Fearless" and Sunmi's "Ballon in Love."

The creators of the music video often use techniques like overhead shooting to create visuals that feel voyeuristic, such as the bridge part after the second chorus of Fearless, where "the dance scene where members lie on the ground and knock on the floor, combined with the use of shadow and light and twisting dance movements, makes people feel that they are imitating some sexual imagery." Sunmi's Ballon in Love is modeled after several scenes from the pedophile film "Lolita, "such as candy bars and hanging underwear at the beginning of the music video.

In addition to the controversial camera angles, actions such as "touching the crotch top, buttocks, or chest spanking" are also seen as sexual innuendo. Both male and female performers face backlash after doing these moves. "For example, some choreographers use male dancers in ways that imply a girl's sex appeal comes from being attached to a man.

We may be able to summarize that when women find themselves in the position of being stared at, it creates a sense of sexual oppression and discomfort, which can be collectively referred to as the embodiment of the male gaze.

When observing the choreographer's flip of Nayeon's solo song *ABCD*, the choreographer presented the same and even more suggestive movements without any sexual implication. Perhaps sexualization and discomfort have less to do with the action itself and more with the form of expression, such as expression management and how the movement is executed. When the choreographer dances with strength, even seductive movements like hip thrusts may not feel sexualized.

"Other styles are not inherently designed to flatter men; women themselves are diverse, and the technique of expression is the key to determining whether something is aimed at pleasing men. Whether a style flatters men depends on the creative perspective of the artistic works rather than the style itself. Whether something flatters men is not about the expression of women but about how women are

perceived."

Social Impact Of K-pop Female Idols

Fan's Imitation of Idols' Fashion The influence of K-pop idols on their fans is powerful, especially in terms of fashion. Many fans emulate their idols' style, purchasing similar items and clothing. In response to the question, "Have you bought music videos, singing clothes, or idols' private clothes in the same style?" 36.2% of the respondents said that they had purchased similar clothing. Among those, 66.7% said they bought the same items because they were aesthetically pleasing. Other reasons included "suiting their style," "wanting to try a new look, "needing to replicate outfits for performances, " and "always liking that brand." Interestingly, only 5.56% of the respondents said their purchase was purely out of love for the dress. This suggests that K-pop fans are becoming more rational, purchasing based on personal needs rather than idol worship. This highlights the need to update and correct some of the fans' stigmatized and irrational perceptions.

Fans' Opinions on Body Anxiety Caused by Idols This rational approach extends to body image issues as well. When asked, "Have you ever experienced body anxiety because of female idols?" only 25.5 percent of respondents said they had. In addition to body anxiety, some respondents reported feeling age-related anxiety, particularly when younger idols achieve fame and success. However, many fans cited self-discipline and a healthy attitude towards life as positive influences that motivate them to improve themselves. Such feelings could be seen as self-improvement inspired by seeing their idols as role models.

Conclusion

Through analyzing questionnaire responses and reviewing existing literature, this research reveals that K-pop artists and fans share a generally positive and mutually beneficial relationship. Fans draw inspiration and motivation from their idols, while idols gain support and energy from their fans. However, the portrayal of female identity within K-pop remains constrained by commercial interests, with a focus on profit over authentic expression. While artists may not always have complete control over their public image, there is a growing awareness among both fans and artists about the importance of self-expression and autonomy. More artists, such as (G) I-DLE's Soyeon and Stray Kids' bangchan, choose to write and compose their own music to express their thoughts and emotions, reflecting a shift towards greater artistic freedom and feminist awareness.

This paper also explores the application and influence of feminism in K-pop, mainly through the lens of the "girl crush" concept. The rise in feminist expression has paralleled the growing number of female audiences, which has accelerated the spread and popularity of the girl crush style. However, due to the entertainment and commercial nature of K-pop, all expressions must navigate commercial considerations. As a result, many expressions of girl crush are not genuine reflections of the artists' or groups' inner beliefs but are instead driven by commercial marketing strategies. Consequently, the industry's focus on profit has led to a fixed training model for artists, resulting in a sense of homogeneity and lack of innovation in K-pop.

From the perspective of fans, there is a noticeable shift towards more rational and critical

engagement with idols. Rather than unquestioningly defending their idols or indulging them unconditionally, fans increasingly evaluate whether specific actions or messages are appropriate and make informed decisions based on their reflections.

Diversity, however, is what the audience truly desires. There is a clear demand for a broader representation of women in K-pop, Yet, the industry is still largely dominated by men executives (e.g., SM Entertainment, JYP Entertainment, YG Entertainment, and HYBE Entertainment), whose decisions are often shaped by the male gaze. In contrast, groups like NewJeans, launched by female producers, offer a refreshing departure from this norm, tapping into the female community's desire for diverse representations, injecting new strength into the increasingly homogenous K-pop landscape.

The limitation of this study mainly comes from the relatively small sample size of 102 valid responses, which may not fully capture the diversity of K-pop fans' thoughts and experiences. Furthermore, the self-reported nature of the questionnaire could introduce biases, as the target audience was relatively limited. Some individuals who might have found the questionnaire too complicated or time-consuming may have had different opinions that were not captured in the data. Additionally, the time when the survey was posted may have influenced the age distribution of respondents. The survey was posted in the afternoon when people with busy work could not see this message, which caused a bias in the audience's ages. Posting the questionnaire at varied times, such as both afternoon and night, could have resulted in a more diverse respondent group.

Finally, this study focuses solely on fan perspectives without directly engaging with industry professionals or idols. Insights from K-pop industry directors, producers, or idols themselves would provide a clearer understanding of the intentions behind performances and marketing strategies. Expanding the questionnaire to include fans from different countries and cultural backgrounds would also help reduce regional biases and provide a more comprehensive understanding of the global K-pop fanbase.

Despite these limitations, this study offers valuable insights into K-pop fan perspectives, but future research is necessary to expand the interviewee group, for example staff from K-pop industry, professionals who delve in K-pop field and people who like to listen to K-pop but do not like K-pop idols. It will be more likely to complete if I conduct a random visual interview on the street and a professional interview. This will lead to a more comprehensive understanding of how K-pop functions and how they deal with female topics.

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Democracy and Authoritarianism: The Case of India and Bangladesh
By Anika Pallapothu

Abstract

India and Bangladesh are two neighboring countries in South Asia, which are characterized by their common history and culture, and have undertaken different journeys in terms of their political regimes since their independence from the British colonial rule. While India in essence has been a democracy with some persisting issues, Bangladesh has oscillated between periods of democratic mechanisms, authoritarianism, and military governance, demonstrating political instability. The first principle should mention that there are such countries, political circumstances, historical backgrounds, and present issues as complicated as the comparison of democracy and dictatorship in these countries.

Research Aim & Objectives

This paper aims to explore the intricate phenomena of democracy and authoritarianism in Bangladesh and India through discussions on the techniques based on culture-politics.

Literature Review

India: A Democracy Amidst Diversity

India is reputed as the largest democracy in the world. However, it embraces a much more profound meaning when viewed against the background of the diversity of its culture, religion, languages, and ethnic groups. Despite the many challenges it faced due to the colonial rule of Britain, India has been successful in standing firm by its democratic ethos (Sen 2021). Yet, among its complexity exists a subtle terrain wherein the democratic ideals are often contrasted with elements of authoritarianism, especially in recent times (Kaul 2023).

India's democratic system is based on free and fair elections, a multiparty polity, and a robust civil society. Regular elections at the national, state, and local levels enable citizens to become involved in political processes and keep their leaders under control. In addition, the Indian Constitution provides for fundamental rights and freedoms, where the right to express and associate stand as pillars of the democratic rule.

However, Indian democracy has its own share of challenges, and its democratic institutions often suffer from problems associated with corruption, caste-based politics, and regional disparities. In fact, corruption has been a consistent challenge, with India ranking 93rd among 180 nations, as per the Corruption Perception Index of 2023 by Transparency International (The Hindu 2024) (Figure 1).
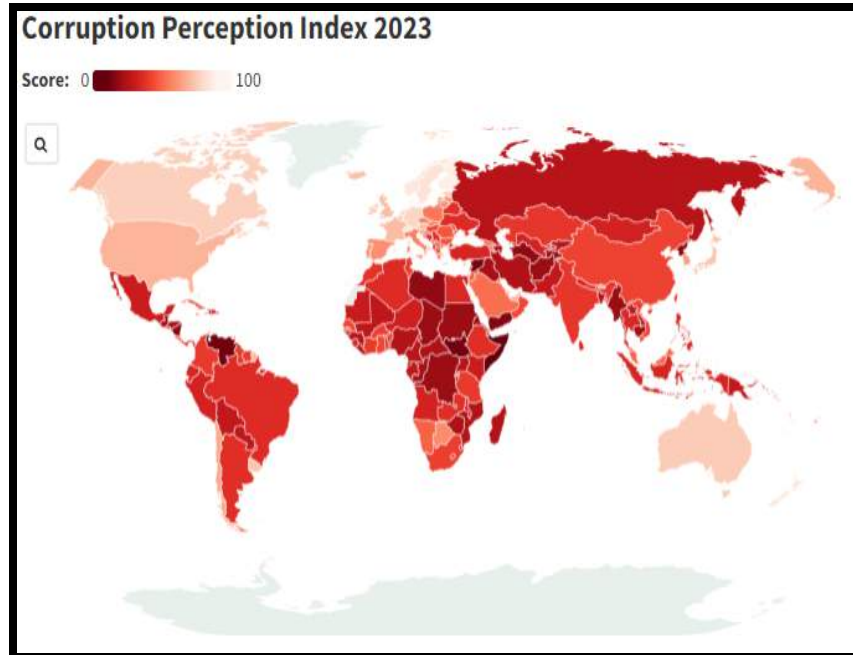
Fig 1: Corruption Perception Index 2023
Source: Transparency International

The dominance of money and muscle power in elections, along with the shadow of dynastic politics, disrupts the notions of fair representation and responsibility. Moreover, India's democratic texture is threatened by increasing religious and ethnic polarization. Further, the dominant party's centralization, might be a reflection of the fears regarding democracy and the weakened efficiency of institutional counterbalances. They comprise the rebellion which leads to the instability and fall of independent institutions (Vaishnav 2019). In the past few years, Indian peoples' civil liberties have been under attack, particularly by means of violation of freedom of expression and a combination of two factors: excessive police surveillance and violation of privacy. Human rights activists, writers, journalists, political tradesmen, and dissidents have endured harassment, intimidation, and even injury. The imprisonment of critics under laws, such as the Unlawful Activities (Prevention) Act (UAPA) and the sedition law, as well as the restriction of media outlets that do not align with governmental goals, are some of the harshest actions of the state to limit the space for protest and democratization (Alam 2020).

However, the country's efforts over time to combat these menaces have resulted in a civil society, an independent judiciary, and a free press that impairs any dictatorial tendencies. The federal model exists in the country under which political power is shared between the central government and the states, while an individual enjoys full decentralization and pluralism. Moreover, the acts of political and social activism in India also reflect the right-to-information movement led by popular journalists, the movement to curtail corruption under the leadership of Anna Hazare, and the recent protests of farmers against some new agricultural laws, among others, indicating that India is indeed an actual democracy and that the rights of the people are being fought for (The Hindu 2016).

Bangladesh: Struggles with Authoritarianism

Bangladesh has been characterized by a turbulent political environment oscillating between democracy and authoritarianism in its journey since its independence from Pakistan in 1971 (Abeyratne 2023). To understand the subtleties of democracy and authoritarianism in Bangladesh, it is necessary to analyze in detail some historical events and political dynamics that are crucial points of tactics used by succeeding governments in consolidating their power.

After independence, Bangladesh had a parliamentary system of democracy with multiparty system, which was subsequently scarred by political confusion with the assassination of the country's father, Sheikh Mujibur Rahman, in 1975, which led to the military rule (Macdonald 2024).

The era of the military regimes of General Ziaur Rahman and General Hussain Muhammad Ershad, which lasted from the late 1970s to the early 1990s, was characterized by the repression of political dissent, media censorship, and the fraudulent conduct of elections. The imposition of martial law, creation of totalitarian rule, breakdown of rival political parties, and one-party system constituted the authoritarian tactics employed by these regimes (Brown 2019).

Unfortunately, the re-establishment of democracy in the 1990s did not bring an end to Bangladesh's problems with its legacy of authoritarianism, including the hostile competition between the country's two main political forces: the Awami League and the Bangladesh Nationalist Party (BNP).

The governments by opposition parties, which alternately came to power, often had to deal with scandals of electoral fraud, political violence, and violation of human rights, which completely violated the underlying democratic institutions, and the country never bounded at the conceptual level by democracy (Hassan and Raihan 2017). In recent years, under the leadership of the Prime Minister Sheikh Hasina and her party Awami League, Bangladesh had become increasingly autocratic and dictatorial. Initially, Sheikh Hasina's government was acclaimed for restoring democracy and restructuring the economy, but of late, critics have stated that the success of their authoritarian rule has made them intolerant of opposing opinions, as they continue to restrict the freedom of the press and intervene in the electoral process (The Economic Times 2024).

The democratic space, an account of the abolition of the country by the ruling governing party, is one of the ways in which they passed controversial laws. In December 2018, the Bill was adopted despite mass protests, which were followed by an accordion of condemnation regarding the wide and vague provisions that granted the authorities the power to imprison anyone for dissention through the Internet as well as for the criticism of the state. The freedom of speech of the media was impacted by the information disclosure law, and politicians from the opposition were restricted in the country, further leading to a fall in the freedom of the press (Gupta 2020).

Moreover, the Awami League government has been charged with using extra-legal means to stifle political opposition and dissent. Numerous cases of enforced disappearances, extrajudicial killings, and arbitrary arrests have been documented by human rights organizations

as perpetrated by the state's security forces who go unpunished. These tactics, acutely similar to that of the authoritarian governments of the past, have provoked the fear of the unbeatable dominance of the ruling party, further undermining the democratic norms (Bangladesh: 86 Victims of Enforced Disappearance Still Missing 2021).

Unlike Bangladesh, India has taken a different course in its fight against dictatorships. Although India has had its setbacks, such as phases of emergency rule and political suppression, the democratic institutions, a lively civil society, and the independent judiciary of the country have remained anchors against authoritarian tendencies (Bhatia 2022). The federal character of the Indian political system, which is based on the sharing of power between the central and the state governments, allows for the development of political pluralism and decentralization. Moreover, India's strong legal system, which has constitutionally guaranteed fundamental rights and freedoms, ensures accountability and transparency in governance. The American institutions of democracy, including a free press, an independent judiciary, and an active civil society, are intended to withstand the assault on democratic norms and values and to provide opposition with a voice. The ability of India's democracy to deter authoritarian pressures is guaranteed by the rule of law, accountability of the government, and responsiveness of power to the people.

Discussion

There are many significant differences in how India and Bangladesh might develop in terms of democratic governance and authoritarian tendencies in future. As a federal nation, India shares some competency between the central authorities and individual state heads, resulting in a uniformity of political entities that leads to decentralization. Under a clearly defined distribution of interests, any kind of party or stake intensifies, based on opinions expressed with the help of authorities in the national sphere. This eliminates authoritarian power. In addition, citizens in India, through civil society, which is the frontline to check the powers of the governments, exercise their civic duties and conduct affairs of the society, politics, and security. In addition, the non-government organizations (NGOs), public interest advocacy services, and grassroot-level groups are powerful in keeping politicians on the ground and are the voices that ensure that individuals and minorities have the right to be heard.

However, in case of Bangladesh, the main representative figure is the ruling class, primarily the two major parties: the Awami League and the BNP, not leaving much for the common people. The phenomenon of this "big two" trap has polarized people in many countries, and has now become a struggle between the two biggest parties in most democratic countries, leading to the creation of a single-party system that makes every election a complete dictatorship in which one dominant party wins, reducing the chances of multiparty democracy. Bangladesh has also seen coups and dictatorships, which have had a negative impact on its democratic institutions and have resulted in more repetitive cases of presidential reach beyond due and justified powers. Despite these challenges, both India and Bangladesh face similar threats to democracy: corruption, inequality, and party politics.

Conclusion

Political parties in both India and Bangladesh disagree on issues such as freedom of the press and their political histories, leading to the same political issues: corruption-free governance and inclusive political practices. The polity of democracy and authoritarianism in Bangladesh and India is an intricate interplay of political power, history, culture, and society. This also applies to both Brazil and the United States, which have been facing problems with the preservation of constitutional principles and the democratic system. Nevertheless, the methods and results exploited by the government and the parties differ. Indeed, democracy cannot survive without the constructive participation of citizens, civil society, and leaders who demonstrate and practice democratic principles.

Indian diversity, which leads to the fundamental question of a corresponding government system consisting of both consistency and incompatibility. Despite significant achievements in several spheres, some key issues, such corruption, religious divides, and concentrated administrative powers, remain unaddressed. The process of establishing a democratic state in our country is moving hand-in-hand with our unceasing endeavors to secure people's fundamental rights (which are ultimately important), build democratic institutions, and raise citizen's awareness of the idea of representative governance. Today's Bharat will be a healthy democracy that affirms multiculturalism, secularism, and the rule of law for tomorrow only if this is retained. Overcoming the challenges and continuing the progress of both countries toward real democratic consolidation will be based on the resilience of their democratic institutions, active involvement of their civil society, and the dedication of the political leaders to democratic values.

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Nanocellulose–the Key to Improve the Composition of F1 Tyres to Create a Better Performance While Approaching Net Zero Aims By Alejandro Sánchez Lozano

Abstract

Nanocellulose is a sustainable and versatile nanomaterial derived from natural cellulose (Low et al.), which holds significant promise in the development of actual technologies, predicting a tremendous progression in many engineering fields. Some of which are continuously evolving, such as the automotive industry. Nanocellulose's potential is even up to the biggest challenges presented in the most competitive side of the industry, for example, pointing to enhancing the performance of Formula 1 tyres. This research paper explores the integration of nanocellulose into tyre composition, aiming to find an improvement and address the demanding requirements of F1 racing, including grip, sustainability (subject to the future 2026 regulations) and durability. Through a comprehensive analysis of experimental data on the mechanical properties of both actual materials used in tyres and nanocellulose-reinforced tyres plus the comparison of pertinent factors that affect the nanocellulose-reinforced compound, this paper demonstrates that the incorporation of nanocellulose into F1 tyres can lead to significant improvements in performance and sustainability. The findings suggest that nanocellulose-reinforced tyres could become a transformative innovation in Formula 1 racing, offering a combination of enhanced mechanical properties and environmental benefits.

Introduction

Formula 1 (F1) is the pinnacle of motorsport, featuring the most technologically advanced race cars in the world. These cars are sophisticatedly engineered for aerodynamics, speed, and agility, incorporating advanced materials like carbon fiber, polymer composites and resins (creating sandwich structures) for lightweight strength. The combination of speed, aerodynamic, and complex materials makes F1 cars the fastest racing cars to this day. Due to its competitiveness, F1 teams are continuously pushing the boundaries of technology to improve efficiency, reduce environmental impact, and enhance the performance of their cars. Although these improvements primarily involve the sport, they have a long-term effect in the automotive industry, as most of these innovations are subsequently implemented in road cars. A Formula 1 car's superior performance relies on the specific development of its various components, such as the power unit, chassis, braking system and tyres. Each of these elements are studied and analyzed in absolute detail, aiming to refine the characteristics of the car. Tyres (Tremlett, A. J., and D. J. Limebeer.) are a representative fraction of the components that play a vital role in the car's behavior, as the fluctuations in lap times are mainly caused by the employment of multiple tyre compounds, formed with different combinations of natural or synthetic rubber. These compounds are classified, depending on their durability and grip to the asphalt, in slick and wet tyres, and subsequently, slick tyres are grouped from C1 to C5 (first one being the most durable but with less grip and last one with the best grip but less durability).
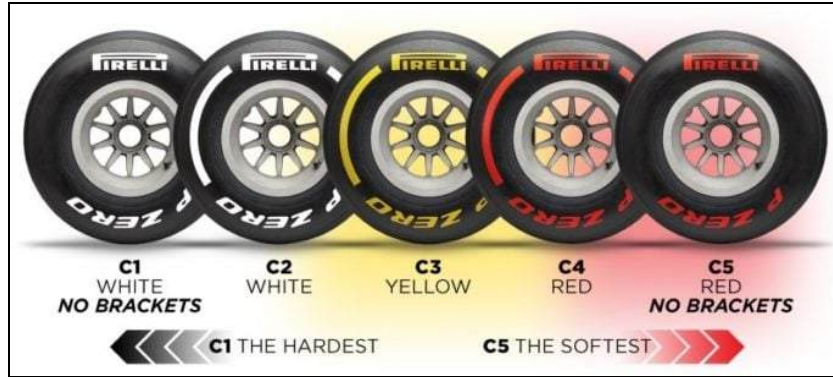
Figure 1: Classification of F1 tyre's slick compounds used in the present day

Tyres are divided into multiple elements, but this study will focus on its thread layer, which is the most important element in terms of performance and with the biggest amount of rubber compounds, meaning also that it is the component where the mounting of nanocellulose would be more remarkable. The rubber compounds used in Pirelli F1 tyres, specifically in the thread layer, are reinforced with carbon black and silica as fillers. Both of the fillers are used to improve the compound's properties: carbon black, a fine black powder made of pure carbon, enhances tensile strength, but limits elongation at break; while silica (SiO_2), a naturally occurring mineral composed of silicon and oxygen, enables the percentage of elongation at break narrowed by the carbon black. Giving the composite high elasticity, with an elongation at break varying from 300 and 500%; an important tensile strength between 15-25 MPa; and a young's modulus of 4 to 8 MPa. However, mechanical properties in these compounds vary depending on the addition of fillers and type of rubber used as matrix, producing less elastic but harder and long-lasting materials, or the opposing situation. The compound used for this study is C2, the most commonly used hard compound, with an specific composition (Anand, G., and S. Vishvanathperumal.) consisting in a combined rubber matrix of natural rubber (NR 35% wt) and synthetic styrene-butadiene rubber (SBR 35% wt), with carbon black (20%) and silica (10%) as fillers. Presenting some differences with the mechanical properties' general values for the compounds: 300-400% of elongation at break, a tensile strength of approximately 20-26 MPa and a young's modulus between 4 and 6 MPa. However, the high-speed degradation, frequent replacement and non-recyclability of F1 tyres result in substantial waste, posing a challenge for sustainable concerns mentioned in the future regulations for 2026 and 2030. Additionally, the production process of F1 tyres involves the use of synthetic rubber and other non-renewable resources, leading to considerable carbon emissions and environmental impact. As these tyres wear down, they release microplastics and other pollutants, which can contaminate soil and water sources.

Figure 2: Worn wheel at the end of the race with rubber debris from the asphalt, that can't be reused or recycled

Nonetheless, F1 teams are constantly searching for technological evolution, and have the potential to implement nanotechnology, particularly nanocellulose materials, to address these environmental and performance challenges. Cellulose itself is the most abundant polymer in nature, coming from plants, or even organic waste produced or fabricated by these plants such as cotton straws, fruit peels or softwood and bamboo pulps (Low et al.). Producing cellulose from these waste can release 3 to 10 times less CO_2 emission than carbon black. Based on data, the approximate emissions (Rosental, Marian, et al.) of CO_2, in kilograms, generated on the manufacturing of 1 kilogram of carbon black is between 1.5 to 2.5 kg CO_2/kg, while for cellulose stands between 0.2 to 0.6 kg CO_2/kg, demonstrating the enormous improvement it would have. Not only by using these organic materials there will be a less dependence on nonrenewable sources, but also it would give a functional use to this waste that is usually burnt (even though the exact amount varies based on the specific material and combustion conditions, burning 1 ton of dry organic waste can release approximately 1.5 to 2.0 tons of CO_2,) or stored in massive landfills (leading to a waste of potential resources), giving solutions to both problems of sustainability and recycling. Moreover, it possesses properties like biocompatibility, low cost, low density, high strength, and good mechanical properties when used as a reinforcement for rubber. For example: a tensile strength varying from 10 MPa to 25 MPa; a percent of elongation at break between 100% and 500%; and a young's modulus going from 1 MPa up to 15 MPa (Datta, Janusz, and Marcin Włoch.). On the other hand, nanomaterials (Shah, Vraj, et al.) (Booker, Richard D., and Earl Boysen.), substances working with dimensions of less than 100 nanometers and with an extensive molecular surface area, exhibit enhanced and more pronounced properties compared to traditional materials. When cellulose is worked down to nano-size, this increased surface area allows nanocellulose (Dufresne, Alain.) to create stronger interactions and better integration with rubber compounds, leading to significant improvements in the mechanical properties of the tyres. By combining nanocellulose, including: cellulose

nanofibers (CNF), cellulose nanocrystals (CNC) and bacterial cellulose (BC),with existing rubber composites, F1 tyres can achieve superior strength, elasticity, and durability. This not only enhances on-track performance by providing better grip and handling but also reduces the frequency of tyre replacements and the associated environmental impact. Implementing such advanced nanomaterials in F1 tyres could set a new standard in both performance and sustainability for the motorsport and automotive industry.

Discussion

These compounds depend on many characteristics and features needed to develop optimal performance and properties, each meticulously engineered to meet specific requirements. The intricate balance of these elements is essential in crafting tires that can withstand diverse conditions and demands.The careful selection and combination of materials ensure that the final product meets the high standards expected in various applications. This process involves a deep understanding of the complex interactions between the compound's components, making it necessary to identify, improve or change them in order to achieve results involving their behavior. Thus, these attributes will be analyzed and explained in order to show the impact that each one has on the compound, and some of the possible alternatives proposed in the paper for their improvement.

Natural and synthetic

The rubber matrix fundamentally constitutes a great part of the compound, usually around 60% to 70% of percentage by weight (wt%). Meaning that the tyre mainly relies on this polymer and its properties, as the characteristics of the tyre will appear similarly as those presented in the rubber it uses (with the existence of some fluctuations due to the placement of fillers, made for the enhancement of different properties). Rubber can be extracted or created from two different origins: natural and synthetic. Natural rubber derives from vegetative sources, particularly certain plants that produce latex (a milky fluid that can be processed into rubber). This latex is collected by making small incisions in the plants, allowing the fluid to be harvested and refined into a flexible, durable material. On the other hand, synthetic rubber is produced through the chemical polymerization of petroleum-based compounds, such as styrene and butadiene. Unlike natural rubber, synthetic rubber is engineered in laboratories by chemical processes and it comes from non-renewable sources.
While both types of rubber share similar characteristics, their origins and production methods set them apart, offering distinct advantages and characteristics between them. When both are reinforced with nanocellulose, they undergo a series of changes that affect in different ways to their composition. Producing divergent alterations of their attributes.

NR OR SBR	Tensile (MPa)	Elongation (%)	Modulus (MPa)	Reference
NR (10 wt %CNC) NC: Bamboo Pulp	From: 9.2 ± 1.3 to 17.3 ± 1.4	From: 554 ± 9 to 455 ± 11	From: 1.7 ± 0.2	[14] Crosslinked natural rubber nanocomposites reinforced with cellulose whiskers isolated from bamboo waste: Processing and mechanical/thermal properties
SBR (10 wt % m-CNF) CNF: Hardwood pulp	From: 10 ± 1 to 55 ± 4	From: 368 ± 25 to 406 ± 13	From: 2.0 ± 0.1 to 6.8 ± 0.3	[5] Rubber materials from elastomers and nanocellulose powders: filler dispersion and mechanical reinforcement

Table 1: (Low et al.) Comparison of the tensile strength, elongation at break and Young's Modulus of two rubber compounds reinforced with 10 wt% of nanocellulose (NC) originated from stiff pulps, one of them natural rubber (NR) and the other one Styrene-Butadiene rubber (SBR) a type of synthetic rubber

As shown in Table 1, natural rubber (NR) when reinforced with nanocellulose (NC) shows a significantly higher elongation at break, but lower values of tensile strength and Young's modulus than Styrene-Butadiene rubber (SBR), a type of synthetic rubber. These phenomenons (Tang, Saifeng, et al.) occur due to NR's more uniform and linear molecular structure (Figure 3), which allows for greater flexibility. NR also benefits from strain-induced crystallization, providing additional strength and elasticity. Additionally, NR's superior elasticity enables it to return to its original shape after being stretched, contributing to its higher elongation at break. In contrast, SBR has a higher crosslink density, making it more rigid and less stretchable; however, this results in higher tensile strength and Young's modulus, also attributed to the presence of styrene, which enhances the material's rigidity and resistance to deformation under stress. Although, the ultimate factor that separates natural and synthetic is the NR's capability to be recycled and reused when reinforced with NC, as well as the substantially less carbon emission that are produced during its manufacturing.

Figure 3: Molecular composition of A) Polyisoprene natural rubber and B) Styrene-Butadiene synthetic rubber
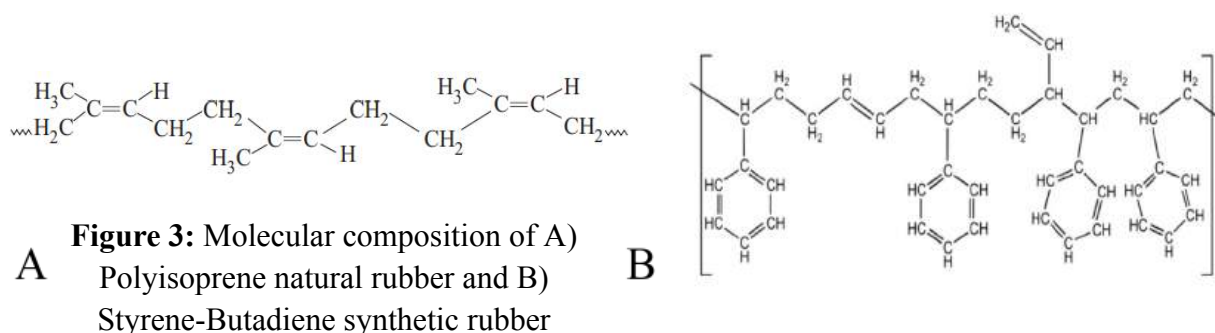
Compatibilizers

Tyre compounds aren't solely made of pure rubber, in fact, they are refined and reinforced with fillers to improve their qualities or even develop new ones. Thanks to this practice materials can be improved in different ways, showing better capabilities than their pure

version. The issue is that the filler must be highly compatible with the rubber polymer to obtain these improvements. In such a way that the amelioration of the properties is proportional to the compatibility between the polymer and the filler. In order to increase their stability and, consequently, attain higher compatibility between a compound and its additive (filler), compatibilizers are crucial. Compatibilizers (Nofar, Mohammadreza.) form an interphase containing some of each component of the composite, showing a better mixture of the components.
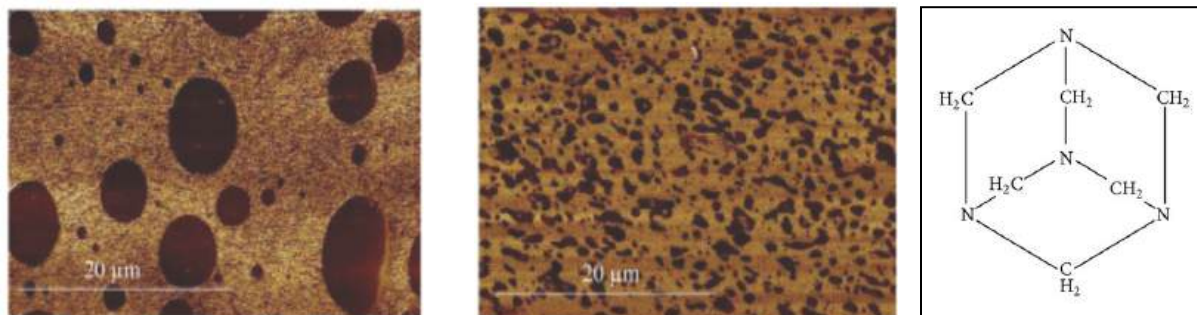
Figure 4: AFM micrographs of uncompatibilized (left) and compatibilized (center) blends, from (Tang, Saifeng, et al.). Chemical structure of resorcinol-hexamethylenetetramine (right)

The compatibilizer used to strengthen this tyre compound reinforced with CNC from cotton straw is known as resorcinol-hexamethylenetetramine (RH), an organic chemical compound usually used as a bonding agent in rubber composites (Low et al.) (Thomas, Seena K., et al.). As a prominent gelation reagent, RH forms strong cross-linked networks within rubber matrices, providing good adhesion properties between filler and rubber chains and improving the dispersion of CNCs, leading to a more uniform and effective cross-linked network. The difference between the composite with and without the addition of this compatibilizer can be visible in the variance of some properties
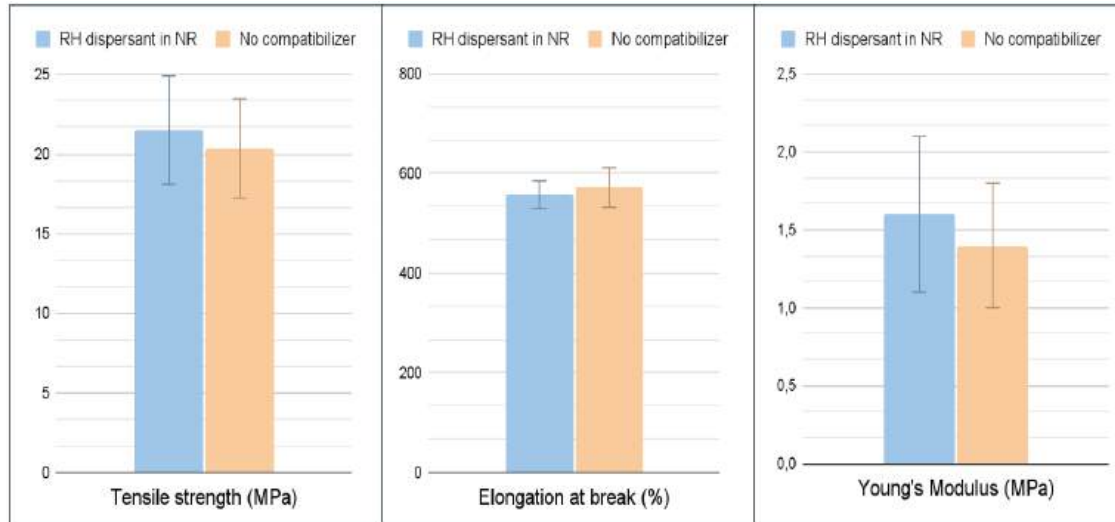
Graph 1: (Low et al.) Mechanical properties' mean value of natural rubber (NR) reinforced with nanocellulose (CNC) extracted from cotton straw with and without resorcinol-hexamethylenetetramine (RH)

Concluding from Graph 1's illustrative information, the application of RH in the rubber compound (Low et al.) results in increased tensile strengths of the composite of 20% compared to samples without RH. Along with another increase in Young's modulus' values by approximately the same percentage. Explained by the uniform and effective cross-linked network that the compatibilizer generates with the promotion of a better dispersion of the CNC added to fortify the rubber matrix. Though, the elasticity and, therefore, the values of elongation at break suffered a devaluation. Linked to restricted mobility caused by stronger interfacial bonding and better stress transfer. This value continues to decrease upon the increasing concentration of nanofiller addition and is attributed to the immobilization of rubber polymer chains by well-dispersed nanofiller networks (Low et al.).

Nanocellulose sources

As the primary filler in the rubber composite under study, nanocellulose plays a crucial role in enhancing the material's strength, elasticity, and overall performance. The source of nanocellulose, whether derived from wood, cotton straw, or agricultural residues, significantly influences the composite's characteristics. This happens due to the inherent differences in the structure, morphology, and surface chemistry of nanocellulose extracted from various origins. Each source produces nanocellulose with unique characteristics, such as differences in aspect ratio, crystallinity, and surface functional groups, which directly influence how the nanocellulose interacts with the rubber matrix. For instance, the surface chemistry of nanocellulose directly affects its compatibility with the rubber matrix, resulting in more enhanced properties. Thus, the selection of nanocellulose source is essential for the final characteristics of the rubber composite, optimizing it for performance and sustainability applications.

NC source	Tensile (MPa)	Elongation (%)	Modulus (MPa)	Reference
Softwood pulp Added compatibilizer: n/a	From 12.6 ± 0.5 to 24.8 ± 3.7 **(18.7)**	From 564 ± 10 to 532 ± 30 **(548)**	From 0.9 ± 0.2 to 1.8 ± 0.4 **(1.35)**	[6] Nanocrystalline cellulose isolated from different renewable sources to fabricate natural rubber composites with outstanding mechanical properties
Bagasse Added compatibilizer: n/a	From 12.6 ± 0.5 to 27.2 ± 2.9 **(19.9)**	From 564 ± 10 to 569 ± 12 **(566.5)**	From 0.9 ± 0.2 to 2.0 ± 0.2 **(1.45)**	[6] Nanocrystalline cellulose isolated from different renewable sources to fabricate natural rubber composites with outstanding mechanical properties
Cotton straw Added compatibilizer: n/a	From 12.6 ± 0.5 to 28.1 ± 2.6 **(20.35)**	From 564 ± 10 to 579 ± 30 **(571.5)**	From 0.9 ± 0.2 to 1.9 ± 0.2 **(1.4)**	[6] Nanocrystalline cellulose isolated from different renewable sources to fabricate natural rubber composites with outstanding mechanical properties

Table 2: (Low et al.) Comparison of tensile strength, elongation at break and Young's Modulus' values (mean values in bold) for the same rubber compound reinforced with three different NC sources in the same quantity: 10 parts per hundred rubber (phr). Red means the lowest value, yellow the medium value and green the greatest value
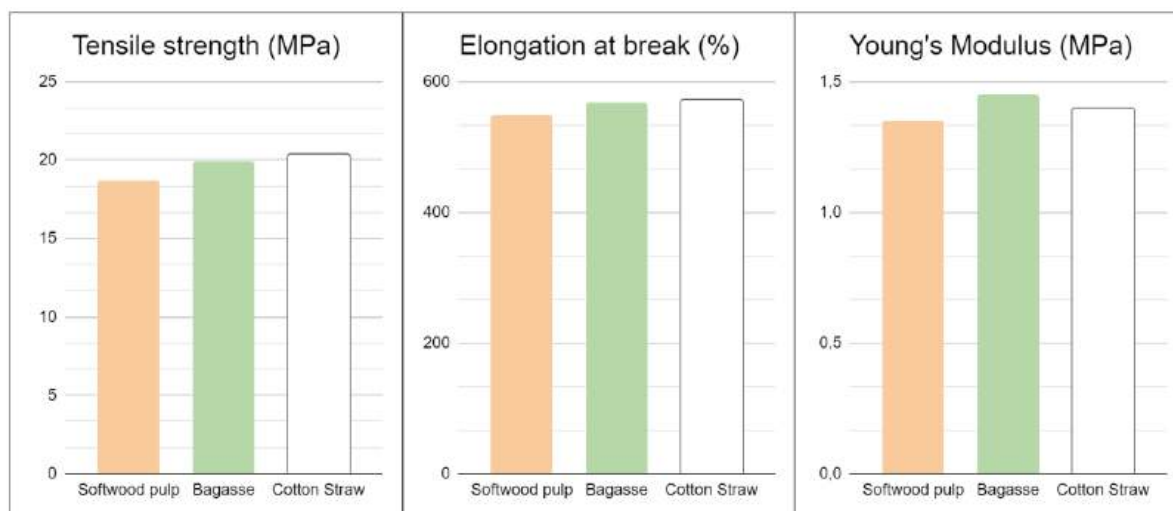
Graph 2: Table 2 mean values arranged graphically

As demonstrated in Table 2 and Graph 2, when comparing mechanically three different NC sources (softwood pulp, bagasse and cotton straw) in the same conditions, considering: rubber matrix, fillers, compatibilizers, quantity of NC and weight, plausible differences can be detected. Softwood pulp (Jiang, Weihui, and Ju Gu.) shows the lowest values in each of the three cases. Even though it produces nanocellulose with high crystallinity (main reason why its elongation at break numbers are the lowest, as it reduces the overall flexibility of the rubber composite), which often leads to increased stiffness and, for that reason, higher values of tensile strength and young's modulus, this crystallinity may not be adequately controlled or the

nanocellulose particles are too large or irregularly shaped, resulting in poor interfacial bonding with the rubber matrix (also considering there is no use of compatibilizers), and leading to this lower tensile strength and modulus. On the other hand, both bagasse and cotton straw present greater values of these properties and their differences aren't as noticeable, but have yet to be compared. As can be seen, cotton straw has higher tensile strength and elongation at break than bagasse. This better tensile strength from cotton straw is due to its finer cellulose structure (Jiang, Weihui, and Ju Gu.), which leads to a more uniform distribution of nanocellulose within the rubber matrix. This enhances the interaction between the rubber and the nanocellulose, giving it better load transfer during stretching. Differently from bagasse which exhibits a coarser structure and larger particle size, causing less efficient dispersion and weaker interaction with the rubber matrix, resulting in lower tensile strength. Similarly, NC from cotton straw provides more flexibility, allowing the rubber compound to elongate more before breaking, giving an increase to the elongation at break. While the less uniform distribution of bagasse NC within the rubber matrix can cause stress concentrations that reduce the ability of the material to elongate and, consequently, lower its elongation at break. However, this factor and its coarser structure permits bagasse to show the greatest value of young's modulus, also taking in account that cotton straw's finer and potentially more flexible nanocellulose leads to a rubber compound that is less stiff, as reflected in a lower Young's modulus than bagasse.

Actual vs cellulose-reinforced tyre compounds

The entire composition of this compound must be evaluated to ensure it is proper and benefitial when incorporated into the sport. Comparing the current rubber compounds used in F1 tyres with nanocellulose-reinforced alternatives is crucial for evaluating the potential of sustainable innovations in high-performance applications. As the motorsport industry pushes for more environmentally friendly practices, exploring materials that can reduce the environmental impact without compromising performance becomes essential. By comparing these two types of compounds, we can assess whether nanocellulose-reinforced rubber can match or exceed the mechanical properties, such as strength, flexibility, and durability, needed for F1's demanding conditions. This comparison could pave the way for more sustainable tyre manufacturing practices in motorsport and beyond, helping meet future regulations and environmental goals. The aim is certifying that mechanical properties are similar in proportion, as there are going to be some differences. However, the variance of some values can be considered advantageous since they might bring better or even new properties to the material.

Material	Tensile (MPa)	Elongation (%)	Modulus (MPa)
Actual (NR 35% / SBR 35% / carbon black 20%/ silica 10%)	20 to 26 **(23)**	300 to 400 **(350)**	4 to 6 **(5)**
NR (10 phr CNC) NC: Cottons straw Added compatibilizer: RH dispersant in NR (5%)	12.6 ± 0.5 to 30.4 ± 2.9 **(21,5 ± 3.4)** **mean values**	564 ± 10 to 550 ± 18 **(557 ± 28)** **mean values**	0.9 ± 0.2 to 2.3 ± 0.3 **(1,6 ± 0.5)** **mean values**

Table 3: Values for the tensile strength, elongation at break and young's modulus of the actual rubber compounds used in F1 tyres (Anand, G., and S. Vishvanathperumal.) [gray] and nanocellulose-reinforced natural rubber compound [green] (Low et al.)
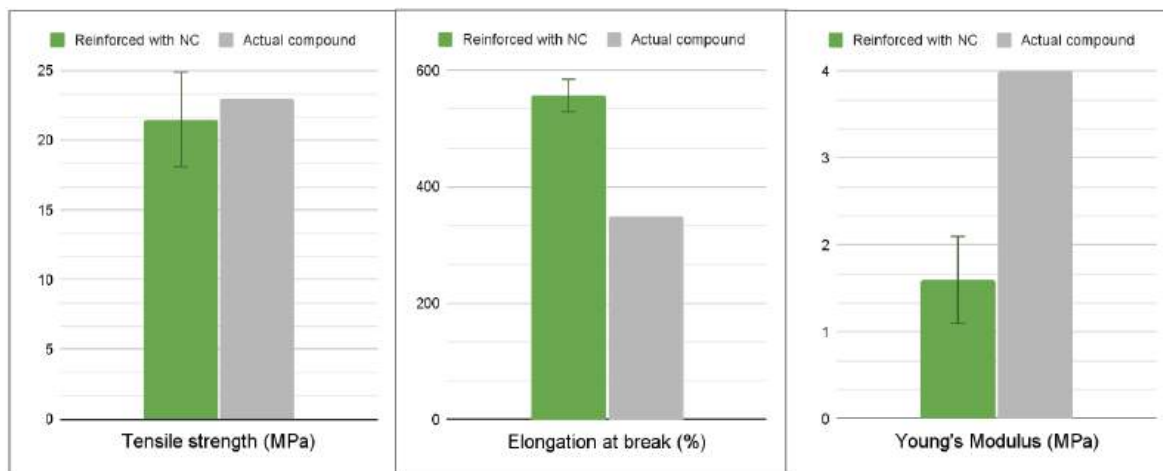
Graph 3: Table 3 mean values (with error bars for the nanocellulose-reinforced compound) displayed in graphs

Disparities between nanocellulose and common fillers are the cause of the variance in the mechanical properties of these rubber compounds. Nanocellulose is a flexible material that when added to a rubber matrix enhances its elongation at break and reduces its stiffness. While other fillers, such as: carbon black and silica, boost its young's modulus, whereby its stiffness, but barely improves its elasticity. This higher stiffness is caused by vulcanization, a chemical process where the rubber compound reinforced with the fillers is heated up with the presence of sulfur. And as defined in Table 3 and Graph 3 it is clearly noticeable the difference in elasticity and flexibility, related to elongation at break; and because of being far more flexible, how the nanocellulose-reinforced rubber compound is particularly less stiff. However, tensile strength presents less variance between both compounds. Although mean values estimate that the actual compound exhibits higher tensile strength, the error bars determine that possibly the nanocellulose-reinforced rubber compound could withstand more stress before breaking. To significantly improve this effect on tensile strength, it is necessary to ensure the development of

nanocellulose's characteristics, in particular: its crystalline structure, its uniform stress distribution and its strong interfacial bonding of its chemical structure. Guaranteeing nanocellulose's tensile strength maximum potential.

Conclusion

After analyzing all of these factors involving the nanocellulose reinforcement in the rubber compound of the thread layer of F1 tires, it is appropriate to conclude which would be the optimal combination to develop an improved tyre with a better sustainability approach, aiming to commit 2030 net zero goals for F1. Firstly, it is certain that the properties presented by synthetic rubber are finer than those from natural rubber, however, the differences can barely be detected and the advantages presented by natural rubber for sustainability aims are much more relevant, also considering that natural rubber is a more elastic polymer, having a higher elongation at break. Furthermore, cotton straw is the foremost NC source to be combined with the rubber compound thanks to its tensile strength and its considerably greater elongation at break, giving it more flexibility. Even though bagasse NC has a superior young's modulus, it isn't high enough to show a remarkable advantage. Also relying on the use of a compatibilizer, in this case RH, which would enhance the young's modulus, alongside tensile strength, of NC coming from cotton straw and reducing the elongation at break by making the composite more stiff. Making the material more balanced. This rubber compound reinforced with nanocellulose will have similar properties as the actual compound used, but, with the capability of being recycled, because of its natural origin and cellulose use, and emitting significantly less CO_2 emissions during its manufacturing process. In addition, the nanocellulose-reinforced rubber compound shows a lower young's modulus and a higher elongation at break than the actual compound, implying that the new compound is more flexible and more durable thanks to its ability to absorb impacts, distribute stresses, and resist cracking or fatigue under various road conditions. Since it provides a longer durability, it will be more suitable for hard compounds such as C2 and will help to reduce high-speed degradation.

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Economic Impact of United States Presidential Election Years: A Comparative Analysis
By Shaan S Guru

Abstract

The United States Presidential elections are held every four years, and they bring a time of economic uncertainty that raises many questions domestically and internationally. In this essay, the relationship between the economy and the presidential election years will be analyzed. Some of those include changes in the investment markets like stocks and real estate, the expectation of the president's policies and how they will affect the economy, what the consumers should expect, how each presidential candidate (Donald Trump and Kamala Harris) has different policies, and how those policies will affect the economy of the US and internationally. By looking at stats from past elections and trends, the confusing connection between the economy and the years that have a presidential election can be further understood, showing how the outcome of United States presidential elections impacts the growth and the power of the economy.

Keywords: Elections, Economy (Growth and Decay), Domestic and International Policy, Consumers, Index

Introduction

The United States of America's presidential elections are held every four years. The main political parties are the Republicans and Democrats. The Republicans are red, and the Democrats are blue. The elections are important not only for politics but also for the global and domestic economy. The election brings a time of economic controversy internationally and domestically. The chance of political change brings attention from the world as it can affect several things, such as investments, businesses, consumers, prices, inflation, and much more. The world will closely follow the election as it unfolds in November.

In the past years, the election years have significantly fluctuated in the investment world, mainly in stocks and real estate. The question of which candidate will win creates a lot of fluctuation in these markets. Some things investors expect are changes in taxes, tariffs, foreign policies, and other domestic rules that can cause the stock market to increase or decrease. People in real estate can also expect changes like interest rates, housing policies, and the growth of the market correlated with whether Donald Trump (Republican) or Kamala Harris (Democrat) wins the election.

The policies each president proposes when running for president give us a forecast of their potential economic impact. Let's rewind to the 2020 election and each presidential candidate. Donald Trump focused on improving domestic manufacturing, deregulation, and tax cuts. On the other hand, Biden focused on healthcare reform, climate change, and social equity. In the election of 2024, we will again see opposing views between Donald Trump and Kamala Harris clash.

One thing that is important in election years is the expectations of the consumer. What the consumer thinks about the economy is often influenced by the president/presidential candidates. The thoughts of the consumer are important because it determines how much money they put into the investment, which is the leading creator of economic growth. A good example is stocks. If the consumer trusts the market, they will invest more money. They will not invest as much money if they are pessimistic about the market. In this paper, I will examine how the United States economy changes or fluctuates every four years during the election years.

This case study paper aims to understand how presidential elections impact the economy globally and locally. This will be done using data from the past and future projections. This research paper will analyze the relationship between the United States presidential elections and the economy in several ways. By looking at the data and statistics of election history, the presidential election creates changes such as the investment market, the expectations of the buyer, and the different expectations from each candidate to the economy. This essay's main objective is to look at how the opinions or views of Donald Trump and Kamala Harris are different and how each candidate's potential policies would impact the economy, whether negatively or positively.

Historical Context/Background

Throughout the history of the United States of America, several presidents have made crucial economic decisions that have affected the domestic and international economy. Each election has many consequences for the economy. The entire world watches the United States election, anticipating what changes will happen.

Since the early 20th century, the United States elections have correlated to the economy. A perfect example is the Great Depression in the United States. This was an economic collapse in the late 1920s when Republican Herbert Hoover was in office. Many people did not like his policies and blamed him for the collapse. Then, Democrat Franklin Delano Roosevelt was elected with his New Deal Plans. He was very active in the government to try to save the United States economy, and he proposed a lot of economic legislation with the New Deal. This was the first time in United States history that much legislation was passed regarding the economy. This would become a major part of the president's job regarding the economy and start a legislative trend (Newman, 2022).

Economic uncertainty has become a concern in recent elections. The 2000, 2008, and 2016 elections were key elections regarding the economy. The 2000 election was, of course, controversial because of the recount and Supreme Court drama. The 2008 election was huge because there was an economic recession. Then, in 2016, the election was marked by a shift from liberal policies to Donald Trump's shifts in taxation, tariffs, and trade (Newman, 2022).

In the 2000 election, Democrat Al Gore ran for president against Republican George W Bush. On November 26, 2000, Florida declared Bush the winner, getting the 25 electoral votes to win the election three weeks after the official election date. It was a very tight and controversial election, and at the time, Florida was a major swing state. Over the next few weeks, Florida

recounted the votes to determine the election winner. It would later come down to a Supreme Court case, where Bush was ruled the winner over Gore, winning the electoral college 271-266. (Kennedy, 2020)

The 2008 election was a major election, and it was controversial due to the economic recession of 2008. In November of 2008, when there was an election between Democrat Barack Obama and Republican John McCain, there was an economic recession known as the Great Recession of 2008. Several steps led to this financial crisis. The housing market was significantly declining, so the Federal Reserve lowered the interest rate throughout 2008 to try and create economic growth. In September 2008, the company Lehman Brothers filed for bankruptcy. For those who don't know, they were an investment banking company from 1850This and ended in 2008. Essentially, this year's big part of the election was who would "save the economy." Barack Obama won the election, and many saw this as a turning point to try and bring back the economy. (Mayorga, 2015)

The 2016 United States election was also heavily correlated with the economy. In this election Democrat Hillary Clinton went up against Republican Donald Trump. Donald Trump would win the election, and it would shift from Liberal policies for the past eight years to Republican policies under Donald Trump. Before running for president in 2016, Donald Trump was a businessman, so many hoped he would benefit the economy. Donald Trump's policies were marked by changes in taxes, tariffs, international trade, and more. His economic policies during the end of his presidency declined due to the Covid-19 pandemic. (Thorbecke, 2021)

In history, the Republicans and Democrats have had opposing views and ideals. Usually, Republicans go for lower taxes to try to grow the economy. On the other hand, the Democrats typically advocate for higher taxes and more money into welfare programs to focus on economic inequalities in the USA. The two always have opposite ideals on what is happening in the world. Going back into history, we had different parties. At one point, it was Federalists and Anti-Federalists/Democratic-Republicans, Then the Whigs and Democrats, and then Republicans and Democrats. Ever since the end of the American Revolution, there has been a concept of the two-party system. (Newman,2022).

Every presidential administration has different policies in several aspects, like the economy. George W. Bush had many tax cuts, and the goal of this was to boost the economy. Obama focused on fixing the economy after the 2008 recession and his healthcare reform plans. Trump went for tax cuts and deregulation (Newman,2022).

The 2024 election is approaching, and the two candidates are Republican Donald Trump and Democrat Kamala Harris. Donald Trump wants to return to tax cuts and deregulation, while Kamala Harris wants to focus on climate change and social equality.

Analysis of Findings

One common trend in presidential elections is re-election. According to these charts, if the president has an economic recession during their time in office, they have not been

re-elected. Two years before the next election, if the president is not in an economic recession, they tend to get re-elected.

No Recession Two Years Before Re-Election		
President	Recession?	Re-Elected?
Obama	No	Yes
Bush II	No	Yes
Clinton	No	Yes
Reagan	No	Yes
Nixon	No	Yes
LBJ	No	Yes
Eisenhower	No	Yes
Truman	No	Yes
FDR	No	Yes
FDR	No	Yes
FDR	No	Yes
Wilson	No	Yes

Recession Two Years Before Re-Election		
President	Recession?	Re-Elected?
Trump	Yes	No
Bush I	Yes	No
Carter	Yes	No
Ford	Yes	No
Hoover	Yes	No
Taft	Yes	No

(Historical Correlation between Election Years and the Market, 2023)

During the presidential election years, many investments are more risky. Things like stocks and real estate tend to fluctuate up and down a lot more during the years of the elections. This is because there is a lot of uncertainty around who will be the next president and their policies. The new president can have long-term and short-term effects on the economy.

A study in the American Economic Review showed that stocks are more up and down in the months before an election. Three months before the 2020 election of Joe Biden and Donald Trump, the S&P 500 had an average daily fluctuation of about 1.2%, and during non-election years, the daily fluctuation was around 0.8%. This is a big difference, and the margin displays how the economy is affected during US election years. (Huberman et al., 2018)

Different types of stocks can react to each type of policy. An excellent example of this is the 2020 election. According to bloomberg.org, the technology stocks had a 15% pre-election rise because of Biden's policy regarding digital infrastructure. Then, the energy stocks that were more in line with Trump's plan went down 10% after he lost the 2020 election. (Bloomberg - Are You a Robot?, 2024)

The next topic is housing policies surrounding real estate. There are many expectations about housing policies during election years. In his presidency(Democrat/Liberal), Biden's aim was to increase affordable housing, so real estate developers were more cautious. In a Republican presidency, let's say, Trump, for example, deregulation is more favorable for real estate developers and investors. Housing policies and real estate are heavily affected by the United States presidential elections every four years.

One important aspect of economics is the consumer. The confidence of the consumer or the investor is very important because that determines how much money will be put in. The confidence of the consumer is affected by the president's policies and, of course, which candidate wins the election. One index of a data point we can reference is the CCI, which stands for Consumer Confidence Index. In 2020, the CCI went down to 132.6 in February(pre-covid), then In April, at the start of Covid, it dropped to 85.7. The reasoning behind this is Covid and the upcoming election, so there was a lot of uncertainty. (Consumer Confidence Index (CCI), n.d.)

The real estate market is a major investment that is impacted by the United States Presidential election every four years. After every election, the new president impacts the regulatory and fiscal policies, which impact commercial real estate because the new president makes different policies. This election, specifically, according to JP Morgan, with either electoral outcome, will likely require continued federal investment into the Infrastructure and Jobs Act. JP Morgan also states that the election outcome does not entirely shift the real estate market, but essentially, it creates volatility during the years of the election. Post-election, the economic uncertainty tends to disappear as time goes on. (Morgan, 2024)

Certain stocks can react differently depending on which political party wins the election. The main point is that stocks do not favor a party, and each president's reaction post-election can differ. According to Edward Jones, the stock market has performed well under several presidents. The average annualized price return (excluding dividends) of the S&P 500 was 9.6% when a Democrat won and 5.7% when a Republican won. These presidents include Republican (R) and Democratic (D) presidents. The most robust returns occurred during the F. Roosevelt (D), Clinton (D), Eisenhower (R), and Reagan (R) presidencies. The stock market does not necessarily favor a party but varies by election. (Jones, 2024). This November, according to LPL Financial, they favor a Trump victory for the United States Stock market. The website states that a Trump victory would be best for the S&P 500 and provides a chart to support this. (Turnquist, 2024)

The last aspect of the analysis findings that will be showcased is the investment behavior during election years. Retail investors sell and buy investments through a bank or broker. They tend to adjust their portfolio during election years. According to a Charles Schwab survey, an interesting statistic is that in 2020, 45% of people adjusted their portfolio as they anticipated a Joe Biden victory in the election. They shifted their stocks towards technology and healthcare. During 2020, Pfizer's stock peaked because of Covid and Biden's policies. It is very interesting how investors shirt their portfolios based on the election. (Kleintop, 2024)
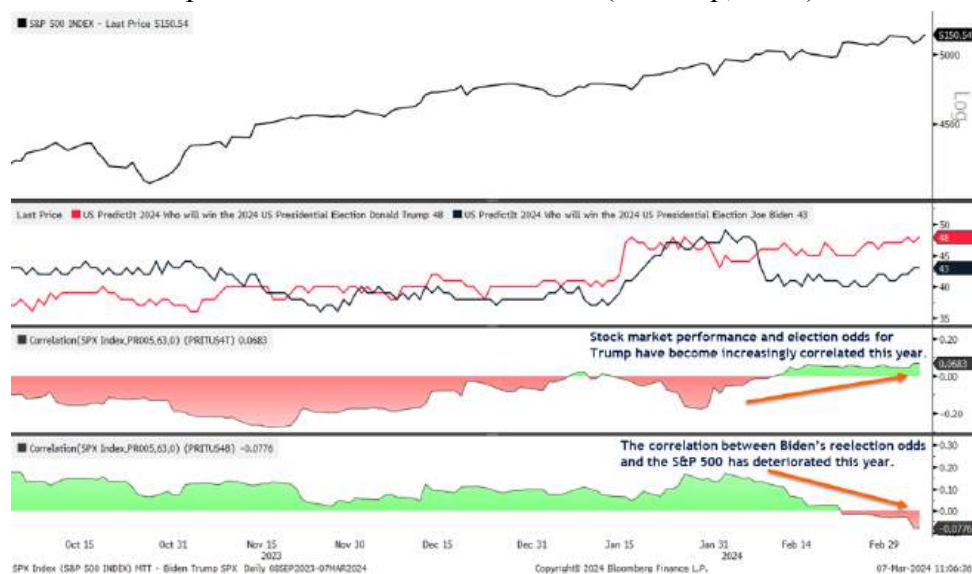
Source: LPL Research, Bloomberg. PredictIt.org 08/22/2024

This data shows the correlation between the daily percent change of Biden's and Trump's probability to win the 2024 election, odds from predictit.org. The outlook is slightly altered, as it is now Kamala Harris vs Donald Trump. It is hard to predict Kamala Harris's economic policies in the election. On the contrary, the market appears to favor a Trump victory, and his correlation shows it to the S&P 500, no matter who the Democrat candidate is. It will be intriguing to see who wins the 2024 election and how the market will shift because it is impossible to predict the effect on the economy perfectly. (Turnquist, 2024).

Methodology

This research methodology was carefully structured and systematically executed. Initially, a mentor was consulted to guide the research process. Following this, the research topic was determined. The subsequent step involved the collection of 20-25 credible sources. Data and evidence were then gathered to support the research objectives. The writing process commenced with the abstract, followed by the introduction, gradually bringing the research paper together. Finally, the data analysis was performed. The mentor vetted all sources to ensure credibility, and the MyBib citation tool was utilized to verify the reliability of each source. After compiling the research, the study's formatting and coherence were meticulously refined. This methodology outlines the research process for examining how the United States presidential election influences the economy.

Limitations

During this research, several limitations and learning experiences were encountered. A limitation is an inherent weakness in the study that falls outside the researcher's control. Firstly, a common challenge in conducting research is the potential for bias, particularly when evaluating sources. It is, therefore, essential to ensure that the sources used, especially those related to policies, are neutral and unbiased. Another limitation involved time constraints; although the research was conducted over a few months, which ensured thoroughness, the limited timeframe imposed certain restrictions. The final limitation was the narrow scope of the study. Due to these time constraints, the research focused primarily on the 2020 and 2024 U.S. presidential elections, necessitating the reliance on prior knowledge for historical context. Despite these limitations, the study was completed and remained largely unaffected by these challenges.

Conclusion

The United States presidential elections, held every four years, profoundly influence the domestic and international economy. The uncertainty surrounding these elections creates significant volatility in various investment markets as consumers and investors grapple with the potential implications of new or continued presidential policies. Historical trends, such as those observed during the 2020 election, underscore the pervasive impact of these elections on economic behaviors and outcomes.

During election years, markets, particularly in stocks and real estate, tend to experience heightened fluctuations. This volatility is driven by the uncertainty surrounding the potential economic policies of the presidential candidates. Investors, wary of the possible shifts in taxation, trade, and regulation, often adjust their portfolios in anticipation of the election outcome. The resulting market instability not only reflects domestic concerns but also indicates the global economy's reliance on the United States' economic policies.

This research highlights how the differing policy agendas of presidential candidates, such as those seen with Donald Trump and Kamala Harris, can lead to varied economic expectations and outcomes. Trump's focus on deregulation and tax cuts contrasts sharply with Harris's emphasis on social equity and climate change, illustrating the divergent paths that U.S. economic policy could take depending on the election results. These differing policies influence investor confidence and have long-term implications for the broader economy, affecting everything from consumer behavior to international trade relations.

Moreover, the analysis presented in this paper shows that consumer confidence plays a critical role during election years. For example, the Consumer Confidence Index (CCI) data from 2020 illustrates how external factors like the COVID-19 pandemic and election uncertainty can significantly diminish consumer optimism, leading to reduced spending and investment, which are crucial drivers of economic growth.

The case study also emphasizes the importance of understanding the broader economic context in which elections occur. Historical precedents, such as the financial strategies employed during past elections, provide valuable insights into how current and future elections might impact the economy. By examining past data and trends, this research offers a nuanced understanding of how presidential elections shape economic policies and outcomes.

This paper has explored the intricate relationship between U.S. presidential elections and the economy. The findings suggest that the economic impact of these elections is far-reaching, influencing not only the immediate market responses but also the long-term economic trajectory of the country. As the world awaits the outcome of the upcoming election and the inauguration of the next president in 2025, it remains clear that the policies adopted by the new administration will play a pivotal role in shaping both the domestic and global economy. The ongoing study of these dynamics is essential for predicting and understanding the future economic landscape in the context of U.S. presidential elections.

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Intermittent Fasting Protects Against Late-in-Life Mental and Cognitive Damage
By Ruhi Deshpande

Abstract

The normal aging process is an inevitable breakdown of the mind and body, altering the manner in which an individual lives their life indefinitely. The decline in working memory and mental well-being is apparent in a large part of the aging process which contributes to a decline in the quality of life. Lifestyle alterations have become increasingly popular methods to alleviate symptoms of such mental and cognitive decline. Intermittent fasting (IF) is a lifestyle diet choice that consists of eating for an "on" and "off" period in order to restrict caloric intake. This period of fasting triggers the release of ketones into the bloodstream, resulting in various other metabolic changes in the body. The metabolic changes caused by fasting have been clearly shown to alleviate symptoms of depression. Anxiety, however, does not appear to be alleviated by IF to the same extent as depression. The effects of IF also result in improvement in memory and learning. This review will include an analysis of existing literature on the effects of IF on mental and cognitive health in older adults and explore the underlying mechanisms. As the growing elderly population increases, we require effective solutions to combat negative lifestyles that result in the loss of cognitive function and poor mental health. IF proves to be a valuable lifestyle modification to address the changes in cognitive and mental health expected with old age.

Key Words: Intermittent fasting, depression, anxiety, cognition, aging, lifestyle

Abbreviations

|	
AD	Alzheimer's disease
ADF	Alternate-day fasting
BDNF	Brain-derived neurotrophic factors
CR	Calorie restriction
GAD	Generalized anxiety disorder
IF	Intermittent fasting
MDD	Major depressive disorder
PD	Parkinson's disease
QoL	Quality of life
TRE	Time-restricted eating

1. Introduction

The aging population is growing at a rapid rate causing concern over the health and lifestyle of the elderly. From 2025 to 2050 the elderly population (65 years and above) is expected to nearly double (1). With this new group of elderly come health risks such as hearing loss, vision loss, diabetes, arthritis, dementia, depression, and many more diverse issues that contribute to a reduction in quality of life. Specifically, declining mental and cognitive health is normally associated with the regular aging process, which may include symptoms such as difficulty with recognition, learning, and retaining new information in addition to confusion, agitation, and mood changes (2). The presence of age-related diseases such as Alzheimer's disease (AD), Parkinson's disease (PD), and Dementia accelerates the rate of cognitive decline and neuronal loss, causing increased concern for the elderly population. In addition, the stress of loneliness, diseases, and disabilities can lead to overall poor mental health in the elderly.

The typical treatment for many mental health disorders is psychopharmaceuticals and psychotherapeutic initiatives. However, such approaches can often be ineffective, as in the case of Major depressive disorder (MDD) where 50% of patients present resistant conditions to conventional treatments (3). Thus, a more unconventional route of treatment is now being considered: intermittent fasting (IF). Fasting is seen to be a therapeutic intervention for common disorders such as depression and anxiety. In addition, fasting has been shown to decrease levels of anxiety and depression without increasing fatigue (4).

The traditional treatments for cognitive impairment and mental health disorders range from various lifestyle changes to pharmacological treatments. Common lifestyle measures include dietary changes/restrictions, exercise regimens, and mental activities in order to prevent further progression of cognitive impairment. Within that dietary changes, specifically IF have been shown to induce change in the metabolic pathway through fatty-acid oxidation and release of fatty-acid-derived ketones which has been shown to improve longevity through improvements in mitochondrial function in addition to the production of brain-derived neurotrophic factors (BDNF) (5). This is significant as mitochondria are the energy-producing organelles of cells and directly influence oxidative stress, neuronal membrane excitability, and synaptic transmission (6). The presence of such changes leads fasting to be a point of interest when looking at cognitive decline in the elderly.

IF is an umbrella term that describes the various methods by which an individual adjusts their eating habits, including periods of fasting and not fasting. There are various types of fasting including time-restricted eating (TRE), alternate-day fasting (ADF), and the 5:2 diet. TRE consists of fasting each day with windows of eating while ADF is a fast every other day, and the 5:2 diet follows a ratio of 5 days non-fasting and 2 days fasting in a week (Figure 1). TRE specifically has gained popularity as a method of weight loss as it is flexible and allows the individual to choose an eating window from 4 to 12 hours. For example, TRE allows for weight loss due to its tendency for the individual to restrict calories by the nature of the diet which itself can be beneficial as it regulates the circadian rhythm and increases autophagy which then leads

to less oxidative stress and neuroinflammation; they both link to the mental well-being of an individual as well as their cognitive abilities (5).
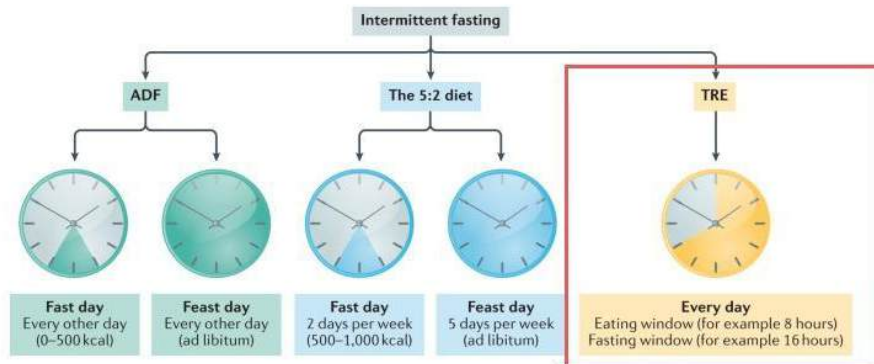
chronic fatigue, irritability, and difficulty concentrating (9). GAD is especially important to watch for in the elderly as it is the only anxiety disorder that is still common in people aged 50 years or more (10).**Figure 1.** Types of intermittent fasting schedules. ADF (alternate-day fasting) shows an alteration between fast and no-fast days. The 5:2 diet shows a weekly schedule of 5 days of nonfasting and 2 days of fasting. The TRE (time-restricted eating)shows a fasting schedule within a 24-hour timeframe Modified from Varady et. al 2022

The growth of the elderly population has increased the need to address the mental and cognitive deterioration associated with aging. Thus, it is imperative to look into treatments and preventative measures to ensure health and longevity in cognitive function. This review will examine the effectiveness of TRE as protection against common mental health disorders and the role it plays in maintaining cognitive abilities.

2. The Effect of Intermittent Fasting on Mental Health
The overall mental health of an individual can be determined by analyzing their psychological, emotional, and social well-being. In today's world, 1 in 5 people live with mental illness, drawing attention to possible solutions to the epidemic facing modern society (7). Specifically, the elderly seem to suffer from poor mental health as social and biological factors such as isolation, loneliness, and progression of disease led to a decline in mental wellbeing; approximately, 14% of people over the age of 60 live with a mental disorder (8). The most common mental health disorders affecting people today are various anxiety disorders and major depressive disorder (MDD). Thus, it is important to address possible lifestyle alterations that may relieve symptoms of such devastating disorders.

2.1 *Lifestyle Interventions and Anxiety: Role of Time-Restricted Eating*

Anxiety is a state of excessive fear, worry, and a constant feeling of being overwhelmed. (10) Anxiety becomes a problem and reduces the quality of life and mental well-being when it develops into an anxiety disorder. The Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) lists 11 specific anxiety disorders, with up to 20% of individuals being affected by one each year (9). Generalized anxiety disorder (GAD) is identified by an individual displaying excessive, persistent, and unrealistic worry about everyday things with additional symptoms such as chronic fatigue, irritability, and difficulty concentrating (9). GAD is especially important to watch for in the elderly as it is the only anxiety disorder that is still common in people aged 50 years or more (10).

The treatment of anxiety is often through an outpatient method of psychotherapy or prescription medication. Cognitive-behavioral therapy is a method shown to improve those diagnosed with anxiety as the face-to-face methods help the individual identify harmful patterns of behavior and thought. In addition, many medications such as selective serotonin reuptake inhibitors, selective serotonin-norepinephrine reuptake inhibitors, and benzodiazepines are commonly prescribed. However, when treating the elderly many have sensitivity to such drugs which may cause side effects such as increased risk of falling, cardiovascular events, and risk of drug-drug interactions (10). Additionally, it is important to consider social factors in treatment as well as therapy and medication, which are often expensive and unaffordable for many.

Thus, lifestyle changes such as fasting, specifically TRE have attracted attention to additional changes individuals may implement. The number of clinical trials testing TRE and its effects on anxiety is limited. Many of the studies were conducted through animal testing or human studies during Ramadan. Such studies often do not find TRE to make a difference in anxiety levels in either humans or animals (11, 12). While there are many individual testimonies of feeling less anxious, the field has not yet been tested to a level that shows true evidence of major improvement in anxiety symptoms. The nature of IF causes calorie restriction (CR) which has been shown to be mildly anxiolytic. However, when measuring signs of anxiety such as certain brain activity, behavioral patterns, and testimony is it clear that the positive association between fasting and anxiety does not demonstrate a clear effectiveness against anxiety.

In a 2014 study done on male rats, 75% calorie restriction of a normal rat diet was tested to measure anxiety effects. 50% of rats followed CR while the other half acted as a control for 18 days. On the 18th day, the rats were tested for anxiety in an open field locomotor activity. The study found that the calorie-restricted rats were somewhat less anxious than their counterparts but that their HPA axis, a system that regulates the body's stress, responses to stress remained relatively unaffected (13). While the data does not show relief of symptoms, it is important to consider that such trials do not test the lifestyle change as a whole and are limited in the time frame. This brings to light how often times IF itself is studied over short periods of time as a temporary treatment rather than a lifestyle change; such a method would be more conducive to reducing anxiety as the implementation of routine is shown to buffer the effects of stress on one's mental health (14).

A 2017 study done in Germany during Ramadan also found that fasting did not show any specific improvements when testing for quality of life (QoL), mood, and fatigue (helpful measurements of anxiety) despite previous research indicating a relationship between fasting and mood enhancement. The study had 50 healthy males split evenly into two groups to either not fast or follow a fast for the month of Ramadan (11). The nature of the Ramadan fast, 19 hours of fasting and a 5-hour eating window, qualifies it to be considered a TRE. Thus, Ramadan studies also demonstrate the same issue of short-term treatment versus full lifestyle change. It is important to question how valid QoL measurements are when the fasting period is no longer than 30 days.

In addition, it is important to note that many studies are done on 100% of the majority male experimental group. This is significant as women are twice as likely to develop an anxiety disorder within their lifetime (12). Additionally, IF has been shown to have huge improvements in women's health in general, especially in post-menopausal women, but many acknowledge that research has been limited (15). Therefore, it is clear that there is reason for further research on TRE and its effects on anxiety as previous research shows that a linkage exists, but has been tested in less suitable circumstances and demographics.

2.2 *Calorie Restriction and Time-Restricted Eating as Lifestyle Alterations to Treat Depression*

Depression is when an individual has a persistently low mood, decreased interest in daily activities, feelings of guilt or worthlessness, lack of energy, and poor concentration. In addition, the ability to function normally is often hindered by appetite changes, psychomotor agitation, sleep disturbances, and/or suicidal thoughts (16). The nature of depression often causes the individual to be unable to do the things they previously liked and needed to do, causing a decline in quality of life. The most common type of depression is major depressive disorder (MDD), with the average lifetime prevalence being 12% (16).

Depression is a disease plaguing the elderly and is often more complicated in comparison to adolescents as they are more likely to display cognitive changes, somatic symptoms, and loss of interest. The older population is also at risk as loneliness and reduction of daily tasks that come with aging can be a pathway to clinical depression. Depression in addition may also appear with a specific set of symptoms when an individual is also suffering from a neurological disease. For example, PD is frequently associated with dysphoria, and AD is associated with irritability and social withdrawal. The complexity and severity of depression in the elderly make it a clear problem plaguing society, and preventative measures and treatments are being studied and tested (17).

Similarly to anxiety, traditional treatments for MDD include pharmacological or therapeutic treatments. Many varieties of therapies such as behavioral therapy, cognitive behavioral therapy, cognitive bibliotherapy, problem-solving therapy, brief psychodynamic therapy, and life review/reminiscence therapy are effective. However, there is concern over the degree of effectiveness as social factors may cause infrequent therapy sessions. (18) The use of drug treatment in the elderly is a nuanced and complex situation with the increased risk of

drug-drug interaction as well as the failure to use effective doses in elderly patients, which can be the reason for a lack of clinical response (18). In addition, drugs such as Tricyclic antidepressants can worsen symptoms of other diseases such as PD. In the same way as anxiety, whole lifestyle changes have been drawing attention.

TRE, and simultaneously CR, have shown to be beneficial for those suffering from depression, with much more solid support in comparison to anxiety. In order to understand why fasting is important, it is necessary to understand how it works to reduce depression. There are many ways in which studies point to TRE and CR reducing depression as both are lifestyle regimens that create large changes in the body. Fasting is associated with an increase in blood ketone bodies which appears to impact brain function by induction of BDNF expression. The change in ketone bodies, brain-derived neurotrophic factor (BDNF), and autophagy (cell breakdown) are significant players when it comes to improving depression (19). Ketones are important in restoring neurotransmitter systems while BDNFS play a huge role in the growth and survival of neurons. All of these processes aid in restoring neuronal pathways and as a result, treating depression.

When looking at individuals of all ages, there are many studies that indicate a wide variety of mental health benefits of TRE, especially for those looking to improve mood when their environment can be the root of depression; many elderly are often in such a situation. A study done in Iran on 313 nurses (56.5% male and 43.5% female) found a 6.5% decrease in levels of depression (20). The test consisted of a questionnaire done before and after Ramadan, a holy month for fasting, and asked the nurses to answer 7 questions relating to anxiety levels with another 7 on depression. The significant difference in depression demonstrates the potential for such measures to be studied further under a more specified population. A sample group of 65+ individuals would provide a more specific understanding of the symptoms of geriatric depression. Additionally, the preliminary data provides a reason to test lifestyle changes for longer periods of time.

A similar study was done on healthy volunteers during Ramadan and looked to analyze depression, anxiety, and stress. This study followed a similar questionnaire format as the previous one and included a total of 73 participants (86.3% male and 17.3% female) by the end of the fasting month. Similar to the study done on nurses, a significant decrease in depressive mood was reported (11% reduction). However, the study acknowledges the limitations of self-reported questionnaires and calls for a deeper analysis of the biological effects of fasting. (21) In addition, a specific study done on 32 aging men found that a fasting regimen showed improvement in mood disturbances, confusion, and anger, symptoms of depression. Half of the men were put on a strict calorie-restricted regime and had a significant improvement in mood according to the Profile of Mood States in comparison to the control group (22).

Thus, there is a clear association between TRE and CR when assessing depression and improvement in mood. In contrast to anxiety, the studies done do not have the lack of a female population, eliminating sex as a conflict of interest. Similarly to anxiety, it is needed that longer testing of TRE as a lifestyle change must be done to see the potential to make large lifestyle

improvements for those with MDD rather than simply an elation in mood and minimizing depression symptoms.

3. The Potential of Fasting to Aid in Cognitive Function Improvement

Cognitive health is generally considered a culmination of an individual's ability to learn, think, and remember clearly. Cognitive health is determined by various factors including environment, genetics, and lifestyle. As individuals age, it is normal for cognitive decline to occur. However, negative lifestyle and environmental factors as well as neurodegenerative disease can cause abnormal decline. The prevalence of subjective cognitive decline among adults aged 65 years and older is 11.7% compared to 10.8% among adults 45-64 years of age (23). This is significant as cognitive decline can be linked with a reduction in QoL due to reduced independence. Many may struggle to do daily tasks such as maintaining personal hygiene, while also struggling with social communication at desirable levels. Such a complex issue calls for intervention and prevention as poor cognitive health and mental health are linked, causing suffrage in general wellness.

3.1 *Intermittent Fasting's Effect on the Learning Process*

A large part of assessing cognitive health is analyzing an individual's ability to learn and retain new information. The process of learning is directly related to cognitive function as processing information is a key element of learning. A specific type of learning known as cognitive learning, emphasizes key features such as gradual memorization, comprehension, and creative problem solving, as opposed to a traditional "cramming" style of memorization. (24) As an individual ages, this ability is often lost or plateaus out as the ability to learn through reinforcement and reward signals decreases in the brain.

In addition, neurodegenerative diseases, such as AD and PD, play a huge role in the loss of learning ability. Common symptoms of AD include difficulty processing new information, anterograde amnesia, and confusion all of which deter the learning process. With the number of people living with AD doubling every 5 years beyond age 65, it is important to be able to retain the learning ability for as long as possible before extreme versions of AD affect the individual (25). In the case of PD, the decrease in dopamine in the brain often disrupts the reward pathway, leading to a loss of learning ability. Additionally, many patients with PD report slower thinking and information processing (26). It is also important to consider social factors and other impairments when assessing the decline in learning ability in older individuals. Hearing loss, limited social contact, smoking, and alcohol consumption may play a role as well.

The effect of IF and CR on learning ability has been assessed through studies on cognition in animal trials. Both have been found to subject neurons to metabolic stress, increasing neuroplasticity and ultimately benefiting cognitive health. BDNFs are protein growth factors that support differentiation, maturation, and survival in neurons. BDNF has been shown to improve synaptic plasticity (5), which implies that it may have a role in some neurological conditions such as AD and dementia, making it an important part of memory. In addition, the

production of ketones has an influence on mitochondrial function, improving energy production and directly influencing neuronal activity and growth (5).

A 2004 study done on rhesus monkeys injected with a neurotoxin to mimic PD showed 30% CR on the monkeys, which showed signs of improvement in cognition. 8 weeks later, the expression of BDNFs has shown to increase indicating possible protection against the symptoms of PD (27). More recently, a 2013 study done on male mice tested the results of a high-fat IF diet. After a period of 11 months, the mice were subjected to a spatial learning and memory test through a Barnes maze. Half of the mice that were on an IF diet showed better hippocampus-related learning and memory. It is noted that much of this improvement is likely related to reduced oxidative stress leading to improvement in brain structure rather than change in BDNF expression (28).

Thus it can be seen that there is a clear relationship between IF and consequently CR through changes in metabolic pathways and brain structure. However, it is important to acknowledge the lack of long-term human trials to test this relationship. In addition, the underlying cause of this improvement in learning cannot yet be deduced to one single change, and it is currently considered to be a conglomeration of changes induced by IF and CR.

3.2 *Intermittent Fasting and Memory Retention: Potential Benefits for Cognitive Health in Aging*

Memory retention is the ability to remember information over a period of time. Similarly to learning, it is a great indicator of an individual's cognitive health and plays a huge role in the learning process. Memory loss has become a huge societal concern, as many individuals often panic when unable to recall information as quickly as they once used to. It is estimated that almost 40% of the population will experience some degree of memory loss by the age of 65 (29).

A person's ability to remember can be hindered by the inability to create new memories, long recall time, or even the inability to recall episodic and semantic memories. Memory loss can be triggered by various factors including but not limited to prescription drugs, depression, anxiety, thyroid issues, AD, PD, and nutritional deficiencies (30, 31). Common ways individuals may try to improve memory retention in midlife is by engaging in active recall, exercising regularly, getting adequate sleep each night, and controlling their diet. This is considered important as there is a clear link between declining cognitive impairment and QoL as motivation and sense of purpose are often lost (32). Such a relationship becomes especially significant when considering an elderly population as they are much more subjected to memory loss as well as the feelings of loneliness and helplessness associated with it.

Similar to learning, many of the trials measuring IF and CR are conducted in the context of neurodegenerative diseases. As they are responsible for a large portion of the memory loss experienced by seniors, many look to address the issue of dementia in the context of AD and PD.

A study done on AD mouse models specifically looks at the effects of TRE on circadian rhythms and the metabolic pathways associated with memory loss. Using a novel objection

recognition test and a radial arm maze test over 5 consecutive days, TRE was shown to restore the performance of a wild-type mouse in comparison to the AD model (33).

A step up can be seen in a 3-year study on 99 elderly adults with mild cognitive impairment, it was shown that IF significantly improved cognitive performance in older adults. Scores on memory tests such as MMSE, MoCA, RAVLT, Digit Symbol, and Digit Span tests were higher among those who practiced IF. Notably, our findings indicate that consistently engaging in IF may help older adults achieve better cognitive function during follow-up, leading to successful or normal aging (34).

The presence of long-term human studies on memory loss and IF is a positive sign for the direction of the future of the field. By promoting neuroplasticity, reducing inflammation, and improving metabolic health, IF and CR may offer promising results for improving memory retention and cognitive function as we age. These lifestyle changes could play a crucial role in addressing the growing concerns of the general well-being of the elderly population in addition to memory loss.
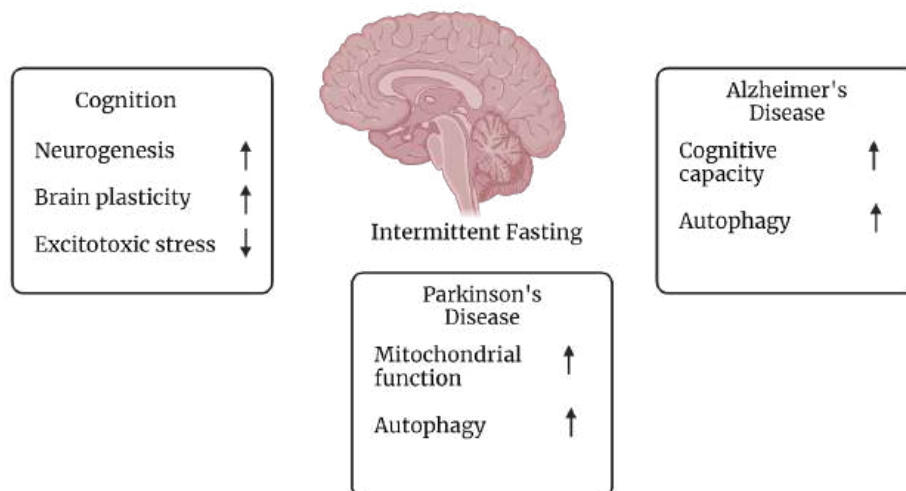
Figure 2. Methods in which IF can improve brain function. Boxes contain issues associated with aging populations. Arrows indicate an increase/decrease in a particular function to aid overall brain function. Modified from Cerqueira et. al 2019

4. Conclusion

IF is a valid method to further test in order to assess protection against cognitive and mental decline, especially in the elderly. As the population ages, addressing cognitive decline and mental health issues in the elderly becomes increasingly important. Traditional treatments often fall short, especially in older adults, leading to interest in alternative approaches like intermittent fasting (IF), particularly time-restricted eating (TRE). IF shows promise in improving mental health and cognitive function. In terms of mental health, there is a strong improvement in reported mood and fatigue as a result of IF. The improvement in memory and

recall as a result of IF demonstrates a future path for testing the benefits of IF in more specific functions of cognition such as language, processing speed, and problem-solving.

While early research suggests the potential benefits of IF in reducing depression and improving cognitive abilities like memory retention, most studies are short-term and lack depth. The population tested on is often middle-aged males disregarding the females and the elderly population. More long-term, diverse human trials are needed to fully understand IF's impact on aging populations. As the concerns for the elderly population arise, IF becomes a valuable tool for individuals to incorporate into their lifestyle to alleviate the risks and symptoms of poor mental and cognitive health.

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A Deep-Learning Approach to Identifying Alcohol Use Disorder Through Abnormal Reductions in Transient EEG Amplitudes Using a Multilayer Binary Classification Learning Model By Krish Patel-Shah, Jacob Taira, and Lawson Woodward

Abstract

Alcohol Use Disorder (AUD), colloquially known as alcoholism, causes 3 million deaths annually and is marked by difficulty in stopping or controlling alcohol consumption despite adverse social or health consequences. Current methods of identifying AUD take several hours, requiring the manual processing of human body samples, and can only be processed in small counts at once. Using patient electroencephalography (EEG) data to train sequential machine learning (ML) models can compensate for the inefficiencies of current practices. Most existing studies do not publicly release the full data, results, or code from the experiments. Consequently, previous attempts to automize AUD detection are non-replicable. To address these issues, we created a program that takes a database of raw EEG data from both AUD and control group patients and passes the restructured data into a deep-learning sequential model that differentiates between subjects using binary classification algorithms. The created program was implemented in multiple tests to find the highest-accuracy ML parameters for a final optimized model. The resulting validation accuracy was 93.1%, and the average loss was 0.35μV on a scale of ±40 μV, indicating that the model was fairly accurate in the context of ML algorithms. Our program provides an easy-to-use source for the application of machine learning processing of large EEG datasets and promotes a new approach to the common identification of AUD in humans.

Engineering Goal

The engineering objective is to construct a multilayer sequential deep learning model that is able to correctly classify at least 90% of all cases from a data set containing AUD-indicative and normal EEG patterns. A secondary engineering goal is to automate data preprocessing and model testing to provide other researchers with the information needed to replicate and build upon the results achieved within this open-source study. The sequential model is predicted to detect an abnormality between EEG records of AUD patients and the control group patients with an accuracy of more than 90%. All code and data will be publicly available for replication, and the code will automate model parameter testing.

Parameters

The experimental parameters include the files of the data set being processed, the ML parameters that the user wishes to change, the layer archetypes within the model, and the percentage of the data that the user wishes to split among the train, validation, and test subsets.

Introduction

Electroencephalography provides a less-invasive approach to measuring brain activity to deduce if an individual is under the influence of alcohol without the need for physical samples

from the subject [1]. Although invasive techniques such as electrocorticography offer better spatial resolution and visibility of the brain's components, noninvasive techniques like EEG, or Functional Magnetic Resonance Imaging (fMRI) possess more precise temporal resolution, fewer safety concerns, and more efficient monitoring of large-scale activity [2]. By constructing an ML model to process and compare EEG data across selective portions of the cerebral cortex, a patient's condition can be identified and assessed significantly faster than traditional methods. Automatic processing of multi-dimensional information with machine learning to identify correlations between variables in a data set is an important frontier in the data science field today. However, the reproducibility of past efforts to create such complex and specialized models is nearly impossible due to a lack of publicly available code and unprocessed data [3]. The creation of an open-source, easily configurable ML model for the identification of brainwave patterns represents a step forward for the publicity of automating EEG brainwave data.

BRAIN PHYSIOLOGY

Parts of the human brain

At its most simplistic level, the brain functions to process sensory information from the environment that it then integrates and outputs as the appropriate motor, immune, or hormonal response. As described in "Overview of the Nervous System," the human encephalon consists of three general sections: the cerebrum (on top of which lies the cerebral cortex), the cerebellum, and the brainstem [4]. The textbook explains that the sections can be further divided into parts with specialized functions involved in the processing of external and internal stimuli.
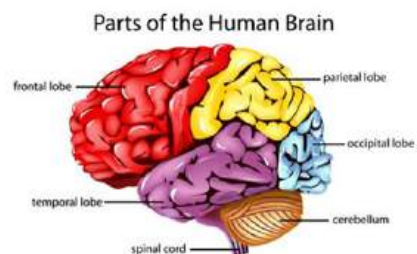
Fig. 1. Human Brain Anatomy [5]

Medical resources describe the cerebrum as encapsulating the majority of the upper portion of the brain and indicate that it is mainly responsible for distilling sensory information involved in logical reasoning and problem-solving while also regulating autonomic (unconscious), endocrine (hormonal), and motor (movement) functions [6][7]. They further detail the cerebrum as having a left hemisphere that is associated with abstract thoughts and speech and a right hemisphere that organizes spatial comprehension. The subcomponents of the cerebrum are described to include the frontal, parietal, occipital, and temporal lobes [6][7].

The frontal lobe functions through executive and motor actions, containing the primary motor cortex, supplementary motor cortex, prefrontal cortex, frontal eye field, and Broca's area [8]. Executive functions detail motivation, judgment, decision-making, learning, and reward,

among others. Motor functions maintain skeletal muscle, facial movement, and speech control, while the primary and supplementary motor cortices work cooperatively to execute and coordinate muscle movement, respectively [8].

The prefrontal cortex is located at the anterior of the brain and is also responsible for executive functions [9][10]. Next to the prefrontal cortex lies the frontal eye field, which enables voluntary rapid eye movement. Broca's Area is the center point between the prefrontal cortex and the supplementary motor cortex that controls speech and its related muscles [9][10].

"The History of the Neurophysiology and Neurology of the Parietal Lobe" locates the parietal lobe in the higher posterior of the brain, explaining that it functions based on physical sensation, auditory stimuli, and visual stimuli [11]. Berlucchi and Vallar explain that the parietal lobe contains the primary somatosensory cortex, somatosensory association cortex, and posterior association area. The primary somatosensory cortex controls the awareness of somatic (bodily) sensations like touch, pain, and temperature, whereas the somatosensory association cortex is associated with memory and the perception of sensations. Additionally, the posterior association area is located next to the somatosensory association cortex and is the point at which the main sensory-processing components all meet to guide spatial awareness of the body [11]

The occipital lobe, as described in "Neuroanatomy, Occipital Lobe," is located at the posterior of the brain and contains the primary and visual association cortex that analyzes, recognizes, and recalls visual information [12]. The visual association cortex functions to receive, segment, and integrate visual stimuli that are then passed to other regions of the brain and are located between the visual cortex, parietal, and temporal lobes [12].

The U.S. Department of Health and Human Services describes the temporal lobe as situated in the lower central area of the brain and indicates that it plays an important role in processing stimuli such as language information, memory acquisition, face recognition, auditory processing, and perception [6]. The National Institute of Neurological Disorders and Stroke explains that the temporal lobe contains the thalamus, the primary auditory cortex, the auditory association cortex, Wernicke's Area, and the primary olfactory cortex [6]. The article further explains that the thalamus organizes data and regulates hormones while relaying information across the brain. Additionally, Wernicke's Area borders the primary auditory cortex and parietal lobe, functioning in the understanding of written and spoken language. The primary auditory cortex processes complex auditory information like language comprehension and switching, while the auditory association cortex is at the center of the temporal lobe and exists to interpret sounds. The primary olfactory cortex is the lowermost portion of the temporal lobe that deals with the awareness and processing of smell [6].

SPECIALIZED BRAIN CELLS AND NEURON ACTION POTENTIALS

Neurons

Khan Academy indicates that each subcomponent of the brain consists of various tissues that house billions of specialized cells called neurons, which can be classified into three main

groups: motor neurons, sensory neurons, and interneurons [13][14]. The articles further explain that motor neurons are located in the central nervous system (brainstem and spinal cord), and transmit signals from the brain to muscular tissues, allowing for physical movement of the body [13][14]. Sensory neurons can be found in groups of neurons known as ganglia within the peripheral nervous system and stimuli from the skin, eyes, mouth, nose, and ears can be used to interpret touch, position, pain, and temperature. Interneurons are only located in the central nervous system and are meant to connect neurons for the intercommunication of signals [15].

MEASURING BRAIN ACTIVITY

Electrodes

"Fundamentals of EEG Measurement" provides an overview of how electrodes are used to measure synaptic activity between neurons throughout the cerebral cortex of the brain [16]. Teplan explains that even though neurons are incredibly small, thousands of excitatory signals can be triggered within a similar time frame to generate an electrical field capable of being measured through tissue and bone. If any of these signals are picked up by an array of electrodes, an EEG signal is generated as a function of amplitude and time. Furthermore, in "Improvement of EEG Signal Acquisition: An Electrical Aspect for State of the Art of Front End", Usakli explains that an electroencephalogram uses electrode configurations known as montages that transform and compare biopotential frequencies for later transformation into electrical signals that can be interpreted by a computer[16] [17]. The brain produces a range of frequency bands that can vary in amplitude from roughly -40 μV to 40 μV, with lower-amplitude signals being harder to detect from the surface of the scalp.

Both invasive and non-invasive approaches to recording subcortical data exist. In "State of the Art of Non-Invasive Electrode Materials for Brain-Computer Interface", Yuan et al describe the major concerns with invasive and semi-invasive electrodes that are associated with high surgery costs, complicated preparation, and potential for great harm to brain health [18]. Health risks are still in the process of being fully eliminated today, hence the more popular use of non-invasive techniques, since electrodes are placed on the surface of the scalp and information is recorded using an electroencephalogram (EEG) without invading the brain tissue [18].

Recording Brain Waves

One electrode is not enough to accurately record and compare changes across the entire surface of the brain. Oftentimes, many electrodes are situated on the scalp using different conductive materials to hold the electrodes in position. The American Electroencephalographic Association provides industry guidelines on the placement of electrodes [19]. The 10:10 placement system establishes a line from the nasion to the inion (front to back) of the head, and points are constructed on this line in 10% increments of distance relative to the length of the line [19]. A 10% increment is assigned to the electrodes closest to the outer edge of the head while the rest are separated along their lines in 10% increments [19]. Electrodes are often placed on the

regions of the scalp that reside over the temporal, frontal, parietal, and occipital lobes. Figure 2 identifies the channel names assigned to the placement. Note that the placement in this diagram is not precise, but is provided to give a general understanding of the locations of channels.
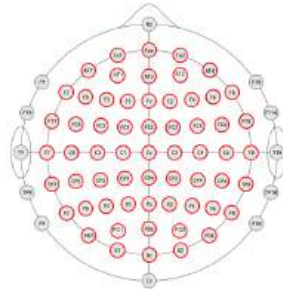

Fig. 2. Electrode placement in a general 64-electrode system

ALCOHOL USE DISORDER

Overview of Alcohol Use Disorder

Alcohol consumption is one of the world's largest contributors to premature deaths and is a causal factor in more than 200 diseases and injuries associated with the onset of mental and physical health issues that can also risk harm to others [21]. The widespread effects of alcohol culminate in a condition referred to as alcohol use disorder, which afflicts more than 105 million individuals across the world today [22]. More than 3 million deaths occur annually from the harmful use of alcohol, which constitutes more than 5.3% of all global deaths in conjunction with significant social and economic losses to individuals and society at large [21]. Furthermore, the United States ranks seventh in the world for the highest rates of overall AUD and remains first in AUD in females [23]. AUD is a medical condition that is characterized by an unhealthy pattern of alcohol consumption and is considered to be a form of substance abuse [24]. One of the primary ways in which alcohol affects the brain is by increasing the release of the neurotransmitter dopamine, mimicking the effect of GABA on postsynaptic inhibitors, and interfering with the normal functioning of serotonin, which also plays an important role in reward, cognition, metabolism, and mood [25]. In addition to neurotransmitter systems, several regions of the brain remain vulnerable to the effects of alcohol, such as the limbic system, thalamus, hypothalamus, frontal lobe, and right hemisphere [26]. Over time, alcohol abuse can lead to significant changes in brain structure and function [26].

EEG Studies of Alcohol Use Disorder

Several recent studies have used deep learning convolutional neural networks (CNN) to classify EEG records into AUD and control categories using the UCI dataset. In 2021, Mukhtar et al. reached a classification accuracy of 95% [27]. Furthermore, Houchi Li and Lei Wu used a CNN-Bi-LSTM model structure to achieve an accuracy of 98% in June 2022 [28]. Additionally, in 2020, Farsi et al. achieved a 93% accuracy for classification [29].

The study "Characteristic changes in EEG spectral powers of patients with opioid-use disorder as compared with those with methamphetamine- and alcohol-use disorders" by Minnerly et al. focused on four groups of patients: those with Methamphetamine Use Disorder, those with Alcohol Use Disorder, those with Opioid Use Disorder, and finally a control group with normal EEG readings [25]. Through five distinct methods of analysis of raw EEG data, Minnerly et al. drew conclusions about comparisons between the different use disorders. There were two major findings from this study, the first being that the largest differences in brain wave amplitudes for those with a substance abuse disorder compared to the control group occurred in the Alpha and Theta waves of subjects (however most significantly in the alpha waveforms). The second major discovery was how different regions of the brain showed changes in amplitude. While there were no observed differences in how the brain of a subject was affected from the right to the left hemisphere, the posterior and anterior regions of the brain showed larger differences in brain wave amplitudes [25].

Publicly-Available EEG Data for Alcohol Use Disorder
The logistics of obtaining data from patients with alcohol use disorder is outside of the scope of this paper. Instead, the authors chose to identify an existing database containing EEG data for control patients and those with alcohol use disorder.

The authors were able to identify only one clinical-grade, publicly-available data source for EEG recordings of subjects with AUD, which was published by the University of California, Irvine (UCI) [30]. In an attempt to find appropriate data sources, the authors conducted numerous Google Scholar searches using keywords such as EEG, electroencephalogram, alcohol, alcoholism, substance abuse disorders, and AUD, and then contacted the authors of published articles that mentioned AUD data sets. Well-known repositories and listings of EEG data sets were searched for, including Temple University EEG Data Corpus, the University of California at San Diego data source listing, and EEG data source listings on GitHub. Henri Begleiter of the Neurodynamics Laboratory (Henri Begleiter Neurodynamics Laboratory) at the State University of New York Health Center in Brooklyn created the data used for this research in 1991. Lester Ingber donated the data set to the UCI in 1999 [30]. As of January 2023, the repository is still used for scientific research related to EEG detection of AUD [31]. It is currently the only existing publicly-available, clinical-grade EEG data set that captures AUD and control EEG data known to the authors [32] [33] [34]. The data set captured EEG data from sites based on the Standard Electrode Position Nomenclature from the American Electroencephalographic Association in 1990 [35]. The set contains over 12,000 trial files across 122 subjects and comes from a large study aimed to examine EEG correlates of genetic predisposition to AUD [30]. As large as it is, the data set is still relatively insufficient when fully training a machine learning model. Each subject was tested with three stimuli to record a reaction in the form of EEG brain wave data.

MACHINE LEARNING

Machine Learning Overview

Machine learning is an aspect of Artificial Intelligence that involves the creation of algorithms (code) that learn from data without being specifically programmed. ML uses large sums of data to identify patterns by using statistical techniques through various types of algorithms, each with different characteristics and uses. The two main types of ML algorithms are unsupervised learning and supervised learning.

Unsupervised Learning

As Andrew Ng details in the Stanford Coursera course *Supervised Machine Learning: Regression and Classification*, unsupervised learning is a collection of ML algorithms that discover relationships in a data set without being given any labeled data [36]. Unsupervised learning uses ML algorithms to run through and organize unlabeled data sets by analyzing and grouping information and discovering patterns without the need for human intervention. Common algorithms include clustering, anomaly detection, and dimensionality reduction.

Supervised Learning

Supervised learning is used in most real-world applications, as supervised learning is a faster and cheaper form of machine learning. As Ng explains, in supervised learning, algorithms are trained using labeled data, in which the data has both input features and corresponding labeled outputs [36]. Further, Ng explains that these types of ML algorithms map a given input (x) to a relative output (y) based on statistical inferences from the provided data ("correct answers") of input-output data pairs. The algorithms use this provided label data to make predictions, which are then tested with a different test data set. Therefore, the accuracy of the model's predictions has a positive correlation with the amount of data fed in to train the machine learning algorithm [36]. Currently, supervised learning algorithms are being used in spam filtering, speech recognition, machine translation, online advertising, and visual inspection. Supervised ML algorithms can be further separated into two main categories: regression and classification. This project uses supervised learning to classify subjects of AUD. The algorithms are trained using the UCI (Henri Begleiter) EEG data set. The input features consist of measurements from 64 electrodes placed on the scalp sampled at 256 Hz for 1 second per trial [30]. The corresponding labeled outputs are alcoholic or control, derived from the fourth character of the subject identifier ("co2a0000364.rd"). A subset of the data set was used to train the model, a second subset was used to validate the data, and a third subset was used to test the predictions with a different test data set.

Classification

Classification is a type of supervised learning that is used to predict specific categories or classes in qualitative or quantitative data [37]. Different from regression algorithms, classification models only predict a finite number of outputs. A classification algorithm divides

the data set into different classes by looking for the decision boundary in the data. An example of this would be an algorithm predicting the type of tumor based on the age of the patient and the size of the tumor. There are many types of regression and classification algorithms, each with its own uses. This research study uses a binary classification model. The supervised learning model predicts between the categories of "Alcohol Use Disorder" or "Control."

Binary Classification and Logistic Regression

Binary Classification is a type of classification algorithm in supervised learning where the model is trained to predict one out of two possible outcomes or classes. The output is either 0 (false, negative class/category) or 1 (true, positive class/category). Linear regression cannot be used to solve binary classification problems as linear regression predicts continuous values and not binary outcomes. As a result, logistic regression is used for binary classification as it creates an s-shaped curve called a sigmoid function that allows the output values to be between 0 and 1. The closer the value is to 0, the more likely it is to be false, and the closer the value is to 1, the more likely it is to be true. The sigmoid function equation where e $\sim$ 2.7 is shown below:

$$f(x) = \frac{1}{1+e^{-(wx+b)}} \qquad \rightarrow \qquad f_{w,b}(x) = g(w\ x + b) = \frac{1}{1+e^{-(wx+b)}}$$

By passing through the previous linear regression function as z into the sigmoid equation, the logistic regression model is created, where the output is a value between 0 and 1. This value can be thought of as the "probability" that the function is 1 or true. The logistic regression model is demonstrated by the function above on the right.

Cost Function for Logistic Regression

In logistic regression, the cost function is used to measure the difference between the predicted probability of the model and the actual class label. For binary classification, the target $\hat{y}$ takes on only two values, 0 or 1. The cost function for linear regression, the squared error cost function, cannot be used since logistic regression is a classification algorithm while linear regression is a regression algorithm. If used for logistic regression, the squared error cost function becomes a non-convex function, making gradient descent inaccurate due to many local minima. In order to change the cost function for logistic regression, the loss part of the equation needs to be changed to incentivize the algorithm to make more accurate predictions when y is equal to 1, since the loss is the lowest when it predicts values close to 1. The overall cost function is now a convex function, and gradient descent can find the global minimum reliably. Since y(i) can only be equal to either 0 or 1, the loss function can be rewritten as:

$$L(f_{w,b}(x^{(i)}), y^{(i)})) = -y^{(i)}\log(f_{w,b}(x^{(i)})) - (1 - y^{(i)}\log(1 - f_{w,b}(x^{(i)}))$$

When this new loss function is plugged into the cost function and becomes simplified, the cost function for logistic regression is created, which is the basis for the binary cross-entropy loss function that most binary classification machine learning algorithms use.

$$-\frac{1}{m}\sum_{i=1}^{m}[y^{(i)}\log(f_{\vec{w},b}(\vec{x}^{(i)})) + (1 - y^{(i)}\log(1-f_{\vec{w},b}(\vec{x}^{(i)}))$$

Gradient Descent

In order to minimize the cost function in logistic regression, Gradient Descent is used. Gradient Descent is an optimization algorithm used to find the values of weight and bias such that J(w,b) (the cost function) is minimized. Gradient descent adjusts w and b and takes steps in the direction that reduces the cost until the minimum is reached. The algorithm for gradient descent is listed below, where both w and b get updated simultaneously:

Repeat until convergence {

$$w = w - \alpha\frac{\partial}{\partial w}J(w,b)$$

$$b = b - \alpha\frac{\partial}{\partial b}J(w,b) \ \}$$

In the equation above, the learning rate, or Alpha (α), is a small positive number (0 to 1) that controls how large of a step the algorithm takes when traversing a gradient descent. If the learning rate is too large, the algorithm may overshoot the minimum and oscillate around it. However, if the learning rate is too small, the algorithm may get stuck in a local minimum or converge very slowly. The derivative term determines the step's direction in gradient descent. The two equations are simultaneously calculated and updated until convergence is achieved.

Feature Scaling

In machine learning with multiple features, if the input features are not on a similar scale, then the classification algorithm can perform poorly. As a result, the inputs must be scaled by lowering the weight of the larger feature and increasing the weight of the smaller one. However, this creates an unusual graph that can be difficult for the algorithm to navigate. By applying feature scaling, these graphs become more traversable for the algorithm. Methods for feature scaling include Mean normalization and Z-score normalization (also known as standardization). Z-score normalization is usually used for data with a Gaussian distribution, while Mean normalization is used when the data is non-Gaussian. Mean normalization involves averaging all the values of x1 in the training set (μ1, the mean), then subtracting that number from each value of xi, and dividing that by the difference between the maximum and minimum:

$$X_i = \frac{x_i - \mu_i}{max - min} \qquad \rightarrow \qquad X_i = \frac{x_i - \mu_i}{\sigma_i}$$

Z-score normalization is the same as mean normalization, but (x1- μ1) is instead being divided by σi. Z-score normalization transforms the values of the input features to have a mean of zero and a standard deviation of one.

Regularization: (Overfitting and Underfitting)

In a machine learning model, overfitting creates a graph that passes through each training set point exactly but is not aligned with any other data points that may be added in the future. Underfitting occurs when the prediction graph does not align with the data and when the training set is not very closely aligned with the points that compose the prediction function. This produces a higher bias, causing the algorithm to predict a very strong linear relationship in contrast to nonlinear data points. Generalization allows the algorithm to fit the data well while not making too many assumptions as to how the relationship between the input and output will be represented on the graph. Some ways to address overfitting are to collect more training examples, implement feature selection, or perform regularization. The main idea of regularization is to have smaller weights so the model becomes simpler and is thus less prone to overfitting. For example, if there was a data set that needed a quadratic function for the line of best fit, having more than two features would create a higher-order polynomial function that would overfit the data (a function that would follow the data too precisely). To account for this, large coefficients can be added to the extra weights in the cost function. If the weights are too large, it will penalize the algorithm, so they must be close to 0 to not tamper with the graph. Lambda ($\lambda > 0$) is a regularization parameter, and to slightly penalize all of these features (wj parameters), a new term is added to the original cost function for linear regression that sums all of the features in a training example. L2 Regularization is represented as [$\lambda*\sum w2$], which is added to the cost function and takes the square of the weights in order to shrink weights evenly and optimize the mean cost, which is better when working with codependent features in larger neural networks. Squaring the weights also means the loss is more sensitive to larger errors since they will stand out more after being squared (penalizes the algorithm further).

L1 Regularization is another form of regularization that can be represented as [$\lambda*\sum|w|$], which is added to the cost function. The Least Absolute Shrinkage and Selection Operator (LASSO) is better for highlighting key features in smaller neural networks while shrinking irrelevant variables to 0, creating sparsity and thus becoming more robust to outliers.

$$J(w, b) = 12mi = 1m(fw, b(x(i)) - y(i))2 + 2mj = 1mwj2$$

Artificial Neural Networks / Deep Learning

Artificial neural networks (ANN) or deep learning algorithms, are ML algorithms created to mimic the biological human brain, where one neuron output becomes the input for another neuron [38]. They have become popular due to their ability to learn nonlinear relationships in data. ANNs are used in tasks such as predictive modeling, image recognition, and natural language processing as they can handle large amounts of complex data while being scalable [39].

Neural Network Layers

At a very basic level, a digital neuron (referred to as a node) takes in an input value and outputs a number to a different neuron, with many nodes doing this process simultaneously. These interconnected artificial neurons form three different layers in a basic neural network: the input layer, the hidden layer(s), and the output layer [40].

In a neural network, the input data is first divided into batches, with each batch containing a number of training examples defined by the batch size [41]. The input layer, layer 0, takes in information into the neural network, where input nodes categorize and/or process the data, which is then passed to the next layer through activations (functions that generate the node's output).

As Géron explains, hidden layers use the previous layers' output to analyze the information further and pass it on to the next layer via activations [40]. In complex networks, there are multiple hidden layers that take the output of the previous layer [40]. The output layer then returns the final result of all the data processing by the different layers in the neural network from an activation function. Géron further explains that the cost function is then applied to the final result and the respective gradient descent is used to update the model parameters [40]. This process is repeated for a set number of times defined by the number of epochs, with the model parameters being updated for each batch of training examples in each epoch. As a result, the model will see more data and have a higher chance of learning complex patterns as the number of epochs increases. The number of nodes present in the output layer depends on the type of problem the neural network is solving.

For binary classification problems, the output layer will contain one node, returning a 1 or 0, and uses a binary cross-entropy cost function. However, in order to handle different types of data, various types of neural networks, layers, and activation functions are used [42].

Feedforward Neural Networks

Feedforward neural networks are the simplest types of neural networks. They consist of an input layer, one or more hidden layers, and an output layer. Forward propagation is used to process data by passing input data through the network and generating an output. The inputs are transformed by weights and activation functions at each layer [43].

Recurrent Neural Networks (RNNs)

RNNs are neural networks designed to process sequential data and are most commonly used in data where the order of the inputs is important. RNNs are especially useful in tasks that have a temporal dimension, such as time-series prediction and speech recognition [44].

Long short-term memory (LSTM) layers

LSTMs are more advanced implementations of RNNs that are able to better handle sequential data because they learn long-term dependencies [45]. LSTM layers use past information to inform their current decision, as neurons in an LSTM act as a type of memory, determining which information to store and which information to discard [45].

Convolutional Neural Networks (CNNs)

A convolutional neural network is a specialized type of feedforward model that abstracts information with fewer weights than a fully connected network [46]. CNNs compress an input

matrix through trainable weights and biases to differentiate between classes of data, which provides greater analysis of spatial relationships and faster computation. As the matrix is passed through the convolutional layers of the model, only strong features are preserved while the overall dimensions and redundant data are reduced [47]. The kernel is a filter of specified dimensions that traverses the input matrix of a layer and extracts key features while removing noise and unnecessary dimensionality (the number of input variables). By the nature of the kernel itself, the matrix will continuously shrink throughout each convolutional layer. An n by n image convolved by a j by j kernel will result in a size of dimensions (n-j+1) by (n-j+1). As this continues, the matrix will get smaller and smaller. Furthermore, cells on the outer edge or corners of the matrix are not covered as often by the kernel as cells more toward the middle, so they are by default not being weighed as heavily. To combat this, padding is used in which an extra layer of empty cells is placed around the outside of the matrix to create an output of the same dimensions (same padding) or no padding (valid padding, p = 0). Therefore, the dimensions of the output matrix would be (n+2p-j+1) by (n+2p-j+1). 'Stride' is the number of cells skipped over for every scan the kernel makes on the input matrix as it moves left/right and up/down. For instance, a kernel of 2x2 on a 4x4 matrix with a stride of 2 (s=2) would jump over 2 cells for each scan, rather than just one, with the equation of the size of the output layer shown below:
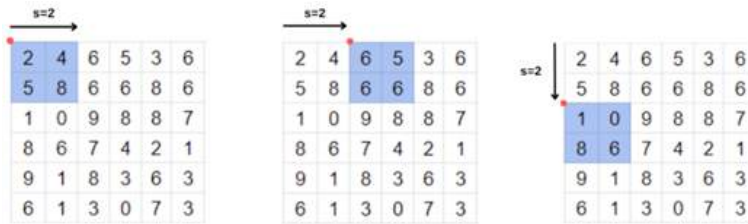
Fig. 3. Stride on Matrix

$$n_{out} = \frac{n_{in} + 2p - k}{s} + 1$$

Pooling layers

A pooling layer downsamples the output of a convolutional layer by reducing the number of unnecessary dimensions [47]. Fewer dimensions result in less complexity and thus faster computation time. Max pooling is a technique in which the kernel returns the highest value of all the cells within its scope on any given scan. This methodology is used as a noise suppressant (similar to a high-pass filter for data) and as a way of reducing dimensionality.

Fully-Connected Layers

Once the input matrix has been compressed and processed, the flatten() method is applied in order to transform the data into a format for a feedforward multilayer perceptron [47]. In a fully-connected layer, or Dense layer, all neurons are connected to one another between layers, meaning each neuron applies a transformation to the input vector through a matrix of weights,

where the number of rows is dependent on the length of the input vector and the number of columns is dependent upon the output vector. However, not all weights affect all outputs, since they are only applied to the elements in the vector array that are eventually represented as a single output. There is an output for each single input array that is represented as a single element in the output vector, which cannot be affected by weights meant for other elements in the input vector. Several lists of weights are applied to the input array to help analyze/isolate each layer and create a final prediction for an input matrix of data.

Activation functions

Activation functions can help introduce complexity into neural networks by allowing the neural network to learn more complex data structures. An activation function, regardless of the neural network architecture, will take the values created by a given layer of the network and apply a transformation to these values in order to map them to a specific range. Some popular activation functions include the rectified linear activation unit (ReLU), hyperbolic tangent (Tanh), logistic regression (Sigmoid), and Linear functions [49]. The use of a certain activation function depends on the target y value. For example, if working on a binary classification problem where the target y value (the output) is either 0 or 1, a sigmoid function would be used in the last layer in order to return a 0 to 1 value. Further, if solving a regression problem, the last layer would be a linear activation function. If the output can only take on non-negative values, this would be indicative of a ReLU function [48].

Binary Cross-Entropy

Over several epochs, the CNN and its consequent Dense layers are able to distinguish between dominating and certain low-level features in images and classify them using binary cross entropy [49]. The binary cross entropy loss function generates a score that describes the averaged differences between the model's predictions that data belongs to class 1 and the actual labels (either 0 or 1), where the loss should be minimized (ideal cross-entropy loss is 0), the probability score should be as close as possible to the actual class label, and the algorithm penalizes the probabilities based on how far off they are from the actual class labels. The prediction of the algorithm can be referred to as $\hat{Y}$ (y hat), and the real label of the data can be referred to as Y.

$$Y_i * log(\hat{Y}_i) \qquad\qquad (1 - Y_i) * log(1 - \hat{Y}_i)$$

Error calculation for positive labels   Error calculation for negative labels

Combining the two terms to account for both negative and positive labels/ predictions and averaging the loss:

$$-\frac{1}{n}\sum_{i=1}^{n}(Y_i * log(\hat{Y}_i) + (1 - Y_i) * log(1 - \hat{Y}_i)$$

In which *i* represents the sample number, and *n* represents the total number of samples. Note that the function is multiplied by negative 1 because the prediction (Ŷ) is a number between 0 and 1, meaning that the traditional function would be negative and approach 0 based on the loss.

Scientific Reproducibility of Machine Learning and EEG Studies

A secondary objective of this research is to provide a framework by which other researchers can replicate and build upon the results of this experimentation. A study is considered reproducible if, given access to data and code, a different group can obtain the same result [50]. A 2015 survey published in Nature indicated that of 1,500 scientists, 70 percent had tried and failed to reproduce another scientist's experiment, and over 50 percent had failed to reproduce their own experiment [51].

Beam et al. stated that "the mainstream machine learning community has embraced fairly radical notions of open science, transparency, and reproducibility" and that "many reports are first available as preprints, code is usually available as open source, and most articles rely on data sets available in the public domain" [52]. However, in their review of 154 papers that applied to deep learning and EEG, Roy et al. found that "studies often suffer from poor reproducibility: a majority of papers would be hard or impossible to reproduce given the unavailability of their data and code" [4]. Though there are large numbers of public repositories of data sets that are contributing to recent developments in deep learning with EEGs, 42% of the studies reviewed by Roy et al. used data not publicly available—notably in domains such as cognitive monitoring [4]. Recent initiatives to develop best practices will likely help to improve reproducibility in the future, though the availability of privately held data could still be an issue. At a minimum, taking an approach that can be termed "data preprocessing as code (DPaC)," similar to "infrastructure as code" (IaC) would enable greater reproducibility in that manual intervention is minimized and even small changes are embedded in code [52].

METHODOLOGY

The methodology for this project involved building an optimized machine-learning model through experimentation while simultaneously developing code that enables more efficient experimentation. The process of this project included: **1)** identifying a data set; **2)** developing code to automate the transfer of data to the working directory; **3)** processing the data; **4)** creating referenceable copies of data to be altered for experiments, including groups and targets files; **5)** creating an ML model through experimentation; **6)** parameterizing key variables to ensure more efficient experimentation; **7)** running and testing the ML algorithms; and **8)** making the experiment replicable by providing access to all data processing, deep learning models, experimental output, and coded experimental execution available in a public repository. Additionally, this program uses the pandas, os, pathlib, tarfile, gzip, shutil, logging, re, numpy, datetime, sklearn (scikit-learn), keras, and Tensorflow libraries/modules.

The data set

As previously mentioned, the authors performed extensive searches to identify and evaluate publicly available data sets or private data sets that other researchers were willing to share. The EEG Data Set provided by the University of California, Irvine Machine Learning Repository was used for research and training data extraction.

Any data with time dimensionality that was manipulated from its original form raises potential challenges that may occur for others when replicating the research results. This project's code requires downloading the entire "eeg_full" directory from the UCI data folder at /ml/machine-learning-databases/eeg-mld to a locally-available drive. The EEG_full directory contains 120 trials for 122 subjects. The entire set of compressed data is about 700 MBytes. The subject files from the original UCI data set are in .tar.gz format, so they must be unzipped and untarred in order for both humans and the program itself to be able to access the data inside these files. The os, pathlib, tarfile, gzip, shutil, logging, and re libraries are used to put each file into a new folder called "processed" that follows the structure of the originally zipped file.

Each piece of the code is strategically broken down into functions, which not only give the code more readability and modularity but also make troubleshooting and debugging much faster. After the uncompressed data is transferred into the processed folder, it must further be organized into a comma-separated (.csv) file using the Pandas and Numpy libraries. Data is transferred from its original structure of a long list containing thousands of data points into a 2-dimensional array that contains the names of the specified channels as the header, followed by each channel's column of data.

Fig. 4. Output of sample channels   Fig. 5. Output of sample data points

The original data files included a row for each electrode with one data point in space-separated format. See Figure 2. It included comments throughout. Initial processing included removing extra comments throughout the data file, converting spaces to commas, and removing channels "nd" and "Y" that could not be mapped to the standard 64-channel map from 1991. The data contain a 1-second epoch of amplitudes recorded at 256 Hz, meaning there are 256 data points in each channel of a subject's trial file. Afterward, the array is simply copied into a newly created file within the subject folder, in comma-separated format, as shown in Figure 3.

Create referenceable copies of data altered for experiments with groups and targets files

In addition to reformatting the subject files, the program creates both a groups.csv and targets.csv file. The purpose of the groups file is to have a referenceable record of how the entire

data set was split into three groups: the train, validation, and test sets. Oftentimes, data is grouped to an approximate 80/10/10 percent split for the train, validation, and test sets respectively. The groups.csv file contains subject file names with a following comma, and then a 1, 2, or a 3 depending on the group that the file is assigned to.

Fig. 6. Format of groups.csv file   Fig. 7. File naming scheme

Additionally, each group includes an equal number of AUD and control patients. This process is randomized, so the files are rearranged each time that the data is transformed from its raw format to the processed files. A parameter "create_new_groups_and_targets" with options of 1 and 0 allows the researchers to keep the same data configuration or reshuffle. This holds the data files constant while other variable changes are made. The targets.csv file uses the name of the subject files (organized into the same rows as the groups.csv file) to categorize a subject as part of the AUD or control group using the fourth character of the subject file name. If the character is 'a', the patient has AUD, and if the character is 'c', the patient is part of the control group [30]. All data files within a subject folder contain the same group and target value and are treated as such. After all the new files have been created (see Figure 6), the EEG data is passed into three new matrices (one for each data set group). For each two-dimensional array, there is a column of subject trial file names and another containing the respective target IDs of the files.

Create a simplistic machine learning model

The first model was a simple LSTM time series model but eventually developed into a large and complex convolutional neural network, refined by the tuning parameters and adjusting layers [53][54][55].

Fig. 8. Model 1 - Simple LSTM Model
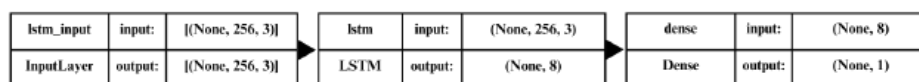
The initial model was chosen to be sequential, containing an input layer, an LSTM layer, and a Dense layer with a Sigmoid activation. After validating and verifying the code using this 3-layer model, inefficiencies were seen. Because of this, the approach was completely changed. Layers were added throughout the experimental phases, and changed to better fit the random input data.

Variables passed to the final CNN model are defined as follows: **1)** the number of Conv2D units is changed for each layer, but only one layer is changed at a time; **2) seq_len** - the sequence length is 256. Each trial includes 256 samples of data; **3) n_channels** - The code automatically derives this from the list of channels specified in the channels variable; **4) lr** - a common heuristic is that the starting value is usually between 0.0005 to 0.001; **5) batch_size** - number of samples processed before the model is updated (must be more than or equal to one and less than or equal to the number of samples in the training data set); and **6) epochs** - The number of epochs is the number of complete passes through the training data set. After validating and verifying the code using this 3-layer model, a new 5-layer model was created in order to more efficiently train, validate, and test the data set.

conv_1_input	input:	[(None, 256, 61, 1)]		conv_1	input:	(None, 256, 61, 1)		maxpool_1	input:	(None, 256, 61, 32)		conv_2	input:	(None, 128, 30, 32)
InputLayer	output:	[(None, 256, 61, 1)]		Conv2D	output:	(None, 256, 61, 32)		MaxPooling2D	output:	(None, 128, 30, 32)		Conv2D	output:	(None, 128, 30, 64)

maxpool_extra	input:	(None, 64, 15, 64)		conv_extra	input:	(None, 64, 15, 64)		dropout	input:	(None, 64, 15, 64)		maxpool_2	input:	(None, 128, 30, 64)
MaxPooling2D	output:	(None, 32, 7, 64)		Conv2D	output:	(None, 64, 15, 64)		Dropout	output:	(None, 64, 15, 64)		MaxPooling2D	output:	(None, 64, 15, 64)

conv_3	input:	(None, 32, 7, 64)		maxpool_3	input:	(None, 32, 7, 128)		conv_4	input:	(None, 16, 3, 128)		maxpool_4	input:	(None, 16, 3, 128)
Conv2D	output:	(None, 32, 7, 128)		MaxPooling2D	output:	(None, 16, 3, 128)		Conv2D	output:	(None, 16, 3, 128)		MaxPooling2D	output:	(None, 8, 1, 128)

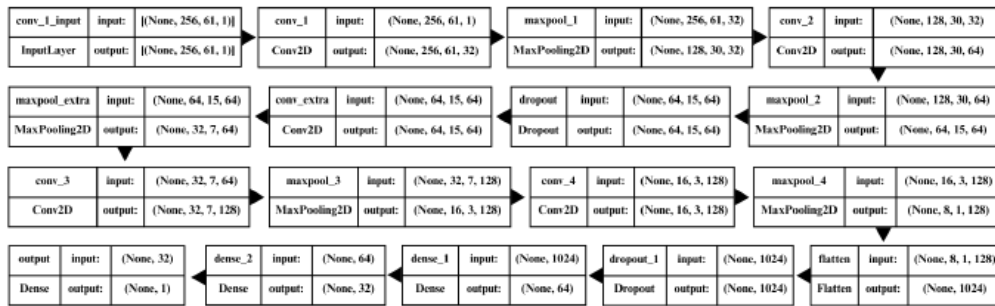| output | input: | (None, 32) | | dense_2 | input: | (None, 64) | | dense_1 | input: | (None, 1024) | | dropout_1 | input: | (None, 1024) | | flatten | input: | (None, 8, 1, 128) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Dense | output: | (None, 1) | | Dense | output: | (None, 32) | | Dense | output: | (None, 64) | | Dropout | output: | (None, 1024) | | Flatten | output: | (None, 1024) |

Fig. 9. Final CNN model with 5 layers

The program initializes a list of variables prior to the start of the algorithm, providing extra feasibility for others to replicate the experiment and change the program's representative values. A user is able to create a list of values for a certain parameter, and the program will produce an experiment for each value specified. This concept allows many run-throughs of the model to be produced in a single run of the program, significantly reducing the amount of code manipulation done on the user side. The main changeable parameters for the ML model include the subject activity (a subset of the trial files), channels, learning rate, CNN layer units, epochs, and batch size. Variables relating to the path name of the processing and experiment files will allow the user to locate the data from the file's .tar.gz format. The code is designed to define as many variables as possible before the functions are defined in order to allow for faster manipulation of the program's dependencies, which also means that the code can also be replicated more easily. Note that the ML model itself is not an independent variable and remains constant for a given set of experiments. When using a new ML model, the experiments using that new model should be treated as a new set of data, separate from the sets of experiments using other models.

The final aspect of the program is the implementation of the machine learning algorithm and the summaries that allow the interpretation of program results. To accomplish this, the algorithm uses the TensorFlow, Keras, and Matplotlib libraries.

The machine learning algorithm first passes data in batches of specified size through the input layer of the sequential model. Learning rate, number of epochs, and units of the CNN

layers are also passed into the model as variables, in which the user can edit in the configurable section of the code. As mentioned previously, one variable would be turned into a list of values in order to test a particular parameter. The program loops through experiments to deduce the value that produces the highest possible accuracy using the model. The final model consists of 5 main layer groups: the input layer, the first and second sets of Conv2D layers, the flatten layer, and the set of dense layers.

After data is passed through the model, the program runs through the defined number of epochs, recording the history of the accuracy and loss for both the validation and test data set groups as graphs in the experiments folder. After all epochs of the data have been processed, the program will copy a diagram of the model, the time that the program executed, the graph of the best-fit gradient descent model, and the run's targets.csv and groups.csv files.

Finally, the overall accuracy score and details of the trained model will be printed in the terminal to signal when the program is properly executed. All the above files and information for an experiment will be output for each individual run of the model (each value of a specific parameter inputted into the for-loop).

Access is provided to all data processing steps as captured in code available on GitHub. Deep learning models, experimental configurations, and experimental results are automatically saved to a folder when the program runs, so that they can be accessed in the future.

PROCEDURE

The procedure describes the steps to set up the program and execute automated experiments on the UCI data using the program.

Materials Required

1x Personal Computer/Laptop that should have: **1)** Windows 10/11 operating system, **2)** at least 16 gigabytes of RAM, **3)** a minimum of 30 gigabytes of available SSD memory, **4)** VS Code version 1.74 with the Python extension, and 5) a browser compatible with Google Drive and Google Docs.

Software and Libraries:

1) Latest version of Visual Studio Code; **2)** Python 3.7 extension for Visual Studio Code; **3)** the latest version of Miniconda; **4)** Pandas, Matplotlib, Numpy, and Scikit-learn libraries; **5)** TensorFlow; and **6)** Keras.

The first part of the procedure is to set up the system for experimentation. This involves installing all prerequisite software, including the research software as follows: **1)** installed Prerequisite Software (VS code, Python extension, and Conda (miniconda)); **2)** downloaded the 'main.py' program file from the GitHub repository; **3)** created a folder on the Windows-SSD ('C:' drive) named 'eeg' and inside this folder, made two new folders named 'sciencefair22-23' and 'Untouched Dataset' (the 'sciencefair22-23' directory became the GitHub repository in this experiment's case); **(4)** Made a folder inside the 'Untouched DataSet' folder named 'eeg_full'

and downloaded all the files inside the 'eeg_full/' directory from the website: https://archive.ics.uci.edu/ml/machine-learning-databases/eeg-mld/. (this was a backup for the data folder, which was modified); **5)** created a folder called 'data' inside the 'sciencefair22-23' folder and made a copy of the 'eeg_full' folder and pasted it into the 'data' folder; **6)** downloaded a '.gitignore' file with this code in the folder 'sciencefair22-23' and added 'data/processed/' on the first line of the file (so that the data does not upload to GitHub): https://github.com/Lawson-Woodward/sciencefair22-23; **7)** downloaded the visual C++ redistributable packages from Microsoft's website, then restarted the computer to add them to VS code; **8)** created a conda environment using the Anaconda prompt as an administrator; **9)** installed the TensorFlow and Keras libraries; **10)** still in the Anaconda prompt, installed the libraries of Pandas, Matplotlib, Numpy, and Scikit-learn (restarted VS Code to ensure the functionality of the libraries and chose the new conda environment, '3.9.15('tf':conda)', as the Python interpreter)

After setting up the system, the next part of the process involves defining and executing experiments. The authors performed the following steps to execute experiments: **1)** kept all variables the same, except for the independent variable; **2)** varied the following variables in sequence, leaving all other parameters unchanged for each set of experiments: **batch_size**, **Lstm_units**, **lr: learning rate**, **datasubset**, **epochs**, and **channel** (To execute a series of experiments, edit the for-loop (line 289)); **3)** executed the program to identify performance and "tune" the parameters of the model; **4)** viewed the output of execution (dependent variable of "Accuracy Score") and graphs in the "experiment" folder to determine further parameter changes; **5)** repeat the steps until the desired accuracy is reached; **6)** opened the 'experiments' folder created in the 'eeg_full' folder to access the data and execution summaries.

Results

Using all of the data across all channels led to the best results. The training group contained 80% of the total data set, while the validation and test sets each contained 10% of the data set. The final model consists of 5 main layer groups: the input layer, the first and second sets of Conv2D layers, the flatten layer, and the set of dense layers. The experimental parameters of the model for the best experiment were a learning rate of 0.0005, 150 epochs, and a batch size of 32. These parameter values demonstrated the highest accuracy across all experiments.

The accuracy and loss graphs also displayed general improvement across the 94 experiments. The accuracy of the first experiment was 0.5 but reached 0.931 by the final experiment, demonstrating that the methods of model tuning were effective. The loss function showed an error of only 0.35 for the last experiment, and it is safe to assume that this level of loss does not majorly invalidate conclusions made from the results of the experiments. The graphs of the accuracy and loss both showed some minor oscillations (early stopping methods from the model compilation stopped the model compilation at 55 epochs).
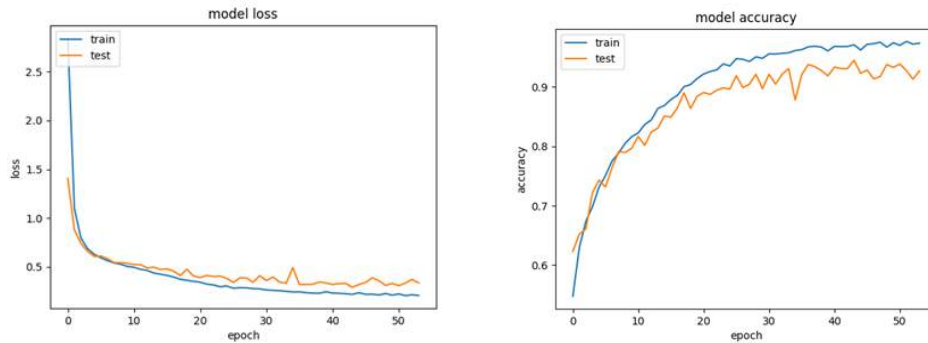
Fig 10 and Fig 11. Accuracy and loss graphs for the final or "best" CNN model

Conclusion

The results of the project aligned with the expectations of the primary engineering goal, as the ML algorithm reached an accuracy of 93.1% and surpassed the target accuracy of 90%. This was not quite as accurate as other previously created algorithms that have dealt with the same data set, including a study by Houchi Li and Lei Wu in 2022 that used the same dataset, producing an accuracy of 98%, and another study in 2020 by four senior IEEE members that produced an accuracy of 93% [28][29]. However, due to the lack of available specifics from their studies, the public is unable to replicate the findings that experts have claimed in their studies. Because this project's code is open-source on Github, as well as the fact that the code is able to be easily changed by a user, the secondary engineering goal has also been met.

Many improvements to the project could be made, and iterations could be added to enhance the classification capabilities of the model. Fully automatic testing describes a concept that is used in ML frontier technologies and would allow for the nearly-automatic parameterization of this ML model. Additionally, an enhancement to the code in the next step of the development of the open-source project would be to create a sentinel value that asks for an input and outputs the prediction, or breaks the loop depending on the input of the user.

The major limitations of the project surprisingly didn't occur because of overfitting or underfitting, but instead were mainly due to a need for further testing and a larger dataset. In the future, a data set of a larger magnitude would allow for more accurate predictions. Additionally, more tuning of the CNN model layers would be beneficial for the reliability of the program.

In totality, this model was successful in providing an easily replicable form of testing a data set, and also is able to accurately make predictions using that information. "Preprocessing of Data as Code" is a new idea sparked by the troubleshooting process of this project in which taking a raw data set and turning it into a usable set of numbers becomes automatic through programming. Other machine learning projects have processed many large datasets, however, they focus more on the machine learning aspects of their programs rather than the data processing aspects. The program in this experiment, however, focuses on creating a nearly universal way to process large online datasets using a variety of data processing libraries.

Although this project's machine learning program is not a new technology, it serves as the foundation for the replicability of current sequential binary classification ML algorithms.

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Impact of Artificial Intelligence on Autism Spectrum Disorder By Ishaan Nikunj Nirmal

Abstract

Autism, also known as Autism Spectrum Disorder (ASD), is a condition that affects how people communicate and interact with the world around them. It can make social interactions, communication, and understanding emotions challenging. However, with the help of Artificial Intelligence (AI), new tools and technologies are being developed to support individuals with autism. AI can help in many ways, such as early diagnosis, improving communication, offering personalized learning experiences, and providing emotional support. This technology is opening up new possibilities for people with ASD to thrive and better navigate their daily lives. This paper evaluates which technologies may be most beneficial to which level of autism, and comes up with recommended solutions.

Introduction

Autism Spectrum Disorder (ASD), commonly known as autism is a neurodevelopmental disorder which is characterized by difficulty in social settings and repetitive behaviors. The prevalence of autism has been increasing at a rather alarming rate. In 2006, one in every 110 kids had autism in the United States, in 2021, that increased to one in every 44 kids, which further increased to one in every 36 kids in 2023 ("Data and Statistics on Autism Spectrum Disorder"). One potential way to manage the rise of autism is through leveraging artificial intelligence. Artificial intelligence has started to play a vital role in healthcare recently. More medical professionals are turning to this technology than ever before for help with various tasks, from gathering vitals of patients to prescribing drugs to even diagnosing illnesses. Artificial intelligence is starting to be implemented in helping patients of ASD as well. It is assisting in all sorts of ways, from diagnosis to treatment. However, AI is still not being used to its full potential to help autistic individuals (Iannone and Giansanti 14,41). This paper aims to offer potential solutions involving AI that would significantly better the lives of those suffering from autism by exploring and analyzing several different options. As AI continues to become more prevalent in other medical situations, it is time that the right type of AI is used for the right type of ASD patient.

Background on Autism

In 1943, Leo Kanner identified the classic autistic syndrome for the first time. 20 years later, Victor Lotter published for the first time an epidemiological study that identified that 4.5 children per 10,000 displayed the symptoms originally described by Kanner. In 1979, Lorna Wing and Judith Gould expanded the set of original symptoms defined by Kanner to include difficulties with social interaction, communication and imagination (which they referred to as the 'triad' of impairments), as well as a repetitive stereotyped pattern of activities. Using the expanded set of symptoms, they determined that 20 in every 10,000 children had autism, about four times more than Lotter's original estimate. In 1944, Hans Asperger introduced a new form

of autism called Asperger syndrome, which included many similarities to previous types of autism, in addition to other abilities, including grammatical language, in the average to superior range (Wolff 201-208). In 2005, the Office of National Statistics in Great Britain conducted a survey about the prevalence of all forms of autism, calling it the autism spectrum. In total, they found a prevalence rate of around 0.9%. Unfortunately, that rate stands at 2.8% ("Autism Prevalence Higher, According to Data from 11 ADDM Communities | CDC Online Newsroom") today, making the research in this paper essential.

Cases of autism are found in all racial, ethnic, socioeconomic, gender, and age groups. However, there is a large disparity of cases of autism between these groups. The male to female autism ratio stands at 3:1 (Loomes et al. 466-474). However, this is not entirely because males are more likely to get autism in females. Rather, females are less likely to display overt symptoms of autism and make more of an attempt to 'camouflage' their symptoms, delaying the process of diagnosis. Similarly, autism is significantly more prevalent in Caucasian individuals rather than other racial groups like African-American or Hispanic. Once again, this is not entirely because Caucasians are more likely to get autism than African-Americans, Latinos, or Asians. It is more likely due to the fact that Caucasians have access to high-quality healthcare and English as the primary language, while other racial groups do not (Hodges et al. 4).

In addition, autism hinders progress of the economy significantly. Between 1990 and 2019, a projected 7 trillion dollars of social costs have been lost. Over the next ten years, it is predicted that if rates of autism do not change, then another 4 trillion dollars will be lost (Cakir et al. 2). Given historical trends, the prevalence of autism spectrum disorder (ASD) is projected to continue rising, potentially leading to substantial economic implications. Conservative estimates suggest that associated costs could escalate to approximately $15 trillion within the next decade. This significant economic impact underscores the urgent need for innovative and efficient interventions. The lifetime per capita societal cost of autism is estimated at $3.2 million, with lost productivity being one of the largest components. This includes not only the productivity losses of autistic individuals but also the impact on family members who may need to provide care (Ganz 343-349). In light of these projections, this paper aims to propose coordinated, evidence-based solutions that leverage artificial intelligence (AI) technologies. The integration of AI in ASD management strategies offers promising avenues for enhancing diagnostic accuracy, personalizing treatment approaches, and optimizing resource allocation. The economic considerations, coupled with the potential for AI to revolutionize ASD care, provide a compelling rationale for exploring and developing these technologically advanced, coordinated solutions. This approach not only addresses the financial aspects but also holds the promise of significantly enhancing the quality of life for individuals with ASD and their families.

Autism Spectrum Disorder has multiple variations in the spectrum, ranging from mild to moderate to severe:

Level 1 of the Autism Spectrum Disorder can be classified as mild autism. People with level 1 autism often have a hard time with certain parts of talking and getting along with others. They

might struggle with casual conversations or understanding social signals. Making and keeping friends can be tough for them. Changing from one activity to another can be difficult or stressful for someone with level 1 autism (Dudhnath) ("What Does Level 1 Autism Look Like in Children? | Autism Level 1").

Level 2 of the Autism Spectrum Disorder can be classified as moderate autism. Level 2 autism is in the middle of the spectrum and indicates that a person needs more support to function independently and successfully in everyday life. According to the diagnostic criteria, people with level 2 autism require substantial support. This means they need more help or accommodations compared to those with level 1 autism. Individuals with level 2 autism often face greater challenges with communication and social skills. They frequently have stimming behaviors, which are repetitive actions common among autistic individuals. While stimming can help them manage stress, some of these behaviors can have negative consequences and distract them from important tasks. Overall, people with level 2 autism need more assistance to navigate daily activities and social interactions (Hodara).

Level 3 of the Autism Spectrum Disorder can be classified as severe autism. Someone with level 3 autism is said to need very substantial support. This means they need a lot more help and accommodations in their daily life, including at home, school, work, in the community, and in relationships, to function independently and successfully. People with level 3 autism might not speak with verbal language, though some do. They might have very challenging behaviors like frequent meltdowns, aggression, or self-harm. Their stimming behaviors are often more frequent and intense. They may struggle to understand others. Someone with level 3 autism might need a lot more supervision, even as a teenager or adult, compared to people with level 1 or level 2 autism.

A large problem in the diagnosis of autism is that it almost always occurs quite late. Often, when kids are little parents do not notice the warning signs of autism, passing them off as just childish behavior displayed by young kids. The signs only start to become more prevalent around 3-4 years of age, and a diagnosis can take another year to be confirmed. By that time, it is too late to significantly improve the condition of the autistic child (Gabbay-Dizdar et al. 1). As per The National Autism Data Center, the average age of intervention is 4.3 years and average age of diagnosis is 4.9 years ("Age of Diagnosis"). Though treatments and therapies are still an option, they are widely regarded as ineffective because they do not address the root cause, and only try to make the autistic child seem 'normal' to others in social settings. This can cause even further mental problems for the autistic child, rather than helping him or her.

How to help people with ASD?

Several studies have found that early detection and treatment of ASD is one of the best mechanisms to help people with ASD (Siegel 15). Autism is generally present in the first year of life, but appears to onset only in the 2nd or 3rd of life (Cohen 9) because early detection is

difficult with current methods of diagnosis. One way to help people with ASD is to look at it from the perspective of autistic learning disability (Siegel 4-10). This helps in identifying specific tools and holistic solution approaches to assist. The majority of kids diagnosed with ASD are not intellectually disabled (having less than 70 score for IQ) (Pinder-Amaker, 1). A combination of factors such as individual (age, gender, health), family, peers, education system, healthcare system, and cultural beliefs affect the individual's growth and hence the support needed for individuals with ASD (Pinder-Amaker, 128). The previous section covered different levels of ASD and challenges faced by the individuals. Given the myriad of challenges and factors affecting those challenges a more coordinated Autism Assistance is needed for effective support for ASD individuals. A comprehensive treatment approach for individuals with autism spectrum disorder (ASD) that integrates advanced technological solutions can significantly enhance coordination across multiple therapeutic domains. This multifaceted strategy addresses various challenges associated with ASD and optimizes the efficacy of interventions. By leveraging technology to facilitate seamless collaboration among healthcare providers, educators, and caregivers, this approach offers a more cohesive and personalized care plan. Such an integrated system has the potential to markedly improve outcomes and quality of life for individuals on the autism spectrum, providing a more efficient and effective framework for support and development. The following sections explore the use of technology, particularly AI, to bring in this coordinated assisted solution for early detection, treatment, and support for ASD individuals.

Background and History on Artificial Intelligence

Before going into the Artificial Intelligence (AI) based solutions, this section covers the background and basics of AI. The first applications of AI were seen in the 1940's, soon after World War II, when people began to realize the importance of automating the translation of text. This, now, is known as Machine Translation, or MT. Early researchers in the field of MT were not so much linguists as they were experts in the field of computers (Jakubková and Varga). This led to a fundamental flaw in the early methodology of MT. They approached MT with the overly simplified view that the only difference between languages were the words used and the order in which those words were used. As a result, when these machines were tested, the results were poor. This approach towards AI led to many early systems being unsuccessful (Hutchins). After a few years of experimenting, researchers realized that a deeper understanding of linguistics needed to be acquired for an AI system to be successful. One of the first to realize this was University of Pennsylvania graduate Noam Chomsky. In 1957, he proposed a grammatically correct sentence that had no semantic value. The sentence was "Colorless green ideas sleep furiously." He found it problematic that an AI system could not recognize that as grammatically correct, and put it in the same category as a sentence like "Green sleep furiously ideas colorless." Chomsky furthered his ideas by authoring Syntactic Structures in 1957. This book is considered one of the most important works in the advancement of computational linguistics in the twentieth century.

AI saw a brief boom in the next decade, especially with early advancements in speech recognition technology. Due to all this, people began to be over-enthusiastic that instant translation machines were just an arm's reach away. However, this was unrealistic, given the state of natural language processing at the time. This led to the ALPAC report of 1966, which concluded that machine translation was not possible currently, causing the first AI winter, or a time where there is a lack of interest and funding in artificial intelligence ("AI Winter: The Highs and Lows of Artificial Intelligence").

This winter was not to last. Soon after the report, MIT researcher Joseph Weizenbaum created ELIZA, the first chatbot. However, Weizenbaum never intended to be a true AI. In fact, ELIZA just uses the words in the input from the user to reply (Law). In reality, Weizenbaum wanted people to understand how AI truly works. Soon after ELIZA came SHRDLU, which manipulated blocks on a tabletop. During this time, many other chatbots, like PARRY and LUNAR were also created (Clarke).

It wasn't until McKeown's TEXT and McDonald's MUMMBLE that AI as we know it came about. TEXT was a summarization machine which actually took steps to 'understand' the text. This was also the case with MUMMBLE, just in the form of a chatbot. AI continued to rapidly grow in the last two decades of the twentieth century (Johri et al. 365-375).

Today, AI is as strong as ever, with modern AI systems like ChatGPT being trained on large language models, or LLMs. This means that they have access to more information than ever before and are extremely powerful. Today's AI systems possess capabilities like writing poems, giving information, playing chess, and even debating with the user. With the availability and affordability of computing power, advanced research, and curation of data, AI has evolved to play a pivotal role in all fields. For example, a lot of trading in stock markets is done by algorithms leveraging AI (Shen et al. 378-385) (Hseih et al. #). AI is used in sports for enhancing athletic performance, predictive modeling, smart wearable devices to measure body vitals, strategy improvisations, content enhancement and fan engagement, etc. ("AI Transforming Sports: 7 Impactful Trends") (Peranzo). Artificial Intelligence (AI) has begun to significantly impact the healthcare sector, revolutionizing processes from diagnosis to treatment planning. Computer vision, a specialized branch of AI, is being increasingly utilized in medical imaging analysis. This technology enhances the interpretation of diagnostic scans and x-rays, facilitating more accurate and efficient detection of tumors, cancerous cells, and various other pathologies (Alowais et al. 1-9). The integration of AI in healthcare not only augments the capabilities of medical professionals but also has the potential to improve patient outcomes through earlier and more precise diagnoses ("Artificial Intelligence in Healthcare: Revolutionising Diagnosis and Treatment"). The National Library of Medicine states that "we expect to see limited use of AI in clinical practice within 5 years and more extensive use within 10." ("The potential for artificial intelligence in healthcare" 94-98) Given the advances, AI based solutions have a high potential to be effectively utilized in helping autistic patients as well.

Artificial Intelligence is increasingly starting to play a role in the diagnosis, treatment, and eventually, cure of autism. The greatest role AI is playing in the field of autism is diagnosis. There are hundreds of models being developed that analyze brain scans, eye images, and social interaction to determine if a child is autistic or not with extremely high accuracy. Companies are starting to build applications that specialize in education of autistic kids, monitor stimming behavior, and help calm down autistic kids. Robots are being developed that help autistic kids with social cues or assist them with impaired motor skills (Rudy). I also want to help autistic kids in various aspects of their lifestyle by leveraging AI.

Existing Solutions and Need for Improvement

Treatment and therapy are the main options for helping individuals with ASD. The most common therapy for ASD is Applied Behavior Analysis (ABA). ABA is a therapy used to help people with ASD gain and apply new skills in daily lives. ABA promotes positive behavior and reduces negative behavior to improve memory, social skills, communication skills, attention and focus, and academic skills (Kearney 20-26). ABA has been criticized for ineffectiveness. ABA treats the individuals by modifying behavior to align with societal expectations, rather than addressing the underlying neurological differences and individual needs of autistic individuals. This approach, which raises ethical questions, prioritizes the appearance of neurotypical behavior over the required development and well-being of the autistic person while respecting sensory sensitivities, and unique cognitive processes (Garey). Critics suggest that a more holistic, person-centered approach that acknowledges and supports the autistic person's intrinsic traits while fostering adaptive skills might be more beneficial and tehical. Various autism rights and neurodiversity groups have protested against ABA treatment, claiming it to be equivalent to abuse.

Another form of treatment, the Early Start Denver Model (ESDM) requires highly trained professionals and is very expensive. This makes it so that it is accessible only to a small number of families (Vivanti and Stahmer #) ("Early Start Denver Model (ESDM)"). It is aimed to help very young children under 5 years of age by reducing the symptoms of autism and target development in all areas. As opposed to ABA where therapists work with the children on repeated learning of a skill, in ESDM, the therapist plays with the child and introduces opportunities to learn in the play routine. ESDM attempts to make the training natureal for the children ("Overview of the Early Start Denver Model (ESDM) | Soar"). Typically the therapists social skills training with therapists or parents is limited and may not translate well to real-world circumstances. In addition, it does not address the anxiety that comes with interacting in social situations with large groups.

Method

The research deals with the intersection of medical and technology fields. Searches are conducted through medical journals, scholarly research papers, AI research papers, not-for-profit websites for helping Autism, and Google scholar searches. Of the research material searched, the

study focused on key challenges for Autistic people, medical definition of ASD levels and symptoms, impact of the conditions on individuals, data on socioeconomic impacts, current treatments options and effectiveness. Further, the study followed a similar approach to understand the evolution of Artificial Intelligence and maturity of the technologies for ASD applications by leveraging robotics and Internet of Things (IoT) along with AI. The information on symptoms was analyzed based on the narrative of the different levels of ASD, common themes across multiple studies, and examples of data provided in the research papers. The study further correlated the potential of technology solutions with highest impact per area of application along with the levels of ASD. The quality of the research study was assessed by number of citations, the data driven approach in the study, the background of authors, and derivation of common themes across multiple research studies.

Proposed Artificial Intelligence Solutions

Artificial Intelligence (AI) is increasingly used in solutions for all sorts of problems, within the medical field, and mental health disorders as no exception. Autistic children face severe challenges that could potentially be solved utilizing AI. The recommendation is to use the below outlined solutions more holistically rather than as point solutions for each problem. The challenges faced by ASD individuals are complex and intertwined. We should not look at solving a particular behavior, but rather use the below tools to augment each other to assist ASD individuals. These are symptoms of autism and AI could potentially be leveraged to help. The following section covers the details of how AI can impact the different life facets of individuals with ASD. In the charts in the following sections, the impact of AI is ranked from level 1 to 5 represented on the Y axis with 5 being the best. X axis represents the ASD level. The title in the following section refers to the challenges faced by individuals with ASD the following numbers in braces refer to the corresponding levels of Autism Spectrum Disorder where AI can assist. The information on symptoms was analyzed based on the narrative of the different levels of ASD, common themes across multiple studies, and examples of data provided in the research papers. The study further correlated the potential of technology solutions with highest impact per area of application along with the levels of ASD. The current maturity of the technology is studied to understand the potential of making an impact for ASD along with how the different technologies can be utilized together to amplify the impact (eg. Robotics with AI, AI with Internet of Things - IOT).

1) **Early Diagnosis (ASD Level 1, 2)** - The current behavioral tools make it difficult to diagnose signs of ASD at an early age. There are multiple factors leading to this such as social and communication skills do not develop until after 1st year of life, the abnormal behaviors are considered abnormal only if continued beyond infancy, and certain repetitive behaviors may emerge later. Also, parents are not necessarily looking for signs for Autism in the babies. Often the signs can get disregarded as childish behavior. However, there are cues that can be observed objectively in early life using computer

vision and interactive observations. A robot with AI software that follows young children around the house monitoring symptoms of ASD to provide an accurate diagnosis using artificial intelligence. A robot can have interactive games for kids to play with and inturn observe the signs of ASD. This technology should be viewed as a potential complement to, rather than a replacement for, professional clinical assessment and diagnosis. Its primary aim would be to support earlier identification of children who may benefit from further evaluation and early intervention services.

Early intervention and treatment is one of the most effective ways to help ASD patients (Siegel 15). This requires early diagnosis. The below chart shows the impact AI can have for individuals with different levels of ASD. Given the effectiveness of early intervention, AI will have the highest impact (5) in all three levels of ASD.
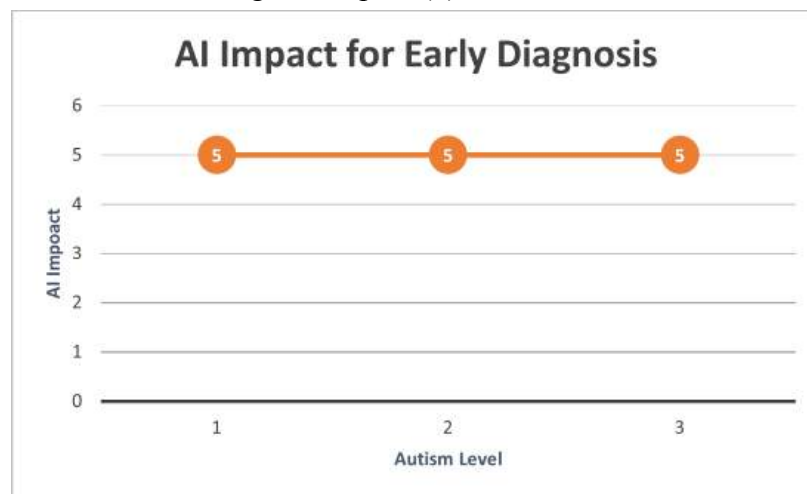
2) **Hard to make friends (ASD Level 2, 3):** Leveraging advanced Large Language Model (LLM) technologies, we propose the development of an AI-powered conversational agent specifically designed to support individuals with autism spectrum disorder (ASD). This innovative solution aims to address two critical areas of need:

   1. Social-emotional support: The AI chatbot would function as a virtual companion, providing consistent, non-judgmental interaction to help mitigate feelings of loneliness and social isolation often experienced by individuals with ASD. This could potentially contribute to improved emotional well-being and stress reduction, offering pathways to transition from virtual to real world to make friends.
   2. Social skills development: Through carefully crafted scenarios and interactions, the chatbot would offer a safe, controlled environment for individuals with ASD to practice and refine their social communication skills. This virtual training ground could help users develop strategies for navigating real-world social situations more effectively.

The implementation of state-of-the-art LLM technologies enables the creation of a conversational agent capable of engaging in near-human-like dialogue. This high level of

interaction fidelity is crucial for providing a meaningful and beneficial experience for users. Moreover, the skills and confidence gained through consistent interaction with the AI chatbot have the potential to generalize to real-world social encounters. This transfer of learning could significantly enhance the overall social competence and quality of life for individuals with ASD (Mishra and Welch,1-9).

LLMs have matured significantly, with being able to hold human-like conversations. While promising, it is important to note that such a tool should be developed and implemented in consultation with autism experts, ethicists, and the autism community to ensure its appropriateness and effectiveness as a complementary support to existing therapies and interventions.

The chart shows the impact AI can have for individuals with different levels of ASD. It is hard to make friends for patients with ASD levels 2 and 3, and hence the level 1 is not applicable for AI impact. While AI will be able to help with social training, the impact is limited to 2 and 1.5 for ASD levels 2 and 3 respectively at this time, because the interactions with AI are still controlled. Real world can throw more unknown scenarios, making the transfer of learned skills difficult. However, as AI systems evolve, we will be able to see the impact also increase.
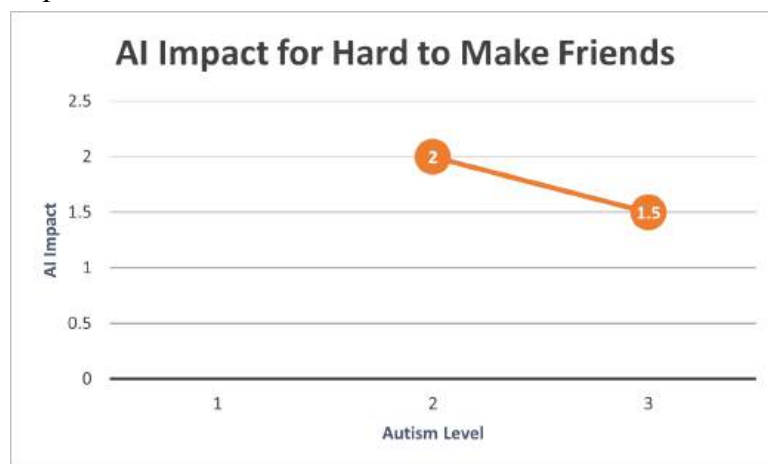
3) **Stimming Behavior (ASD Level 2, 3)** - Artificial Intelligence (AI) can be utilized to monitor stimming behaviors in kids with ASD and provide reminders to help manage these behaviors. One effective strategy is scheduling stimming activities and encouraging them to be conducted in private settings. The AI system can monitor these behaviors, offer reminders, and suggest alternative activities, such as listening to music through headphones, to facilitate a more constructive approach to self-regulation ("6 Strategies to Reduce Stimming in Autistic Children").
However, it is essential to recognize that stimming often serves as a vital coping mechanism for many autistic individuals. As per YellowBUS Autism Therapy, the

therapists have been using Applied Behavioral Analysis ("Stimming in Autism: How to Manage It") to break down the the complex behaviors to smaller and manageable steps (eg. replace head banging stimming behavior with squeezing stress ball or feet-tapping). Therefore, an enhanced approach would be to track these behaviors using AI and inform the child's guardian. AI is used to recognize the audio patterns through Machine Learning (ML) and physical movements through Computer Vision and ML. This allows the guardian to make informed decisions and interventions based on the child's needs and preferences. As per Healthline, by providing guardians with insights into their child's stimming patterns, an alternative can be pursued (eg. squeezing a ball) (Legg). Further, visual support and social stories provide cues (eg schedules, cue cards, charts) and stories (eg. situations, emotions, and responses) that help with understanding and navigation of their environment ("Stimming in Autism: How to Manage It"). The AI can support a collaborative and augmented approach to managing these behaviors, ensuring that the child's coping strategies are respected while also promoting their overall well-being. The below chart shows the impact AI can have for individuals with different levels of ASD. Stimming behavior patients with ASD levels 2 and 3, and hence the level 1 is not applicable for AI impact. Since AI can augment and not fully control the remediation, the impact is moderate, marked as 3 out of 5. The impact will be similar for ASD levels 2 and 3.
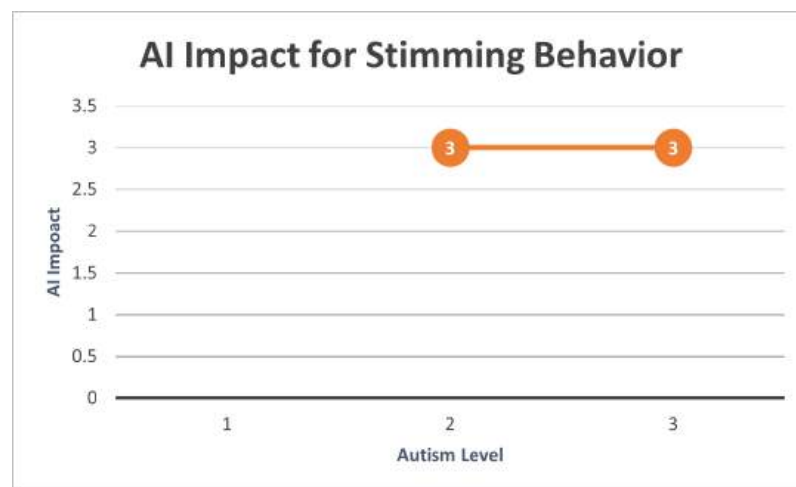
4) **Sensory Sensitivities (ASD Level 1, 2, 3) -** Sensory Sensitivities can significantly impact individuals across multiple domains. Up to 90% of people with ASD experience some form of sensory sensitivity, which can manifest as Hypersensitivity wherein one takes too much information or Hyposensitivity wherein one takes too little information (Zeliadt). Management strategies include environmental modifications, gradually exposing sensory experiences in a controlled manner, and providing extra sensory inputs in case of hyposensitivity ("Sensory sensitivities & autism: 4-18 years").
Integrated smart home systems, powered by artificial intelligence (AI), offer the potential to create dynamically adaptive sensory environments tailored to the unique needs of

individuals with autism spectrum disorder (ASD). These systems utilize a network of intelligent sensors and actuators to monitor and adjust environmental factors in real-time, effectively mitigating sensory overload and enhancing comfort (Hameed et al. 1-8). Therapists have been using

Key features of this AI-driven smart home ecosystem include:

1. Adaptive Sensory Modulation: Smart lighting and sound systems can automatically adjust based on the observed reactions and presence of the individual with ASD, creating a more conducive sensory environment.
2. Continuous Learning and Personalization: The AI system employs machine learning algorithms to analyze data collected from various sensors, enabling it to identify specific sensory sensitivities unique to each individual.
3. Predictive Environmental Adaptation: As the AI system accumulates data and refines its understanding of the individual's sensory profile, it can proactively adjust environmental parameters to prevent potential sensory overload situations.
4. Multi-modal Sensory Management: The system can coordinate multiple environmental factors simultaneously, such as lighting intensity, color temperature, ambient sound levels, and even haptic feedback, to create a holistic sensory experience.
5. Data-Driven Insights: The collected data and AI-generated insights can provide valuable information to caregivers and healthcare professionals, potentially informing broader therapeutic strategies.

This AI-enhanced smart home approach represents a significant advancement in creating supportive living environments for individuals with ASD. By leveraging AI to provide personalized, responsive sensory management, these systems have the potential to significantly improve quality of life and promote greater independence for individuals on the autism spectrum.

The below chart shows the impact AI can have to help with Sensory sensitivities. The impact is lower with ASD level 1 as the symptoms are less compared to those in ASD levels 2 and 3. Further, there are multiple sensory inputs that affect ASD patients such as sight, sound, touch, taste, smell, balance, and body awareness. AI in its current state of maturity cannot address all of these inputs. AI needs to evolve further to be able to measure and correlate the sensory inputs while learning the impact of the outcome of the recommendations.

AI Impact for Sensory Sensitivities
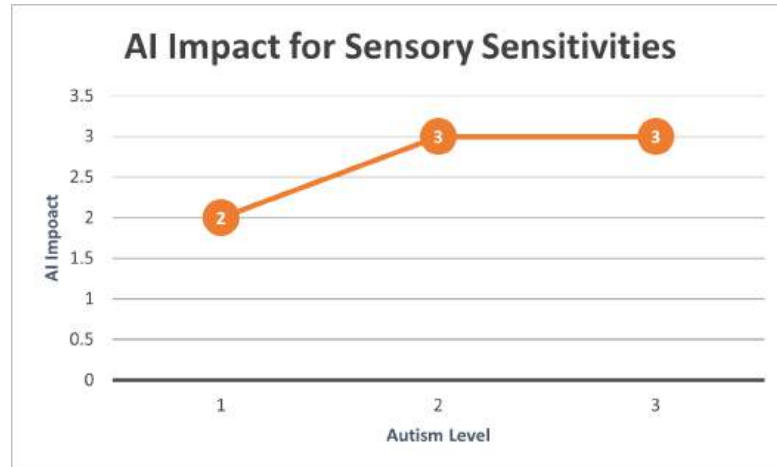
5) **Difficulty During Transition (ASD Level 1, 2, 3)** - Artificial Intelligence (AI)-powered scheduling applications offer innovative solutions to support children with autism spectrum disorder (ASD) in managing daily routines and transitions. These advanced tools can generate personalized visual schedules and provide timely reminders, helping children with ASD to anticipate and prepare for changes in their environment or activities. By leveraging AI algorithms, these applications can adapt to individual needs and preferences, offering a tailored approach to support (McClure).

The integration of visual and auditory cues within these AI-driven scheduling tools can significantly enhance the effectiveness of transitional support. Visual representations of tasks and activities, combined with customizable auditory prompts, can create a multi-sensory approach to schedule management. This comprehensive sensory input can help reduce anxiety and stress often associated with transitions for children with ASD. As research in this field progresses, AI-powered scheduling apps have the potential to offer increasingly sophisticated and personalized support, potentially contributing to improved daily functioning and reduced stress for children with ASD during transitions and throughout their daily routines.

The below chart shows the impact AI can have to cope with transition stress. The transition stress is lower with ASD level 1 and hence AI has the lowest impact. ASD level 2 patients can benefit more from AI as they are able to absorb the recommendations from AI powered tools, however, this requires active engagement limiting the impact mark at 2 for AI. With ASD level 3, there is more active support needed and hence the impact of AI tools drops down to 1.

AI Impact for Transition Stress
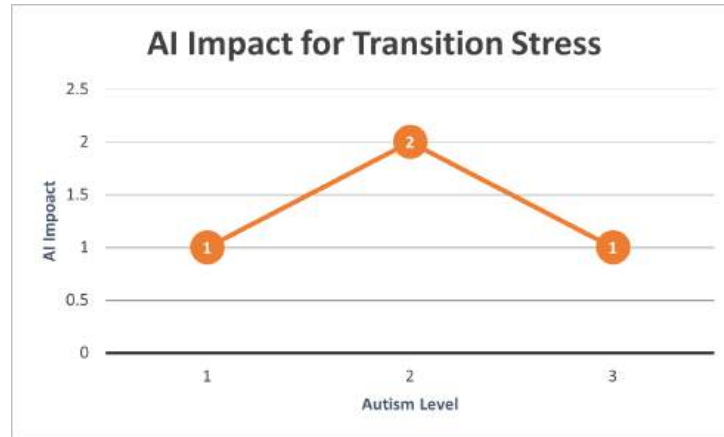
6) **Learning Disabilities (ASD Level 1, 2, 3)** - Artificial Intelligence (AI)-powered educational tools offer significant potential in providing personalized learning experiences for children with autism spectrum disorder (ASD). These advanced systems leverage machine learning algorithms to create tailored educational content that adapts to each child's unique cognitive profile, learning pace, and individual needs (Grynszpan et al. 346-361).
Key features of AI-driven adaptive learning platforms include:
   1. Dynamic Content Adjustment: The system can automatically modify the difficulty level of educational materials in real-time, based on the child's performance and engagement metrics.
   2. Targeted Skill Development: By analyzing patterns in a child's responses and progress, AI can identify specific areas requiring additional support and generate customized exercises to address these needs.
   3. Multimodal Learning Support: AI systems can present information through various sensory channels (visual, auditory, tactile), catering to different learning styles and preferences common in children with ASD.
   4. Progress Tracking and Reporting: Advanced analytics can provide detailed insights into a child's learning trajectory, enabling educators and caregivers to make data-driven decisions about educational interventions.
   5. Engagement Optimization: AI can identify which types of content and interaction styles are most effective for each child, maximizing engagement and learning outcomes.

These AI-powered educational tools have the potential to significantly enhance the efficacy of educational interventions for children with ASD by providing a level of personalization and adaptability that would be challenging to achieve through traditional methods alone. However, it's crucial to note that these technologies should be implemented as part of a comprehensive educational strategy, in consultation with education professionals and ASD specialists.

The below chart shows the impact AI can have for individuals with different learning disabilities. AI powered tools can be highly adaptive making the impact one of the highest for this category, especially with ASD levels 1 and 2. With ASD level 3, there are additional challenges that cannot be fully solved by AI and hence the impact drops slightly to 4.

7) **Difficulty in social interactions (ASD Level 1, 2, 3)** - AI can be leveraged to develop sophisticated conversational support tools for individuals with autism spectrum disorder (ASD). These AI-powered systems can analyze the nuances of ongoing conversations in real-time, offering contextually appropriate response suggestions to the user with ASD. Furthermore, the AI can break down complex social cues and implicit meanings within the conversation, presenting them in a more explicit and comprehensible format. This feature aids in enhancing the user's understanding of social interactions, potentially improving their ability to formulate independent responses. By providing this scaffolding, the AI tool aims to support the development of social communication skills while promoting autonomy in social interactions. However, it is crucial to note that the effectiveness of such tools may vary depending on the individual's specific needs and the severity of their ASD symptoms. Implementation should be carefully considered and monitored by healthcare professionals to ensure it complements existing therapeutic approaches and supports the individual's overall social development goals.
The below chart shows the impact AI can help with social interactions. This is an area of overall high impact with highest in ASD level 1 and 2. ASD one is a point lower than ASD 2 because of the lesser need to support. ASD 2 individuals can absorb the inputs better from AI tools and hence can benefit the most. With ASD 3, the impact drops because of the higher challenge in absorbing and responding to the inputs.

AI Impact for Social Interactions
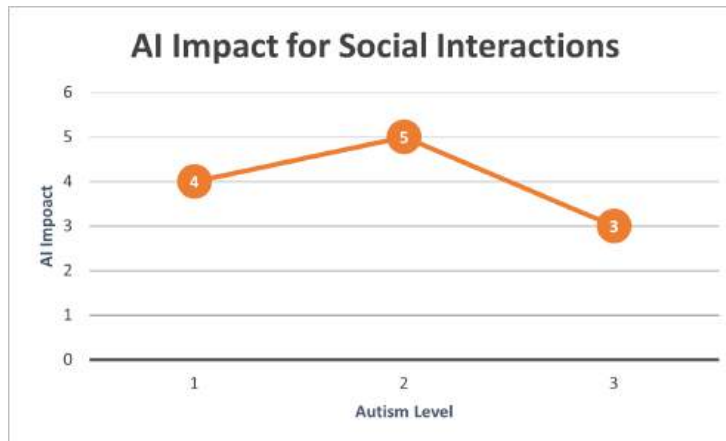
Conclusion and Recommendations

Let us examine the aforementioned potential solutions. The first proposed solution for early diagnosis has a very large potential impact. It can be expensive to implement, but the early diagnosis means that the autistic child can live a better life with less symptoms of autism. The second solution addressing making friends is effective but with limited impact with current maturity of AI solutions. It is trying to help autistic kids feel more comfortable in social settings by creating a chatbot. However, several of these chatbots already exist and are being used as supplementary to traditional therapy options. It has the potential to improve with the evolution of AI. The third solution attempts to address stimming behavior. While stimming behavior can cause self-harm and other problems, autistic kids often use it as a coping mechanism. An artificial intelligence repeatedly telling the autistic kid to stop the stimming behavior might cause stress and frustration, which may lead to more self harm. The better approach in this case would be to simply track the stimming behavior, and rather than taking any direct action, report it to the parents and/or therapist so that they can take more effective steps. The fourth solution aims to reduce stress and sensory overload on the autistic child through lighting and sound blocking systems. However, this solution is near impossible to test on a large scale to make sure it is effective as they would have to be implemented in a physical space. For the fifth proposed solution, the use of artificial intelligence makes limited impact, and such scheduling apps already exist, without the need for autism specialization or artificial intelligence. The sixth proposed solution is specialized education for autistic kids. In the status quo, such education plans are present but are taught by human teachers in schools. An AI powered tool can not only supplement this learning, but also provide an avenue for autistic children to learn effectively at home without a specialized teacher. The last proposed solution to help with difficulty in social interactions, helps reduce awkwardness and stress for autistic people in social situations. This solution could take the form of glasses, a barely noticeable device on the shirt, a smart-belt, or any other form. It would be able to receive audio input and suggest responses to the autistic kid.. In conclusion, I think the best options that would help autistic people are: 1) early diagnosis because of long-term life changing impact, and 2) Help kids at school especially because social awkwardness is one of the main daunting symptoms of autism, and being able to help it

effectively is absolutely crucial along with addressing the learning disabilities. The below chart summarizes the impact of each of the proposed solutions on the ASD symptoms.
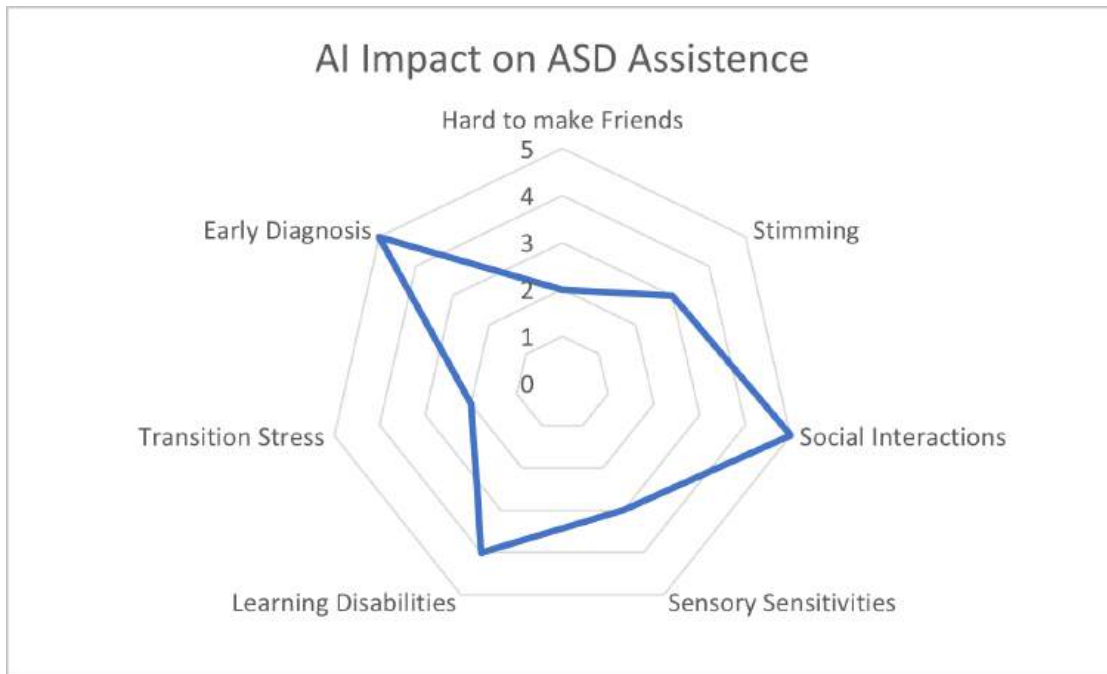
Developing a comprehensive suite of Artificial Intelligence (AI)-driven solutions for Autism Spectrum Disorder (ASD) has the potential to significantly enhance outcomes across the lifespan for individuals with ASD as well as drive the economic impact for individuals and society. This integrated approach encompasses three key phases: 1) Early Diagnosis: AI-powered diagnostic tools can potentially identify subtle indicators of ASD at earlier stages of development. 2) Optimized Treatment: AI systems can assist healthcare professionals in developing personalized intervention strategies. 3) Lifelong Support: offering potential support throughout an individual's life. By implementing this comprehensive, AI-enhanced approach, we can potentially create a continuum of support for individuals with ASD. This strategy aims to improve quality of life, promote greater independence, and enhance social integration from early childhood through adulthood.The goal is to augment and enhance existing support systems, not to replace human care and interaction.

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An Ethical Comparison on Gender Abuse in Fast Fashion By Alina Q. Huang

Thesis

This research paper explores solutions to widespread gender-based abuse in fast fashion and demonstrates, through case studies, how the actions of the FashionABLE clothing company more effectively mitigate abuses than those applied by the multinational fashion retailer H&M.

Introduction

In fast fashion, the least prioritized rung of the stakeholder ladder tends to be the employee. Working against harsh production expectations, female garment workers in Ethiopia earned starvation wages of $26 per month and faced gender-based violence for "not working faster" (Salaudeen; Hodal). This reality affects at least 540 factories and thousands of women, not just in Ethiopia, but throughout Sri Lanka, Indonesia, and several Asian countries. Allegations against Gap, a major fashion retailer, revealed that a Bangalore female tailor was physically beaten for not meeting her quota. Several girls in an Indonesian factory were threatened with contract termination if they spoke out against verbal insults, and female garment workers were referred to as a lower "caste" (Hodal). Women are most easily exploited by the loose regulatory environment in developing nations, which gives companies the freedom to impose their own conditions onto workers. Further, womens' perceived "lack of skills and education" lead to weaker bargaining power (Glöyer). Despite these deplorable conditions, substantial profit margins are hard for companies to resist. The faster the fashion the higher the profit margins, averaging 16% in fast fashion compared to 7% earned by regular retailers (Walsh). By relinquishing some control to factories in developing nations, company leadership significantly reduces overhead costs (reducing manufacturing-related direct expense) and gains significantly cheaper labor. The money speaks for itself, especially in a publicly-traded company where quarterly earnings reports can make or break a business's year. This therefore satisfies the second stakeholder, the company executive, at the expense of the first—the employee.

As with other ethical dilemmas, this short-term mindset leads to a long-term supply downfall. In the short-term, factories appear to be productive. The typical factory in a developing nation overworks employees by requiring them to produce 180 to 200 units per hour, while those workers could only produce 100 to 120 units in an average workday—essentially compressing more than 8 hours of work into a single hour (Jenns). The mental and physical strain required to maintain that production speed makes it unsustainable over the long-term. Garment worker retention rates in Bangladesh dropped from 80% for women in the 1980s to 53.65% in 2021. While factors like childcare and family obligations were the primary causes for the high turnover rate, the significant drop was also indirectly fuelled by harassment and harsh working conditions. Moreover, limited upward mobility for females perpetuates an environment that facilitates gender-based abuses (Jenns). While it might look like fast fashion companies are quickly and effectively responding to rapidly changing fashion trends, the industry is indirectly undermining the long-term health of its supply chains.

Due to increased globalization and the prominence of digital media, awareness of fast fashion abuses among consumers—the third stakeholder—is increasing rapidly. Insofar as companies support unethical production, whether in their own production facilities or outsourced factories, they may face backlash from growing activist movements. Customer activism can drive stock price declines that counteract even the effects of a solid earnings report, demonstrated in the 1990s, when Nike's sweatshop scandal drove boycotts to the point where Nike had to exclusively focus on regaining its reputation to reverse a 20% share price decline (Conway). Although general activist pressure can encourage industry giants to improve, research shows that this awareness does not "necessarily translate into purchasing behaviors" on the individual level (Chmelik). Since the 1990s, cheap prices and fashion trends have kept fast fashion impulse buying affordable for consumers. Fast fashion companies would likely take more decisive, transformative action if their valued stakeholder, the customer, changed their purchasing behavior. Whether through boycotts, choosing competitors, or buying out of need rather than impulse, customers can pressure companies toward a greater focus on supply chain management.

From a governance point of view, very little has been regulated due to jurisdictional challenges: when companies outsource, governments are less able to influence factories' international operations. Instead, oversight mainly focuses on mitigating environmental effects and product circularity, issues in which jurisdiction has been historically widened (Shao).

A similar situation can appear in multinational organizations. The International Labor Organization (ILO) actively works with businesses, unions, and underserved areas to create labor standards that uplift its partners and member countries (ILO editors). However, despite the ILO's wide jurisdiction, the vast majority of member fast fashion businesses are not bound by its regulations. Moreover, the ILO does not exclusively focus on gender abuse in fast fashion, meaning there is less attention paid to this issue than others, like the gender pay gap.

Although corporate social responsibility (CSR) standards discourage gender abuses in the garment industry, limited outside oversight and minimal legal consequences effectively incentivize companies to produce without interruption while abuses continue.

Case Studies

Multinational clothing company H&M operates more than 4,000 stores in 77 markets. Featured among the company's publicized corporate values are inclusion and gender equity (H&M Group editors). While some initiatives pushed for internal diversity, program scope appears to often be limited to the upper-level management of the firm and does not trickle down to its production factories. In 2018, the Department for Global Labor Justice uncovered flagrant gender-based abuses at many of H&M's 235 Asian factories. From frequent female assaults to supervisor retaliation, the violations were, the allegations stated, driven in large part by the company's fast fashion production deadlines (Jenns). While H&M cannot directly influence operations at its factories in developing nations, its business model creates unrealistic supply pressures that indirectly drive these abuses.

To combat the report's concerns, this clothing industry giant created a unique partner program with the International Labor Organization (ILO) one year later (ILO editors). By investing $2.8 billion USD, the initiative supported 20,000 workers in Ethiopia with job certification training, enforced in-factory consultancies for Turkey supervisors, and created bi-partisan committees to improve female union leadership. Under the Markkula Center's Framework for Ethical Decision-making, H&M implemented its solution most prominently using the Rights lens, an ethical problem-solving perspective that puts human dignity and rights before profitability targets. H&M prioritized its workers' rights to safety, upward mobility, and offered formal job certifications based on hours worked or experience in a position (Velasquez et al.).

9 years before H&M launched its program, a start-up clothing company called FashionABLE was actively counteracting female prostitution through fashion. By providing traditionally exploited women with livable wages and training in safe clothing production job skills, ABLE's production spread across Ethiopia. With growing profits, factory-based screening standards, and careful enculturation (gradual acquisition of a country's culture and norms), ABLE reached Brazil and Peru (SustainabilityChic editor). By incorporating culture into its business, ABLE understood the gender norms at each production location and designed a system to combat worker abuse. The start-up further developed its social impact tool AccountABLE to gauge wage, quality, and safety in its production partners, then monitored the implementation of its standards with rigorous, publicly-released audits. The same year H&M's abuses allegations came out, ABLE became the first fashion company to publish its factories' lowest wages, especially emphasizing their progress in countries where starvation wages had become the norm. ABLE's production system inherently pursues the Rights lens by allowing its workers to pursue a balanced lifestyle with fair wages. The company also implements the Justice lens in its systemic action and adherence to gender equality beyond its headquarters.

Comparison

Key differences appear in how H&M and FashionABLE combat fast fashion abuses. Unlike H&M, ABLE created an integrated system of values and business operations rather than separate, retroactive programs, which served to limit gender-based abuses more effectively. Without changing its internal operations, H&M spent millions to fund thousands of female job certifications and supervisor training sessions (ILO editors). While these programs improve prospects for workers, they do not address the workplace abuses driven by the production pressure required by H&M's business model. In effect, H&M has addressed the symptoms of the 2018 report rather than the root causes. Considering the Markkula Care lens, an ethical perspective that accounts for the feelings of all stakeholders, this makes sense: if the company were to slow its production deadlines, the decreased output would translate to more lost dollars than the $2.8 billion H&M invested in the ILO partnership programs. Therefore, H&M chose a solution that would smooth over potential negative reactions or adverse public statements from the company's shareholders while still seemingly improving the livelihoods of the at-risk worker

stakeholder group. On the other hand, ABLE's business model started without a reliance on fast fashion deadlines, embracing lower profit margins to protect its workers from unethical workplace pressures.

Recommendations

Incorporating conscience and long-term production stability into a company's top-to-bottom operations and supply chain, as well as its corporate culture, sets the stage for genuine ethically oriented transformation, while ethics training and social initiatives serve as the action to spread that awareness among internal stakeholders, partners, and customers (Byars and Stanberry). A reasonable recommendation must therefore include both factors: internal operational action and a well-communicated company culture shift. Given that H&M's fast fashion business model inherently contradicts its advertised corporate culture of inclusion and gender equity, its Ethiopian female certification campaign—a social initiative—will realistically serve as window-dressing if the company's core operations undermine its project-by-project initiatives. This lack of alignment between the company's business model and its project-by-project values-based initiatives has further been evidenced by a class-action lawsuit against H&M for sustainability misrepresentations and a Quartz investigation proving greenwashed advertisements (Sierra).

Therefore, H&M should gradually shift its business model to reduce its reliance on fast fashion. While such a shift would fundamentally transform H&M, ethical and financial arguments justify the shift. H&M has already lost significant market share to new entrants like SHEIN due to its inability to compete on price and delivery efficiency (Boyd and Strazzeri). This medium-term loss could bleed into a long-term decline considering the steady uptick in competition, so H&M could pivot to higher quality fabric, support longer-term fashion trends, and slightly increase price points (Boyd and Strazzeri). This brand reintroduction could begin with a test product anchored to a social mission and manufactured with transparent reporting throughout its supply chain. A significant percentage of profits could support gender equity programs. Moreover, to justify higher price points, H&M could focus on the 30-40s female demographic (25-40 years), who have the spending power to "prioritize long[er]-lasting, quality products over cheaper, disposable ones" (Mutairi). Whether through trendy maternity clothes or durable office-friendly attire, H&M could take an industry leadership role by steadily shifting its core customer profile and fashion portfolio over time.

To facilitate this shift, the clothing giant could temporarily reduce the millions that it spends on short-term social initiatives. In effect, H&M must ensure its fundamental business model does not facilitate gender abuses issues before it contributes to 'surface-level' social initiatives. Its pivot should also be accompanied with procedures that evaluate its supply chain, including outsourced facilities, as H&M has historically taken a hands-off approach to its 235 Asian factories (Jenns). With female skill education programs and regular evaluations that focus on counteracting gender abuse—components of ABLE's system—H&M could significantly alleviate the systemic pressure that drives factory abuses (Buss). H&M could develop female

garment workers' skills beyond mandatory assembly line tasks. Moreover, by paying living wages, H&M could help its female garment workers escape current gender-related pay constraints. Female workers' wages are often mere supplements for male breadwinners.

Only once the strategic corporate overhaul is complete should funds be reintroduced to project-based initiatives such as H&M's ILO partnership, bi-partisan union committees to uplift female leadership and wages, or separate CSR initiatives to educate female workers beyond their current "assembly line" knowledge. A project-based initiative with ILO would be easier to justify when the company's core supply chain does not systemically contribute to the gender equity issue it is attempting to resolve. In other words, the ILO initiative should not be launched to cover up—or inadequately address—ongoing ethical wrongdoing, but to further heighten awareness of gender equity. A research survey by Harvard Business Review further supports these proposed recommendations: 82% of the surveyed business executives believed that a business model transformation towards CSR promised long-term gains, with 94% saying that aligning operational improvements (such as improving worker conditions) with CSR would improve the company's social standing (Rangan et al.).

Aside from marketing its CSR initiatives, H&M seems to have no other incentive to pursue sustainability past its current superficial level. H&M must therefore be motivated to see social responsibility as part of its bottom line, and this change begins at the consumer level: what would it take for a shopper to select an ethical company?

The market research behind this question is compelling. 77% percent of consumers and 73% of investors are motivated to purchase and invest in companies committed to corporate social responsibility (Stobierski). Moreover, this investment trend has potential staying power: 41% percent of millennial investors put "significant effort into understanding a company's CSR practices," compared to the 27% percent of Gen X and 16% percent of baby boomers that precede this generation (Stobierski). In fashion, McKinsey reports that "approximately 50 percent of millennials and Gen Zers expect to purchase more garments secondhand" due to fair labor issues, showing the rise of a conscious demographic (Loughlin).

Based on this growing long-term trend, H&M will likely be outpaced by competitors on three critical dimensions: reputation, profitability, and investor support. Early signs of competitive pressure are already appearing. H&M's stock price declined from $358.20 (2015) to $142.38 USD (2024) (Yahoo Finance editors). The previously-mentioned test product release model could help reverse these trends and encourage H&M to pivot, but it is largely up to consumers to increase pressure on H&M to change. Since research has shown that consumer awareness and action will likely increase soon, it is up to H&M to anticipate potential disruptions to its business or wait and react as scrutiny and consumer pressure ramp up.

If H&M has to choose a more proactive path, it could expand its focus on female customers beyond the middle-aged demographic. From Freedonia's market research, women were "at least nine percentage points more likely to purchase an item than men" for every aspect of clothing except accessories, which women still bought more of than men, though by a narrower margin (Schmidt). H&M could therefore drive higher purchase volumes by tailoring its

social responsibility imperatives to its audience, namely by creating an empathetic situation where abuse-free supply protocols inspire both female workers and consumers. Moreover, if H&M takes on the United Nations Sustainable Development Goals (primarily 5 and 8) associated with bettering its supply chain, it can not only contribute to an agenda supported by 193 member states but also embrace an internationally accepted indicator of the company's progress, potentially reversing its current negative reputation. In summary, by moving away from fast fashion, H&M stands to gain long-term reputational benefits (including investor support and purchases from socially minded customers), a feasible industry niche, and a competitive motivator that can encourage the female fashion demographic to choose H&M over competitors (provided its social responsibility actions are credibly executed and marketed well).

In the Markkula framework's context, this solution focuses primarily on the Rights lens, which values human dignity through systemic supply chain transformation. In an industry infamous for unregistered sweatshops, health-threatening labor, and notoriously low wages—mainly directed at women in developing nations—the Rights lens refers specifically to an abuse-free workplace and, more optimistically, the right to a higher standard of living through livable wages. Moreover, this recommendation uses the Care lens to take the company shareholders into account: with H&M's profit-earning imperatives in mind, the recommendation reconciles H&M's current industry position in relation to its competitors with its potential to redirect funds from its current initiatives to a plan that better achieves a socially responsible, sustainable future. Considering the company's financial well-being, the recommendation recognizes that a robust supply chain and profitable retail operation is necessary for H&M to thrive in both the sustainability and business spheres — embodying Rockefeller's concept of stewardship, capital with responsibility that provides more than just economic value (Byars and Stanberry).

Due to its consideration of the shareholders' wishes, this recommendation relies less on utilitarian values, namely, creating the greatest good for the most people. It recognizes that compromise between profit and workers' rights is crucial for a solution to thrive in the long run, and that there are other stakeholders to consider in this modern business context.

Conclusion

Gender abuses in the global fashion industry tend to be driven by systemic supply chain pressure and a dated corporate perception of "uneducated" women in developing nations leading to diminished bargaining power for women. As a strong female activist who has personally consumed products from both case study companies, the author chose these contrasting enterprises as a specific window into a broad topic: gender equity. The author wishes to use the worldwide prevalence of H&M to draw attention to how corporate social responsibility in fashion extends to social issues as well as the more visible environmental ones. Despite spending millions on labor sustainability initiatives, the multi-national fast fashion brand is guilty of gender exploitation in its manufacturing processes. In the long-term, H&M has been losing ground in both the fast fashion industry and the growing social responsibility movement, whether

it be to new industry entrants like SHEIN or small corporations like FashionABLE building successful companies and robust reputations on social responsibility. Considering how H&M is already facing backlash from lawsuits and news investigations, a business model shift is required to reverse both its falling profits and its poor gender equality track record. To remove the exploitation inherent in its operations, H&M should focus on bettering its supply chain—even if it means moving funds away from its historic labor initiatives. This ensures the company's culture does not structurally infringe on human dignity (as outlined in the Markkula Rights perspective) before spending on supplemental actions.

Moreover, H&M would benefit if it designed and produced higher quality clothing, slightly increased price points, and shifted from fast trends to short to medium-term fashion design. This would not only alleviate the supply chain pressure that facilitates gender abuse, but also give H&M a responsibility niche that appeals to its female customer demographic if executed well. After temporarily rerouting funds to transform its operations and establishing a genuinely integrated corporate culture of equality, H&M could feasibly return to funding its current supplemental initiatives. This would be a positive shift following the lead of FashionABLE's business model, which ensures responsibility from the bottom-up through providing living wages to females who are typically trapped in male-dominated spheres of influence at home and at the workplace (Glöyer). Based on ABLE's clear model of labor transparency, its accountABLE auditing system, and its workplace female skills support, it is clear that ABLE's actions do more to combat gender abuses in developing nations than H&M's current system—which underscores the need for a radical shift in H&M's company culture.

Among consumers, the long-term trend towards supporting socially responsible companies is encouraging, yet more action is required to convince industry giants that their business models are compromised in the long-term. Whether it be Gen Z's promise to purchase more garments secondhand or millennials' evident preferences for social brands, consumers can accelerate improvement if they take on activities such as thrifting and buying for the long-term, creating bottom-line pressure on H&M and its peers to change their ways (Loughlin).

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ALS: Exploring Interactions Between Caregiver and Patients Stress and Mental Health in Amyotrophic Lateral Sclerosis By Jacob A. Lee

Abstract

Amyotrophic Lateral Sclerosis, also known as ALS, is a rare neurodegenerative disorder that is characterized by progressive muscle weakness: leading to loss of mobility, speech, and ultimately death. While the disease's impact on patients is well-studied, there is a significant burden placed on caregivers that is often overlooked. This research paper explores the relationship between ALS patients' and caregivers' mental health, highlighting the psychological burden caregiving takes over time, which usually intensifies as the disease progresses. The paper begins by discussing the basics of ALS, including its genetic, and molecular structure, and the fundamentals of ALS, then highlights the disease's relentless and progressive nature, as well as the limited scope of research, especially regarding diverse populations and ethnic groups. The paper also examines how ALS patients experience significant mental health challenges, such as depression, anxiety, and a reduced quality of life, which are often directly related to the disease's worsening stages. Caregivers are tasked with managing numerous complex emotional, physical, and financial responsibilities, leading to chronic stress, depression, anxiety, and caregiver burnout. Current treatment options for ALS, such as Qalsody (Tofersen), Riluzole, and Edaravone, alongside multidisciplinary care for symptom management, offer some relief. Yet, there remains a significant lack of attention to caregiver stress and trauma, which have long-term detrimental effects on their health. The paper concludes by emphasizing the urgent need for more research into caregiving stress, improved caregiver support systems, and continued advancements in treatment options for ALS patients, to enhance the quality of life for patients and their caregivers.

Introduction

ALS, also known as Amyotrophic Lateral Sclerosis, is a rare neurological condition where the muscles slowly start to weaken over time, limiting muscle function and movement and leading to death. However, ALS patients are not the only ones in danger; the caregivers around the patients are as well. Plenty of overlooked caregivers spend their time worrying about the patients, leading to their health declining. This paper explores the interactions between caregiver and patient stress and mental health in amyotrophic lateral sclerosis by going over the fundamentals of ALS, the mental health of ALS patients and caregivers, and finally, treatment options.

ALS Fundamentals

ALS is a scarce condition that is clinically heterogeneous and only affects 40,000 citizens in the United States each year (Total et al., 2021). Out of these numbers, 1/400 or 1/500 people in the United States and Europe would die from ALS each year as well (Total et al., 2021). The average prognosis of patients with ALS is around 3-5 years (Total et al., 2021). 10% of the cases

are inherited from previous ancestors when inherited. The TDP43 mutations are very present in familial ALS (Total et al., 2021). 90% of cases of ALS are sporadic (Total et al., 2021). Understanding ALS's genetic and molecular fundamentals is crucial because it would help identify potential therapeutic targets and ways to improve patient outcomes.

ALS is a focal-onset disease that relentlessly spreads throughout the body (Total et al., 2021). ALS also spares the sensory neurons, showing that motor neurons are not the only affected neurons. The average prognosis of patients with ALS is around 3-5 years (Total et al., 2021). The nervous system is most affected by ALS, as motor neurons degenerate in the spinal cord and brain, losing the ability to control different muscles (Total et al., 2021). ALS affects the proteins in an individual's body, getting clumped and ubiquitinated together. The proteins involved in ALS are TDP43 proteins, a nuclear protein, a transcription repressor, and a splicing apparatus. This protein is cleaved, hyperphosphorylated, and ubiquitinated in the cytoplasm. This process happens in early ALS and FTD. Understanding the molecular changes is critical to potentially developing therapies that target the affected proteins.

The survival of the patients depends on the different motor neurons involved in ALS. Mutations in various types of proteins in the human body can lead to ALS, including a *SOD1* mutation (Total et al., 2021). Proteins could also be misfolded (Total et al., 2021), meaning their correct structure and function still need to be achieved. This may lead to cellular stress and the progression of ALS further. ALS genes can trigger toxicity through different pathways: for example, protein quality control (*SOD1*), process extension (PFN1), and RNA metabolism (*C9orf72*), which result in progressive loss of muscle control. *SOD1* is an enzyme that prevents oxidative damage. When it is mutated, toxic protein aggregates, and the enzyme's loss of function contribute to the disease pathology. High levels of NfL, a cylindrical neurofilament in the cytoplasm of neurons, contribute to fast disease progression, leading to earlier death. When an individual experiences neuronal damage, NfL is released from the CSF and plasma.

There are several disparities in ALS research. Most of the research on ALS patients is based on European and American white men, who make up a small minority of people with the disease (Total et al., 2021). Limiting the research population prevents the generalization of research. There are also disparities in clinical trials: certain racial/ethnic groups are overrepresented in the study population, and more diverse populations need to be included in ALS intervention studies. There are also environmental risk factors disparities: exposure to environmental risk factors for ALS may differ based on socioeconomic or geographic characteristics. (Total Health, Oncology, 2021)

Mental Health: What We Know

ALS affects the mental health of patients and their ability to adapt to living with the disease. Quality of life for patients decreases as the disease progresses (Stephens et al., 2016). Many pain symptoms come with ALS, resulting in a severe impact on daily activities (Albert et al., 2007). In a study of 197 ALS patients, researchers found moderate pain levels, pain interference with daily activities, and suboptimal pain relief from treatments on average (Albert

et al., 2007). The quality of life in ALS patients has varied: many ALS patients can maintain a quality of life in different aspects despite their physical health decline (Albert et al., 2007). As death approached, family involvement, engagement with friends, and leisure activities became even more critical. Furthermore, the amount of satisfaction with these aspects of life was largely independent of their physical functioning (Albert et al., 2007).

Depression and anxiety were both widespread in ALS patients across multiple studies (Albert et al., 2007; Stephens et al., 2016; Averill et al., 2007). The higher pain self-efficacy scores predicted lower pain severity (Albert et al., 2007), indicating they are more aware of their own body. The prevalence of depression among ALS patients at the end of life was around 9% (Averill et al., 2007), which is low compared to initial thoughts. The ALS patients did not have an increase in depression as they were getting closer to death (Albert et al., 2007). However, about 19% of ALS patients have expressed that they wished to die; they have reported higher levels of depressive symptoms, pessimism, and hopelessness (Averill et al., 2007). Those who could plan and "control" their approaching death reported to have less suffering and a greater sense of control of their condition (Averill et al., 2007).

There are many cross-cultural differences in the mental health of ALS patients. American patients were reported as the least distressed overall among all the ALS patients (Albert et al., 2007). This could be because of the quality of hospice care and the availability of more improved technology compared to less fortunate countries. Israeli patients were reported as the country with the highest levels of distress, pessimism, and suffering (Albert et al., 2007). This could be because of the quality of the care and the quality of the technology as well. German patients were reported between the American and Israeli patients in terms of distress and other mental health indicators (Albert et al., 2007).

Qalsody + Other treatment options

Qalsody, also known as Tofersen, is an antisense oligonucleotide that is becoming a potential treatment for the rare disorder of amyotrophic lateral sclerosis, also known as ALS. Tofersen was recently approved about a year ago, but only for patients with a mutation in the 6the superoxide dismutase 1 (*SOD1*) gene. Tofersen can bind to the *SOD1* mRNA, degrading the *SOD1* mRNA and reducing the synthesis of the *SOD1* protein. The Tofersen was tested on patients with the *SOD1* mutation, reducing the total cerebrospinal fluid *SOD1* by 35% and 2 % in placebo patients (Blair, 2023). The Tofersen also reduced the plasma NfL by 55% and 12% increase in placebo patients (Blair, 2023). The cerebrospinal fluid's (CSF) maximum concentration is reached after the third dose of Tofersen. The Tofersen is transferred from the CSF into the systemic circulation, which helps get the maximum plasma concentrations after 2-6 hours. No statistical differences exist between age, sex, race, and body weight and the impact on tower exposure in the plasma (Blair, 2023). Metabolism of Tofersen is expected to happen because of exonuclease-mediated hydrolysis (Blair, 2023). Qalsody (Toferson) is a very significant advancement in the treatment of ALS, especially for individuals who have the *SOD1* mutation

There are many symptoms of ALS, and there are symptom management for the different symptoms. Other pharmaceutical treatments include Riluzole and Edaravone. Riluzole, an FDA-approved medication that can slow down the progression of ALS, is often prescribed early in the disease course.; Edaravone, e: an FDA-approved drug that may slow the decline in daily functioning for some ALS patients. Additional treatments may include multidisciplinary care: ALS treatment typically involves a team of specialists, including neurologists, physical therapists, occupational therapists, speech therapists, nutritionists, and respiratory therapists. Finally, physical therapy is recommended to maintain mobility and prevent complications from inactivity.

There are some "Upstream" therapies, for example, Target DNA (CRISPR/Cas9), where the gene itself "heals" or the mutation is deleted; target RNA, Antisense oligonucleotides (ASO) and micro-RNA; target protein-immuno-depletion; and Target Transcriptional networks. "Personalized" biological therapies may be particularly beneficial in FALS caused by *SOD1* and *C9orf72* gene mutations.

Caregiver Stress: Mental Health Disorders in Caregivers and Genetics

Caretakers have many different responsibilities for patients with ALS, including assisting with daily activities (bathing, dressing, eating, medicine, secretions, etc.), operating medical equipment and learning how to use it, coordinating medical appointments, providing emotional support, and making decisions about care and treatments.

Caregiver burden, or caregiver stress, is the strain or load a caregiver feels helping ill, disabled, or elderly family members. Stress is a self-perceived, multifaceted strain (physical, emotional, social, and financial) and a temporal aspect (burden over time). Many caregivers need more financial resources, multiple responsibility conflicts, and a lack of social support systems. As time progresses with the disease, provisions decrease, quality of life declines, and physical and psychological health deteriorates (Cabral et al., 2014).

ALS caregivers are exposed to a variety of stressors, ranging from financial, physical, emotional, and more. High costs of medical care and equipment, loss of income, expenses for home modifications, and costs of medications and treatments not covered by insurance all contribute to financial stress. Physical demands include assisting with mobility and transfers, helping with personal care tasks, managing feeding and nutrition needs, and lack of sleep due to nighttime care requirements. Emotional and psychological challenges encompass watching a loved one's progressive decline, anticipatory grief, feelings of isolation and loneliness, stress from constant vigilance and decision-making, and potential depression and anxiety. There are also logistical stressors, such as time management: balancing caregiving with other responsibilities, coordinating medical appointments and therapies, and managing medication schedules. Communication challenges between a patient and caregiver develop throughout the disease; adapting to changes in the patient's ability to communicate and learning to use assistive communication devices can cause substantial stress. There are also behavioral changes that come with ALS, which for the caregiver include dealing with mood swings or personality changes,

managing frustration or depression in the patient, and handling potential cognitive changes in some ALS patients. Beyond physical tasks, there are specific medical and nursing tasks: learning to use and maintain medical equipment, administering medications, and monitoring for complications, as well as navigating the healthcare system: coordinating care between multiple specialists, advocating for the patient's needs and understanding and making decisions about treatment options. Social impacts are inevitable, given reduced social life and personal time and strain on relationships with other family members or friends. Finally, self-care challenges are expected, including neglecting one's own health needs and difficulty finding time for respite care.

Several adverse mental health outcomes come with being a caregiver for ALS patients. This includes chronic stress, depression, anxiety, grief, burnout, isolation, guilt, and strains in relationships. In terms of chronic stress, the constant demands of caregiving lead to stress, which affects both physical and mental well-being (Schischlevskij et al., 2021). In regards to depression, you need to witness a loved one's physical decline slowly and face different daily challenges, leading to sadness and depression (Penning & Wu, 2016). Research on caregiving anxiety shows that worrying about the future, managing medical care, and financial concerns can lead to increased anxiety symptoms and anxiety disorders (Penning & Wu, 2016). Grief and guilt are also a significant concern; witnessing the gradual decline of a loved one could lead to grief (Liu et al., 2020), and caregivers may feel guilty about taking time for themselves or have a negative mental perception of situations leading to guilt caregivers feel guilty about taking time for themselves or have a negative mental perception on situations leading to guilt. Taking care of ALS patients can lead to exhaustion, detachment, and a sense of hopelessness, which encapsulates caregiver burnout (De Wit et al., 2018). Caregivers also see ripple effects in their social network - taking care of an ALS patient could take time away from social support systems (De Wit et al., 2018); relationships also change, leading to emotionally challenging relationships (Penning & Wu, 2016).

Over 50% of caregivers reported chronic health issues: heart problems and hypertension. Sleep deprivation: caretaking may ruin sleep patterns, leading to changing mental health and cognitive function (Burke et al., 2015). Overall, there is a decrease in caregivers' overall health.

Conclusion

This review sought to explore the mental health effects of caregiving, specifically in the realm of ALS. As a neurodegenerative disease, we know that ALS is a focal onset disease that has relatively fast disease progress. However, there still needs to be more research about the core biology of ALS, its genetics, and more research about ALS in different ethnic groups. Some data shows that ALS patients' and caregivers' mental health is affected as the disease progresses into further stages, with evidence supporting correlations between quality of life and psychiatric disorders, including depression and anxiety, as well as others. Although we know these effects are devastating and last beyond the disease for caregivers, research on caregiving stress and caregiving trauma is scarce. Given the deficit of research on caregivers, definitive conclusions

cannot be made on the long-term effects of caregiving stress, which includes financial, physical, and emotional stress. More research is necessary to determine potential treatment options or ways to create healthier bonds between patients and their caregivers, as well as efforts to treat caregiver stress while ALS patients are receiving treatment. While federal funding supports ALS research, specific financing must also be allocated for caregiving research. In regards to treatment options for ALS, more widespread and efficacious treatment options need to be developed and widely advertised to ALS patients and caregivers. Both ALS patients and their caregivers deserve adequate and practical support during ALS treatment and beyond.

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Analyzing the Correlation between Corruption and Income Inequality in Vietnam, Thailand, and the Philippines (1970-2023) By Erin Beall

Abstract

This paper studies the relationship between corruption and income inequality in Vietnam, Thailand, and the Philippines over the years 1970-2023 using Ordinary Least Squares (OLS) methods. The results show a positive correlation between corruption and income inequality except for Vietnam due to a lack of observations. As corruption increases, income inequality will also increase. This paper also considers additional variables, such as the unemployment rate, GDP per capita growth, school enrollment, health expenditure, democracy index, and tax revenue, and their impact on income inequality in these countries. The variables provide a broader context for understanding how socioeconomic and governmental factors interact with corruption in influencing income inequality. These results have overarching implications for how governments address corruption and reveal a need for effective anti-corruption policies/reforms. As such, this paper offers valuable insight for the countries' governments and adds to the existing literature about government and inequality.

Introduction

Corruption can distort political processes but augment disparities between the rich and poor and stark differences in wealth and opportunity. This paper aims to contribute to the existing literature by studying the relationship between corruption and income inequality and other variables in Vietnam, Thailand, and the Philippines. It provides insight into the political, economic, and social contexts of these countries. These specific countries were chosen because they each represent a diverse political and economic environment. Vietnam is a one-party socialist nation, while the Philippines is a republic, and Thailand is a constitutional monarchy. Thailand is a more developed nation in comparison to Vietnam and the Philippines and all three countries have experiences of corruption in their government. This study of these countries will allow for a greater understanding of the governments, economies, and development levels in the selected countries. It also provides useful policy insights for these countries.

Literature Review

Existing literature on the relationship between corruption and income inequality is extensive, however, there are mixed results in the studies. Gupta and Abed (2002) conducted a cross-sectional analysis of the effects of corruption on the Gini coefficient in a selection of countries over the period of 1980-1997 using OLS and instrumental variables (IV) and found that corruption increases the Gini coefficient significantly. Li, Xu, and Zou (2000) found an inverted U-shape relationship between corruption and income inequality, such that both low-corruption countries and high-corruption countries have low-income inequality.

Several studies were conducted on the effects of corruption and income inequality in specific regions of the world. For example, Gyimah-Brempong (2002) used panel data from

various African countries in the 1990s to test corruption on the growth rate of per capita income and income distribution. The results indicate that corruption decreases the growth rate of per capita income and is related to high-income inequality in the sample countries. Ojo, Eusebius, Ifeanyi, and Adaremi (2020) specifically focused on the relationship of inequality and corruption within Nigeria. They found that corruption and income inequality have a negative relationship in Nigeria, meaning high corruption lowers income inequality, and found that corruption has a unidirectional causality on inequality. Similarly, Dwiputri, Arsyad, and Pradiptyo (2018) studied the effects of corruption on income inequality in 14 Asian countries using Ordinary Least Squares (OLS) and Tobit methods and found as well that corruption had a significant effect in increasing income inequality. Nguyen, Vo, Le, and Nguyen (2020) studied the relationship between fiscal decentralization, income inequality, and corruption in Vietnam. They found that all three variables interact significantly with each other and each has a two-way relationship with the other two variables. Specifically, they found that a decrease in corruption correlated with an increase in income inequality, and fiscal decentralization has a positive relationship with income inequality and vice versa. Additionally, Dincer and Gunalp (2008) found robust results that corruption increases income inequality and poverty in US states using data on the number of government officials convicted of federal crimes in each state and various inequality indicators and poverty data. Corruption was found to negatively affect the lower end of the income distribution more than the upper end by regressing varying degrees of inequality aversion for Atkinson indexes. Batabyal and Chowdhury (2015) found that corruption also negatively affects income inequality in Commonwealth countries, even when financial development helps to reduce it. . Studies similar to Batabyal and Chowdhury's compared the influence of external factors that play in the relationship between income inequality and corruption. Keneck-Massil, Nomo-Beyala, and Owoundi (2024) looked at the influence of political power in the relationship between corruption and income inequality. The results show that while, at a world level, low corruption is correlated with low-income inequality, in developing countries, specifically, corruption will decrease income inequality due to the uneven distribution of political power.

There were also studies conducted examining the opposite: the effect of income inequality on corruption. For instance, Samahedi and Fahranmadour (2013) studied how income inequality affects corruption and how a country's economic freedom influences this relationship. In free and mostly free countries, as income inequality increases, corruption also appears to increase. However, the opposite was found to be true in mostly unfree countries, in which an increase in income inequality is correlated with a decrease in corruption. Khagram and You (2003) conducted a similar study, however, distinguishing between authoritarian and democratic regimes. They found that high income inequality is correlated with high corruption overall and that the effect of income inequality is greater in democratic regimes rather than in authoritarian regimes. Policardo and Carrera (2018) found, using a panel of 50 countries, that higher income inequality leads to higher corruption, but corruption did not appear to affect income inequality. However, they recognize that in individual countries a causal relationship between corruption and income inequality may exist.

Data and Methodology

This paper uses Ordinary Least Squares (OLS) to conduct a statistical analysis of the chosen variables with panel data from 1970 to 2023. The variable used to measure income inequality is the Gini index taken from the World Bank DataBank and the variable used for measuring corruption is the Transparency International Corruption Indicator. The Gini coefficient measures inequality on a scale of 0 to 100 with 0 meaning perfect equality and 100 meaning perfect inequality (World Bank, 2024). The Transparency International Corruption Indicator measures corruption on a scale of 0 to 100 with 0 meaning "highly corrupt" and 100 meaning "very clean" (Transparency International, 2024).

In addition to variables for corruption and income inequality, this paper utilizes the unemployment rate, GDP per capita annual growth rate, school enrollment rates - primary and secondary, democracy index, current health expenditure as a percentage of GDP, and tax revenue as a share of GDP. Tables 1-4 contain the descriptive statistics of the variables used and their sources. The unemployment rate represents the share of the labor force that does not work and are actively seeking work. The GDP per capita growth rate represents the annual growth rate of GDP per capita using constant local currency. School enrollment rates represent the ratio of enrollment of the population that corresponds to the respecting level of education. The democracy index is a scale from 0-10 (0 being less democratic, 10 being more democratic), which represents the competitiveness of political participation, openness and competitiveness of recruiting the executive branch, and the limitations of the executive branch in a country. Current health expenditure as a share of GDP represents consumption of healthcare goods and services as a percentage of GDP. Tax revenue as a share of GDP represents the compulsory transfers to the government as a percentage of GDP.

Figure 1. Descriptive Statistics Table

Variable	Observations	Mean	Standard Deviation	Minimum	Maximum
Gini index*	118	42.119	32.513	4.439	49.800
Unemployment rate (%)	96	2.220	1.069	0.250	4.050
Corruption Perception Index	85	16.607	16.186	2.300	42.000
GDP per capita growth (annual %)	144	3.404	3.456	-10.978	11.312
School enrollment - secondary* (%)	111	67.299	27.020	17.273	134.440
School enrollment - primary* (%)	147	104.670	7.787	81.251	125.090
Democracy	141	1.553	13.763	-88.000	9.000
Current health expenditure - share of GDP (%)	64	3.928	0.633	2.638	5.607
Tax revenue - share of GDP (%)	83	13.839	1.614	10.173	17.414

Notes:
Gini index: World Bank - https://data.worldbank.org/indicator/SI.POV.GINI, Our World in Data - https://ourworldindata.org/grapher/economic-inequality-gini-index,
Unemployment rate: World Bank - https://data.worldbank.org/indicator/SL.UEM.TOTL.ZS
GDP per capita growth: World Bank - https://data.worldbank.org/indicator/NY.GDP.PCAP.KD.ZG
Secondary school enrollment: World Bank - https://data.worldbank.org/indicator/SE.SEC.ENRR
Primary school enrollment: World Bank - https://data.worldbank.org/indicator/SE.PRM.ENRR
Democracy level: Polity - https://www.systemicpeace.org/polityproject.html
Current health expenditure: World Bank - https://data.worldbank.org/indicator/SH.XPD.CHEX.GD.ZS
Tax revenue as a share of GDP: World Bank - https://data.worldbank.org/indicator/GC.TAX.TOTL.CN?locations=K%20H

*An average was taken for years where data was not available from the two years surrounding

The dependent variable is the Gini index and five equations are used for the independent variables. The baseline equation includes the unemployment rate, corruption perception index, GDP per capita growth, and the secondary school enrollment rate. Equation 2 adds the primary school enrollment rate to the variables from the baseline equation. Equation 3 adds the democracy index to the variables from the baseline equation. Equation 4 consists of baseline equation variables plus the current health expenditure as a share of GDP. And finally, Equation 5 consists of baseline equation variables plus tax revenue. OLS is the method used to regress the equations mentioned above. Statistical regressions using these equations are run with the data of the three countries (the Philippines, Thailand, and Vietnam) combined as well as each country individually.

Empirical Results
The correlation matrix of the variables used in this paper is shown below in Figure 2.

Figure 2. Correlation Matrix

	Gini index	Unemployment rate	Corruption Perception Index	GDP per capita growth	School enrollment - secondary	School enrollment - primary	Democracy index	Current health expenditure - share of GDP	Tax revenue - share of GDP
Gini index	1	0.704	−0.421	0.163	-0.582	0.036	0.049	-0.118	-0.457
Unemployment rate		1	-0.210	-0.102	-0.183	0.122	0.459	0.151	-0.850
Corruption Perception Index			1	0.107	0.649	-0.194	-0.416	0.551	0.218
GDP per capita growth				1	-0.275	0.012	-0.207	-0.241	0.069
School enrollment - secondary					1	0.523	0.254	0.283	0.267
School enrollment - primary						1	0.445	-0.737	-0.285
Democracy							1	-0.133	0.269
Current health expenditure								1	0.003
Tax revenue - share of GDP									1

There are several instances of high correlation and moderate correlation exhibited in the correlation matrix. Tax revenue and unemployment rate exhibit a strong negative correlation on the matrix. This makes intuitive sense as it means fewer people have a source of income and thus are paying less taxes. Additionally, current health expenditure as a share of GDP and primary school enrollment have a strong negative correlation. This is less intuitive, however, it may be because when more resources are allocated toward one sector, there will be fewer resources allocated to the other. To continue, the Gini index and the unemployment rate have a moderately strong positive correlation as well. Theoretically, this can be explained because if more people do not have employment and thus have little to no source of income, it can widen the gap between the rich and the poor.

The regression analysis results using the OLS method are shown in Figures 3-6. Figure 3 shows the results of the full sample with the data of the three countries combined, and Figures 4-6 show the results of each country individually.

Figure 3. Full Sample - Impact of Corruption on Income Inequality
Dependent Variable: Gini index

	(1)	(2)	(3)	(4)	(5)
Unemployment Rate	1.012** (0.468)	0.926** (0.448)	1.027*** (0.346)	1.410*** (0.364)	1.086** (0.456)
Corruption Perception Index	-0.073*** (0.022)	-0.047* (0.023)	-0.057*** (0.016)	-0.038** (0.017)	-0.856*** (0.017)
GDP per capita growth	0.135** (0.060)	0.096 (0.060)	0.112 (0.055)	0.075 (0.048)	0.130** (0.048)
School enrollment - Secondary	-0.033* (0.017)	-0.056*** (0.019)	0.044 (0.095)	-0.032** (0.013)	-0.039** (0.213)
School enrollment - Primary	–	0.108** (0.046)			
Democracy index	–	–	0.044 (0.095)	–	–
Current health expenditure - share of GDP	–	–	–	-1.453*** (0.355)	–
Tax revenue - share of GDP	–	–	–	–	0.206 (0.213)
Observations	55	55	43	44	48
R-squared	0.67	0.71	0.83	0.87	0.82

Numbers in parentheses represent standard errors.
*p < 0.1 ;
**p < 0.05 ;
***p < 0.01

Figure 3 reveals that corruption has a significant negative correlation with income inequality in the three countries. As corruption perception decreases (higher CPI), income inequality decreases. The results show that the unemployment rate, GDP per capita growth, primary and secondary school enrollment, and current health expenditure as a share of GDP significantly influence income inequality.

A higher level of unemployment translates to higher inequality. GDP per capita growth only produced significant results in Equations 1 and 5. This could mean that the inclusion and/or exclusion of variables in Equations 2-4 might be influencing the significance of the variable or that there is a multicollinearity issue with the variables in Equations 2-4. Secondary school enrollment displays a similar issue in which Equation 3 is the only equation without a significant value for secondary school enrollment. This may affect the robustness of the results.

Primary school enrollment is significant. As primary school enrolments increase, inequality increases. This relationship is not expected and is counterintuitive, as, theoretically, basic education should give individuals the skills and knowledge needed to compete in the labor market. However, this can be possibly explained because the quality of primary education may

vary greatly for different socioeconomic groups and rural/urban areas or might not be sufficient to greatly impact an individual's contribution to the labor force.

And lastly, health expenditure in the fourth equation displays a significant negative correlation with inequality. The variables that did not have a significant effect at all on income inequality are the democracy index and tax revenue as a share of GDP. The analysis of the impact of corruption on income inequality concludes that corruption negatively affects income inequality. If corruption is decreased in the countries studied, then income inequality will decrease.

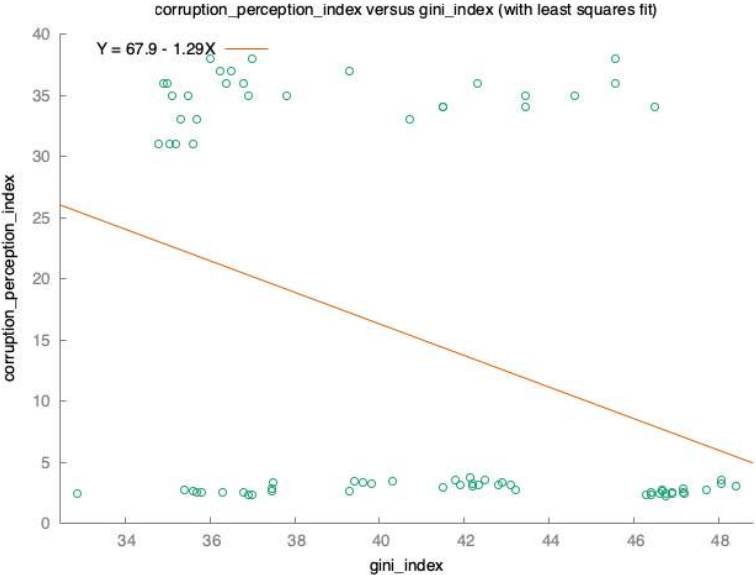Figure 4. Full Sample - Regression Graph

Figure 4 shows the respective regression graph for the full sample regression results. The Gini index is represented on the x-axis and the Corruption Perception Index is represented on the y-axis. The points plotted represent data points for each year observed. All regression graphs in this paper are formatted in this manner. The full sample regression graph displays a downward slope, which indicates a negative relationship between corruption and income inequality. The points plotted form two distinct horizontal arrays– one along the top and one across the bottom of the graph. This reflects the different patterns in the regressions across the countries studied and the dispersion of the points likely suggests there is some variation over time or between the countries.

Figure 5. Philippines - Impact of Corruption on Inequality

Dependent variable: Gini index

	(1)	(2)	(3)	(4)	(5)
Unemployment Rate	1.523** (0.709)	0.712** (0.386)	2.193*** (0.528)	1.899*** (0.480)	1.280** (0.660)
Corruption Perception Index	-0.054* (0.030)	-0.060*** (0.016)	-0.024 (0.019)	-0.026 (0.022)	-0.019 (0.032)
GDP per capita growth	0.036 (0.065)	0.013 (0.034)	-0.016 (0.090)	-0.016 (0.050)	0.013 (0.060)
School enrollment - Secondary	-0.165* (0.082)	-0.039 (0.046)	-0.101* (0.053)	-0.020 (0.079)	-0.292*** (0.096)
School enrollment - Primary	–	0.200*** (0.028)			
Democracy index	–	–	–	–	–
Current health expenditure - share of GDP	–	–	–	-1.547*** (0.327)	–
Tax revenue - share of GDP	–	–	–	–	-0.571* (0.2371)
Observations	23	23	20	18	23
R-squared	0.84	0.96	0.90	0.92	0.87

Notes: The variable Democracy index is not included because of insufficient observations. Numbers in parentheses represent standard errors.

*p < 0.1 ;
**p < 0.05 ;
***p < 0.01

Figure 5 represents the impact of corruption on inequality in the Philippines. As seen in the table, the coefficients of unemployment are slightly higher in Figure 3 than in Figure 4, however they demonstrate the same trend. The coefficients of corruption are significant in Equations 1 and 2 but not in Equations 3-5. The loss of significance for corruption in Equations 3-5, could be because additional variables are either reducing the relative importance of corruption in explaining income inequality or interacting with corruption in ways that make its direct effect on income inequality less clear. This suggests that corruption plays a bigger role in influencing income inequality when considering a more basic set of economic and educational variables in the Philippines rather than a more complex set of variables. While GDP per capita growth exhibited some significance in the full sample regression table, it appears to not be significant for the Philippines individually. Secondary school enrollment is significant in

Equations 1 and 5. This means that secondary school enrollment's relationship to income inequality is influenced by the presence of other variables in these models. Equation 1 is relatively simple, meaning that secondary school enrollment is a key factor for explaining income inequality when included with a basic set of economic variables. In Equation 5, however, tax revenue is introduced alongside the baseline variables, which might interact with secondary school enrollment in a way that increases its significance. Primary school enrollment is highly significant in the Philippines. However, its positive correlation still remains strange, as it should have a negative correlation with inequality theoretically. Health expenditure is highly significant as well and shows a negative correlation with inequality.

Finally, while tax revenue in the full sample regression table was not significant, it appears to be significant in the table for the Philippines. As tax revenue increases as a share of the GDP, then income inequality will decrease.

Figure 6. Philippines - Regression Graph
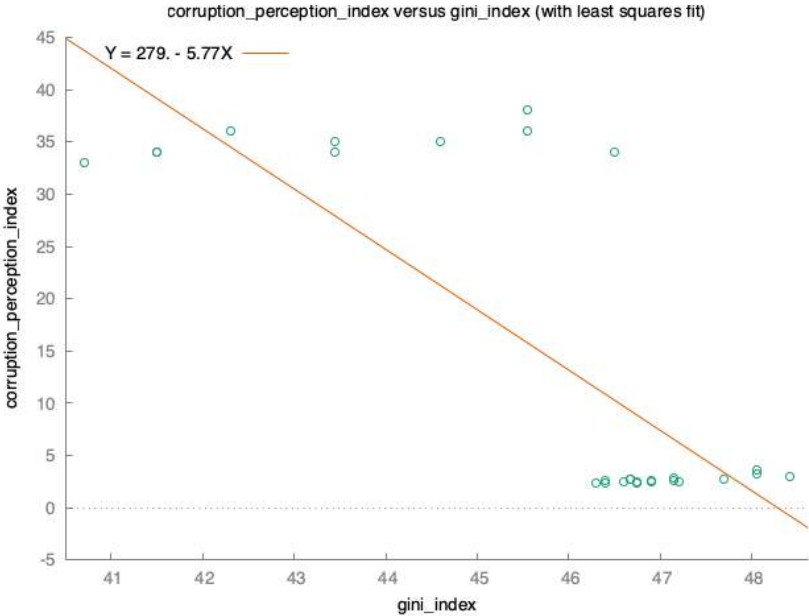
Figure 6 shows the regression graph for the Philippines. It shows a downward trend, which indicates a negative correlation between corruption and income inequality. The observed year points form two horizontal arrays, with one spread across the top graph and distributed along the entire x-axis and the other concentrated in the bottom-right part of the graph. This distribution suggests that, over time, the Philippines experienced distinct phases in the relationship between corruption and inequality. The separation of points implies some variations in the relationship between the two variables across different periods.

Figure 7. Thailand - Impact of Corruption on Income Inequality

Dependent variable: Gini index

	(1)	(2)	(3)	(4)	(5)
Unemployment Rate	0.764 (0.481)	0.764 (0.493)	2.193*** (0.528)	1.347** (0.501)	2.046*** (0.675)
Corruption Perception Index	-0.055* (0.481)	-0.056 (0.035)	-0.024 (0.019)	-0.017 (0.025)	-0.051* (0.026)
GDP per capita growth	0.178** (0.070)	0.179** (0.080)	-0.016 (0.090)	0.113 (0.094)	0.223*** (0.066)
School enrollment - Secondary	-0.059*** (0.019)	-0.059 (0.026)	-0.101* (0.053)	-0.021 (0.019)	-0.043** (0.018)
School enrollment - Primary	–	-0.001 (0.070)			
Democracy index	–	–	0.061 (0.108)	–	–
Current health expenditure - share of GDP	–	–	–	-3.390** (1.352)	–
Tax revenue - share of GDP	–	–	–	–	0.865** (0.351)
Observations	25	25	22	20	25
R-squared	0.85	0.85	0.86	0.92	0.89

Note: Numbers in parentheses represent standard errors.

*$p < 0.1$;

**$p < 0.05$;

***$p < 0.01$

     Figure 7 represents the regression results for Thailand individually. The unemployment rate has significance in only equations 3, 4, and 5. This is rather perplexing as unemployment should have a highly strong relationship with income inequality. However, perhaps the relationship between unemployment and income inequality in Thailand may be conditional to the broader economic and political context of the country. Corruption is only significant for equations 1 and 5. This lack of significance could be due to the interactions with the variables of the models. GDP per capita growth is only significant in equations 1, 2, and 5 and secondary school enrollment is only significant in equations 1, 3, and 5 as well. Again the differences in significance among the different equations are disappointing, but it is also likely due to the interactions with other variables. Health expenditure produced a significant coefficient intuitively. As health expenditure as a share of GDP increases, income inequality will decrease.

Tax revenue as a share of GDP also has a significant coefficient in the table of Thailand. As tax revenue increases, income inequality will also increase. This might occur because higher tax revenues are not effectively redistributed or are used for policies that may exacerbate income inequality.
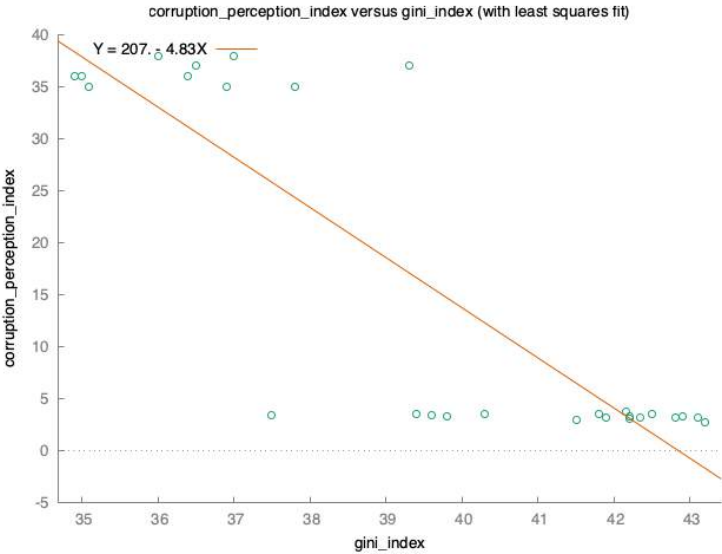
Figure 8. Thailand - Regression Graph

Figure 8 shows the regression graph of corruption and income inequality in Thailand. It shows a downward-sloping line, which demonstrates a negative relationship between corruption and income inequality. The observed year points are arranged in two distinct clusters. One array is clustered in the top left part of the graph and the other array is clustered in the bottom right. This shows a clear division in how the relationship between corruption and inequality has changed over time. The downward trend between corruption and inequality supports the conclusion that higher corruption is associated with lower income inequality in Thailand, though the distinct grouping of points indicates different periods or dynamics that influenced the relationship.

Figure 9. Vietnam - Impact of Corruption on Income Inequality

Dependent variable: Gini index

	(1)	(2)	(3)	(4)	(5)
Unemployment Rate	-0.802 (1.020)	-0.255 (0.313)	–	-0.212 (0.000)	–
Corruption Perception Index	0.111 (0.181)	0.050 (0.053)	–	0.081 (0.000)	–
GDP per capita growth	-0.325 (0.196)	-0.127 (0.070)	–	-0.163 (0.000)	–
School enrollment - Secondary	–	0.069 (0.014)	–	–	–
School enrollment - Primary	–	–	–	–	–
Democracy index	–	–	–	–	–
Current health expenditure - share of GDP	–	–	–	0.247 (0.000)	–
Tax revenue - share of GDP	–	–	–	–	–
Observations	7	7		6	
R-squared	0.96	1.00		1.00	

Note: Equations 3 and 5 were omitted due to an insufficient number of observations. Numbers in parentheses represent standard errors.

*p < 0.1 ;
**p < 0.05 ;
***p < 0.01

Figure 6 shows the regression table for only Vietnam. None of the variables in the regression equations for this table produced significant results. This can likely be explained by the small sample of data collected for this country, as it was difficult for me to procure enough high-quality data for Vietnam and the specific variables. While this reason is likely to be the most accurate reason for an absence of significant results, multicollinearity is still a potential reason or the relationship between the independent variables and the Gini index may be non-linear (for instance, U-shaped), or there might be unique situational economic and social dynamics that are

A regression graph for Vietnam was not included in the results due to the insignificance of the regression results.

Conclusion and Policy Recommendations

This paper investigated the relationship between corruption & additional variables and income inequality in the Philippines, Thailand, and Vietnam from 1970 to 2023 using Ordinary Least Squares. The results of this paper highlight important findings about the impact of corruption and socioeconomic factors on income inequality in these countries.

Firstly, corruption has a significant negative effect on income inequality across the three countries combined. This means as corruption decreases (the CPI increases), income inequality will also decline, which supports the theory that corruption makes economic disparities worse by undermining resource allocation and government efficiency. However, the relationship between corruption and inequality tends to be less clear when additional variables like the Democracy Index and health expenditure are added, especially in the Philippines and Thailand. This suggests that the impact of corruption is greater when a smaller set of variables are added.

The unemployment rate and secondary school enrollment largely had significant negative correlations with income inequality, which reaffirms their role in addressing economic disparities. Their significance tended to fluctuate slightly across equations, especially in Thailand and the Philippines, which might signal issues regarding the robustness of the results. It was interesting to see that primary school enrollment had a counterintuitive positive correlation with income inequality, especially in the Philippines. This may be due to the disparity in primary education quality between socioeconomic groups or between urban and rural areas, which might limit its effectiveness in reducing inequality in these three countries. Health expenditure had a significant negative correlation with income inequality, which indicates that more investment in public health will likely contribute to reducing economic disparities.

For Thailand specifically, tax revenue and income inequality's relationship was significant but showed an unexpected positive correlation. This might suggest inefficiencies in the redistribution of tax revenues or fiscal policies that worsen income inequality. Vietnam, however, did not have significant results in any of the equations, which is likely due to the small sample size and potential multicollinearity.

Because of the strong negative correlation between corruption and income inequality, a priority to reduce corruption should be taken in these countries. This can be done by having greater transparency in public spending and creating or making better anti-corruption agencies. The strange positive correlation between primary school enrollment and inequality likely signals a need for better quality and accessibility of primary education, especially for poor and rural populations. Better education can improve economic opportunities for these groups and hence reduce income inequality. I would also suggest greater investment in healthcare in order to expand access to it, especially for low-income groups. In Thailand, the positive relationship between tax revenue and inequality might signal a need for better tax redistribution mechanisms, so that it is being used to promote economic equality instead of making it worse. Additionally, more research and data collection in Vietnam would aid in the revealing of the causes of income inequality in the country.

To conclude, this paper affirms the relationship between corruption, education, health expenditure, and fiscal policy play important roles in affecting income inequality in Southeast Asia. Better policies such as anti-corruption policies, education reform, and investments in healthcare are recommended to promote more equality in this region.

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The Relationship Between Sleep Spindle Characteristics and Working Memory Load
By Anya Pramanick

Abstract

   The present study explores the relationship between the characteristics of sleep spindles during non-rapid eye movement (NREM) sleep and working memory load. Sleep spindles, oscillatory events occurring between 10-16 Hz, are associated with memory consolidation, but their connection with working memory load requires more research. Using electroencephalography (EEG) data from 17 subjects who performed a working memory task and then took a nap period where the EEG data recorded, sleep spindles were auto-detected and analyzed for various characteristics, including power spectral density (PSD), amplitude, duration, and total count, across different working memory loads. The present study utilizes the filter-based and thresholding (FBT) model to identify sleep spindles and compares spindle characteristics between low and high memory loads (Load 2 and Load 5). The results indicate significant differences in spindle power spectra across multiple spindle frequency bands. There was also a significant difference between the upper quartile of high amplitude sleep spindles between both memory loads in each subject. The findings suggest that differing working memory loads influence sleep spindle activity. They also show the potential role of sleep spindles in altering working memory which can lead to further investigation into their neural mechanisms and methods such as sleep spindle manipulation for the improvement of memory.

Introduction

   The role of sleep in the facilitation of memory processes has been long debated. One theory concerning the influence of sleep on memory consolidation is through neural events that occur during sleep called sleep spindles[1]. Sleep spindles refer to brief oscillatory events that recur periodically in mammalian brains during non-rapid eye movement (NREM) sleep. NREM sleep has three stages: N1 (drowsiness), N2 (light sleep), and N3 (deep and restorative sleep) which make up about 80% of a normal night's sleep[1]. Sleep spindles during NREM sleep appear as a burst of electrical activity in the brain in a sequence of 10-16 Hz sinusoidal cycles and are identified using electroencephalography (EEG). EEG measures activity in different areas of the brain using electrodes that are attached to the subject's scalp. The brain's electrical activity is measured through neural oscillations, which can be studied for patterns or unusual activity. Sleep spindles last between 0.5 to 3 seconds and are characterized by a pattern of high frequency sinusoidal curves of higher amplitude between low frequency waves with lower amplitude (see Figure 1).

Figure 1: Sleep Spindle Visual
This figure shows what a sleep spindle oscillation looks like when looking at EEG data.

They are primarily prevalent in Stage 2 sleep and are considered the hallmark of Stage 2 NREM sleep, but can be found in any stage of NREM sleep; however, they are not found in rapid eye movement (REM) sleep. REM sleep is rather known for rapid movements of the eyes and dreaming[4]. Sleep spindles are predominantly local thalamocortical events and can be categorized by their frequencies into fast and slow spindles. Fast spindles are frequencies higher than 13 Hz and are prevalent in the centroparietal region of the brain. On the other hand, slow spindles are frequencies lower than 13 Hz and are found in the frontal region of the brain.

The purpose of sleep spindles has been extensively researched, where sleep spindles are found to correlate with memory consolidation in both humans and animals across many studies[1]. For example, Sejnowski & Destexhe (2000) discovered through experimental models that spindle-like activity induces huge influxes of calcium ions into cortical pyramidal cells as well as triggers intracellular mechanisms involved with long-term potentiation—a neural mechanism of memory[2]. Manoach & Stickgold (2019) found that spindle deficits in schizophrenia patients correlate with impaired sleep-dependent memory consolidation[3].

Manual annotation has been used to identify sleep spindles, but it is time consuming and suffers from substantial intra- and inter-rater variability[4,5]. Because of this, auto-detection methods of identifying sleep spindles have been researched and developed. Kaulen et al. (2022) presents a U-Net-type deep neural network model to automatically detect sleep spindles based on a consensus of manual spindle annotations[4]. Mei et al. (2017) developed and evaluated an optimized filter-based and thresholding (FBT) model and machine learning models using naïve features. Machine learning models derived from the FBT model are shown to improve sleep spindle classification. The automated approach applied to a DREAMS dataset and a public dataset provided by Ellmore et al. (2016) shows excellent sensitivity and can classify spindles across multiple channels, which has the potential to accelerate and improve the objectivity of manual annotation[6]. The FBT model is designed to classify spindles with parameters that capture temporal and spectral characteristics of the EEG representations of spindles such as frequency, duration, amplitude, and total number of spindles.

The FBT approach was utilized by this study to auto-detect sleep spindles in the public dataset provided by Mei et al. (2017)[5]. The dataset is part of a larger study by Ellmore et al. (2016) examining the effect of memory load on the generation of sleep spindles. [5, 6] For this experiment, 41 subject completed memory tasks both before and after nap EEG recordings. Over the course of two days, subjects came in at the same time each day for a two-hour session (a total

of four hours of participation in the experiment). During sessions, subjects performed a Sternberg working memory paradigm task which was either high load (Load 5) or low load (Load 2). These trials had two to five naturalistic scenes presented for 2 seconds each. After each presentation of scenes, there was a 6 second delay with a blank screen. Then, a probe stimulus is shown for 2 seconds. If that probe stimulus was a part of the original set of scenes, subjects had to press the left (green) button on a response pad; if the probe was not a part of the original set of scenes, subject had to press the left (red) button on the response pad. The load order for testing sessions was randomized. The subjects then performed a recognition test and took a short nap in a sound-attenuated chamber while continuous EEG recording was conducted. Subjects performed another recognition task after the short nap. While Mei et al. (2017) used this dataset to develop their FBT model and algorithm, the authors did not analyze if there was an association between sleep spindle characteristics during the nap period with the load level of the working memory task. The purpose of this investigation is to determine how characteristics of sleep spindles relate to working memory load. The present paper is studying sleep spindles after a recognition task with differing memory loads.

Much research has been done on the relationship and correlation between sleep spindles and memory consolidation, but less research has been done on the relationship between sleep spindles and working memory. Zhu et al. (2023) found that the power spectral density (PSD) of fast and slow spindles in the group of patients with obstructive sleep apnea syndrome (OSAS) was significantly reduced compared to the healthy control group and that sleep spindle PSD was positively correlated with working memory[7]. PSD is a measure used in signal processes, like EEG analysis, to describe how the power of a signal, or sleep spindle in the present study, is distributed across different frequency components. Zhu et al. (2023) also investigated omega complexity (Ω-complexity) and its differences between the OSAS group and the control group. Omega complexity is a measure used to quantify how complex a time series data is, especially with EEG signals. Memory-related cognitive functions were assessed for both groups: logical memory, digit ordering, pattern recognition, spatial recognition, and spatial working memory. Spindle hyperconnectivity in the prefrontal and central regions was also found to underlie declines in working memory. The working memory tasks used included tests from the Cambridge neuropsychological test automated battery (CANTAB): Digit Ordering Test (DOT), Logical Memory Test (LMT), Pattern Recognition Memory (PRM), Spatial Recognition Memory (SRM), and Spatial Working Memory (SRM). The complexity of the spindles in the prefrontal and central regions decreased significantly.

There is a need for further research into the association of working memory with sleep spindles. The analysis of the present study utilizes the FBT algorithm by Mei et al. (2017) to identify spindles across 30 channels from the working memory dataset from Mei et al. (2017) and determine if there are differences in PSD, amplitude, duration, frequency, and/or total count[5]. The study highlights that sleep spindles during NREM sleep are linked to memory consolidation, but their specific relationship with working memory is yet to be explored further. Research indicates a correlation between spindle power spectral density (PSD) and working memory,

particularly in obstructive sleep apnea patients. Further research is needed to investigate the characteristics of sleep spindles (e.g. frequency, amplitude, duration) in relation to working memory, especially in healthy individuals. Understanding these characteristics could deepen our knowledge of how sleep spindles affect cognitive functions like working memory. With the results of this paper, scientists can have additional information to research how to improve working memory through characteristics of sleep spindles. Novel sleep spindle manipulation methods to improve working memory can lead to sleep spindle manipulation in dementia, OSAS, and other relevant. This paper gives the general and scientific community an understanding that sleep, specifically NREM sleep, and sleep spindles are influenced by working memory, in addition to memory consolidation.

Electroencephalography (EEG) data from 17 subjects who performed a working memory task and then took a nap period where the EEG data recorded in a public data set, sleep spindles were auto-detected and analyzed for various characteristics, including power spectral density (PSD), amplitude, duration, and total count, across different working memory loads. The present study utilizes the filter-based and thresholding (FBT) model to identify sleep spindles and compares spindle characteristics between low and high memory loads (Load 2 and Load 5). Data analysis was performed using Python but was limited to Jupyter Notebook's free resource. The scope of this research is limited to the data availability in the data set.

Methods

The Nap EEG data set is available on Open Science Framework (OSF) (https://github.com/nmningmei/Get_Sleep_data). Briefly, these EEG recordings were taken after the subjects completed a working memory task (described above). The dataset includes 17 subjects recorded on two separate days (6 female, mean age 25.5 +/− 7.03 standard deviation, range 18 − 42 years old). 64 channels of EEG data, including 2 electrooculography (EOG) electrodes, were recorded continuously at 1 kHz sampling rate with an antiCHamp active electrode system (Brain Products, GmbH). Subjects took a short nap on a bed inside a sound-attenuated testing booth (IAC industries). The experiments were done in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki). Subjects gave written informed consent and completed the procedures of the study according to a Institutional Review Board of the City College of New York approved protocol.

All analyses were performed using Python version 3.10.9. First, data was pre-processed to remove artifacts as described in Mei et al. (2017)[5]. Artifacts were corrected using independent components analysis using an automated pipeline that utilized the MNE package[8]. The sleep spindles were auto-detected using machine learning models derived from the optimized FBT model created by Mei N. et al. (2017)[1]. The auto-spindles for each subject and each day were manually checked for accuracy and then processed to determine their onset, amplitude, duration, and total count. Onset, amplitude, and duration were calculated using the FBT model. The total count was calculated manually by the number of auto-spindles detected per subject per day. Q-Q plots and the Shapiro-Wilk test were used to determine the normality of the data. Median

amplitude and duration for each subject on each day were calculated due to the distributions being right skewed. The Wilcoxon signed-rank test was used for assessing statistical significance between the repeated measures (Load 2 vs. Load 5) for amplitude and duration, and a paired sample t-test was used for assessing statistical significance for the total spindle counts.

A time-frequency analysis of EEG spindle events was also conducted to compare neural oscillatory activity between the two working memory loads. To facilitate the time-frequency analysis, a filtering and thresholding approach was used that segmented the continuous EEG recordings into epochs centered around the identified spindle events. The time-frequency representations (TFR) of the spindle events were calculated using a moving windows approach. The moving window step size was 0.25 seconds and the window duration was 1.5 seconds to balance temporal resolution and capture full spindle events. Power spectral density (PSD) values were extracted from the TFR data, showing the distribution of power across different frequency bands for each spindle event.

To assess the statistical significance of the differences in spindle power between Day 1 and Day 2 of each subject, mean power was calculated across frequency bands by averaging the PSD data over the duration of the spindle and across EEG channels. The Shapiro-Wilk test and Q-Q plots were used to check for normality in the power distributions within each frequency band. Because distributions were non-normal, the Wilcoxon signed-rank test was used to compare spindle power for each frequency band (1 through 61) between the two days (Load 2 vs. Load 5). A False Discovery Rate (FDR) correction was used to account for the multiple comparisons performed across the frequency bands. The FDR correction helps control the rate of type I errors, ensuring that the reported significant differences are not simply due to chance. The statistical threshold is $p < .05$.

Results
Amplitude, Duration, and Total Sleep Spindle Count

The medians of the amplitude and duration of all auto-spindles was used to calculate statistical significance as the data is skewed right for both plots. The median amplitude for Load 2 was 0.000009545 microvolts (MAD = [6.61754E-06]) and for Load 5 it was 0.000009645 (MAD = [6.19255E-06]), which was not statistically significant (p = 0.904) (refer to Figure 2). The median duration for Load 2 was 0.000009545 microvolts (MAD = [6.61754E-06]) and for Load 5 it was 0.000009645 (MAD = [6.19255E-06]), which was not statistically significant (p = 0.256) (refer to Figure 3). The total spindle counts were uniformly distributed for both Load 2 and Load 5; the difference in total spindle counts between Load 2 and Load 5 was not statistically significant (p-value = 0.7745855854173527) (refer to Figure 4). However, total sleep spindle counts were generally greater in Load 5 in comparison to Load 2. Statistical significance was found on the absolute differences between the total spindle counts for Load 2 and Load 5 with the Wilcoxon Signed-Rank Test on Absolute Differences (statistic=0.0, p =1.526e-05).

The amplitude distribution and duration distribution using all auto-detected sleep spindles were graphed by their amplitude or duration and frequency using histograms on the same axis and were overlaid; a difference in the maximum spindles amplitude between the two loads was shown (refer to Figure 2). To look into this difference further, the number of high amplitude spindles was taken as a percentage of the total spindles to normalize the spindle count for each day. In post-hoc testing, it was discovered that the distributions of Load 2 vs. Load 5 amplitudes appear different, with more higher amplitude sleep spindles in Load 5. The top 25% of high amplitude spindles was greater in Load 5 than the top 25% of high amplitude spindles in Load 2.
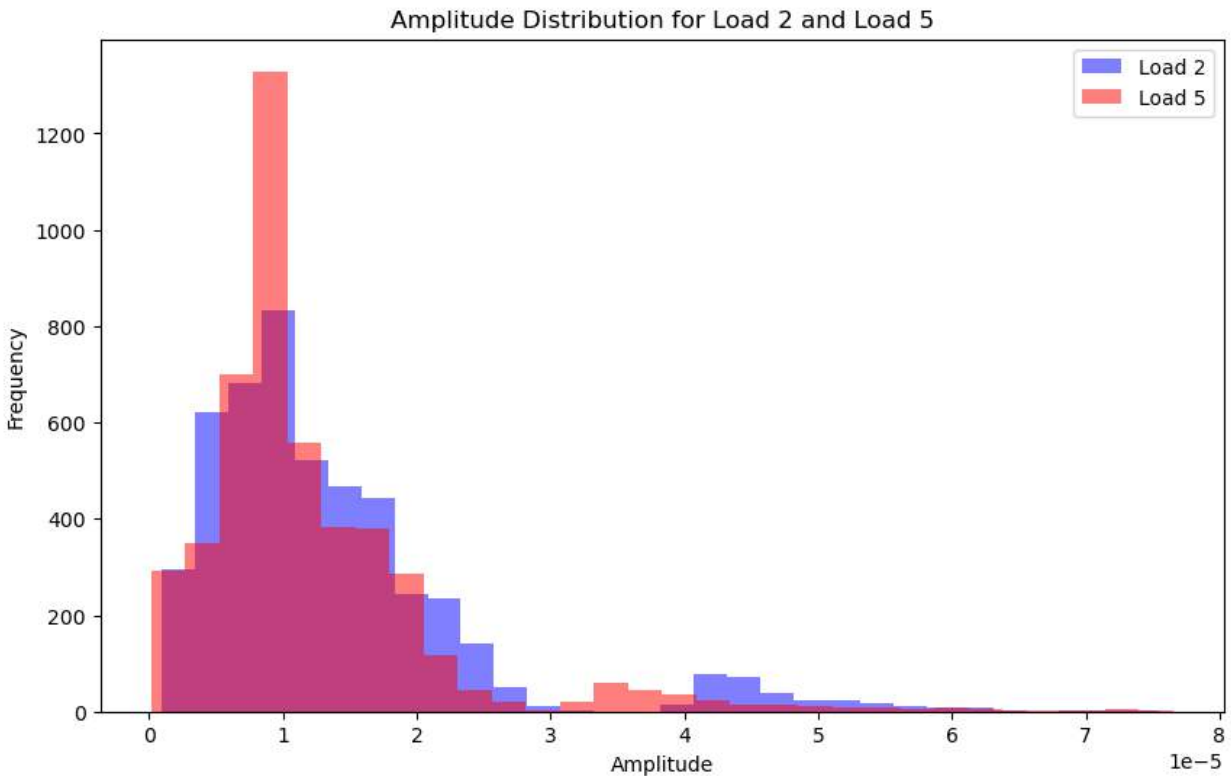

Figure 2: Amplitude Distribution for Load 2 and Load 5
This figure shows the amplitude distribution against frequency for Load 2 and Load 5 across all subjects.
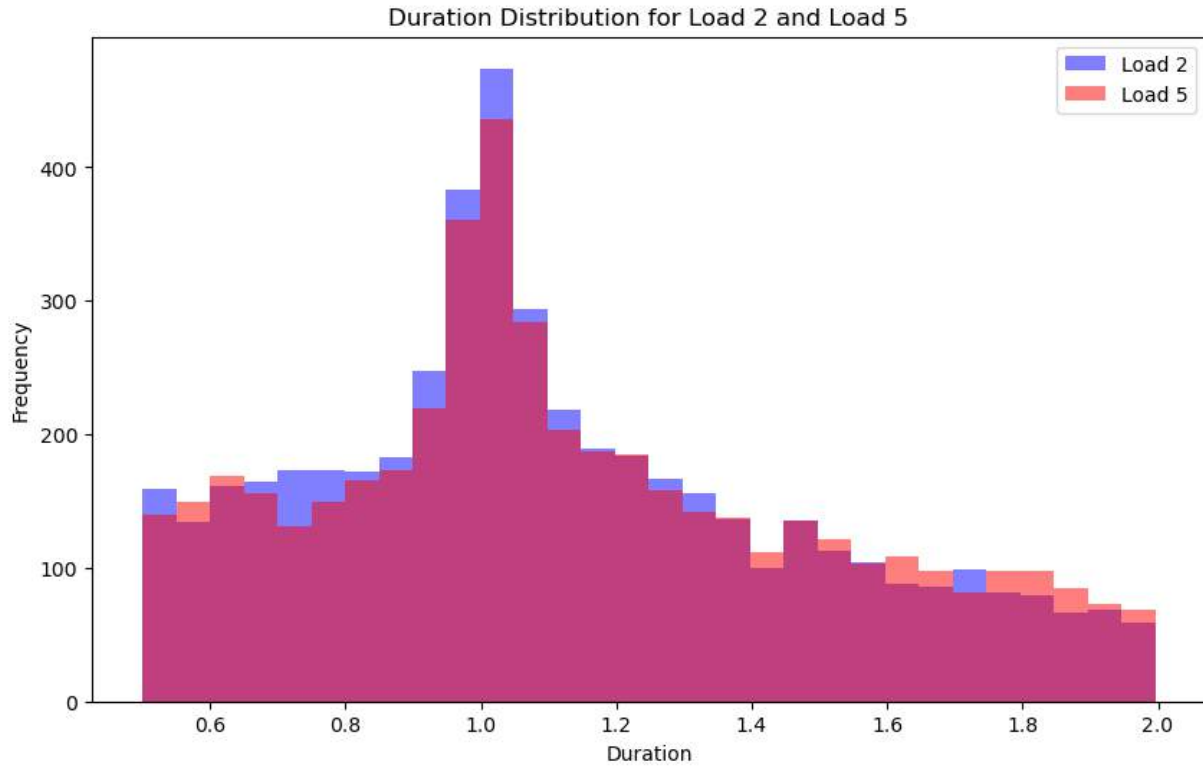
Figure 3: Duration Distribution for Load 2 and Load 5
This figure shows the duration distribution against frequency for Load 2 and Load 5 across all subjects.
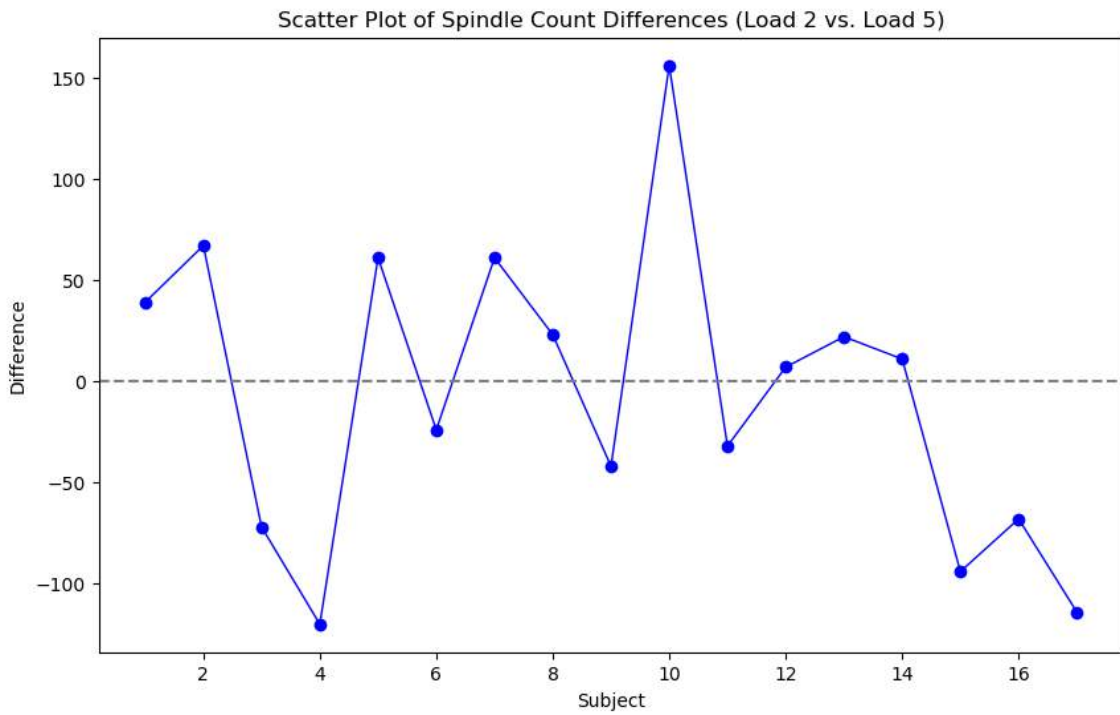

Figure 4: Scatter Plot of Spindle Count Differences Between Load 2 and Load 5

The figure shows the graph of the scatter plot of spindle count differences between Load 2 and Load 5, with the difference being calculated by subtracting Load 2 total spindle count from Load 5 total spindle count.

Power Spectral Density and Frequency Bands

Statistical testing revealed several frequency bands that had statistically significant differences in spindle power between Day 1 and Day 2 and therefore statistically significant differences in spindle power between the conditions of Load 2 and Load 5. After applying FDR correction, specific frequency bands were identified where the difference in spindle power remained significant, suggesting potential alterations in neural oscillatory events and dynamics between Day 1 and Day 2, and between Load 2 and Load 5. The frequency bands that had statistically significant differences in spindle power between Day 1 and Day 2 and therefore statistically significant differences in spindle power between the conditions of Load 2 and Load 5 with p-value < 0.05 include: frequency band 15 ($p = .022$), frequency band 16 ($p = .021$), frequency band 17 ($p = .049$), frequency band 19 ($p = .032$), frequency band 22 ($p = .045$), frequency band 35 ($p = .039$), frequency band 46 ($p = .041$), frequency band 47 ($p = .026$), frequency band 49 ($p = .037$), and frequency band 50 ($p = .009$) (Wilcoxon Signed-rank Test). Since some potential outliers in the p-values of the data from both sides may have skewed the calculated means, total counts were also taken of the number of subjects that had p-values < 0.05 for that specific frequency band. The threshold for the number of subjects with a p-value of 0.05 for a specific frequency band to be considered significant was 9 subjects out of the 11 subjects. These frequency bands include: frequency band 3 (9 subjects), frequency band 4 (9), frequency band 7 (9), frequency band 8 (9), frequency band 11 (9), frequency band 12 (9), frequency band 15 (10), frequency band 17 (9), frequency band 19 (10), frequency band 20 (10), frequency band 24 (10), frequency band 37 (9), frequency band 39 (9), frequency band 43 (9), frequency band 44 (9), frequency band 46 (9), frequency band 48 (9), frequency band 49 (10), frequency band 50 (10), and frequency band 58 (9).

To complement the statistical analysis, the mean power spectra of spindle events for both Day 1 and Day 2 across the frequency bands for Subject 11 are visualized as an example (refer to Figure 5). This was achieved by plotting the average spindle power for each frequency band, providing a clear graphical representation of how spindle activity varied between Day 1 and Day 2, and therefore between Load 2 and Load 5.
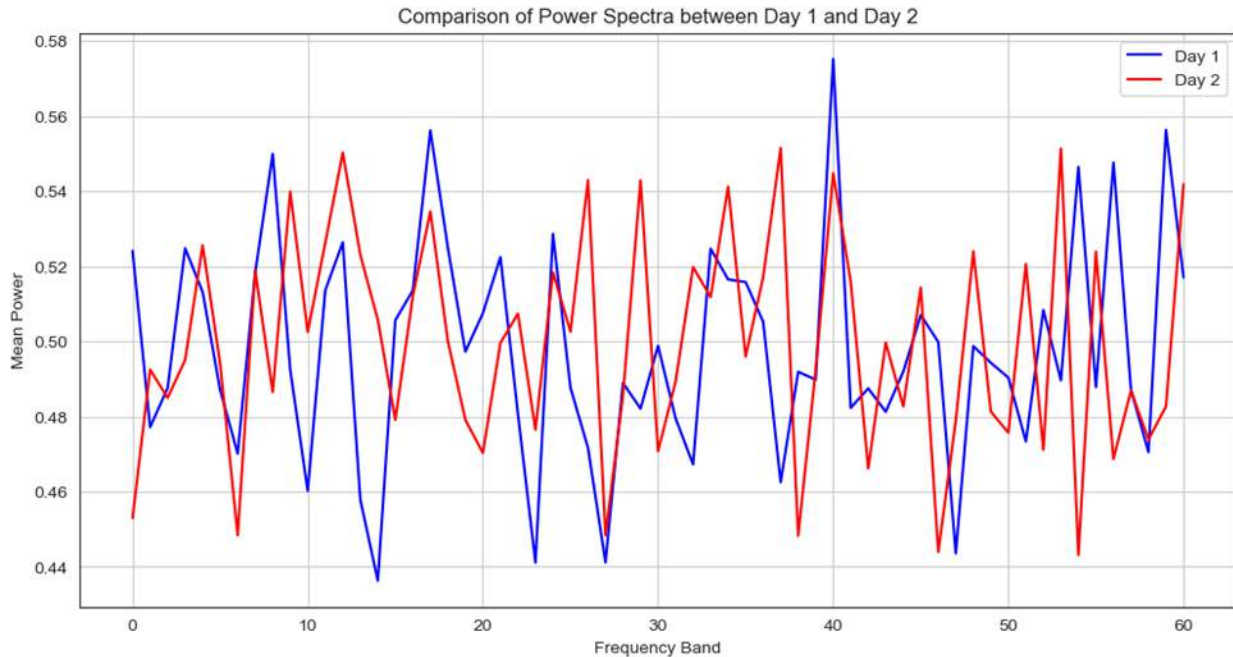
Figure 5: Comparison of Power Spectra between Day 1 and Day 2
This figure shows the distribution of the power spectra in the 61 frequency bands analyzed for day 1 and day 2 for Subject 11.

Discussion

In the present paper, statistical analysis revealed significant differences in spindle power across multiple frequency bands between Day 1 and Day 2, and thus between Load 2 and Load 5. Following FDR correction, differences in many frequency bands were still found to be statistically significant, suggesting changes in sleep spindle activity between conditions. In the power spectral density (PSD) data, frequency bands 15, 16, 17, 19, 22, 35, 46, 47, 49, and 50 were significant ($p < 0.05$) using the Wilcoxon Signed-Rank Test. Given potential outliers in p-values, the number of subjects with p-values < 0.05 for each frequency band was also calculated with a threshold of 9 out of 11 subjects indicating significance. Frequency bands 3, 4, 7, 8, 11, 12, 15, 17, 19, 20, 24, 37, 39, 43, 44, 46, 48, 49, 50, and 58 met this criterion.

Amplitude and duration distributions revealed more high-amplitude spindles in Load 5, with a greater percentage of top 25% spindles in Load 5 compared to Load 2. Despite this, there was no statistically significant difference in median amplitude and duration between Load 2 and Load 5. Total spindle counts were similarly distributed across both loads, but the Wilcoxon Signed-Rank Test on absolute differences in counts demonstrated statistical significance ($p < 0.05$).

These findings suggest that although spindle amplitude and duration remain relatively consistent, there are significant changes in specific frequency bands and power spectral density when the working memory load is altered. This highlights that sleep spindle events can vary between different working memory loads. Further investigation into amplitude, duration, and spindle power can build upon these results.

The results of the data analysis go hand in hand with the results of the Zhu et al. study on the relationship between sleep spindle activity and memory ability in Obstructive Sleep Apnea-Hypopnea Syndrome (OSAS) patients[7]. Utilizing PSD and omega complexity to analyze the characteristics of brain regions of sleep spindles and assessing memory-related cognitive functions (logical memory, digit ordering, pattern recognition, spatial recognition and spatial working memory), sleep spindle PSD was found to be positively correlated with working memory. In this paper's data analysis, mean p-values across subjects identified specific frequency bands from spindle PSD data as statistically significant.

These results are significant because they can lead to research on sleep spindle manipulation or using sleep spindles to improve working memory and memory consolidation. It also further confirms the finding that working memory and sleep spindles have a relationship. One limitation of this study was using the publicly available EEG dataset that had a small number of subjects, so my analysis was limited to these subjects. Future research should be performed on a larger cohort of subjects and could investigate other types of working memory tasks with different conditions. The next steps would be to use a larger sample size to confirm these results and use that information to start more research on sleep spindles and their relationship with memory altogether. This research paper can help scientists gain an understanding of how sleep spindles and working memory relate and can lead to future research on how to improve working memory in patients such as OSAS patients and dementia patients by working with sleep spindles through manipulation or other methods. In the paper by Astori et al., the authors state that spindles appear to be an area for selective manipulation that spare other sleep rhythms with recent technological advancement[9]. Also, genetic manipulation of T channels and SK2 channels has proved to assist in selectively modifying sleep spindles. The study shows that CaV3.3 and SK2 channels are promising targets for the goal of spindle manipulation through manipulating the nRt intrinsic oscillations in these channels that underlie spindle generation in mice. However, the only published papers in relation to sleep spindle manipulation have been tested on rodents.

With the additional information found in this paper, scientists can have additional information to research neurobiological and other factors that influence sleep spindle PSD and frequency bands, high amplitude, etc. Finding these factors can allow for further discovery of methods of manipulation of sleep spindles, an area that hasn't been researched greatly. Finding novel methods of manipulating sleep spindles can lead to sleep spindle manipulation in dementia, OSAS, and other relevant patients to improve memory and sleep. This paper gives the general and scientific community an understanding that sleep, specifically NREM sleep, not only relates to memory consolidation but is also influenced by working memory load prior to sleep. This is important as high load generally leads to an increase in spindles, an increase in spindle PSD great difference in frequency bands, greater high amplitudes, and more. This can also lead to research about how working memory can be improved based on the knowledge of what characteristics of sleep spindles are related to working memory. This could be a source of hope for dementia patients as well as other memory deficiency issues.

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Unlocking the Potential of mRNA Therapies: A Review of Design and Targeted Delivery
By Wuyan Li

Abstract

The review article brings out the various possibilities of mRNA vaccines in treating certain diseases including Covid-19 and Cystic Fibrosis (CF) and also the use of mRNA in synthesizing chimeric antigen receptors in treating cancer. mRNA are single stranded nucleic acids that contain a sequence of nitrogenous bases which stands for a certain protein. Recent studies and proposals indicate that the mRNA molecules act as versatile molecules in gene regulation. mRNAs can be used to synthesize any protein in the transfected cells by using the process of protein synthesis. This way they have the ability of focusing on several diseases at once and make the right protein for the right disease. Because of their applicability in curing diseases, in vivo tests on mRNA-based drugs have been proven to transform cancer and genetic disorders treatment. In this review article, the author discusses the different ways through which mRNA has been altered in order to enhance the therapeutic application of the material, and how mRNA has been implicated in many diseases. This article also looks at why the mRNAs vaccines have been the most efficient and simultaneously the most promising in genetic therapies. The notion of changing mRNAs for particular proteins may help elucidate the process to generate favorable sequences for the development of targeted therapies.

Intro

Genetics and biotechnology has led to the discovery of many new medical therapies. mRNA vaccines have been identified as anutshelletic therapy for many diseases to be used as vaccines. These vaccines have proven to have a high potential of curing diseases such as CF and also synthesizing CARs to cure cancer. In a nutshell, CF is a disease which is result of a single gene mutation of the protein called cystic fibrosis transmembrane conductance protein (CFTR). A particular mRNA sequence will produce an accurate copy of CFTR and this will be transported to the cells with a view of manufacturing a proper and healthy CFTR protein (Cystic Fibrosis Foundation). mRNAbased vaccines can be rapidly designed by the researchers. A more detailed view of a single messenger RNA (mRNA) molecule shows that there are several features that can affect translation and efficiency of the process. Some of these are the 5' cap, the 3' poly (A) tail, and the 5' and 3' untranslated regions (5' and 3' UTRs). Another benefit of this therapy is that it does not produce other proteins coded by the different mRNA sequences before being synthesized by in vitro transcription. One benefit is that only healthy protein is manufactured for a short time through in vitro transcription to treat the disease and there is no chance of genomic integration (Kim et al., 2021). It is possible to expand the list of possible treatments for other diseases as well. New mRNA medications may be created from the existing technology through a modification of the nitrogenous base template DNA sequence. Most of the diseases that are being reported today as critical have been estimated to have the possibility of being treated through the use of mRNA therapies. As you may recall from the introduction, CF is

a genetic disease which is caused by the defective CFTR gene. 1 Some of them are dry cough, dyspnoea and chest pain. The next paragraph will shortly describe the function of mRNA encoding chimeric antigen receptors (CAR). This review focuses on the structural changes in mRNA vaccines that enable the efficient delivery of the molecule and protein synthesis—the treatments for CF and COVID-19 and the relationship with CAR T-cell therapies. The paper also seeks to establish the effectiveness and reliability of mRNA vaccines as opposed to other techniques of gene delivery. We examine the possibilities of using mRNA vaccines for the further development of the pharmaceutical industry and its impact on the future of medicine (Pardi et al., 2018).

Cap Structure

Before being transferred from the nucleus to the cytoplasm for protein translation, eukaryotic RNA undergoes several changes. mRNA capping, also known as 5'-capping, is a process that modifies the 5' end of messenger RNA (mRNA) to create a five-prime cap. Caps are needed to improve mRNA stability, processing, release, and translation (Shuman, 2002). The three-step process is controlled by RNA triphosphatase, guanylyltransferase, and methyltransferase. It adds a 7-methylguanosine (m7G) to the 5′ end of the mRNA and connects it to the first nucleotide (m7GpppN, Cap0) (Ramanathan et al., 2016). The three capping enzymes are coupled with RNA polymerase II, and this process takes place during transcription. The resulting 5′ cap then serves to control pre-mRNA spicing, the process of exporting out of the nucleus, to protect the RNA from exonuclease cleavage, and recruit translation initiation factors for protein production. The cap structure is also used to distinguish between self and non-self RNA molecules. Therefore, synthetic mRNA vaccines with modified cap analogs have to be made to imitate fully processed mRNAs and avoid being recognized as non-self and stimulate an immune response. Generally, there are four identified cap structures, which include cap 0, cap 1, cap 2 and the N6, 2′-O-dimethyladenosine (m6Am) cap (Andries et al., 2015). To evade immune responses, synthetic mRNAs need to achieve either cap 1 or cap 2 structures. Cap-0 is an N7-methyl guanosine connected to the 5′ nucleotide through a 5′ to 5′ triphosphate linkage, typically called m7G cap or m7Gppp-. Cap 1 is formed by the addition of a methyl group (-CH3) to the 2′-hydroxyl group (-OH) on cap 0, and subsequent 2′-O-methylation on the second nucleotide will form cap 2, which often exists in nearly 50% of transcripts (Figure 1). An innate immune receptor called Retinoic Acid Indueble Gene-I (RIG-1) recognizes uncapped RNAs or RNAs with cap 0. As mentioned above, RNAs with cap 1 modifications will remain unrecognized by RIG-1 (Ramanathan et al., 2016). Although most mRNAs possess the cap 2 structure, the molecular function of cap 2 mRNA are still extremely vague. One method is to produce cap 0 or cap 1 RNAs using vaccinia virus capping enzymes; this method is expensive. The other method used for RNA capping is adding a cap analog during transcription. This is the process of carrying a methoxy group (-OCH$_3$) in place of the 3' hydroxyl group. In a nutshell, the primary function of capping is to prevent the mRNA from degrading.
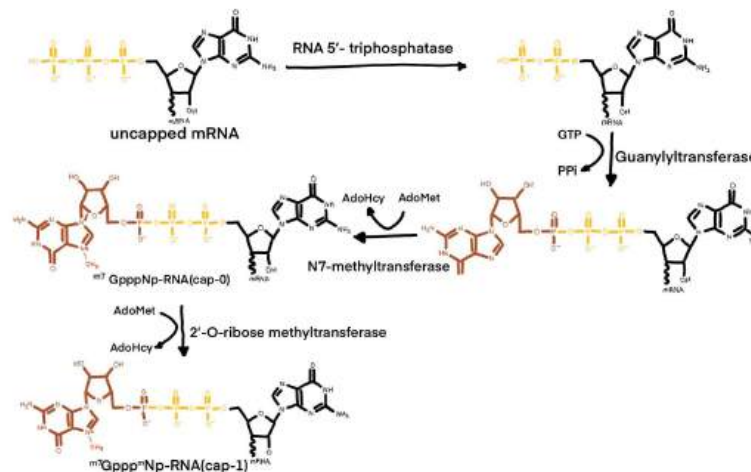
Fig 1: Three enzymes are needed to make post-transcriptional changes to mRNA with cap0: triphosphatase, guanylyltransferase, and N7-methyltransferase with S-adenosylmethionine (SAM) as the methyl source. The cap0 is then changed with 2′-O-ribose methyltransferase to make the cap 1 structure. *Image created with Procreate.*

Poly (A) Tail

The poly (A) tail also helps to stabilize the mRNA and the length of this tail has been claimed to influence the translation rates. Poly (A) tails are normally made of 10 to 250 ribonucleotides which are units of RNA molecule. First, poly (A) tail has to be added to a plasmid template (Nicholson et al., 2019). There are a number of methods which can be employed to incorporate the poly (A) tail to the template and one of them is PCR. For example, in the mRNA therapies, the poly (A) tail of about 100 nucleotides was preferred owing to the potential shortening of the molecule's half-life (Schlake et al., 2012). When the researchers found out that the poly(A) tail had a facilitative role in translation initiation, the assembly of polysomes was observed to increase gradually with the length of the poly(A) tail up to 68 nucleotides (Eckmann et al., 2010). Translation of in vitro produced mRNA was also observed to be slightly improved when the length of poly(A) tail was increased from 54 nucleotides to 98 nucleotides.

5′- and 3′-UTRs or Secondary Structures

mRNAs also consist of 5' and 3' UTRs the last structures of which differ from each other. These changes are important as they are involved in the process of stabilizing the mRNAs and also; affect the regulation of expression of proteins that are being synthesized. For example, the current study examines and confirms the broad use of approaches that use various 5′UTR and 3′UTR to enhance the production of Arginase 1 (ARG1) protein. This water soluble protein

works like an enzyme in the urea cycle, which is one of the amino acid metabolism pathways. As mentioned earlier, ARG1 is one of the proteins that have been defined to be an operational target of mRNA interference (Warren et al., 2010). The enhancement of overall protein synthesis of ARG1 was concluded to be due to translation rather than mRNA stabilisation. The term 5′ UTR and the 3′ UTR commonly referred to as mRNA UTR is very vital in the regulation of mRNA and its translation to proteins bodies. Warren and colleagues used artificial 5′ UTR with strong Kozak sequence which is a translation initiation site in eukaryotic mRNA which is derived from the transcription process Translation initiation site is a part of the 5′ untranslated region of mRNA which is derived from its transcription. A part of this sequence is integrated usually following the 5'-UTR sequence for efficient translation and the 3'UTR of the alpha-globin to enhance protein production as well as during the reprogramming of fibroblasts into the pluripotent stem cells (Asrani et al., 2018). As for the research objectives some findings were made. This increase of protein levels may be due to the up-regulation of the proteins' translation efficiency rather than the mRNAs' stability (Wang et al., 2023). Furthermore, the effect of changing 5′ UTR seems to be the most significant on protein synthesis rate (Ross, 2024).

Modified Nucleotides

The makeup of mRNA is also essential for the process of translation and codons represent it. The GC mRNA sequences that are related to the genes having a large number of guanine and cytosine nucleotides were proposed to be connected with the high rate of protein synthesis but not with the enhancement in the rate of translation. This is because it is now clear that GC sequences have higher transcription rates than the other sequences due to the fact that they are transcribed more often than the other sequences (Kudla et al., 2006). It was found that the presence of GC-rich sequence in mRNAs containing 5-methylcytidine (m5C) and pseudouridine (Ψ) increases the translation rate of mRNAs (Weng et al., 2020). In particular, mRNAs that code for the same polypeptide but with codon have been recognized to produce vastly different amounts of proteins. Such synonymous codons changes may influence such shape, change locations of post-translational modifications, change functions of proteins and even change conformation of the protein. Therefore it is expected that synonymous mutations should be associated with different hereditary diseases. Thus, to ensure the safety of the mRNA drug, future studies on the codon usage have to be carefully assessed especially in the regions where the changes of codons may affect the structures of RNA and protein. A key issue emerged with regards to the issue of immunogenicity of these drugs when used as vaccines and as protein replacements. Viral RNA molecules are automatically identified by cells through pattern recognition receptors that are present in cells and the identification is followed by signaling events. TLR3, TLR7 and TLR8 which are localized in the endosomal compartments recognize both, the double-stranded and the single stranded RNA (Figure 2) (Nance et al., 2021). However, the cytoplasmic receptors such as RIG-I and MDA-5 have the ability to recognize both the double stranded RNA as well as the RNA which is associated with 5'-triphosphate group. Vaccination is always good in the development of the immune response but sometimes over

activation of the immune response may cause an allergic reaction or anaphylactic shock. Another interesting finding is that human RNA contains molecular components such as pseudouridine, thiouridine and 5-methylcytidine which are biosynthetic modifications that decrease the immunostimulatory property of RNA (Karikó et al., 2005). More experiments were then conducted to determine whether such kinds of alterations in nucleobases may enhance the rates of protein synthesis from artificial mRNAs. Alterations of this kind have been beneficial in numerous areas including the creation of induced pluripotent stem cell. The advancement of this concept resulted in N1-Methylpseudouridine (m1Ψ) that was discovered to enhance protein synthesis and repress TLR3 in mRNA (Andries et al. 2015). At least three mechanisms have been proposed to explain how m1Ψ and other modifications that affect m1Ψ can decrease the immunogenicity of synthesized mRNA. The altered nucleotide assists the mRNA vaccines to escape the immune system's detection and thus prevent elicitation of an immune response. This may also lead to the enhancement of the synthesis of antigens by cellular structures involved in protein synthesis at certain times. Currently, the examined and applied mRNA vaccines are nucleoside-modified mRNAs, unmodified mRNAs, and optimized in sequence mRNAs. Such mechanisms involve the modulation of the activation of Toll-like receptors (TLRs), the retinoic acid-inducible gene I (RIG-I) like receptors, the protein kinase R (PKR) and the 2′-5′-oligoadenylate synthetase (OAS) by nucleoside-modified mRNA. Moreover, nucleoside change enhances the translation activity and provide defense against RNase L mediated degradation.
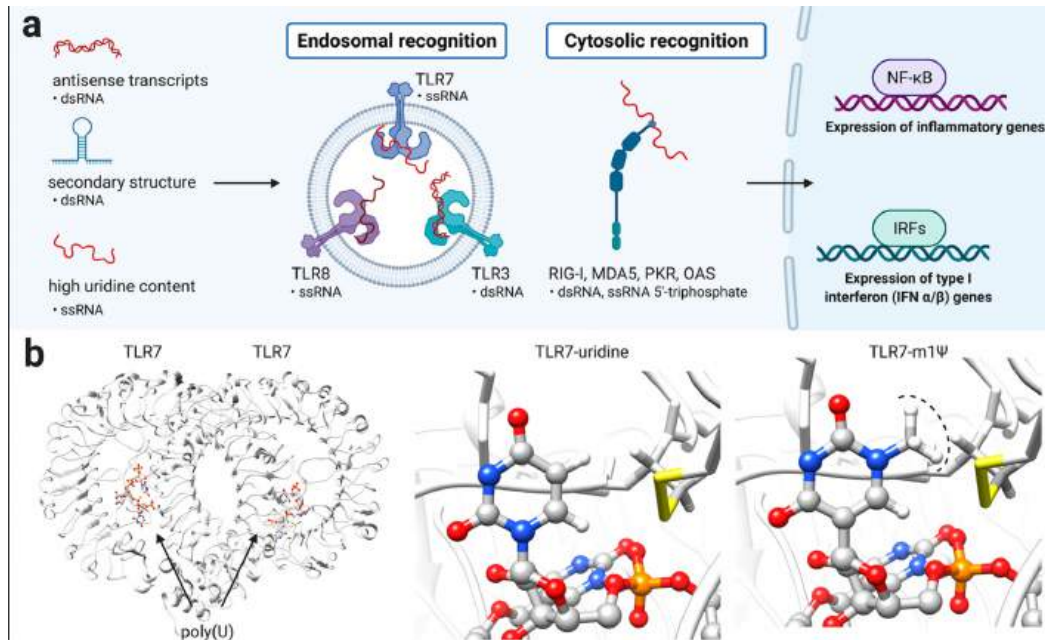
Fig 2: (a) Induction of the innate immune response by secondary structures of mRNA (b) The configuration of the TLR7 single-stranded RNA sensor when it is bound to a polyuridine (poly(U)) ligand. Substituting uridine with m1Ψ reveals the incompatibility of the altered nucleobase with TLR7 binding and immunological activation due to steric factors. Reprints with permission from Nance et al. (2006). *Copyright 2021 American Chemical Society*

Synthetic mRNA Vaccines

Mostly, mRNA vaccines are produced through in vitro synthesis through an enzymatic process. Functional synthetic mRNA may be prepared by in vitro transcription by using a cDNA, which is usually a plasmid DNA (pDNA), and a bacteriophage RNA polymerase (Krieg et al., 1984) For a plasmid DNA (pDNA) template that is used for transcription in a laboratory application, there is need to include a bacteriophage promoter, an open reading frame (ORF) and, optionally, poly(dA/T) which when transcribed becomes poly(A). Moreover, the template should have a special restriction site that will help linearize the plasmid, thereby having a specific transcription stop. The cap is not specified in the template (Juan Carlos Martínez et al., 2023). The RNA transcription process uses a pDNA template, recombinant RNA polymerase (T7, T3, or SP6) and nucleoside triphosphates to synthesize mRNA (Konarska, 1984). There will be need to cap the mRNA again. It issues a rapid degradation of uncapped mRNA and harbours a 5-ppp group, eliciting a robust immunogenic response (Galloway et al., 2019).

mRNA Isolation

It has been noted that a lot of RNA can be synthesized by in vivo transcription with DNA templates of phage RNA polymerase. Altered nucleosides are able to suppress the activation of the innate immune system and at the same time stimulate the process of mRNA translation. Nevertheless, there is still an ongoing activation of type I interferons (IFNs) and proinflammatory cytokines. Via dissection, one can establish that factors such as dsRNA in nucleoside-modified in vitro-transcribed RNA induce innate immunity. In order to remove these contaminants we have employed high-performance liquid chromatography (HPLC) and synthesised mRNA that does not induce IFNs and inflammatory cytokines (Karikó et al., 2011). Also, the specificity assays are based on the translation of these mRNAs in primary cells with rates that are 10- to 1000-fold higher than those observed in primary cells. Karikó et al. compared the effect of HPLC-purified mRNA on human dendritic cells (DCs). Lipofectin, a lipid-based delivery system, was used to introduce HPLC purified Ψ- or m5C/Ψ-modified RNA and transfection did not cause TNF-α or IFN-α and β production (Mant et al., 2007). The authors demonstrated that the enhancement of protein expression after HPLC purification is due to eliminating contaminants like dsRNA which activates the PRRs and subsequently leads to the downregulation of protein expression.

mRNA Delivery with Lipid Nanoparticles (LNPs)

LNPs have recently emerged as a potential tool for mRNA as well as many other gene therapies. LNPs contain an aqueous core which is surrounded by a lipid bilayer containing several lipids, each of which has a particular function (Reichmuth et al., 2016). The size and the efficiency of encapsulation of the mRNA in LNPs are dependent on the synthesis approach. Phospholipids, cholesterol and lipid anchor polyethylene glycol (PEG) are some of the lipids that are used in LNP formulation. The main function of LNP is structural and phospholipids has a vital part in this structure. They enhance the biophysical properties of lipid bilayer allowing for

its formation and disruption to promote endosomal escape. Generally, LNPs are synthesized by the process of mixing aqueous and ethanol solution of lipids and letting them undergo a process of condensation. According to the LNP synthesis method the mRNA is either in the liquid phase and encapsidated during condensation or is conjugated to the LNP after their formation in a separate step. The formation of vesicle hypothesis indicates that formation of LNP is based on the presence of disk shaped bilayer fragments with their edges being maintained by ethanol. A large number of LNP formulations rely on the cationic lipids to facilitate the interaction with the negatively charged RNA molecule. Nonetheless, it has been shown in various studies that the cationic lipids with long term positive charge are more toxic and less effective. Therefore, the researchers have now started to employ ionizable lipids. Such lipids are neutral in the normal pH levels in the body but they can take up a positive charge at a low pH level. Such a charge favours the formation of complexes between nucleic acids and lipids in an acidic buffer. When the complexes reach the target cells, they can fuse with the negative charged endosomal membrane; this fuses the lipid bilayer and releases the mRNA into the cytoplasm. Thus, LNPs can protect mRNA from degradation by enzymes. A positively charged LNP will increase the chances of mRNA to attach to the negatively charged cell membrane and can be taken up by endocytosis. Both the LNP and the endosome have to be crossed by the mRNA in order for it to be translated.

Tissue Targeting

The following are the strategies to enhance the effectiveness of the mRNA vaccines especially for organs such as the heart and lungs. To treat these organs it is crucial to have better delivery systems suited for each organ. Lungs are easy to access through the respiratory system and this can be done by inhaling hence the use of small amounts of drug with less side effects. Thus, Pulmonary delivery systems provide a rapid and non-invasive route to the Alveoli and the lung parenchyma. However, there are still some problems which have to be solved in order for the delivery to take place. The surface area of about 100 m2 and the protective mucosa on the epithelium of the lunch might decrease the effectiveness of mRNA delivery. A successful pulmonary RNA therapeutic must maintain the stability and the integrity of the mRNA. This entails being able to cross the mucosa barrier and enter the cells and then deliver the mRNA cargo.

Approximately twenty years since the first use of mRNA in live organisms, mRNA-based vaccinations have proven themselves to be a revolutionary method for treatment and prevention. The scientific community is currently anticipating the initial clinical outcomes' data. However, more advancement and enhancement can still be made in developing mRNA-based immunizations. The ability of antigen synthesis depends on the structure and uptake of the mRNA. Other factors include the novel RNA designs and the formulation as well as the distribution of the mRNA.

mRNA in Treating CF and Other Diseases

CF is one of the many genetic diseases which has given a ray of hope to mRNA therapies. CF is a genetic disease that shortens life expectancy and currently presents in more than 70,000 people across the globe. The condition arises from mutations in the coding region of the CFTR gene which codes for an ion channel namely the cystic fibrosis transmembrane conductance regulator and is involved in the transport of chloride ions from the apical surface of secretory epithelial cells. This is simply because the dysregulation of ion transport systems affects many organ systems, and as these fail, the patient dies within the shortest time. There is over 300 different types of mutations that lead to diseases and the diseases can progress in different ways. Some of the symptoms that are associated with this condition include; breathing difficulties which may include reduced moisture in the air sacs of the lungs, poor ability to clear mucus, long-term colonization of bacteria and lung disease. The main goal of creating drugs for CF is to correct the disrupted ion balance in patients' bodies. As discussed earlier, existing approaches employ altered nucleotides including m5C and Ψ. Then the LNP formulations contained the mRNA encoding human CFTR which was referred to as cmCFTR. These LNPs were able to introduce the cmCFTR mRNA into immortalized bronchial epithelial cells of patients. Therefore the cells were able to regain the normal movement of chloride ions.

It is a disease whose causative agent is the novel coronavirus, SARS-CoV-2, which primarily targets the respiratory system (Rohner et al., 2022). SARS-CoV-2 is one of the Betacoronavirus species and this virus is one of the RNA type viruses which has a single stranded RNA (ssRNA) positive sense enclosed in the envelope (Fang et al., 2022). In short, Covid-19 mRNA vaccines enable the body to produce antibodies to prevent the binding of viral membrane proteins to cell membrane proteins. As has been mentioned earlier, mRNA has a negative charge and is quite unstable, which is why it is usually encapsulated within a carrier to ensure that it enters the target cell.

For instance, during the case of the vaccine in which the mRNA is conveyed by lipid nanoparticles (LNPs), the mRNA is internalized only through endocytosis. This process does not in any way leads to the disruption of the cell membrane as it generates an endosome. After fusion with the plasma membrane the endosome is transported to the lysosome for breakdown. It has been established that ionizable lipids in LNP affect the mRNA release and its escape from endosomes. The head group of the ionizable lipid will be cationic in the acidic environment of endosomes. This mRNA then exits the endosome and gets into the cytoplasm and here the mRNA will follow the central dogma. It is synthesised from DNA by means of transcription and is translated into proteins by ribosomes and thus acts as an endogenous antigen. It is degraded in the proteasome to antigenic peptides. These peptides are then presented to CD8+ cytotoxic T cells via the Major Histocompatibility Complex (MHC) class I molecular pathway. This is the primary reason as to why mRNA vaccines are effective in the activation of cell-mediated immune responses.

However, the proteins that are synthesized based on the information contained in the mRNA molecules can be transferred to the extracellular environment and can be present in the

blood stream. After entering the circulation these proteins are endocytosed by dendritic cells, which are cells that antigenically activate other immune cells to initiate the adaptive immune response. The exogenous antigen is than processed and presented to CD4+Tcells through MHC class II molecules. The presenting process will also cause the cytokines to be released, which are forms of communication proteins in the body's cells. Also, it stimulates the B cells to produce and secrete antibodies that help neutralize the Covid-19 virus. (Figure 3)
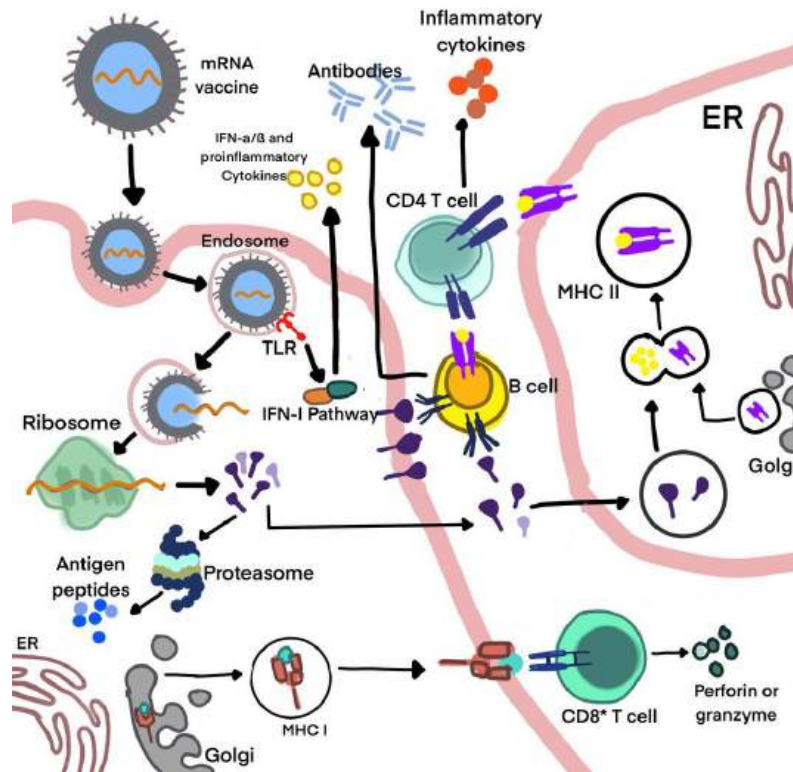

Fig 3: The mRNA in an mRNA vaccine is taken up by cells through endocytosis and, once released from the endosome, is converted into protein by ribosomes. Translated proteins can subsequently stimulate the immune system primarily through two mechanisms: i) Proteins undergo degradation by the proteasome, resulting in the formation of peptides. Major histocompatibility complex (MHC) class I molecules present these peptides on the cell surface. The MHC class I molecules bind to the T cell receptor (TCR), activating CD8+ T cells. The activated CD8+ T cells eliminate infected cells by releasing perforin and granzyme. ii) Proteins secreted outside the cell are taken up by antigen-presenting cells (APCs). The APCs then degrade these proteins into peptides, subsequently presented on the cell surface by MHC class II molecules. CD4+ T cells recognize these peptides and can activate cellular immune responses by secreting cytokines and humoral immune responses by co-activating B cells. Furthermore, mRNA vaccines contain single-stranded RNA and double-stranded RNA that attach to Toll-like receptor (TLR) in the endosome. This attachment triggers the activation of the body's natural antiviral immune responses by producing type-I interferon (IFN-I). As a result, various IFN-1-stimulated genes involved in antiviral innate immunity are induced. This process is referred to as the self-adjuvant effect of a sequence-engineered mRNA. *Image created with Procreate.*

Synthesis and Delivery of Chimeric Antigen Receptors

Another area of interest is the use of mRNA therapies in synthesizing of chimeric antigen receptor for T cells with a view of curing cancer through expression of receptors and interaction with tumor antigens to perform cell death. This has made the use of CAR-T-cell therapy to be very effective and have long term results. CARs also known as chimeric antigen receptors are artificial receptors which are programmed to guide lymphocytes especially T-cells to recognize and destroy cells with a specific antigen of interest. It is upregulated in a manner that does not require the interaction of the CARs with antigens presented on the cell surface by the MHC receptor. This results to effective stimulation of T cells and development of efficacious antitumor immunity (Sterner, 2021).

Numerous studies have been conducted in an attempt to discover other techniques of gene transfer which are feasible, accurate, efficient, and safe. The use of mRNA to achieve CAR expression on the surface of T cells for a short period is a viable non-viral option to the problems faced with CAR T cell treatment. Similar to the CF, the CARs have adopted the use of LNPs in order to transport mRNA into the immune cells. To this end, in the year 2020, C14-4 LNPs, a synthetic mRNA delivery carrier was developed to create CAR T cells. The experiments were performed using primary human T cells treated with CAR mRNA encapsulated in C14-4 LNPs; this method yielded comparable CAR expression and cancer cell killing compared with the use of electroporation. Nevertheless, the cytotoxicity of treatment with LNPs was significantly lower than in the other groups (Billingsley et al., 2020).

Although many years of development and enhancement, LNPs have shown great promises in being a great carrier for therapeutic agents. It has been observed that they have enhanced capability to transfer genetic material and have over time lessened the damage they cause to cells. The two CAR-T cell engineering strategies have the possibility to treat cancer (Figure 4). The results presented here show that the LNP are able to effectively deliver the mRNA to the primary human T-cells, which in turn translated to functional and healthy proteins. LNPs have been also reported to increase the efficiency of CAR and the efficacy of CAR T-cell therapy. Subsequently, A. G. Hamilton et al. attempted to transfer CAR mRNA and siRNA targeted to PD-1 (CD279) to T cells at the same time by means of C14-4. The aim was to engineer the CAR-T cells to have short CAR expression time and blocking the PD-1 signal at the same time. This was done in controlled conditions, that is in the laboratory (in vitro) (Schlake et al., 2012). PD-1-The PD-1 is a receptor that is situated on the surface of T cells and it is involved in the control of apoptosis that is the process of cell death. The study team optimized the C14-4 formulation and developed a method to deliver mRNA and siRNA at the same time and established the best combination for protein expression. It was also observed that addition of siRNA improves the C14-4 mediated mRNA transport and leads to the synthesis of more IVT mRNA. The results showed a 15% improvement of the delivery efficiency of C14-4 for co-entrapping the mRNA and siRNA than the LNP that only contain the mRNA (Zhang et al., 2017)

Twenty-four hours post-transfection, CAR-T cells demonstrated a highly statistically and pointedly reduced PD-1 level due to siRNA. The downregulation of the PD-1 gene was maintained for seven days post transfection which is considered to have positive impact on the modulation of the immune checkpoint.

Expression of the CAR-related protein encoded by mRNA

In 2014, G. L. Beatty et al. identified a promising approach by transducing CAR mRNA into T cells with CD3ζ and 4-1BB domains to target mesothelin for solid tumor treatment. This solution helped to overcome the side effects of cancer treatment with the help of engineered CAR T-cells. It proved that mRNA CAR transfection may be the best approach to treat tumors as shown in Figure 4. T-cells were then nucleofected with mRNA giving rise to CAR molecules that selectively recognize tumor antigens. The application of mRNA have been proven in many cancer types including melanoma, lung cancer and breast cancer (Beatty et al., 2014).

CAR mRNA is associated with different forms of cancer and the specific antigens expressed by CAR mRNA are different forms of cancer. For instance, H. G. Caruso et al. showed the potential of mRNA CAR-T cells in Terms of its toxicity against glioma cell lines (U87, T98G, and LN18) (Caruso et al., 2015). The authors of the study H. Meister et al. found that the application of multi-target mRNA CAR-T cells, which are sensitive to the natural killer group 2D (NKG2D) receptor, and pro-inflammatory cytokines IL-12 and IFN2 increased the activity of angioma in both laboratory and live mouse glioma models. Importantly, this approach did not result in any toxicity and was efficient in three immunocompetent mouse glioma models (Gross et al., 1989). The number is. Tumors of the same type can produce several antigens and this is why it is possible to direct the treatment to different subtypes or forms of cancer.

For instance, K. Schutsky, and colleagues established the efficiency of intravenous delivery of mRNA CAR-T cells that bind to FRα. This protein controls cell division, in managing ovarian cancer in mice. Harrer et al. identified the CSPG4 as one of the target antigen for ovarian cancer. It was established that ovarian carcinoma cells exposed to decitabine died specifically with an emphasis on CSPG4. Strengthening of the treatment approach can improve the effectiveness of the treatment and the delivery of medical regimens whereby treatment regimens can be changed to suit the specific conditions of each patient.
Using a specific approach can enhance the treatment results and allow the medical staff to adjust treatment plans following the patient's individual conditions (Xiao et al., 2023)
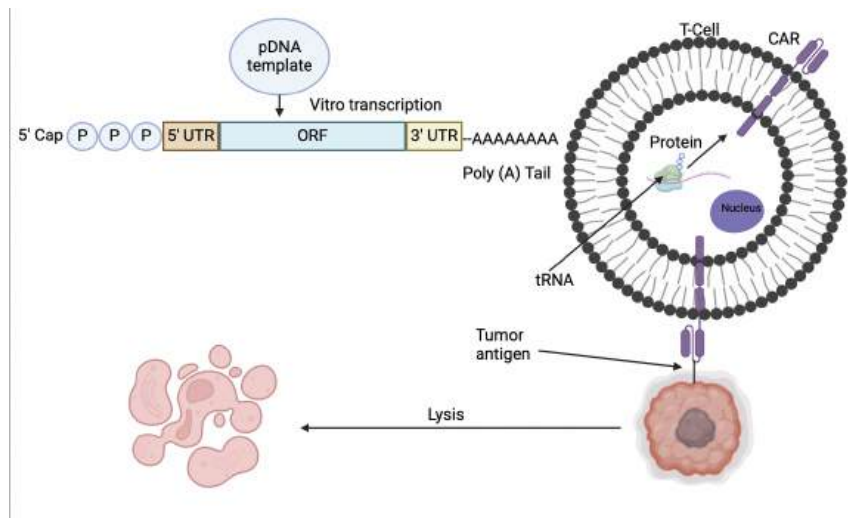
Fig 4: Before modifying T-cells, the mRNA encodes CAR, is introduced into a laboratory setting, and then converted into proteins in the cytoplasm. This allows for the expression and presentation of CAR on T-cells. Subsequently, the CAR molecule engages with tumor cells, triggering the process of apoptosis. Image created with Biorender.com

Conclusion

mRNA has been proved to be very useful in many fields of medicine such as treating genetic diseases and in synthesis and delivery of CARs to fight cancer. The mRNA vaccines are subjected to several modifications such as capping and nucleotide modification in order to come up with the best vaccine to be translated and expressed and to minimize the immune response. In terms of therapies, particularly in the current year, there has been a tremendous rise in the research & development and usage of vaccines against COVID-19 which are based on the concept of mRNA. These vaccines give a possible solution to the challenges posed by mRNA stability, and immunogenicity which has been a major challenge. The new mRNA vaccines may provide effective prevention and cure to people affected by the virus according to the researchers and scientists. The subsequent generation of COVID-19 vaccines is expected to introduce new and better changes that shall increase efficacy, expand access, and provide longer immunity. Also, these enhancements are expected to increase the generation of cross-neutralizing antibodies that are capable of fighting VOCs including Delta and Omicron. New possibilities have also been created in noninfammatory mRNA vaccines to treat autoimmune diseases. Krienke et al. established a modified mRNA vaccine platform which is devoid of adjuvant properties and mediate the delivery of Multiple Sclerosis autoantigens into the lymphoid dendritic cells. This method is based on the expansion of a given subset of Tregs that can control autoimmune agaisnt specific self-antigens and also modulate the activity of effector T cells that target other myelin

related self-antigens. The vaccination also showed a delay in the onset and reduction in the severity of the already existing disease in the mice models of MS without showing generalised immunosuppression. The unique advantages of mRNA-based drugs over other biomedicines have made the industry and academia to carry out researches in this area.

The advantages of mRNA are manifold and encompass the following: The following are some advantages of mRNA therapeutics: (1) Much shorter, less complicated, and less expensive development and manufacturing processes than traditional biologics that require systems such as cell lines or E. coli; (2) There is no risk of pathogenic infection in the enzymatic mRNA synthesis in vitro; (3) The production of any protein can be easily modulated and switched to by just changing the mRNA sequence; (4) There is no chance of mRNA integration into the genome, thus making it safer than DNA therapies; (5) It has the potential of targeting intracellular proteins that were previously considered undruggable by antibodies or proteins; (6) This technology has the potential of being applied in the production of vaccines for diseases such as infectious diseases including the COVID 19. It can also be used in cancer vaccines and immunotherapy, cell therapy, protein replacement therapy and gene editing among others. (7) The potential of genetically modifying diseases to either block the expression of certain genes (which code for detrimental proteins) or replace any non-functional proteins by introducing proteins to the body. It also triggers both the cellular and humoral immunity which is broad and strong and results to better protective immunity than the usual vaccines.

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Understanding Allergies from Molecular Mechanisms to Personalized Treatment Strategies
By Robin Jeon

Abstract

      Millions of people globally suffer from allergy symptoms yearly, with minor symptoms like sneezing to more severe symptoms like anaphylaxis. Allergy reactions are defined as the immune system's adverse reaction to harmless substances. This report discusses the mechanism of allergic reactions, the prevalence of different allergies, and the risk factors associated with allergy development. This review will also include the current solutions to allergies, including pharmaceutical treatments, therapeutics, and preventative treatments. With this overview, we aim to provide practical guidance to patients and caregivers in managing allergies with the ultimate goal of improving public health outcomes.

Introduction

      Despite our society becoming increasingly hygienic as technology advances, in recent years the number of allergy patients has been on the rise. According to the Center for Disease Control (CDC), a third of U.S. adults and a quarter of U.S. children were diagnosed with seasonal allergy, eczema, or food allergy in 2021 (*More Than a Quarter of U.S. Adults and Children Have at Least One Allergy*). An allergic reaction is the result of our immune system producing an inappropriate immune response to harmless substances called allergens. Allergens include respiratory particles like dust mites, animals, pollen, and mold; consumed allergens like peanuts, tree nuts, and soy; insect stings are also a common type of allergen that does not fall under the two categories above ("Types of Allergens"). Unlike others, some individuals' immune systems mistakenly perceive allergens as harmful, leading to a range of allergic symptoms. Mild symptoms include sneezing, coughing, itching, and swelling, while severe reactions such as anaphylaxis–difficulty breathing due to airway constriction–can be life-threatening ("Anaphylaxis"; "Overview: Allergies").

      Allergies can develop due to a variety of factors. Some people might have a higher risk of developing allergies due to hereditary aspects, meaning they have a family history of allergies (Aldakheel). Others may have been born or have inherited specific genes like MALT1 in their DNA that cause them to be more inclined to have an allergy than others. But even if we disregard these genetic and hereditary aspects of allergies, allergies can also develop due to other external factors: drastic changes in allergen exposure, the route of exposure, and environmental factors like pollution (Aldakheel).

      As of now, allergy treatments include medications like antihistamines and steroids, which help treat symptoms immediately (Aldakheel). In addition, monoclonal antibody injections called Xolair, immunotherapy, and even parasitic worm infections are options that help suppress allergic reactions or even get rid of them in the long term ("FDA Approves First Medication to Help Reduce Allergic Reactions to Multiple Foods After Accidental Exposure"; "Why Catching a Parasite Might Be the Best Thing for Your Allergies"; Frew). Preventative treatments are also

available; such as early exposure to allergens and avoiding allergens ("Overview: Allergies"; Trogen et al.).

This report will review the biological underpinnings of allergies, the prevalence of different allergies, and the risk factors that cause allergy development. It will also cover currently available solutions to allergies and emerging preventative treatments. Understanding the complexities of allergies, their prevalence, and the factors influencing their development is crucial for improving outcomes and quality of life for allergy sufferers worldwide.

Mechanism Behind Allergies

Allergies are triggered by errors in the immune system, which is the key defense system in our body that fights off diseases to prevent people from falling ill. One of the most important actions in this defense system is recognizing whether a substance is potentially harmful. If the substance is harmful, the system will prepare an attack to fight off the substance, releasing an immune response tailored to it. In the case of an allergic reaction, that substance is called an allergen.

Once the immune system misidentifies the allergen, an immune response is released to attack it and prime the sensitization process. By the end of the response, the immune system produces specific antibodies–often IgE for allergens–targeted to the allergen; these antibodies are the immune system's main tools of defense when they attack specific antigens (Aziz et al.). These antibodies then bind to immune cells responsible for releasing inflammatory chemicals. At this point, we say that the body is sensitized to the allergens. In other words, the IgE antibodies that target the allergen are present and ready to launch a full-on allergic reaction whenever the allergen is encountered again. During the subsequent exposure to the allergen, we experience typical allergy symptoms like swelling in the skin, runny noses, and watery eyes due to the release of inflammatory chemicals.
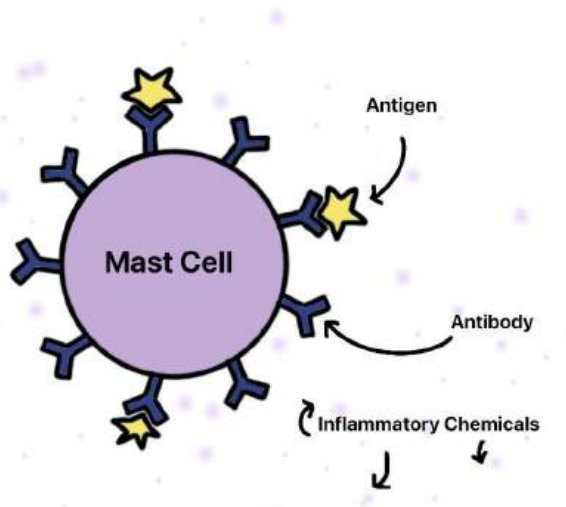

Fig 1. Antigen encounter after sensitization
When the body encounters the allergen after sensitization, an inflammatory response is released as the allergens trigger the release of inflammatory chemicals by binding onto the antigen on the mast cell's surface.

Allergens that cause these reactions can be anything (Aldakheel). Some can be from foods, animals, plants, insects, or even from the air, like pollen ("Types of Allergens"). When these allergens are inhaled, consumed, or absorbed into our skin, there is always a chance that the immune system might become sensitized to them. Some allergies are more common than others because we have more exposure to them (Galli et al.). For example, pollen allergies like tree, grass, and weed allergies are common because every year, we are exposed to pollen produced by these flourishing plants all around us (James). During this season, the immune system has a greater chance of being sensitized to the pollen by frequent exposure ("Overview: Allergies"). Now that we understand the basics of how allergies develop, we can then dive into risk factors and treatments of allergies with greater clarity.

Risk Factors for Allergy Development

There are multiple risk factors associated with allergy development. They can be developed due to eczema, a skin condition that increases its vulnerability to skin infections, changes in exposure to the allergens, or from air particles in the environment we live in (Aldakheel; "Why Do I Have Allergies after Moving to a New Place?"; "Risk Factors for Food Allergy"; *Eczema (Atopic Dermatitis)*). Principally, all allergies are developed when our immune system becomes sensitized to an allergen; and for sensitization to occur, we must be exposed to an allergen in some way. During these exposures, a misinterpretation of the allergen by the immune system can lead to its development. The primary risk factors include: 1) changes in exposure to allergens, 2) route of exposure, 3) environmental factors, 4) inheritance, and genetics.

1) Changes in exposure to allergens: There is a greater chance of allergen sensitization when the body is deprived of an allergen and exposed to it after several years ("Why Do I Have Allergies after Moving to a New Place?"). Due to the drastic change, the immune system's sensitivity rises and causes greater difficulty in determining whether the allergen is harmful or not during the sudden exposure. This can be observed when we compare allergy prevalence to those in urban areas and rural areas (Tizek et al.). People who live in rural areas are consistently exposed to many bacterial and viral substances from their outdoor environment. The constant exposure to these substances causes people to become desensitized to them, lowering the likelihood of the immune system to stimulate an immune response against them (Tizek et al.). In contrast, those living in urban areas are often protected from these foreign substances in nature. Consequently, their immune systems are much more vulnerable to release a response to a sudden exposure to a foreign substance (Tizek et al.). In a way, one can say that a person born in a rural area has an immune system that is better trained compared to those in urban areas (Tizek et al.). The same can also happen when people migrate from one area to another (Amoah et al.). For example, when a person raised in a cold region with a lower pollen count for several years moves to a much warmer region, his or her immune response might be triggered to stimulate an immune response towards pollen because it has never been precedent to it.
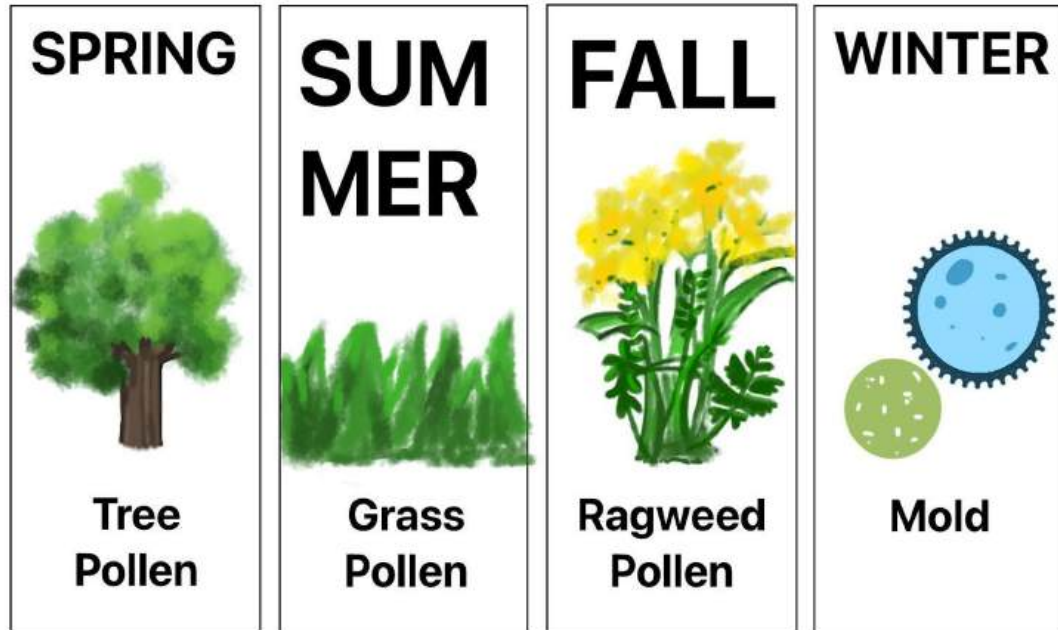
Fig 2. Common Types of Seasonal Pollen: Not all pollen allergies are caused by the same type. In different seasons, there are seasonal allergens more common than others. For this reason, when a person migrates from a place that is cold to a place with four distinct seasons, they may encounter new types of pollen that his or her body is not used to.

2) Route of exposure: Along with the changes in exposure, the routes by which the allergens enter a body also play a key role in allergy development ("Risk Factors for Food Allergy"). Usually, allergens enter our body through inhalation or consumption. However, eczema patients can also be exposed to allergens through their skin ("Risk Factors for Food Allergy"). Due to their dry skin, eczema patients have weaker skin barriers. Since the skin acts as the first line of defense against foreign substances, eczema patients' skin is more prone to allergen invasion than others.

Some even connect this new exposure route to a risk for food allergy development (Papapostolou et al.). For example, food allergens are usually consumed orally. This is considered the usual route to both us and to our immune system. But when these food allergens are introduced through an eczema patient's skin, the abnormality of this route raises a higher risk of sensitization ("Risk Factors for Food Allergy"). The prevalence of food allergies is 33% to 39% in severe eczema patients while it covers 0.1% to 0.6% of the general public (Papapostolou et al.). For this reason, eczema can be seen as a risk factor of food allergy development.

3) Environmental factors: Another risk factor promoting allergy development is pollution. In addition to exposure patterns to airborne allergens, gaseous pollutants like nitrogen oxide, produced by factories and cars, also increase the likelihood of developing sensitization to airborne allergens (Aldakheel).
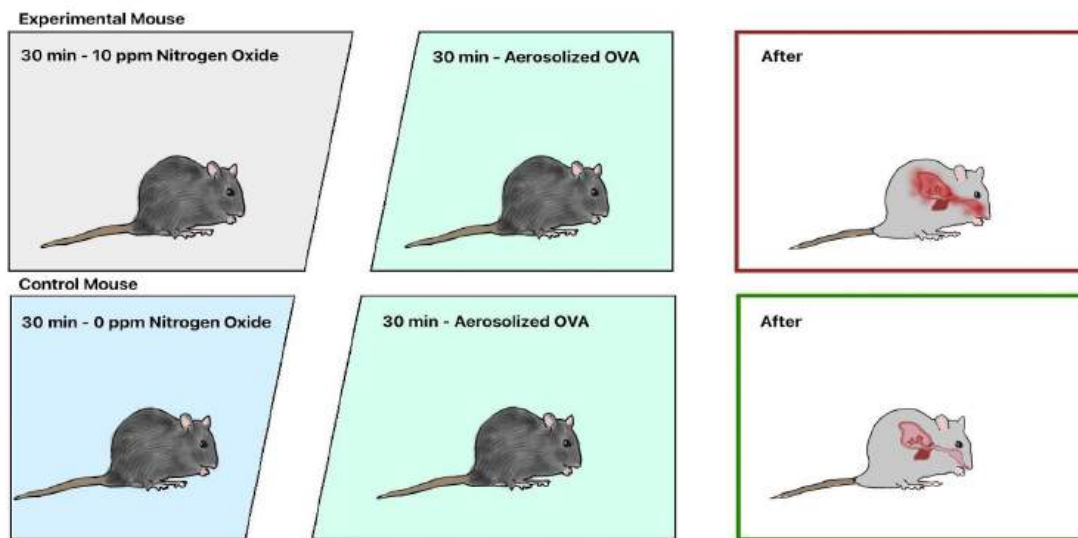
Fig 3. Mice Experiment on Nitrogen Oxide's Effect on Sensitization
In the experiment, the experimental group of mice that were exposed to nitrogen oxide ended up with inflammation in their airways. In contrast, the control group of mice did not show any signs of adverse reactions (Bevelander et al.).

To study the correlation between allergy development and nitrogen oxide exposure (Bevelander et al.). Researchers tested with two groups of mice, the experimental group was exposed to aerosolized ovalbumin (OVA)–a common protein used in research–and nitrogen oxide and the control group was only exposed to aerosolized OVA. Since purified OVA–a harmless protein found in egg whites used to study immune responses–does not generally provoke an immune response, researchers studied whether nitrogen oxide affected allergy development to OVA. The experimental group of mice was administered an hour of nitrogen oxide before being exposed to aerosolized OVA for thirty minutes. The control group was placed in room air free of nitrogen oxide before the thirty-minute exposure to aerosolized OVA. By the end of the experiment, researchers observed that the mice that had undergone nitrogen oxide exposure had evident airway inflammation present. On the contrary, the control group of mice did not exhibit any signs of airway inflammation during observations. Through the inflammation observed in the experimental mice, the study concluded that nitrogen oxide promoted allergic sensitization to airborne allergens (Bevelander et al.). Connecting this study to humans, in Mexico City, many children with asthma–a lung disorder that causes difficulty breathing due to airway inflammation–demonstrated a high correlation between respiratory symptoms and pollution caused by traffic (Aldakheel). Since asthma can also be triggered by airborne allergens, we can hypothesize that airborne allergies would also be greatly affected by pollution. For this reason, people, especially those at a higher risk, are advised to avoid living in areas with poor air quality to prevent airborne allergy development.

4) Inheritance and Genetics: Though there are many external factors that may trigger the development of an allergy, allergies can also be triggered by genetics. In the immune system, MALT1 is identified as a key regulatory protein in the immune response. A person with a

defective MALT1 gene is often considered immunodeficient meaning they have defected immune responses (Jaworski and Thome). In a study, National Institute of Allergy and Infectious Diseases (NIAID)-funded researchers concluded that among the subjects who had not consumed peanuts before the age of five, those who had a gene called MALT1 tended to have a higher risk of developing peanut allergies in comparison to those that did not have the gene ("Risk Factors for Food Allergy"). Initially, the study Learning Early About Peanut (LEAP) focused on peanut allergy prevalence by experimenting with allergen exposure timing (Trogen et al.). Among a group of high-risk infants, one group had peanuts before the age of five while the other group avoided them. Although the early exposure proved effective by ending up with fewer children with peanut allergies, researchers realized that even within this group, MALT1 was associated with provoking an antibody, IgE, response to certain proteins in peanuts (Winters et al.). In addition to the consumption group, MALT1 carriers within the avoidance groups showed higher levels of IgE compared to non-carriers. Through these observations, we can see how MALT1 ties to peanut allergy development (Winters et al.). Through the interplay between genes and peanut allergy development, we can see how nobody is born with allergies, but some others are born with a greater risk of developing allergies compared to others.

      With genetics being a risk factor, allergies can be inherited. Children born under allergic parents have higher immune system sensitivity compared to those born from non-allergic parents. Even if only one person is allergic, the chances that their children would develop an allergy is around 30-50% (Aldakheel). While children with both non-allergic parents have only a 12% chance of developing an allergy (Aldakheel). Many risk factors contribute to allergy development. They can be inherited, exhorted by certain genes, triggered by conditions like eczema, or provoked by environmental factors. With many risk factors causing allergies, allergy patients can be seen all around us.

Pharmaceutical Treatments

      Pharmaceutical treatments are one of the most accessible forms of solutions to immediately alleviate allergic symptoms like inflammation, hives, swelling, rash, congestion, watery eyes, and breathing problems ("Overview: Allergies"). Treatments can be in the form of pills, liquids, nasal sprays, inhalers, eye drops, skin creams, and shots ("Allergy Medications: Know Your Options"). Depending on the medication, some may need a prescription from the doctor, while others can be bought in drugstores. In this section, we will go over 1) antihistamines, 2) corticosteroids, and 3) Xolair injections (Aldakheel; "FDA Approves First Medication to Help Reduce Allergic Reactions to Multiple Foods After Accidental Exposure").

      1) Antihistamine: Antihistamines are drugs that are used to treat symptoms caused by histamine (Farzam et al.). Some common antihistamines in the drugstore include Allegra, Claritin, and Zyrtec ("Antihistamines"). Though antihistamines can be used to treat many different types of allergy, they are generally used to treat allergic rhinitis: an atopic disease that often proposes nasal irritation to inhaled allergens (Akhouri and House). To understand how antihistamines work, first, one must know about histamines and how they work. Histamines are

chemicals released during an allergic reaction that promote inflammation and blood vessel dilation. As chemical messengers, histamine binds to receptors to initiate the swelling from the allergic reaction. To counteract this effect, antihistamines bind to these same receptors, preventing histamines from attaching and initiating an allergic response (Farzam et al.). With the lack of receptors available for histamines, allergic symptoms induced by histamines are reduced.
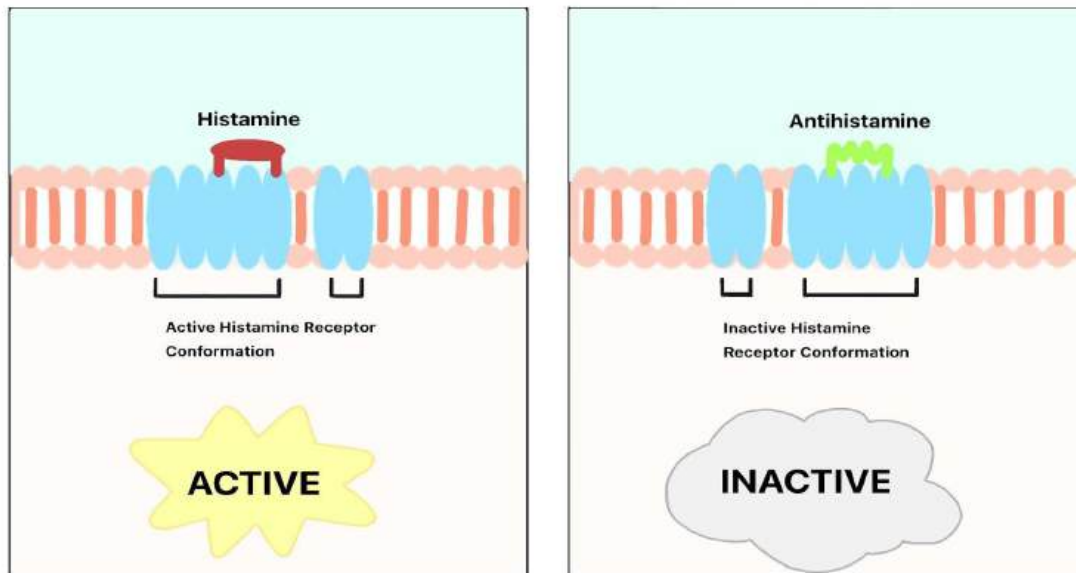

Fig 4. Cellular Histamine and Antihistamine Mechanisms
While histamine activates the receptor to create inflammation in the body, antihistamines give the opposite effect. Though they both bind to the same receptor, antihistamines deactivate it to prevent the body from producing an inflammatory reaction.

But along with the ease that antihistamines provide, there are also some side effects to it. For instance, users sometimes experience a dry mouth, dizziness, insomnia, and drowsiness. When the dose increases, delirium and decreased coordination are also experienced (Farzam et al.).

2) Corticosteroids: Corticosteroids are man-made steroid hormones that mimic the properties of glucocorticoids and mineralocorticoids produced in the adrenal cortex (Hodgens and Sharman). In our lives, they are commonly found in drugs like Nasonex, Prelone, and Medrol ("Allergy Medications: Know Your Options"). Corticosteroids are a type of medication often used to treat allergic rhinitis and anaphylaxis. When corticosteroids are administered to the body, they bind onto the glucocorticoid receptor and take effect at the nucleus, inhibiting the production of inflammatory cells and immune cells responsible for producing an inflammatory response. Through this process, allergic symptoms due to inflammation and the overall immune system become suppressed (Hodgens and Sharman).
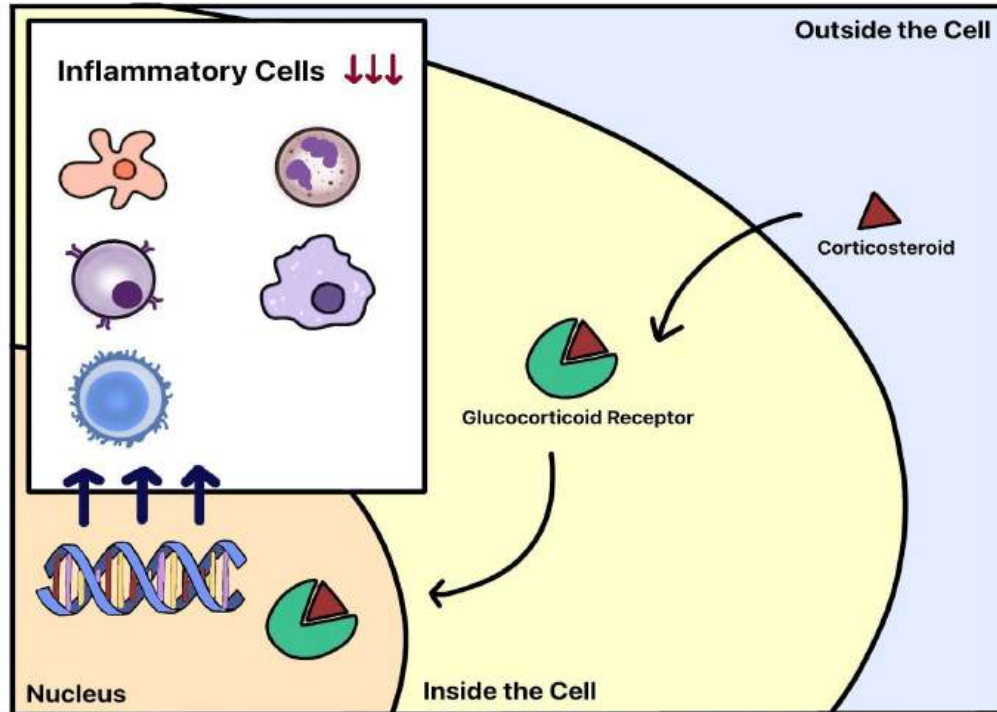
Fig 5. Corticosteroid Function
Up above is a brief process of how corticosteroids alleviate allergic reactions caused by inflammation. Corticosteroids enter the body and bind to the glucocorticoid receptors inside the cell. This then takes effect into the nucleus, where the production of inflammatory cells is inhibited, leading to a dampened allergy response.

In general, corticosteroids taken at a normal dose and duration do not carry many side effects. However, when they are given at higher doses with greater frequency, corticosteroids can cause many adverse effects in the body. Some of the common side effects include weaker bones and muscles, diabetes development, and impaired immune function (Hodgens and Sharman). Among these, impaired immune function is especially unavoidable since corticosteroids reduce inflammatory responses by suppressing the entire immune system. This causes the body to be susceptible to infections due to the body's weakened defense system against viruses and bacteria (Hodgens and Sharman).

3) Xolair Injections: Xolair monoclonal antibody injection binds onto IgE–an antibody that triggers an allergic reaction–and prevents it from binding into its receptors ("FDA Approves First Medication to Help Reduce Allergic Reactions to Multiple Foods After Accidental Exposure"). Unlike the previous options, Xolair injections are not used to provide immediate relief to allergic reactions. Instead, they are intended to reduce the severity of allergic reactions in the case of accidental exposure to food allergies. This makes them particularly useful for allergy patients who come across life-threatening situations during allergic reactions. Common side effects of Xolair injections are reactions at the injection site and fever. Besides the side effects, there were also cases of anaphylaxis upon administration of Xolair injections. Subsequently, although self-injections are approved (Murphy et al.), it is recommended that Xolair injections are given in a healthcare setting well equipped to prepare for anaphylaxis

("FDA Approves First Medication to Help Reduce Allergic Reactions to Multiple Foods After Accidental Exposure").

Therapeutics

For several years, we have thought that allergies had no cure. For this reason, most people focus on treating their symptoms with the pharmaceutical treatments mentioned above. But through further research, we developed more options that help reduce or even get rid of allergy symptoms in the long run. One of them is immunotherapy (Aldakheel), which can be divided into two types: subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) (Incorvaia et al.). The other is administration of parasitic worms. In this section, we will go over these three therapeutic methods to improve allergic symptoms in the long run.

1) Immunotherapy: During allergy immunotherapy, patients are given increasing doses of allergens to improve their immune system's tolerance towards them. As the immune system is consistently and frequently exposed to the allergen, it slowly becomes desensitized to the allergen and suppresses IgE antibodies involved in allergic reactions (Aldakheel). Immunotherapy can be administered subcutaneously or sublingually. Although both of them follow the same concept, subcutaneous immunotherapy is injected under the skin while sublingual immunotherapy is administered orally under the tongue (Boltansky).

    a) Subcutaneous Immunotherapy: Subcutaneous immunotherapy is more commonly known as allergy shots ("Allergy Shots - What You Need to Know"). Allergy shots are commonly used to treat allergic rhinitis and insect venom allergies. At the injection site of the allergy shot, local reactions like redness and swelling can be commonly found among patients. More severe reactions are systemic reactions like wheezing, coughing, flushing, or tightness of the throat can also occur. Due to this, patients who receive an allergy shot are required to stay in the office for thirty minutes to watch out for these symptoms ("Allergy Shots - What You Need to Know").

    b) Sublingual Immunotherapy: Sublingual immunotherapy can be in the form of a tablet or an allergy drop (Boltansky). While the tablets work better for airborne allergens like ragweed pollen, grass, and house dust mites. Allergy drops are also effective with trees, cats, and dogs, and feathers as well. Both options can be administered at home. For this reason, sublingual immunotherapy gets rid of the hassle of reaching out to the clinic for every drop or tablet. But even if they can be taken at home, sublingual immunotherapy may also have some moderate symptoms in the first few weeks like skin reactions, oral irritation, nausea, or itching eyes. However, the chances of having a severe allergic reaction like anaphylaxis are extremely rare (Boltansky). An advantage of sublingual immunotherapy is that it can also be used against food allergies. In 2003, a kiwi-allergic patient was successively desensitized after taking increasing

amounts of kiwi extract (Schworer and Kim). As the immunotherapy continued, the number of specific IgE antibodies decreased in the patient's system. Moreover, when the patient resumed immunotherapy after four weeks of rest, the patient did not have any side effects (Schworer and Kim). Through this case, sublingual immunotherapy might be a rising option for treating food allergies in the future. For the best effects, both sublingual and subcutaneous immunotherapy should be done for at least three to five years (Boltansky; "Allergy Shots - What You Need to Know").

2) Parasitic Worms: Yes, parasitic worms are a type of parasite that can cause the same harm as a virus or bacteria. However, in the context of an allergic person, parasitic worms present surprising benefits for allergy symptoms ("Why Catching a Parasite Might Be the Best Thing for Your Allergies"). When a parasitic worm enters the body, the immune system identifies them as a foreign invaders and attempts to release an immune response. In response to the immune system, parasitic worms release messengers intended to shut down the immune cells in action. Subsequently, the immune system weakens, allowing the worms to survive inside the body. Though this may alert many people, the weakened immune system also makes them less sensitive to allergens. Coming back to allergies, the immune system's hypersensitivity is the cause of an allergic reaction. Therefore, when the immune system is down, they would not be as reactive to an allergen. But despite this notion of parasitic worms helping allergy symptoms, there are many risks and downsides. One of them is malnutrition. Without the immune system attacking them, parasitic worms settle in the intestines to absorb the nutrients in our body to survive ("Why Catching a Parasite Might Be the Best Thing for Your Allergies"). Further research and experimentation are needed to fully understand the impact of parasitic worms on overall health, particularly in the context of allergy treatment.

Preventative Treatments

Although treating existing allergies is also important, learning how to prevent them from developing is also crucial. Especially with the number of allergy patients increasing globally each year, there must also be future parents who want to prevent their children from developing an allergy as well. One thing we need to understand here is that people are not born with allergies. Even though there may be some individuals more susceptible to allergies due to hereditary factors, there are ways to lower the likelihood of developing them. For instance, food allergies can be prevented by early allergen exposures, while allergen avoidance prevents allergies to animals (Trogen et al.).

1) Early Exposure: Previously, we have touched on the LEAP study (Trogen et al.). LEAP is the first study that suggested early introduction to allergens to prevent allergy development. In this study, one group of high-risk infants was given increasing amounts of peanuts in their diet during four to six months of age. To compare the outcomes, the other group of infants avoided peanuts during the same period. When the participants

were tested for peanut allergies back at the age of five, the prevalence of peanut allergies decreased by approximately 80% compared to those who avoided peanuts. Though this part of the study was enough to convince people about the power of early exposure, a new study, Persistence of Oral Tolerance to Peanut (LEAP-On) proved that the peanut tolerance built from the early exposure persisted even when the peanut consumption paused for a year (Trogen et al.). With LEAP and LEAP-On highlighting the idea of early exposure, it is now advised that other allergens like eggs, milk, and fish (Chin et al.).

2) Allergen Avoidance: Though there are some allergens that are better off in early exposures, there are some others where simply avoidance is the answer. This option may help prevent allergies caused by cats and dogs ("Overview: Allergies"). While it is practically impossible for airborne allergens like pollen. After all, avoiding allergens does not give the immune system a chance to become sensitized in the first place. Even if avoidance may not be best in prevention, in the case of people who are already allergic, avoidance also prevents allergic symptoms from occurring.

Conclusion

Many people around us suffer from allergies every day. Due to the watery eyes, coughs, nasal irritation, and even anaphylaxis, the quality of their lives is constantly nagged by rising pollen levels, foods to look out for, or animals and insects that cause a fuss to their immune system ("Types of Allergens"; "Overview: Allergies"). Although our immune system was simply trying its best to protect us from potential danger, it ended up mistakenly attacking allergens that are technically harmless in reality. In addition, risk factors like inheritance, genetics, air pollutants, changes in allergen exposures, and eczema promote our chances of developing allergies (Aldakheel; "Why Do I Have Allergies after Moving to a New Place?"; "Risk Factors for Food Allergy").

To treat patients with allergies, healthcare providers offer pharmaceutical solutions such as antihistamines, corticosteroids, and Xolair injections to relieve allergic symptoms (Hodgens and Sharman). A therapeutic option, immunotherapy, is also receiving attention with the successful reduction in allergic symptoms after consistent treatments (Frew). While more research is encouraged, preventative strategies such as early exposure to food allergens and allergen avoidance have emerged as key areas of focus in allergy research ("Overview: Allergies"; Trogen et al.).

However, even though allergies have a lot more to be uncovered, research on allergies is not as focused as it is on more recently discovered illnesses like COVID-19. While encouraging current researchers in the health field to provide innovative, effective treatments with minimized side effects, ordinary people should also recognize the severity of allergies and participate in helping the world for allergy patients. We can help improve allergy patients by reducing pollution through simple tasks like reducing plastic use or encouraging carpools to minimize the release of harmful byproducts in our environment. Through these efforts, we can only hope allergy patients worldwide receive the help they need.

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Targeted Drug Therapies for Mantle Cell Lymphoma: A Review by Sakura Nakanishi

Abstract

Mantle cell lymphoma (MCL) is a type of B cell non-Hodgkin lymphoma that is rare but very aggressive. The median age of diagnosis is age 60 to 70, and it has a significant sex ratio of affected individuals, with 3 males affected for every 1 female affected. The hallmark of the disease is a translocation of chromosomes 11 and 14 that results in the overexpression of cyclin D1, a protein associated with cell cycle dysregulation and excessive proliferation and division. Other proteins and molecular pathways are also altered in the disease, such as the BCL-2 pathway, SOX-11 pathway, and the NF-kB pathway. Traditional treatment options are limited, as the disease is widespread, preventing surgery from being an option, and it is diagnosed at later stages preventing radiotherapy from also being appropriate. Thus, chemotherapy is the only viable standard option, but it is ridden with side effects and other issues. Recently, other therapies such as targeted therapy, immunotherapy, and epigenetic therapy have become more commonly researched and used as viable treatment options. Targeted therapy, the focus of this paper, involves selectively delivering drugs to certain genes or proteins specifically found in cancer cells or the tumor microenvironment, which allows for specific and effective treatment of MCL. Many small molecule drugs have been shown to be effective in treating MCL, and many more are currently being tested in clinical trials, but they come with their own set of issues, notably drug resistance. Thus, further research into potential molecular targets and drug discovery for MCL is vital to help treat and eventually cure MCL.

Keywords: mantle cell lymphoma, targeted drug therapy, drug resistance, chemotherapy

Introduction

Mantle cell lymphoma (MCL) is a rare subtype of B-cell non-Hodgkin lymphoma, characterized by the overexpression of the *CCND1* gene due to a specific genetic translocation (Lynch et al., 2024; Stephens & Spurgeon, 2015). It is often a rather aggressive cancer, although indolent variants do exist (Lynch et al., 2024). This disease has a prevalence of about 1 in 200,000 people per year, and accounts for approximately 5% of non-Hodgkin lymphomas. The male-to-female ratio among those affected is 3:1, with most diagnoses occurring between ages 60 and 70 (Lynch et al., 2024). Many variants of this disease exist, often making it difficult to diagnose (Lynch et al., 2024). Survival rates vary depending on the aggressiveness of the variant, with most patients surviving from 1.8 to 9.4 years post-diagnosis (Lynch et al., 2024). At the time of diagnosis, MCL is usually widespread, with common manifestations such as splenomegaly, gastrointestinal infiltration, lymphadenopathy, and bone marrow involvement often found (Lynch et al., 2024; Schieber et al., 2018). Commonly reported symptoms include night sweats, fever, abnormal blood counts, and symptoms of weight loss (Lynch et al., 2024).

Treatment of cancers generally consists of one or a combination of the following: surgery, radiotherapy, and chemotherapy (Debela 2021). For MCL, surgery is not recommended for treatment as the disease is often systemic, and radiotherapy is rarely done as it is recommended for treating stage IA and stage IIA MCL and the disease is often not diagnosed at such an early stage (Lynch et al., 2024). As a result, out of the three standard therapy approaches, chemotherapy is the only method commonly used to treat MCL. However, chemotherapy also has many issues, including severe side effects and depressing the immune system, among other problems (Amjad et al., 2024). Therefore, there is a need for more effective and less toxic therapies, making novel treatment options like targeted therapy promising fields to further study.

Herein, this review paper aims to explore the molecular pathophysiology of MCL, followed by an in-depth discussion on the use of targeted therapy and chemotherapy. It will also highlight newly identified drug targets for MCL and address the challenges and future directions in precision medicine for the treatment of MCL.

Pathophysiology of Mantle Cell Lymphoma

Genetic Hallmark of Mantle Cell Lymphoma
The main abnormality found in MCL is a translocation of chromosomes 11 and 14 (t(11;14)), which places the *CCND1* gene at llqI3 with the IgH regulatory region (Jain & Wang, 2019; Navarro et al., 2020). This chromosomal mutation occurs during the pro/pre-B stage of differentiation during VDJ recombination (variable-diversity-joining rearrangement) and is caused by recombination activating gene (RAG) enzymes (Navarro et al., 2020). Cyclin D1 constitutive overexpression results in genetic abnormalities, which dysregulates cell cycle progression from the G1 to S phase (Navarro et al., 2020). Cyclin D1 is also involved in regulating gene expression of transcription factors, and histone and chromatin modifying enzymes, regulating apoptosis, and responding to DNA damage (Navarro et al., 2020).

However, not all cases of MCL have the t(11;14) mutation (Navarro et al., 2020). Some small subsets of MCL overexpress cyclin D1 without the CCND1 gene rearrangements (Navarro et al., 2020). There are also cases where cyclin D1 overexpression is completely absent (Navarro et al., 2020). In these cases, cyclin D2 and D3 are often overexpressed due to insertion of a small IGK region near *CCND2* and *CCND3* genes, respectively (Navarro et al., 2020; Schieber et al., 2018).

MCL Types
Conventional mantle cell lymphoma (cMCL) is a subtype of MCL that originates from naïve-like B-cells that do not enter the follicular germinal center as seen in Figure 1. It is the more common subtype of MCL. This subtype of MCL often overexpresses SOX11, develops many alterations to chromosomes, and is genetically unstable (Jain & Wang, 2019; Navarro et al., 2020). SOX 11 overexpression has been found to be independent of cyclin D1 status in MCL (Schieber et al., 2018). Patients with cMCL often have generalized lymphadenopathy and the

subtype is extremely aggressive (Navarro et al., 2020). *SOX11* overexpression is one genetic change that differentiates cMCL from other subtypes of MCL (Navarro et al., 2020). This gene is not expressed in healthy B cells or other mature B cell cancer except in MCL (both cyclin D1+ and cyclin D1- strains) and 25-50% of Burkitt lymphoma (Navarro et al., 2020). SOX11 has many effects, including inducing angiogenesis via PDGFA. It also targets *CXCR4* and *FAK*, upregulating their expression, and thereby promoting tumor migration, adhesion, and cell division (Navarro et al., 2020). SOX11 may promote MCL by constitutively activating PAX5, which promotes the growth of tumors and also blocks terminal B-cell differentiation. Interestingly, SOX11 is also associated with increased angiogenesis, or the growth of blood vessels that supply nutrients to the tumor (Navarro et al., 2020). The mechanism of action of SOX11 is largely unknown (Navarro et al., 2020).

Leukemic non-nodal mantle cell lymphoma (nnMCL) is the other subtype of MCL, which originates from naïve-like B-cells cells that have entered the germinal center and acquired immunoglobin heavy chain variable region (IGHV) somatic mutations as shown in Figure 1 (Navarro et al., 2020). This subtype of MCL originates from germinal cell memory-like B cells and tends to be indolent and stable for extended periods of time (Jain & Wang, 2019; Navarro et al., 2020). This is associated to low *SOX11* expression, which is one of the defining differences between nnMCL and cMCL (Schieber et al., 2018). Patients with this subtype often have minimal lymphadenopathy and some later develop splenomegaly (Navarro et al., 2020). Genetically, nnMCL cells often only have the t(11;14) mutation, but sometimes evolve to have other mutations that lead to genome instability and a worse prognosis (Navarro et al., 2020). nnMCL tends to have a stable genome with few epigenetic modifications (Jain & Wang, 2019).
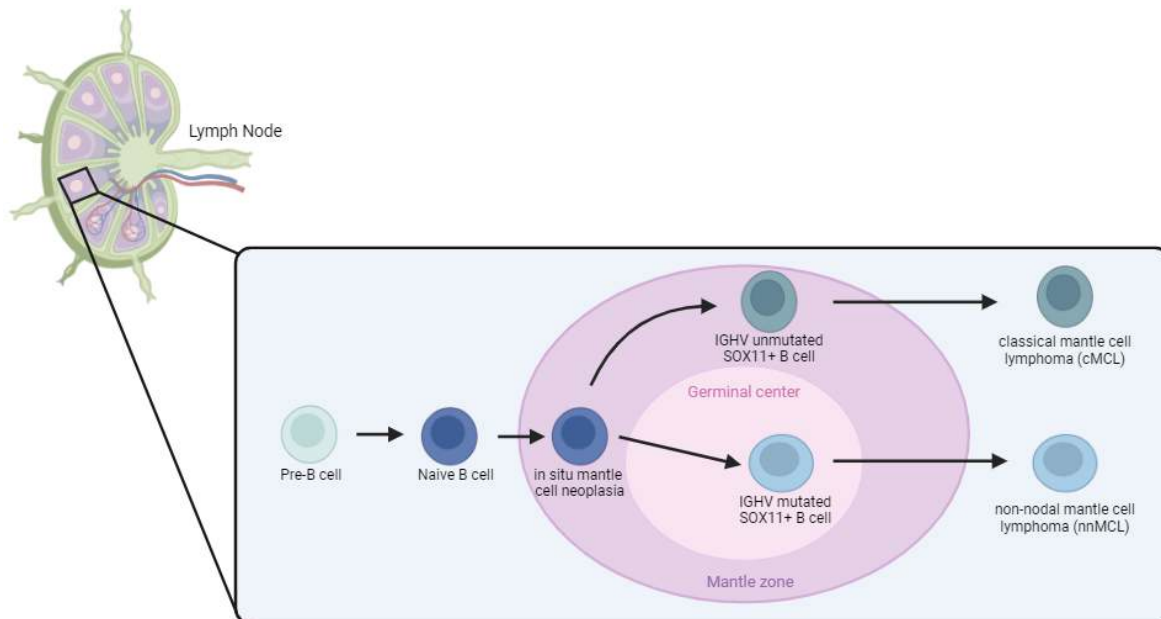

Figure 1: Formation of different types of MCL (Made with BioRender)

The Influence of Genetics on Disease Progression

The progression from t(11;14) mutation to full out MCL is not well understood (Navarro et al., 2020). In fact, studies have shown that 8% of B-cells in peripheral blood may carry the t(11;14) mutation, which suggests that not all cells that develop this mutation ultimately become MCL cells (Navarro et al., 2020). Cyclin D1+ cells are also sometimes found in the mantle zone of lymphoid follicles in a condition called in situ mantle cell neoplasia (Navarro et al., 2020). The number of people with in situ mantle cell neoplasia who ultimately develop MCL is not well known but seems to be quite low (Navarro et al., 2020).

The Hallmarks of Cancer in MCL

Cancer cells are different from healthy normal cells in many ways, and some of the main criteria in determining if cells are cancerous is by identifying whether they have these characteristics. In this section, the hallmarks of cancer in the context of MCL will be discussed. Figure 2 describes these hallmarks.
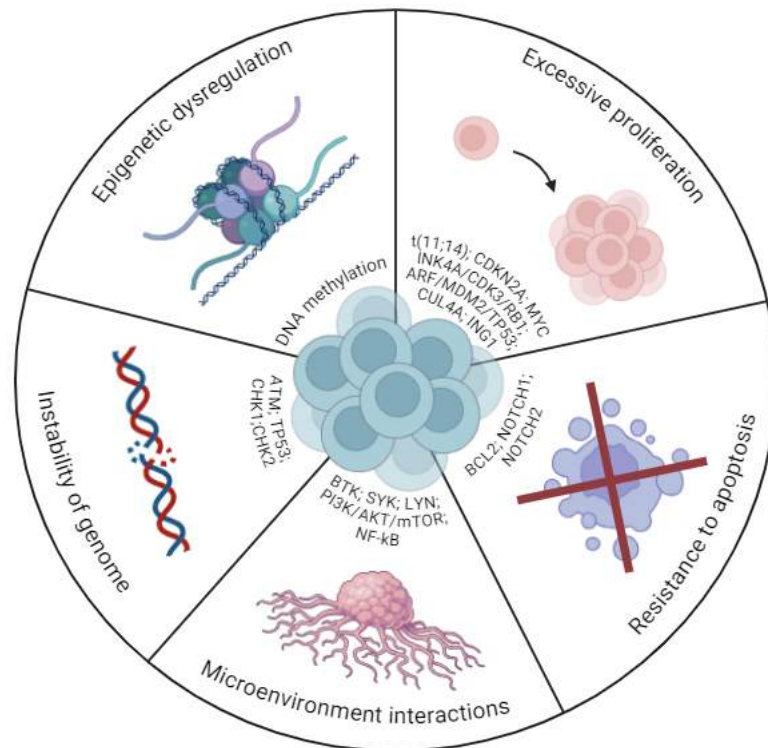
Figure 2: Hallmarks of Cancer in MCL (Made with BioRender)

One trait of cancer cells is their ability to continue to proliferate even when growth suppressors are found in their vicinity (Navarro et al., 2020). In MCL, the t(11;14) translocation that is the hallmark of MCL leads to the dysregulation of cyclin D1, which results in promotion of G1/S phase transition as cyclin D1 binds to CDK4 (Navarro et al., 2020). This binding results in phosphorylation of RB1 (inhibiting it) and the release of E2F (Barbieri et al., 2013; Jain & Wang, 2019; Navarro et al., 2020). Another common genetic mutation found in patients with MCL is the deletion of *CDKN2A*, a gene that codes for pl6, a CDK inhibitor that binds to CDK4 and CDK6, which allows for RB1 to be active, preventing cell cycle progression (Navarro et al.,

2020). *CDKN2A* also codes for pl4, which is a ubiquitin-protein ligase that stabilizes the tumor suppressor gene p53 (Navarro et al., 2020). Other genetic events also lead to cell cycle dysregulation, such as alterations in the INK4A/CDK3/RB1 pathway and the ARF/MDM2/TP53 pathway, as well as MYC translocation and amplification and *CUL4A* and *ING1* deletions (Navarro et al., 2020).

The ability to resist apoptosis is another hallmark of cancer cells. Overexpression of proteins in the BCL family, notably BCL2, an antiapoptotic protein, is found in a chunk of MCL cases (Navarro et al., 2020). Recently, gain of function mutations in *NOTCH1* and *NOTCH2* have been associated with poor prognosis in MCL (Navarro et al., 2020). This pathway is involved in regulating both apoptosis and cell proliferation through the *MYC* gene that is associated with RNA metabolism, B cell receptor signaling, and modifications of chromatin and transcription (Navarro et al., 2020).

Constitutive B cell receptor (BCR) signaling is one hallmark of MCL, and results in increased proliferation and survival in B cell cancers (Navarro et al., 2020). Although not thoroughly understood, Bruton's tyrosine kinase (BTK), spleen tyrosine kinase (SYK), and tyrosine protein kinase (LYN) have been considered as therapeutic targets because they are often constantly active in MCL (Navarro et al., 2020). Constitutive PI3K/AKT and NF-kB signaling is also prevalent in MCL (Navarro et al., 2020). The PI3K/AKT/mTOR pathway affects a variety of processes, from angiogenesis to cell growth and survival, while the NF-kB pathway is associated with increased proliferation of tumors and less apoptosis in MCL (Navarro et al., 2020).

MCL tends to have the highest amount of instability in its genome among B cell cancers (Navarro et al., 2020). In general, cancer cells have a propensity to accumulate genetic mutations and have a high degree of genomic instability (Navarro et al., 2020). Over 90% of cases of MCL have genomes that are highly altered, with deletions in 1p, 6q, 8p, 9p, 9q, 10p, 11q, 13a, and 17p and insertions in 3q, 7p, 8q, 10p, 15q, and 18q being the most common (Navarro et al., 2020). This is likely because *ATM* and *TP53*, the two most commonly mutated genes in MCL, are involved in DNA repair (Navarro et al., 2020). Additionally, *CHK1* and *CHK2* downregulation is found in some cases of MCL, which leads to more instability in chromosomes (Navarro et al., 2020). These genes code for two serine-threonine kinases that are critical in the DNA damage response (Navarro et al., 2020). *TP53* is a gene that is often mutated in patients with MCL, which can interfere with cell cycle arrest mediated by p53 (Navarro et al., 2020). In general, greater chromosome instability is associated with more severe clinical outcomes for MCL (Navarro et al., 2020).

Epigenetic dysregulation is a common phenomenon found to occur in many different cancers. In MCL, DNA methylation appears to be associated with worse prognoses (Navarro et al., 2020).

All hallmarks of cancer can be ultimately attributed to genetics. As more and more mutations accumulate in the B cell, MCL can ultimately develop. It is with these hallmarks that cancerous and noncancerous cells in the body are distinguished from each other.

Current Therapies in MCL

Current therapies for treating MCL include chemotherapy and targeted drug therapy. The most commonly prescribed targeted drug therapies include BTK inhibitors, NF-kB pathway targeting drugs, BCL-2 inhibitors, PI3K inhibitors, and androgen receptor blockers. Each of these therapies will be discussed in detail in this section.

Chemotherapy for MCL

Chemotherapy is a type of cancer treatment whose goal is to reduce cell proliferation and tumor growth in cancers (Amjad et al., 2024). These drugs do this through many different ways, but most commonly, they inhibit nucleic acid and protein synthesis or inhibit the function of specific molecules that are needed for cell growth and proliferation, both of which usually lead to apoptosis (Amjad et al., 2024). However, due to its broad effects, it ends up impacting healthy body cells as well, which is also why side effects are very common (Amjad et al., 2024). They most especially affect rapidly dividing cells in the body, resulting in side effects like nausea, vomiting, alopecia, infertility, and myelosuppression (Amjad et al., 2024). The immune system gets depressed, leading to an increased risk of infections (Amjad et al., 2024). In MCL, the standard treatment is the following: chemotherapy using rituximab and cytarabine is first done, then autologous stem cell transplantation, and then finally, rituximab maintenance for younger patients (Kumar et al., 2022). For older patients, chemotherapy with bendamustine/rituximab along with R-CHOP and VR-CAP are used (Kumar et al., 2022). However, patients with TP53 mutations and those with highly proliferative MCL often do not respond well to chemotherapy (Martin et al., 2017; Novak et al., 2023). Additionally, patients who live in geographically isolated areas that lack access to these chemotherapies as well as those with comorbidities often cannot be treated successfully with chemotherapy (Martin et al., 2017). Recently, chemotherapy is not as commonly used in MCL treatment, and instead, treatment has evolved to consist of a combination of targeted, immune, and epigenetic therapies (Pu et al., 2022).

Targeted Drug Therapies for MCL

Targeted therapy, or molecular targeted therapy, is another kind of cancer treatment that has become more common recently. It involves selectively delivering drugs to certain genes or proteins specifically found in cancer cells or the tumor microenvironment (Padma, 2015). It is a therapy that is specific, allowing for targeted release of the medications in the diseased areas while reducing side effects due to impacts on off-target molecules and pathways. Most targeted therapy drugs are small molecule drugs or monoclonal antibodies (Padma, 2015).

Targeted therapy tends to be very effective at killing cancer, while having fewer side effects compared to traditional chemotherapy methods (Min & Lee, 2022). Chemotherapy is more general in its effects, while targeted therapy is much more specific. Thus, targeted therapy can only be used in patients who clearly have specific mutations or aberrations in specific pathways (Min & Lee, 2022). It also requires a certain amount of understanding of the molecular pathogenesis of a disease in order for effective targeted therapy drugs to be identified and used,

while chemotherapy can be used upon diagnosis and after appropriate staging is identified. The emergence of resistance to targeted therapy drugs has become an increasingly pressing issue in MCL and other cancers (Min & Lee, 2022). On the other hand, use of both targeted therapy and chemotherapy results in some side effects, although traditional chemotherapy usually results in more of these effects.

The main targeted drug therapies for MCL can be categorized into BTK inhibitors, NF-kB pathway targeting drugs, BCL-2 inhibitors, PI3K inhibitors, and androgen receptor blockers, which will be further explored in the next few sections. Some of these are fairly established treatments, while others are still undergoing clinical trials. Various targeted drug therapies are often used in combination to help treat MCL, which will also be discussed.

BTK Inhibitors

Bruton's Tyrosine Kinase (BTK) is a protein that plays a significant role in stimulating B-cell division and growth through the B cell receptor (BCR) signaling pathway, and chronic activation of the pathway has been linked to many types of B cell cancers, such as MCL (Hanel & Epperla, 2020; Stephens & Spurgeon, 2015). BTK plays an integral role in regulating B cell differentiation, survival, growth, and migration, and in the case of MCL, chronic BTK activation appears to promote B cell survival (Stephens & Spurgeon, 2015). Ibrutinib is an FDA approved BTK inhibitor that is used to treat several B cell malignancies including MCL. The drug irreversibly binds to a cysteine in the active site of BTK, preventing it from performing its role (Hanel & Epperla, 2020; Stephens & Spurgeon, 2015; Thomas et al., 2024). It was the first-in-class BTK inhibitor approved for MCL treatment, and was specifically preferred for relapsed/refractory MCL (Pu et al., 2022; Thomas et al., 2024). However, ibrutinib also affects other kinases such as BMX, BLK, and ITK that are found in a variety of tissues, which results in many off-target effects (Jain & Wang, 2019). Acalabrutinib is another BTK inhibitor that has been FDA approved for treating relapsed MCL (Pu et al., 2022). The drug has limited off-target activity and has been shown to have better side effect profiles compared to ibrutinib (Lu et al., 2024; Pu et al., 2022; Thomas et al., 2024). Zanubrutinib is another relatively new irreversible BTK inhibitor that has been FDA approved for treating MCL (Hanel & Epperla, 2020; Thomas et al., 2024). In fact, due to being more safe, acalabrutinib and Zanubrutinib are the BTK inhibitors currently used to treat MCL and ibrutinib is not on the US market for MCL anymore (Thomas et al., 2024).

More recently, pirtobrutinib, or LOXO-305, another BTK inhibitor, has been FDA approved for treating MCL (Pu et al., 2022; Thomas et al., 2024). As it does not bind to the cysteine residue that other BTK inhibitors target, it is effective for treating another B cell cancer, chronic lymphocytic leukemia, when the cancer develops resistance to traditional BTK inhibitors by replacing the cysteine residue with serine (C481S mutation) (Hanel & Epperla, 2020; Thomas et al., 2024). Unlike ibrutinib, acalabrutinib, and Zanubrutinib, pirtobrutinib binds to BTK in a non-covalent manner, which allows it to

also have a greater affinity and selectivity towards BTK (Hanel & Epperla, 2020). This same phenomenon occurs in some MCL cases, such that the FDA has approved pirtobrutinib use in MCL after at least two lines of treatment is already done (Thomas et al., 2024).

Nemtabrutnib is a new BTK inhibitor currently in clinical trials (Pu et al., 2022). It is a reversible inhibitor of BTKs that has been reported to be effective in treating chronic lymphocytic leukemia due to the BTK-C418 mutation, but this mutation is not common in MCL patients, so the efficacy of this drug is still uncertain (Pu et al., 2022). ARQ-531 is another BTK inhibitor but it also inhibits other kinases such as Src, Fyn, and Syk. This ability to target multiple parts of the BCR pathway may make ARQ-531 a better treatment for MCL (Hanel & Epperla, 2020). However, more studies are needed to confirm its efficacy in MCL treatment (Hanel & Epperla, 2020). Orelabrutinib is another BTK inhibitor that is highly selective, but it is irreversible (Pu et al., 2022). It has been approved for treating MCL patients who have previously gotten at least one treatment in China, but its efficacy and safety are yet to be assessed in the United States, making it currently not on the drug market in the United States (Pu et al., 2022).

NF-kB Pathway Targeting Drugs

Proteosomes are proteins that work with ubiquitin to degrade proteins in cells. As a result, they play a vital role in maintaining the balance of pro and anti-apoptotic proteins, regulating signal transduction pathways, and managing cell stress (Pu et al., 2022). Bortezomib is a first-generation proteosome inhibitor that has been shown to be moderately effective in treating MCL patients who have relapsed (Pu et al., 2022). It binds reversibly to the beta subunit of the 20S proteasome, preventing protein degradation, including degradation of lkB, the protein that keeps NF-kB inactive (Thomas et al., 2024). Thus, as overstimulation of the NF-kB is associated with MCL, bortezomib specifically targets this pathway, and allows for the inhibition of MCL growth (Thomas et al., 2024). The NF-kB pathway is also targeted by lenalidomide (Thomas et al., 2024). This drug can inhibit IkB kinase, which inhibits genes that are stimulated by NF-kB from being activated (Thomas et al., 2024). It is FDA approved and currently used for patients with MCL that has relapsed (Thomas et al., 2024).

Carfilzomib is a proteasome inhibitor that has been shown to cause MCL cell apoptosis through inhibition of the NF-kB pathway (Hanel & Epperla, 2020). It is also suggested that carfilzomib may have higher cardiotoxicity but lower neurotoxicity, and it is currently in phase II clinical trials for relapsed MCL (Hanel & Epperla, 2020).

BCL-2 Inhibitors

B-cell lymphoma-2 (BCL-2) is an anti-apoptotic protein that is often used by B-cell lymphomas to allow cells to undergo uncontrolled and excessive growth (Thomas et al., 2024). Venetoclax is a BCL-2 inhibitor that is currently being studied for

consideration in the treatment of MCL (Kumar et al., 2022; Thomas et al., 2024). It mimics the BCL-2 homology domain-3 on BCL-2, and phase-one studies have been done (Thomas et al., 2024).

PI3K Inhibitors

PI3K has been a recent therapy target in MCL (Thomas et al., 2024). Idelalisib is a PI3K inhibitor currently in clinical trials (Thomas et al., 2024). Additionally, parsaclisib, another PI3K inhibitor, is also undergoing clinical trials (Thomas et al., 2024). Currently, there are no PI3K inhibitors that have been FDA approved and are found on the market for treating MCL (Thomas et al., 2024).

Androgen Receptor Blockers

Due to the substantial sex ratio of MCL patients, with 4 males having been diagnosed with the disease for every female being diagnosed, androgen receptor expression has been studied in MCL cells (Schieber et al., 2018). Studies have found that MCL cells surprisingly have increased *AR* gene expression (Schieber et al., 2018). Currently, enzalutamide, an anti-androgen drug that is FDA approved for treating prostate cancer, is being studied, and has been shown to decrease MCL cell proliferation (Schieber et al., 2018). This has led to ongoing clinical studies to be conducted (Schieber et al., 2018).

Combination Strategies

In order to improve treatment outcomes in MCL patients, combination therapy has been a promising approach. Drugs such as rituximab and ublituximab, which are monoclonal antibodies that target CD20, are currently being tested in combination with ibrutinib in clinical trials (Stephens & Spurgeon, 2015). Additionally, combination therapy of NF-kB inhibitor bortezomib with rituximab, prednisone, doxorubicin, and cyclophosphamide has been shown to improve response rate (Pu et al., 2022). Combination strategies are commonly used based on the idea that a combination of drugs with different targets, mechanisms of action, and toxicity can help kill a wider range of subclones of MCL, including those that might persist and lead to drug resistant MCL and recurrence of the disease (Martin et al., 2017). It is an especially important treatment option for subtypes of MCL that are often resistant to chemotherapy, such as TP53 abnormal MCL (Thomas et al., 2024).

Limitations and Future Directions

MCL is a currently incurable cancer with many challenges towards finding a cure, with the main ones being severe side effects from treatment, drug resistance, and relapse. Although effective, chemotherapy, the standard for cancer treatment, can lead to long term and short term toxicities and negatively impact MCL patients' quality of life and overall survival (Jain & Wang,

2019; Martin et al., 2017). Thus, further studies into targeted therapy as well as other developments (e.g., CAR T-cell therapy) and other immunotherapies are essential.

Continued studies on combination treatment will also be important as drug resistance especially to BTK inhibitors and other small molecule drugs becomes more common. Exploring the order in which small molecule drugs should be prescribed and used, as well as prescribing a combination of drugs at once can help reduce resistance development in MCL. However, unfavorable reactions between drugs, toxicity, and other issues need to be carefully studied to ensure effective combination therapies can be formulated. Relapse of MCL is also quite common, making the need for more treatment options greatly needed (Kumar et al., 2022).

Another challenge with MCL is the late age of MCL diagnosis; as the median age of patients with MCL is 68 years old, intensive treatments are often not an ideal approach (Jain & Wang, 2019). This has been a significant barrier to novel treatments, and it severely limits the search for medications to those that are specific (with few off-target effects that could potentially be fatal in older patients) yet effective. As we progress toward chemotherapy-free treatments for MCL, drug discovery and development will continue to be vital to helping combat and hopefully eventually finding a cure to this disease. Continued participation of MCL patients in MCL clinical trials will also be of great importance moving forward (Schieber et al., 2018).

Conclusion

MCL is a type of B cell cancer that was typically treated with chemotherapy, but more recently, targeted drug therapies have become an increasingly promising approach, with many FDA approved small molecule drugs now on the market and many more in clinical trials. However, off-target effects, relapse, and drug resistance continue to be a significant problem in MCL management and treatment. With further studies on MCL, more about its molecular pathophysiology will be unraveled, allowing for more potential drug targets to be identified. This is of upmost importance due to the dire need for different ways to target MCL and help combat its ability to resist drugs. With that, more potential targeted therapy drugs will be found or developed, allowing for MCL to perhaps become a curable disease in the future.

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American Intervention in the Middle East and its Impact on Vote Choice in the 2024 Presidential Election By Aidan Friedman

Abstract

How does American involvement in conflict in the Middle East (sending money, troops, aid) impact Americans' vote choice in presidential elections? In the leadup to the 2024 Presidential Election, this paper will explore how the recent and continued attacks following October 7, 2023, in the Israeli-Palestinian conflict will impact citizens' vote choice. This research is critical to understanding how the American public responds to violence in the Middle East, particularly regarding the changes and continuities they want to see in American foreign policies. Initially, I examined the past presidencies of Jimmy Carter and Ronald Reagan and analyzed how their foreign policies resulted in Carter's removal from office. Then, I conducted a survey which utilized past questions from Gallup to achieve current data points and original questions to analyze the 2024 competing presidential candidates' (Donald Trump, Kamala Harris - seen as an extension of Joe Biden following his dropout from the race, and third party candidates) policies. From this, I will analyze the shifts or continuities in public opinion as a result of conflicts and changes in the media and its impact on vote choice. From the results we can conclude that foreign affairs will play a role in the 2024 election, with Harris's policies either deterring or motivating voters given their respective stances on the Israeli-Palestinian conflict.

Keywords: American Middle Eastern intervention, October 7th, Israeli-Palestinian conflict, 2024 Presidential Election

Intro

The United States has long played a role in Middle Eastern affairs. Intervention has become a more prominent role that the United States has taken on in the Middle East. The US has attempted to mediate and resolve issues and tensions between Middle Eastern nations as "the sole remaining superpower" and has maintained "by far the most important role of any external power in the contemporary Middle East" following the conclusion of the Cold War (Miller 1 and Lieber 1).

For example, the United States has supported Israel since 1987 being a major non-NATO partner and their close alliance can be observed through the US sending Israel about $3 billion each year in aid (Lieber 2).

Interest in the Middle East has become increasingly mainstream and publicized as conflict and US intervention has reached an all-time high. This has been particularly true regarding the Israeli-Palestinian conflict following October 7th, which is regarded as "the region's deadliest fighting in decades" (Rich 1). This has resulted in a multitude of changes in the minds of the American public and has created new divisions between various demographics of American citizens.

This research will explore how American involvement in conflict in the Middle East (sending money, troops, aid) impacts Americans' vote choice in presidential elections. I have chosen to examine presidencies, as the reasons behind who is voted in or voted out of office is profoundly demonstrative of the public's opinion, including around foreign policy and Middle East affairs.

This research seeks to analyze the effect of a variety of news outlets including social media, biased news sources, and the spread of misinformation on the American people. In detail, the mainstreaming of the Israeli-Palestinian conflict has become ingrained in the American people's mind as it has become substantially more evident in the media, especially on the topic of foreign affairs, following the October 7, 2023, attacks on Israel from Hamas, an Islamic organization that the US government has classified as a Foreign Terrorist Organization.

Currently, research has concluded that the American public has a distinct role in deciding key aspects of American involvement in the Middle East, which can be seen through the various doctrines that have been set in place to dictate American actions in the Middle East (Lee 137-138). Additionally, we know that conflict is occurring and has happened for almost a century due to differing opinions from the Israeli and Palestinian perspectives on who has the right to rule the Gaza Strip and the West Bank. However, researchers are unaware of the implications of how modernized media outlets and sources of information, and misinformation, influence public opinion on matters relating to the Middle East. This can be seen through their support of rejection of the president's foreign policies. Even more so, 2024 is a year in which presidential elections will occur for the United States, and the public's approval of the president's conduct towards Middle Eastern affairs will play a crucial role in garnering votes or losing votes to a shifting public opinion.

To analyze these components, I will first examine the research that has been completed to investigate how historical patterns in presidents' actions changed or preserved the public's opinion. Following this, I will conduct my own survey of people who are of voting age to observe their opinions of the president's actions in the Middle East. I will utilize questions that have been posed before to see any continuities or changes in opinion as well as create my own questions to deeper understand the effects of Middle Eastern affairs on the mind and opinions of the American voter.

Literature Review

Public opinion is a prominent factor in the formation of foreign policy. Thus, understanding the relationship between public opinion and foreign policy is necessary to examine its impact on the American people (Rathbun 380; Herrmann, Tetlock, and Visser 562 Holsti 434). Broadly, the ways in which public opinion is stimulated, taking a greater role in paying attention to politics, and what moves public opinion, acting on political beliefs, are factors that are forever changing. Public opinion changes as people's views do not always remain the same over time, especially when impacted by current world events causing shifts or, for example, whether it be influenced by elites, interest groups, media (including social media,

digital newspapers, etc), elected representatives, or other members of the public (Powlick 428-429). Thus, changes in public opinion result from new methods in which people seek out information and in what manner their findings are interpreted.

It is evident that the public has experienced an increased interest in foreign policies and have formulated new opinions on the United State's role in worldly affairs. A Gallup poll asked respondents whether the US should take a leading role in world affairs. 20% indicated support for a leading role, 45% for a major role, 27% for a minor role, and 7% for no role. Furthermore, a nationwide poll from the AP-NORC's Center for Public Affairs Research indicated that the public views foreign policy as one of their top issues in 2024 which marked a significant change from last year's emphasis on the economy and inflation rates (AP-NORC 1). Thus, regarding American involvement in foreign matters, the American public is very opinionated, and different variations of the American people have their own desires as to what role the United States should uphold.

Furthermore, research has concluded that elites and governmental officials create opinions which are then mainstreamed to the public primarily through the media, especially through news outlets like digital devices, television, radio, or print publications (Pew Research Center 1). Yet, the impact of elites forming public opinion "becomes moot if the media does not report what elites are saying in the first place" (Powlick and Katz 38). Thus this reveals how the media plays a large role in the public's news awareness.

As such, due to this high level of attention to and concern for world politics involving US engagements and public opinion, it is necessary to observe the public's awareness of foreign policies and understanding of foreign policies. Although some scholars have previously argued "that the public had little understanding of foreign policy," new studies show that today, a majority of Americans do (Powlick and Katz 30). According to a Pew Research Study that gave a variety of US adults the same 12 questions on international affairs, the average of correct responses was 6.3 demonstrating how a majority of the American public is aware of worldly affairs and the involvements that the US associates itself with. Furthermore, 31% of Americans who participated in this study correctly answered 9-12 of the questions correctly, a group of people considered to have a high level of international knowledge according to this Pew Research study. For instance, Kertzer and Zeitzoff argue against the notion that the public is widely unaware of issues concerning foreign policy. Instead, they point out the discrepancy between the public disagreeing with foreign policies created by elites, hinting towards a bottom-up structure to understanding foreign policy as opposed to the typical top-down structure in which elites form public opinions. Their findings indicate that the top-down theory is at times flawed and the "effect of elite cues was inconsistent" further denoting that "individuals do carry substantively meaningful orientations toward foreign affairs" (Kertzer and Zeitzoff 554).

The media's primary role in mainstreaming opinions on foreign policies generated by elites and governmental officials to the mass public also leaves space for dangerous implications. This is because media coverage and what is being reported has changed over time, especially now. Research has shown that "various ideologies that affect daily life are imposed on society by

political and economic authorities through media and advertisements" (Eren 195). As a result of these advertisements, "new media environments are among the first channels that come to mind that can be used to influence, direct people, and create public opinion because new media is a constantly active world" (Eren 195). Moreover, it is through the new media environment, the advancements in computers and internet technologies which create new digital platforms for the public's engagement, that public opinions are formed and passed on to the general public. Given the media's dominating role in the formation of public opinion, they also have the means to spread misinformation and biased information to substantially more communities. This can negatively affect voters, which can be seen through the misinformation spread throughout the 2016 US Presidential Election (Grinberg et al. 379) Thus, media coverage has a prominent role in the coverage of foreign policies and it is through this coverage, and the commentary on foreign policies, that public opinions are formed on foreign policies.

Yet, the methods in which people obtain information are forever changing with the prevalence of new media and its impact on policy making and the formation of public opinion. Since media coverage has changed drastically, where many people obtain their news from digital platforms as opposed to paper publications, we need to research whether and how public opinion has changed. With the rise of misinformation and falsifying news, there can be inconsistencies regarding specific foreign policies and the public's opinion on those matters, such as Middle Eastern matters involving Israel and American support or disapproval.

Scholars use presidential approval to analyze public opinion (Powlick and Katz 37). An analysis of changes in public opinion are demonstrated through the difference between two polls regarding presidential approval (Powlick and Katz 37). Another study found similar methods on measuring public opinion with the general standard of the president as an indicating variable of how the public views foreign policies. Given that the president is a key figure in serving as a delegate of the country, their presidential approval rating also demonstrates how the public views their actions as a diplomat. Thus, a higher rating would indicate the public's approval of the president as a delegate of foreign policy whereas a low or minority rating would indicate their disapproval (Powlick 428).

The public has watched Middle Eastern foreign affairs throughout history, especially in the conflicts between Israel and other Middle Eastern nations. This is evident through research that illustrates fluctuating variations in the American peoples' support for Israel over the past 40 years (Krosnick and Telhami 537). Additionally, public opinion has indicated that there has been a longstanding notion that Americans support Israel two to three times more than Arabs (Krosnick and Telhami 537). Moreover, this study affirmed the position that Americans have long supported Israel more than they have supported Arabs which can also be observed through foreign policies favoring Israel such as the Reagan Middle East peace plan and the Oslo Accords (Krosnick and Telhami 537).

Historically, foreign affairs have had an effect on voters and their choice in elections. As a result of foreign policies having an impact on voters, presidents are restricted to the desires of interest groups they are responsible for (Mattes, Leeds, and Carroll 289). However, the impact of

foreign policies in elections has also fluctuated over time with its importance decreasing such as when news coverage of foreign affairs decreased from 1989 with 3,733 minutes to 1996 with 1,829 minutes of discussion. Furthermore, in the 1992 election of Clinton, the foreign policies of the presidential choices was only one of the top two issues for 9% of voters (Lieber 6).

Yet, foreign affairs in the Middle East remained important to the public. It has been identified as an "exception to the lessened priority of foreign policy" because the American people have been involved with and have aimed to stay informed on the "security imperatives and threats to American interests" that have continuously risen in the region (Lieber 6). Gallup polling data also corroborates the affirmation that Americans are invested in Middle Eastern affairs as a Gallup poll that prompted "How closely would you say you have followed the recent situation in the Middle East involving Israel and the Palestinians -- very closely, somewhat closely, not too closely or not at all?" Thirty-one percent responded very closely, 41% somewhat closely, 17% not too closely, and 10% not at all in November 2023. This data demonstrates that a supermajority of the American public is aware of the situation and the fighting that is happening between Israel and Palestine. This reality also conveys how the American people are paying more attention to American-Middle Eastern foreign affairs. This results in the formation of new opinions on how the president has acted, represented through approval or disapproval when sending various forms of aid. In fact, the public's inspection of the president's actions regarding the Middle East has made the American people take sides and place their sympathies towards specific Middle Eastern countries.

However these sympathies have not remained consistent recently in 2024, marking a distinctive change from the past's overarching support for Israel over other Middle Eastern nations. A past Gallup polling data graph which prompted respondents to choose whether they were more sympathetic to Israel or to Palesntine revealed the trend that the American public has supported Israel to a far greater extent than Palestine from the period 1988 to the beginning of 2024, and throughout 2023, 54% of people had greater sympathies towards Israel. However, this historic trend regarding overall support has come into question in March of 2024 when the American alignment with Israel and approval of military actions has shifted. This shift in public opinion is demonstrated when Gallup poll administrators re-questioned the American people if they approved or disapproved of the military action Israel has taken in Gaza. The shift from the 50% majority approval rating of Israel's actions has turned into a majority disapproval through the results of 36% approval, 55% disapproval, and 9% no opinion. As the results display, although there are now double the number of people with no opinion from November 2023 to March 2024 (4% to 9%), the data dictates the growing disapproval regarding Israel.

Presently, conflict between the two nations has sustained itself throughout the time following the Reagan presidency. However, the widespread mainstreaming of the Israeli-Palestinian conflict has lured the American public into the events and occurrences of the fighting following the attacks of October 7, 2023. To the American people, the outbreak of the Israeli-Palestinian conflict sparked numerous positions to be upheld by the public. However, according to a Gallup poll that prompted if Americans supported or did not of Israeli military

action in Gaza, a majority of American people approved of the military action that Israel was taking demonstrated through a 50% approval, 45% disapproval, and 4% of people having no opinion on the matter in November 2023.

Additionally, this trend of support has continued which is further displayed through the Gallup question that prompted respondents if they think the US is doing too much, about the right amount, or not enough to provide military aid to Israel in which 31% responded too much, 42% right amount, 25% not enough, and 3% no opinion in November 2023. This data illustrates how another supermajority (a combination of the right amount and not enough categories) of the American public support providing aid to Israel. Specifically, regarding the impacts of the October 7, 2023 attacks, a Gallup question that prompted respondents on the Middle East conflict involving Israel and Gaza and whether the US is doing too much, about the right amount, or not enough to resolve this conflict the respondents reflected how the American people are in support of the United States sending aid (in the form of money, military, and other forms of aid) to Israel through 19% responding too much, 41% the right amount, 39% not enough, and 2% no opinion in December 2023. This data likewise establishes another supermajority of support for Israel (a combination of the right amount and not enough categories) and illustrates the public's approval of the actions of the president in foreign affairs matters.

Furthermore, when analyzing party affiliation regarding this situation, a Gallup poll that prompted respondents if they think the US supports Israel too much, about the right amount, or too little, respondents from the Republican party indicated 26% too much, 37% the right amount, 37% too little, and 1% no opinion. From the Democratic Party, respondents indicated 40% too much, 43% the right amount, 15% too little, and 2% no opinion. From those who identify as an Independent, respondents indicated 40% too much, 36% the right amount, 22% too little, and 2% no opinion from December 2023. These results are demonstrative of the broader historical support for Israel in terms of party as the Republican Party has supported Israel substantially more than the Democratic Party and more than Independents. The supermajority of support for Israel from Republicans in December of 2023 at 74% is representative of their historic support for Israel, especially following the attacks of October 7th, seen through a Gallup graph detailing the trend of "Net Sympathy for Israel (net sympathy for Israel is % more sympathetic toward Israel minus % more sympathetic towards the Palestinians) in the Middle East Situation, by Party ID." This trend graph displays how above a majority 55-82% of Republicans have supported Israel in the Middle East since 2002 ending at 67% in 2023 compared to Independent support for Israel maintaining an average between 31-52% from 2002-2019 and decreasing slightly and ending at 17% in 2023, and compared to a lessened Democratic support for Israel maintaining an average between about 17-35% from 2002-2015 and then rapidly decreasing to -11% ending in 2023.

It remains to be seen whether the recent shift in disapproval towards Israel will lead to a desire to keep Vice President Kamala Harris in office as the next President (with Harris and her policies seen as an extension of President Biden). This is due to Biden's and Harris's

perspectives on the Israeli-Palestinian conflict, such as with their support for the two-state solution, departing from previous affirmations that revealed their support for Israel. This two-state solution would reveal a decreasing support for Israel as this also demonstrates a shift towards support for the Palestinian cause as well. This contrasts former President Trump's unwavering support towards Israel in comparison to other Middle Eastern nations such as when naming Jerusalem the capital of Israel. Thus, I believe Harris's support for the two state solution will cause the American people to side more with her in the 2024 presidential election.

Methods

There are a multitude of methods in which public opinion can be analyzed. This investigation will focus on how the president's action in foreign affairs in the Middle East, especially with the recent conflicts, generates support or deviation from their candidacy in subsequent elections. First, I review a few historical cases; then, I will build on these cases to conduct a survey of public opinion.

In my case studies, I will focus on past presidencies of Jimmy Carter and Ronald Reagan, as a shift in public opinion is displayed through their consecutive presidencies, to examine how their actions and policies impacted public opinion. To elaborate further, these presidents are crucial to American involvement in the Middle East, and in turn are demonstrative of public opinion on Middle Eastern affairs, as these presidents experienced and had to respond to turmoil in the Middle East throughout their tenures.

Thus, we can measure public opinion about foreign policy by analyzing the changes in approval ratings between two presidencies. Building off the theory of the activation of public opinion and how presidential approval ratings are reflective of the public's support or disapproval of their actions, as mentioned in the beginning of the literature review, examining the consecutive presidencies of Jimmy Carter to Ronald Reagan are exemplary examples.

Case Studies

Jimmy Carter's Carter Doctrine did not support full military intervention in the Middle East but rather selective military intervention as his policy to secure the containment of Iran (Lee 2022, 137). Carter was President from 1977 to 1981 and only served one term, witnessing both the Iranian Revolution (ending in February 1979) and the Iranian Hostage Crisis which began in November 1979. Mixed with economic stagflation and inefficiently resolving tensions and issues arising in the Middle East, he lost a majority of his approval which led to his demise and quick replacement in the consecutive presidential election.

Further, Carter's approach to alleviate the tensions in the Middle East did not satiate the public as his approval rating towards the end of his presidency fell to the mid-thirties. Additionally, he had an average approval rating of 45.5% according to a Gallup Job Approval Ratings Trend chart and polling data. The public's involvement with Carter's presidency is a result of the "hostage crisis quickly bec[oming] an important, spectacular, and even melodramatic story on network television news" in which 75% of the US public was able to easily observe (Pach 552). In addition to a substantial number of American citizens constantly

analyzing his actions, Carter's inability to designate a specific date as to when the hostages would be returned to the United States, eventually turning into 444 days, was detrimental to garnering support from those who had previously supported him as it demonstrated to that he was not fulfilling his role sufficiently in the eyes of the public. Carter's subsequent loss in the 1980 election demonstrates the American public's role in determining who is going to be the president and how the president's actions in the Middle East reflects the American public's opinion on their functionality as the president and their views on foreign affairs. By taking Carter out of office, who was focused on selective and not direct military intervention, the public communicated how they wanted more direct policies and intervention in the Middle East which is seen through Reagan's foreign policies as Carter's approval slipped to "30 percent in the foreign area" (Roberts 1).

Moreover, in contrast to Carter's indirect policies, the public demonstrated their approval of Reagan's actions in the Middle East especially in times of intense American intervention with foreign conflicts seen under the Reagan Administration. For example, Reagan initiated the Reagan Middle East peace plan in which the United States "had become Israel's 'full partner,'" taking a direct role, with the objectives in resolving peace between the conflicting Israeli and Palestinian nations being organized under "a framework of absolute Israeli security acquiesces to a long-standing Israeli thesis" (Aruri and Moughrabi 11). In correlation with the federal government's affirmations, the American people demonstrated their support for Reagan's policies in the Middle East. Reagan obtained an average 52.8% approval rating throughout his presidency compared to the last three presidents losing a majority of approval seen through Carter's 45.5%, Gerald Ford's 47.2%, and Richard Nixon's 49% according to Gallup polling data. Thus, this paved the way for Ronald Reagan to obtain a greater level of support in the 1980 election as he aimed to avenge the losses from Carter, running his platform under the notion of "'Elect me and you won't have to take that anymore'" (Pach 560). Reagan drew on the current public opinion to form his own Reagan Corollary which called for the United States to defend against "all military threats, whether from within the region or without" (Brands, Cook, and Pollack 4).

Given this standpoint, Reagan's active military intervention in the Middle East proved to be a high priority to the public and his engagements in the Middle East were something that increased his support. In particular, with the Israeli-Palestinian conflict gaining prevalence in foreign politics, his actions in this conflict, and alignment with Israel found its support within the American people. As demonstrated through his creation of the Reagan Middle East peace plan, the American public supported Reagan's outline for Israel and Palestine, despite clearly defining Israel's terms of the plan while using ambiguous language such as the "legitimate rights of the Palestinians" to refer to the objectives for the Palestinians (Aruri and Moughrabi 12). By utilizing language regarding the "legitimate rights" of Palestinians, Reagan implies that "some rights are not legitimate" which highlights how Reagan and the public favored Israel in the peace-making process (Aruri and Moughrabi 12).

Subsequently, due to a lack of defined terms in this peace plan, the United States as a whole further demonstrated their overall support for Israel when mediating between the two nations in the Oslo Accords. In this peace-making process, beginning within the Reagan Administration, the plan called for the Palestinians' "acceptance of UNSC Resolution 242 along with explicit recognition of Israel's right to exist" (Hassan 66). Resolution 242 and the overall Oslo Accords are in favor of the two-state solution in which Israel withdraws from the stipulated areas in "the West Bank and the Gaza Strip" (Hassan 69). However, radicals within each nation eventually did not agree to full terms of the agreement which has led to the continuation of fighting and conflict in the Middle East between the two nations. Moreover, from these case studies, it is important to understand how past changes in public opinion due to involvements and policies in the Middle East demonstrate a continuity or change when analyzing current day foreign affairs, given the new forms of media coverage and access to news.

Survey Methods

The methods for this research, analyzing how recent events will impact voters and their electoral choices in presidential elections, will be conducted in a comparative format: analyzing the responses garnered from survey questioning and comparing them to historical patterns.

Public opinion has been studied in a variety of ways including surveys, analyzing vote choices, based on literature, and more. I will use a survey to analyze how the current conflicts and present-day news influences voters and what effect new media and current conflicts will have in the 2024 presidential election. Comparing the survey responses to past data will demonstrate either a shift in who individuals vote for or will demonstrate voters fixed political beliefs. This research deepens the examination of how these factors create an impact domestically, such as through how voters will decipher between presidential candidates and what foreign policies they affiliate with. After securing the results, I will compare the results to the historical data to demonstrate the public's shifting opinion and the influence of the mainstreaming Middle Eastern conflicts to the American public.

I used questions provided from Gallup, original questions, and past research and investigations on American involvement in foreign countries in the Middle East and the implications it had on American citizens. I will send this survey to those of voting age as I will be able to analyze a large group of American citizens from a variety of demographics, preferably between 50-75. Sending it to those of voting age will additionally deepen my examination of this research as it will give insight to how foreign policy will impact voters who will be voting in the 2024 presidential election. The survey will be sent out on Google Forms via email with no inclusion of personal identification to ensure anonymity and accurate results.

Regarding the first five questions in the survey, their purpose is to establish the character of the respondent and to get insight on their experiences in life that may have any implications regarding vote choice. These capture the age, race, religious affiliation, and highest level of education of the respondent.

1. How old are you?
2. What is your race/ethnicity?
3. What is your religious affiliation, if applicable?
4. What is your highest level of education?
5. What state is your primary residence located in?

Question 6 is necessary to the content of the survey as understanding their political party affiliation will determine whether or not they will shift or if their opinions will remain the same at the end of the survey. This question will capture the respondent's party affiliation.

6. Which political party do you affiliate with?

Question 7 will help identify how news coverage, the place in which they obtain their political information, impacts their political ideologies and how new media has influenced vote choice. This question will capture the primary source of their news intake.

7. Where do you primarily get your news from?

Questions 8 and 9 set the foundation for the rest of the survey and provide the general information about whether the respondent is aware of the global affairs which involve the United States and the role they believe the US should be taking. These questions will capture the respondents awareness of American foreign affairs and the respondent's belief as to what role the US should take on in regard to foreign affairs.

8. Do you pay attention to America's engagements internationally – foreign affairs?
9. Do you think the U.S. should -- [ROTATED: take the leading role in world affairs, take a major role but not the leading role, take a minor role, (or) take no role at all in world affairs]?

Building off the respondent's global awareness in question 8, question 10 narrows the focus of their knowledge to the Middle Eastern situation, providing the necessary information to set the foundation for their beliefs on the conflict. This question will capture the respondent's awareness of the Middle Eastern situation, specifically the Israeli-Palestinian situation.

10. How closely would you say you have followed the recent situation in the Middle East involving Israel and the Palestinians -- very closely, somewhat closely, not too closely or not at all?

Question 11 is crucial to the survey as it will demonstrate the respondent's preference towards a Middle Eastern country, providing the initial information that will determine which

political party they might vote for in 2024. This question will capture which nation they are more sympathetic to.

11. In the Middle East situation, are your sympathies more with the Israelis or more with the Palestinians?

Questions 12 and 13 present the respondent with the conflicts that have been happening in the Middle East and demonstrate their opinions on their approval or disapproval of American and Israeli engagements in the Middle East. These questions capture their approval of American and Israeli actions in the Middle Eastern situation.

12. Do you think the United States is doing – [ROTATED: too much, about the right amount, or not enough] – to resolve this conflict?
13. Do you approve or disapprove of the military action Israel has taken in Gaza?

Questions 14 and 15 center on the aid that the United States has granted to Israel throughout the conflicts and if they approve of it or not. In this, these questions will help establish their opinions on whether they will approve or disapprove of presidential candidates who plan on sending more aid to Israel or less aid. These questions will capture the respondent's stance on American support for Israel and their belief on if American involvement bettered the US.

14. Do you think the United States is doing too much, about the right amount or not enough to provide military aid to Israel?
15. Do you approve of the military action, monetary support, and other forms of aid that the American government has provided to Israel?

Questions 16-18 prompt respondents on how they believe President Biden has performed in office in regard to his engagements in the Middle East. These questions will capture the respondent's perspective on Biden's presidency and if they believe what he has done is for the betterment of the United States or not.

16. Do you think President Biden's foreign policies and engagements with foreign entities in the Middle East (Israel and Palestine) were beneficial to the United States?
17. Do you think President Biden's foreign policies and engagements with foreign entities in the Middle East (Israel and Palestine) were beneficial to the resolution of conflict?
18. Overall, do you approve of President Biden's foreign policies and engagements with foreign entities in the Middle East (Israel and Palestine)?

Question 19 prompts the respondent with whether or not foreign affairs and policies will impact their vote choice in the presidential election. Thus, this question will capture whether or not the respondent believes that the president's action in other countries will impact their vote choice.

19. Will foreign policy and American intervention in the Israeli-Palestinian conflict impact your choice for president in the 2024 presidential election?

Question 20 asks whether or not the respondent will vote for the Democratic Party or not, indicating their belief on the necessity for a bipartisan effort towards Israel or whether they will vote for the Republican Party, capturing their belief on the necessity for greater support and aid to Israel.

20. Will President Biden's actions and foreign policies directed towards the Middle East, specifically regarding the Israeli-Palestinian conflict, deter you from the Democratic Party or increase support for the Democratic Party?

Question 21 is crucial to the survey as it provides the information on whether or not the respondent's opinion has shifted or has remained the same throughout the duration of Biden's presidency. This question will capture who the respondent voted for president in 2020.

21. What candidate did you vote for in the 2020 Presidential election?

Question 22 provides information on whether or not new media and current events will impact, change, or keep the respondent's opinions the same by prompting the question of who they will vote for in the 2024 Presidential election. Due to President Biden stepping down, I am treating Vice President and Presidential candidate Kamala Harris as an extension of President Biden in this question. This question will capture who the respondent is intending to vote for in the 2024 presidential election.

22. Which candidate will you vote for in the 2024 Presidential election?

Questions 9-14 have been extracted from previous Gallup polls where respondents were asked those questions. I will compare the historical data they have captured and compare it to the new data that I will poll to identify differences or similarities in public opinion.
Based on the current tensions and transitions in support, I hypothesize that the survey will demonstrate decreasing support for Israel which may contribute to more people voting for the Democratic Party and people continuing to vote for the Democratic Party, as they have historically been more reserved in their support for Israel as opposed to the Republican Party. A shift from historical patterns will be demonstrated when there is a decreased support for Israel

and a continuity of historical patterns will be demonstrated as support for Israel. This is due to Americans being bipartisan in their support for Israel, as they have been a beacon of Western ideologies in the Middle East which caused the United States to support Israel.

Thus, I hypothesize that respondents who changed from Democrat to Republican did so because they disapproved of Biden's policies in the Middle East. In terms of survey questions, I hypothesize these individuals have disapproved of Biden's actions and will respond "not enough" to question 12, "no" questions 17 and 18, "yes" to question 19, and "deter" in question 20.

I hypothesize that respondents who changed from Republican to Democrat did so because they approved of Biden's policies in the Middle East. In terms of survey questions, I hypothesize these individuals will respond "yes" to questions 16-18, "yes" to question 19, and "increase support" in question 20.

Further, I hypothesize that respondents who voted for Trump and indicate they will vote for Trump disapprove of Biden's policies in the Middle East. In terms of survey questions, I hypothesize these individuals will respond "Israel" to question 11, "approve" to question 13, "not enough" or "about the right amount" to question 14, "no" to questions 16-18, "yes" to question 19, and "deter" in question 20.

I also hypothesize that respondents who voted for Biden and indicate support for Kamala Harris approved of Biden's policies in the Middle East. In terms of survey questions, I hypothesize that these individuals will respond "about the right amount" to question 12, "yes" to questions 16-18, and "increase support" to question 20.

Results

Overall, I found that the results did support the hypotheses I created. Across the four hypotheses, the majority of the results aligned with the predictions I made in regard to the specific changes and continuities for each respective hypothesis.

The survey was live during the period of August 7, 2024 to August 24, 2024. In total, I obtained 51 responses to the survey.

A large demographic responded to the survey. The ages ranged from 18-78 with each respective generational age group encompassing the following percent of the total responses: 2% who had 18-29 years of age, 17.6% who had 30-44 years of age, 52.9% who had 45-59 years of age, and 27.5% who had 60-78 years of age. The survey covered six different ethnic and racial groups with each encompassing the following percent of the total responses: 76.5% white, 9.8% Asian, 5.9% Hispanic or Latino, 3.9% Black or African American, 2% Middle Eastern, and 2% from mixed races. Regarding respondents' religious affiliations, five major religions were accounted for with a large percentage of respondents also noting religion did not apply to them. Of the total responses, the following percent of people marked an affiliation with the following beliefs: 52.9% Jewish, 23.5% Christian, 15.7 indicated no religious affiliation, 3.9% Catholicism, 2% Buddhist, and 2% Islamic. Three major educational groups were recorded in the responses to my survey - each encompassing the following percent of the total responses: 76.5%

with a graduate degree or higher, 15.7% with an undergraduate degree, and 7.8% with a high school diploma. Lastly, 62.7% of the total respondents marked an affiliation with the Democratic Party, 17.6% marking no party affiliation, 15.7% marking an affiliation with the Republican Party, and 3.9% classifying themselves as independents.

Although my results account for a variety of different cultural, racial, political, religious, and educational groups, I do not think that the results are representative of the entire American population. In the survey, a little more than 75% of respondents were white, 92.2% of respondents were from California, and 52.9% were Jewish. Thus, I think my results were limited in the sense that although a large portion of the population was covered in the survey, the results are highly reflective of the beliefs of people who live in California, are white, and who are affiliated with the Jewish faith. However, my results do capture major aspects of the American population, accounting for many age groups, religions, ethnic/racial groups, educational backgrounds, and party affiliations.

Overall, there was a majority of respondents in support for Biden's policies; however, a large number of respondents did indicate they disapproved of his policies. I found that 43.1% of all respondents disapproved of Biden's policies targeting the Israeli-Palestinian conflict overall, 39.2% specifically noted their belief that Biden's policies were not beneficial to the US, and 52.9% specifically noted their belief that Biden's policies were not beneficial to conflict resolution in the Israeli-Palestinian conflict. In contrast, I found that 56.9% of all respondents approved of Biden's policies targeting the Israeli-Palestinian conflict overall, 60.8% specifically noted their belief that Biden's policies were beneficial to the US, and 47.1% specifically noted their belief that Biden's policies were beneficial to conflict resolution in the Israeli-Palestinian conflict.

Next, the task is to understand how/whether this level of support for Biden's policies is impacting respondents' vote choice this upcoming November.

For my first hypothesis, focusing on individuals who switched from the Democratic to the Republican Party, I hypothesized that this change would occur if Democratic voters in 2020 disapproved of Biden's policies. I coded a respondent as switching from Democratic to Republican if they voted for Biden in 2020 but marked "Trump" or "not sure yet or not sure if I will vote" with the addition of marking that Biden's policies will deter them from the Democratic Party. No respondents who voted for Biden in 2020 said they would switch to Trump. However, we can look at the people who seem hesitant to support the Democratic party because of Biden's policies: Only 4 people said they weren't sure if they were going to vote for Harris or not vote. All of these respondents said Biden's policies had deterred them from the Democratic party.

Of the 43.1% of respondents who disapproved of Biden's policies, four respondents who had voted for Biden in 2020 indicated their hesitation towards choosing Harris in the 2024 election by marking the option detailing how they are not sure who they will vote for or if they will vote. However, the four respondents who voted for Biden in 2020 and marked "not sure yet or not sure if I will vote" when asked who they will vote for in 2024 indicated that Biden's foreign policies will deter them from the Democratic Party. Individually, in regard to my

question predictions, two out of four people who marked the unsure option fully aligned with my predictions, the other respondent chose every predicted answer beside one and the last respondent chose every predicted answer beside two.

For my second hypothesis, focusing on individuals who switched from the Republican to Democratic Party, I hypothesized that this change would occur if Republican voters in 2020 approved of Biden's policies. I coded a respondent as switching from Republican to Democratic if they voted for Trump in 2020 but marked "Harris" or "not sure yet or not sure if I will vote" with the addition of marking that Biden's policies will increase support for the Democratic Party.

Respondents who had voted for Trump in 2020 indicated their decision to vote for Harris in the 2024 election. Individually, in regard to my question predictions, both respondents fully aligned with my predictions:they indicated approval of Biden's foreign policies across all three of my measures and indicated these policies had increased their support for the Democratic party.

For my third hypothesis, focusing on individuals who indicated they voted Republican in 2020 and will vote Republican again, I hypothesized that this would occur if Republican voters in 2020 disapproved of Biden's policies. During the time my survey was live, Kennedy was still in the presidential race, however, given his dropout, I have classified individuals who marked they were going to vote for him as Republican Party voters due to his endorsement. I coded a respondent as remaining a voter of the Republican Party if they voted for Trump in 2020 but marked "Trump" or "Kennedy" or "not sure yet or not sure if I will vote" with the addition of marking that Biden's policies will deter them from the Democratic Party.

Eight people had voted for Trump in 2020. 5 of these people said they would be voting for Trump again, while three said they weren't sure who they would vote for or they weren't sure whether they would vote. Overall, all 8 of these respondents generally disapproved of Biden's foreign policies.

One additional respondent marked that they did not vote in 2020, but would vote for Kennedy in 2024. Due to Kennedy's endorsement of Trump, this voter was classified as someone who would be voting for Trump in 2024. They indicated that Biden's foreign policies would deter them from the Democratic party.

For my fourth hypothesis, focusing on individuals who indicated they voted Democratic in 2020 and will vote Democratic again, I hypothesized that this would occur if Democratic voters in 2020 approved of Biden's policies. I coded a respondent as remaining a voter of the Democratic Party if they voted for Biden in 2020 but marked "Harris" for 2024.

24 people voted Democratic in 2020 and planned to do so again, while one person voted for Biden in 2020 but said they were not sure who they would vote for or whether they would vote in 2024. All 24 people indicated support for Biden's foreign policies while 22 of them indicated strong support, and all said Biden's foreign policies would increase their support for the Democratic party. The one respondent that wasn't sure who they would vote for or whether they would vote indicated that Biden's foreign policies would deter them from voting for Harris.

Although less directly related to my primary hypotheses, I found another trend. Every Jewish respondent besides three out of twenty-seven who responded to the survey indicated their

sympathies are with Israel in the Middle Eastern situation, the US is doing about the right amount or not enough to resolve conflict, and that the US is doing about the right amount or not enough to provide military aid to Israel. However, these results were not surprising to see. Due to Jewish people's high support for Israel and US forms of aid being sent to Israel, this data lends credibility to my overall results.

Moreover, my results confirm my hypotheses regarding party switches and continuities on the basis of disapproving or approving Biden's policies in the Middle East. Compared with historical trends discussed earlier in this paper such as in the case studies and past Gallup questions, this aligns with the perspective that the Republican Party has a stronger affiliation and tendency to favor Israel on the topic of sending aid. Looking back to historical data as well, my results align under the perspective that the Democratic Party is more critical of Israel and more hesitant towards sending aid.

Conclusion

In this research paper, analyzing an overview of the literature, case studies, and original surveying, I set out to answer how American involvement in conflict in the Middle East (sending money, troops, aid) impacts Americans' vote choice in presidential elections. This research is important because of the increasing polarization surrounding the Middle Eastern situation, particularly that of the Israeli-Palestinian conflict. Furthermore, this research is highly impactful to present day conversations regarding the political sphere as the Presidential Election is upcoming. Thus, understanding a multitude of perspectives that would arise out of the election is important to make informed decisions regarding vote choice.

After the case studies involving an examination of the presidencies of Jimmy Carter and Ronald Reagan, I aimed to see how the Middle Eastern situation would impact the current election given there has been a major outbreak in relation to conflict. This situation is similar to the tensions that had resulted from the transition from Carter to Reagan, and the current conflict has placed a lot of pressure on the Biden-Harris administration to respond, similar to the pressure exhibited by Carter. So, I set out to see how the present day conflicts, specifically focused on the Israeli-Palestinian conflict, would impact vote choice and why.

Resulting from the original research I conducted, I found that a supermajority of respondents, 66.7%, noted that the Israeli-Palestinian conflict would have an impact on their vote choice for the upcoming 2024 Presidential Election. This supermajority of people, I believe, is representative of the larger American population and the increasing emphasis that foreign policies and affairs will have in this upcoming election. The respondents of my survey indicated another supermajority (66.7%) of voters intending to vote for Kamala Harris in 2024.

Additionally, I analyzed the relationship between party switches and party continuities. The primary reasoning behind party switching involved the disapproval of the current president's policies, from Democrat to Republican, or approval of the president's policies, Republican to Democrat. However, in relation to party switches, there were a very small number of people who demonstrated an inclination to switch parties. For example, only four respondents were classified

as Democrats who would switch to Republican and only two respondents were classified as Republicans who would switch to Democrat. Based on this, I found that a larger majority of respondents indicated they would remain supporters of the party they chose to vote for in 2020. For example, all eight people who voted for Trump in 2020 were classified as voters who would be voting for Trump again in the 2024 election. Likewise, 24 out of the 25 people who voted for Biden in 2020 indicated that they would be voting for Harris in 2024.

In this research, there were some limitations. The primary limitation of the research was that a very large portion of the respondents were from California, 92.2% of respondents. This was a limiting factor of the research as California is a very Democratic state, which could have resulted in the limiting of perspectives from the Republican viewpoint. However, the survey did encompass perspectives from the Republican party, mildly counteracting the limitation.

In the future, a potential field of research could be analyzing what the actual results would be from voters. In detail, this research could focus on the people who indicated that the Israeli-Palestinian conflict would impact their vote choice and who they actually voted for in the 2024 Presidential Election.

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Benefits and Pitfalls of Alternative Energy Sources on the Economic Development of Republic of Kazakhstan By Sultan Zhorakhan, Almaskhan Nurgalym, Kairatuly Adilzhan, Juvarov Kassymkhan.

Abstract

The research paper explores the growing demand for renewable energy sources in Kazakhstan, driven by environmental, economic, and social factors. The paper highlights the depletion of fossil fuels, rising energy costs, and climate change as key motivations for this transition. Technological advancements and public awareness further enhance the shift toward sustainable energy. The paper analyzes various renewable energy sources in Kazakhstan, such as solar, wind, and hydropower, and examines their economic and environmental impacts.

While renewable energy presents significant economic benefits, including job creation, energy cost reduction, and improved environmental conditions, it also comes with challenges. These include high initial investment costs, infrastructure limitations, and energy production instability. Additionally, developing countries like Kazakhstan face financial risks, as the adoption of renewable energy is often dependent on external factors such as technological development from more advanced countries.

The research concludes by assessing the potential for renewable energy in Kazakhstan, examining successful and unsuccessful projects, and providing insights into the feasibility of further developments in this sector. The paper emphasizes that a strategic, well-supported approach is necessary to overcome challenges and realize the economic and environmental benefits of renewable energy.

Introduction

Currently, there is a significant increase in demand for renewable energy sources. This demand is growing for several reasons related to environmental, economic, and social factors. Firstly, one of the key reasons is climate change and the associated environmental issues. Fossil fuels such as coal, oil, and gas emit carbon dioxide (CO_2) and other greenhouse gasses when burned, contributing to global warming. Alternative energy sources like solar and wind power produce significantly fewer CO_2 emissions. Moreover, traditional energy sources are often associated with air and water pollution, while alternative energy sources have a smaller impact on ecosystems.

The depletion of traditional energy sources is an important factor. Fossil fuels are finite resources, and their reserves are limited. In contrast, solar energy, wind, geothermal energy, and other renewable resources are available in unlimited quantities. Additionally, the prices of oil and gas can fluctuate significantly due to political and economic factors, making them less reliable in the long term.

Technological progress also plays a significant role in the growing demand for alternative energy sources. Modern technologies are becoming more efficient and accessible, increasing their competitiveness compared to traditional energy sources. Technological advancements and mass

production lead to reduced costs of alternative energy technologies, such as solar panels and wind turbines.

Finally, public opinion and social responsibility also contribute to the increasing demand for clean energy. Growing public awareness of the consequences of climate change and the need for sustainable development encourages individuals and organizations to switch to renewable energy sources. Many companies strive to improve their environmental image and meet sustainability requirements, prompting them to use clean energy.

All these factors together contribute to the growing demand for alternative energy sources and their integration into the energy systems of various countries. Increasing attention to environmental issues and the need to reduce carbon footprints promote the development of solar, wind, and hydro energy. Countries worldwide, including Kazakhstan, aim to reduce their dependence on fossil fuels and invest in sustainable energy solutions, accelerating the transition to a more environmentally friendly and economically viable energy system.

Between 2007 and 2017, the total capacity of renewable energy sources worldwide more than doubled, indicating a significant increase in interest and investment in these clean energy sources. The economic benefits of using renewable energy can be substantial: reducing dependence on imported energy carriers, creating new jobs, improving environmental conditions, and reducing healthcare costs.

For example, in Kazakhstan, in the village of Shubar in the Ordabasy district of the Turkestan region, a solar power station allows private entrepreneur Bakhtiyar Yusupov to power his greenhouse and sell surplus energy, earning an additional profit of 500,000 tenge ($1,073). The use of alternative energy sources has also benefited a medium-sized sugar refining enterprise located in the village of Baskuduk in the Munailinsky district of the Mangystau region. This solar power station benefits nearby residents and company employees, and it has reduced the use of diesel generators by almost 90%, positively impacting the polluted area's environment.

However, renewable energy sources can negatively impact economic benefits due to high initial installation and maintenance costs. Infrastructure limitations, energy production instability, and the need for additional investments in grids and energy storage also pose significant financial risks. Moreover, insufficient technological development and dependence on subsidies can hinder achieving economic sustainability and competitiveness in the long term. The role of corruption and the irrational use of budgets cannot be overlooked either. Overall, the introduction of renewable energy sources can adversely affect the economic conditions of many developing countries that cannot afford such investments. For example, in Kazakhstan, the development of renewable energy directly depends on more developed countries like China or Russia.

The aim of this research is to assess the economic benefits or losses from the introduction of alternative energy sources in Kazakhstan. The study will examine current trends in renewable energy development in the country, the economic and environmental aspects of their use, and analyze examples of successful and unsuccessful projects in this field. The results will allow conclusions to be drawn about the prospects and feasibility of further developing renewable energy

in Kazakhstan.

Literature review

1. Present (conventional) energy resources

Coal. Kazakhstan's coal reserves comprise approximately 37 billion tons (4% of world estimated reserves). The primary coal mining areas are the Karaganda and Ekibustuz basins, with enough reserves to last over a century. However, smaller coal deposits in other regions remain underutilized. Nowadays, Kazakhstan produces 120 million tons of coal. Up to 80% of the produced coal is used within the country for the production of electricity and heat generation in thermal power plants. The rest, 22 million tons, is exported. The Government has plans to increase the volume of coal production nearly two times to almost 200 million tons by 2030. Its applications include coal combustion in furnaces, providing heat to mine facilities, and the generation of coke used at industrial enterprises. Unfortunately, it is coal of a high ash content that contributes to pollution, because sulfur and nitrogen oxide flue gas scrubbers are not common in power plants using this fuel. Efforts at promoting alternative fuels can be in the form of coal-bed methane and coal-mine methane. A pilot plant installed in the Lenina mine gives 1.4 MW of electrical power from coal-mine methane. However, such technologies as carbon capture and storage and underground coal gasification are not currently included in Kazakhstan's intentions.

Oil. Kazakhstan has proven on-shore oil reserves in the west of the country which will allow extracting oil for over 30 years, estimated at 30.0 billion barrels (3.9 billion tons) of oil representing 1.8% of world reserves. The country has 172 oil fields and 42 gas condensate fields at the Caspian Sea and overall production in 2013 was 81.8 million tons. Particularly remarkable is that the Fields of Tengiz, Kashagan, and Karachaganak account for more than 50% of the oil produced.

Uranium. Kazakhstan is the world's leader in uranium production. The country has 15% of global uranium resources. This year the country yields 22,550 tonnes of uranium per year and its share in total world production is 38%. Significantly, 90% of Kazakhstan's uranium production is exported. The country's only nuclear power plant, the 90-MW Mangyshlak fast reactor in Aktau, was closed down in 1999 after 27 years of operation, but a cooperation agreement with Russia aims to commission a new nuclear power station as of May 2014.

2. Renewable energy resources and potential in Kazakhstan

Hydropower. Hydropower accounts for roughly 13% percent of Kazakhstan's total generating capacity delivering around 7.78 TWh from 15 large (>50 MW) hydro power stations with a total capacity of 2.248 GW. Large hydropower plants in the country include those at Bukhtyrma (750 MW), Shulbinsk (702 MW) and Ust-Kamenogorsk (315 MW) on the river Irtysh, Kapshagai (364 MW) on the Ili River, Moinak (300 MW) on the Charyn river, and Shardarinskaya (104 MW) on the Syrdarya River. Small (1-10 MW) and medium-scale (10-50 MW) hydropower projects have grown in popularity due to being less costly, reliable and environmentally friendly. There are seven small hydropower plants (<10 MW), with the total installed capacity amounting to 78 MW and the

estimated potential–13 TWh, located in the east and south of Kazakhstan, Zhambyl and Almaty provinces.

Wind Power. The vast steppe geography of Kazakhstan makes it an ideal setting for wind power projects. The country's economically realizable wind energy potential is estimated at 760 GW. About 50% of the territory of Kazakhstan has average wind speeds adequate for energy generation, from 4 to 6 m/s. It should be noted that the greatest wind potential in the country is in the area of the Caspian Sea, central regions, and northern regions. The best sites would appear to be in the Almaty region in the Djungar (Dzhumgarian) Gates, 600 km northeast of Almaty close to the Xinjiang border, and the Chylyk Corridor, 100 km east of Almaty. Estimates are that these sites have wind potentials of 525 W/m² in the Djungar Gates and 240 W/m² in the Chylyk corridor. Consequently, wind turbines established here can, therefore, realize energy generation of 4400 kWh/MW and 3200 kWh/MW, respectively. Besides, it has initiated the construction works for Kazakhstan's first wind power plant in Yerementau of the Akmola region. It is designed by 22 FWT2000 2 MW turbines with an installed capacity of 45 MW and a production capacity of 172.2 kWh.

Solar energy. Kazakhstan has areas with high insolation that could be suitable for solar power, in the first place, particularly in the south of the country, receiving between 2200 and 3000 hours of sunlight per year, which equals 1300-1800 kW/m² annually. There are no intentions of building a concentrated solar thermal plant although the government of Kazakhstan has ambitious plans to introduce 1.04 GW of renewable energy capacity.[1]

3. Economic implications.

Economic Value of Renewable Energy.

Job Creation: Investments directed at renewable energy ventures will bring about job creation. For example, installation of wind power creates more jobs in relation to manufacturing, installation, and maintenance. *Reduced Energy Costs:* Renewable energy sources will gradually reduce the cost of energy to consumers and businesses. Electricity generated using solar panels and wind turbines is created without any fuel cost.

Diversification: Moving to renewables diversifies the energy mix in Kazakhstan and reduces overdependence on fossil fuels, which enhances the security and resilience of the energy system.

Export Opportunities: As a renewable energy champion, Kazakhstan can export excess clean energy to neighboring countries, contributing to cross-border trade and economic growth[2]

Challenges and Considerations.

Initial Investment: Renewables are beneficial in the long term but are often characterized by high initial investments. This, however, is offset with long-term savings.

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[1] 1. Marat Karatayev , "Current Energy Resources in Kazakhstan and the Future Potential of Renewables: A Review," Energy Procedia, December 4, 2014, https://www.sciencedirect.com/science/article/pii/S1876610214017214.

[2] Anett Großmann et al., Economy-wide effects of adaptation in the Energy Sector, accessed July 22, 2024, https://www.giz.de/en/downloads/giz2021-en-kazakhstan-economy-wide-effects-of-adaptation-in-the-energy-sector.pdf.

Infrastructure Development: Renewable energy infrastructure, including such things as wind farms or solar parks, requires planning and financing and coordinated activity.

Policy Support: For promoting the use of renewable energy, effective policies and incentives are vital. Entrepreneurs face challenges like high interest rates and short loan terms when adopting green technologies.[3]

Current Scenario in Kazakhstan.

In 2019, around 16% of Kazakhstan's Gross Domestic Product was associated with the energy sector, including mining and energy supply. But the share of renewable energy remains small compared to that of fossil energy.

The country aims to achieve 50% electricity generation from non-coal or oil sources (including renewables) by 2050, as part of its Green Economy Concept[4]

Renewable energy sources (RES) have the potential to contribute to economic, social, and environmental sustainability. They improve access to energy, reduce emissions, and create local development opportunities. This paper highlights the economic benefits of RES for sustainable development, environmental impact including global warming, advantages and disadvantages, and strategies for optimum exploitation.

Access to affordable and reliable electricity is crucial for eradicating poverty and achieving long-term success. Factors such as livelihoods, water availability, agricultural production, healthcare, and equality for women are impacted by energy access. Social and environmental considerations must be addressed when selecting renewable technologies. The use of renewable energy sources helps protect natural resources and reduce the risks associated with fossil fuels. Solar and wind power have less serious environmental impacts compared to traditional sources.

Renewable energies include land and resources such as sunshine, air, rainfall, waves, and geothermal energy. Solar and wind power are quickly regenerated and can be tied into the local power grid. Biofuel production historically has cost more than fossil fuels, but it includes various commodities that can be used for human consumption. The high cost of solvent extraction is a challenge for producing biofuels from phytoplankton. Dependence on environmentally friendly resources is limited by factors such as weather conditions.

The world will heavily rely on renewable electricity sources in the future. Oil, coal, renewables, and nuclear power are the three main types of energy available. Solar, wind, bioenergy, and groundwater are among the sources used to produce power. Renewable technologies offer opportunities for employment generation, decrease emissions, and improve the quality of life in

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[3] "Transition to Renewable Energy Sources: Economic Benefits for Entrepreneurs in Kazakhstan," UNDP, February 12, 2024, https://www.undp.org/kazakhstan/stories/transition-renewable-energy-sources-economic-benefits-entrepreneurs-kazakhstan.

[4] Iea, "Kazakhstan Energy Profile – Analysis," IEA, accessed July 22, 2024, https://www.iea.org/reports/kazakhstan-energy-profile.

remote areas. Implementing renewable energy projects in rural areas can boost the local economy.

Conventional power production using fossil fuels is inefficient and harmful to the environment. There is a global push to include more renewable energy sources like solar and wind power to meet energy needs sustainably. Renewable sources have the potential to supply the country's energy needs multiple times over. Achieving a decent standard of living through sustainable development requires the adoption of renewable energy sources.""[5]

The document discusses the environmental impacts and economic benefits of renewable energy sources such as solar, wind, biomass, hydropower, and geothermal energy. It highlights the challenges and provides recommendations for the effective and efficient utilization of renewable energy in Nigeria. The key points are:1. Renewable energy sources have lower environmental impacts compared to conventional fossil fuels, but face challenges such as financial constraints, technological incapability, lack of comprehensive national energy policy, and low public awareness.2. Recommendations include increased government support, subsidies, and funding for renewable energy research and development, as well as bridging the gap between research institutions and manufacturing industries.3. The document discusses the global status and trends for different renewable energy technologies, their advantages, disadvantages, and strategies for optimum exploitation.4. Renewable energy is crucial for sustainable development, as it can positively impact various aspects of social, economic, and environmental development.""[6]

This pioneering study examines the relationship between renewable energy consumption, urbanization, financial development, and environmental outcomes in South Asian nations. Using panel quantile regression analysis, the study finds that renewable energy consumption has a negative impact on CO2 emissions, particularly in higher quantiles. Urbanization has a positive effect on GDP, while natural resource rent positively impacts both GDP and CO2 emissions. Broad money boosts GDP in lower quantiles but has a negative impact in higher quantiles. The findings suggest that governments should focus on promoting renewable energy consumption and sustainable urbanization to combine economic development with environmental sustainability.

South Asian nations like Pakistan, Bangladesh, and India face challenges in sustaining environmental quality due to factors such as population expansion, urbanization, and industrialization. These nations experience issues like water and air pollution, deforestation, and

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[5]Algarni, Salem, Vineet Tirth, Talal Alqahtani, Sultan Alshehery , and Pravin Kshirsagar . "Contribution of Renewable Energy Sources to the Environmental Impacts and Economic Benefits for Sustainable Development." Sustainable Energy Technologies and Assessments, February 21, 2023. https://www.sciencedirect.com/science/article/abs/pii/S2213138823000917.

[6] Sani, Garba Danjumma, Abubakar Ibrahim, Suleiman Sahabi, and Bashar Badamasi Lailaba. "Renewable Energy: Environmental Impacts and Economic Benefits for Sustainable Development." International Journal of Engineering Research & Technology, September 2, 2019. https://www.ijert.org/renewable-energy-environmental-impacts-and-economic-benefits-for-sustainable-development.

insufficient waste management. Environmental degradation affects the economy, society, and health, leading to productivity loss, higher healthcare expenses, and vulnerability to natural disasters.

The study focuses on the South Asian Association for Regional Cooperation (SAARC) countries: Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan, and Sri Lanka. These countries are chosen for their unique attributes and provide a comprehensive framework for analyzing sustainable development patterns in South Asia. The availability of relevant data facilitates a thorough analysis of the complex relationship between economic development and environmental sustainability.

Urbanization and natural resource utilization are key factors affecting environmental quality in South Asian countries. Urbanization leads to increased demand for resources and energy, resulting in pollution and waste. The overuse of natural resources leads to environmental degradation. Broad money, which refers to the total quantity of money in circulation, also impacts environmental quality. Investigating these factors is essential to understand their consequences on the environment.

Renewable energy consumption is another crucial aspect that affects South Asia's environmental quality. Switching to renewable energy sources can reduce CO2 emissions and mitigate climate change. However, the region faces challenges in adopting renewable energy due to factors like cost. Examining the impact of renewable energy consumption on the ecosystem is therefore crucial.

The study utilizes panel data analysis to evaluate the impact of these variables on CO2 emissions and environmental indicators. The data sources include national statistics and the World Bank's KOF Globalization Index. The results can assist regional stakeholders and policymakers in developing strategies to address environmental deterioration in South Asian nations.

The research aims to contribute to the discourse on balancing economic development with ecological conservation in the SAARC region. The findings provide insights into the relationship between carbon emissions and sustainable economic growth. By informing policy decisions, the study has the potential to mitigate environmental degradation in the region.

Overall, the study highlights the importance of renewable energy consumption and sustainable urbanization in achieving economic development with environmental sustainability in South Asian countries. By addressing environmental challenges through effective policies, governments can promote a greener and more sustainable future.'"[7]

This study examines the relationship between economic growth, carbon emissions, and industrial structure. It highlights the importance of sustainable urban communities and the need to transition to renewable energy sources. The effects of climate change are impacting regions worldwide, and it is crucial to address environmental degradation and cooperate between developed

[7] Imran Khan, Ihsan Muhammad , Arshian Sharif, Inayat Khan, and Xiangbo Ji. "Unlocking the Potential of Renewable Energy and Natural Resources for Sustainable Economic Growth and Carbon Neutrality: A Novel Panel Quantile Regression Approach." Renewable Energy, December 4, 2023. https://www.sciencedirect.com/science/article/abs/pii/S0960148123016944.

and less developed countries. The UN conference on climate change has emphasized the urgent need for greenhouse gas emission reduction and the acceleration of renewable energy transition.

The study focuses on two groups of emerging economies in different regions and their efforts to balance economic growth with environmental protection. The growth rates of these economies have been driven by attracting foreign investments in energy-intensive industries. Previous research has confirmed the pollution haven hypothesis for these countries, but there are differences between the European countries and the ASEAN countries. The European countries, now EU members, have adopted stricter environmental regulations and targets for carbon neutrality. Asian economies, particularly the ASEAN countries, have made progress in renewable energy and energy intensity reduction.

The key features of a developed economy include sustained economic growth, urbanization, and industrial development. These features contribute to human welfare and economic development but also pose challenges to the environment. Therefore, policymakers need to find optimal policies to promote growth while curbing environmental degradation. Economic growth is especially important for developing economies, and strategies that prioritize renewable energy and innovation can contribute to both economic development and climate change mitigation.

This research analyzes several emerging economies and their potential for sustainable development. The study aims to fill gaps in the existing literature and explore the nexus between urbanization, financial development, economic growth, industrial structure, and environmental degradation. Achieving sustainable growth and contributing to climate change mitigation are crucial objectives for these economies.'"[8]

Methodology

The facts revealed by the survey on the use of the alternative energy resource in Kazakhstan and how it will affect the economy are helpful for the general understanding of the public opinion and regions' outlooks. Here's a comprehensive analysis based on the data collected:

1. Demographic Breakdown

Respondents of the survey are young and 35 percent of them are between twenty and thirty years old. 8 % in the age group of 18-27 years. This implies that the young people are very active in debates relating to renewable energy. For instance, none of the respondents are of 60 years and above, which implies that older people's perceptions could not be captured through this survey.

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[8] Florian Marcel Nuţă, Ali Sharafat, Oliver Joseph Abban, Itbar Khan, Muhammad Irfan, Alina Cristina Nuţă, Alex Boadi Dankyi, and Muhammad Asghar. "The Relationship among Urbanization, Economic Growth, Renewable Energy Consumption, and Environmental Degradation: A Comparative View of European and Asian Emerging Economies." Gondwana Research, November 30, 2023. https://www.sciencedirect.com/science/article/abs/pii/S1342937X23003222.
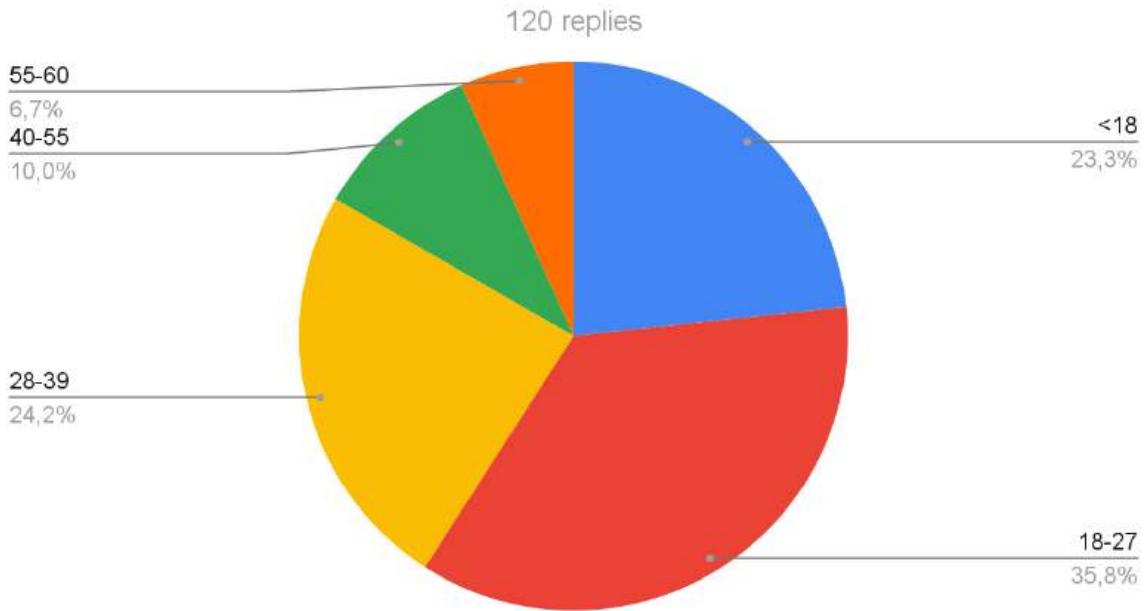
Figure 1: Average age of the respondents

2. Regional Distribution

Thus, according to the geographical distribution of the respondents South Kazakhstan has the maximum number of responses 35% while Northern Kazakhstan responded 29.2%. This may mean the institutions in these regions may be more interested in or have a better access to the alternative energy resources. On the other hand, western Kazakhstan has a comparatively low respondent rate 8.3 % which may in a way mean less interested or fewer available sources for the alternative energy. Equally allowed but less represented is Central Kazakhstan claiming 17. 5%, and East Kazakhstan with 10% representation.
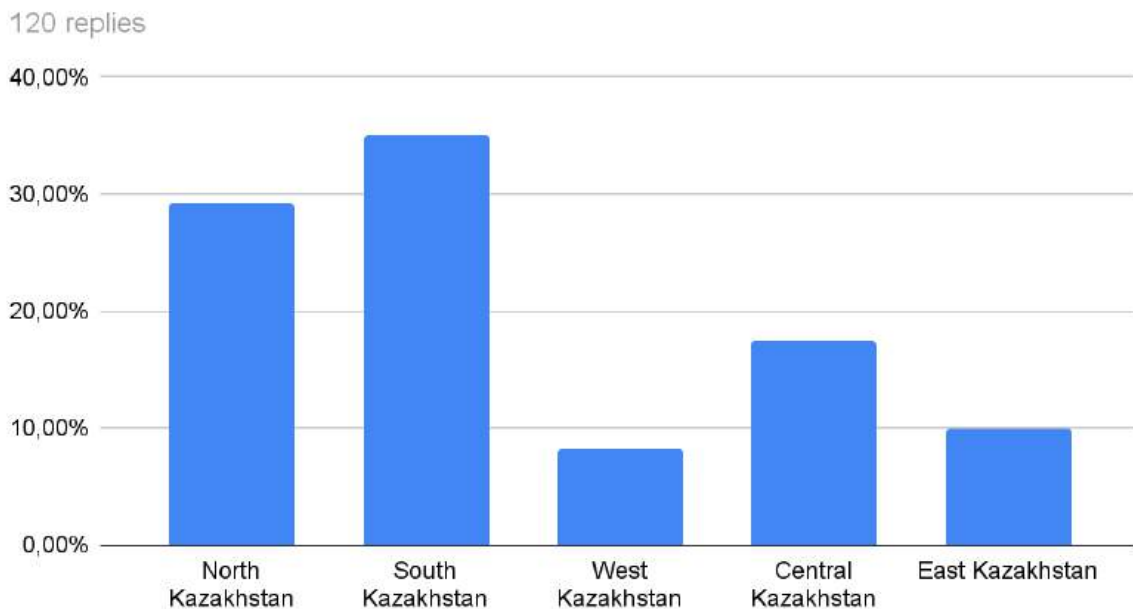
3. Accessibility of the Other Forms of Energy Supply

The option that comes out on top of the poll is solar energy as 70 of the respondents designate it as the most available type of alternative energy. 8% of respondents. Hydro power is the second with 53. 3% of the population Using coal power, 20. 7% of respondents. No respondent reported they are using geothermal energy, possibly because the area of the country is not endowed with the resource, or has not invested in it. Additionally, 19. Finally, there are the respondents who reported that their region does not offer any sources of alternative energy, which implies a highly prospective field.
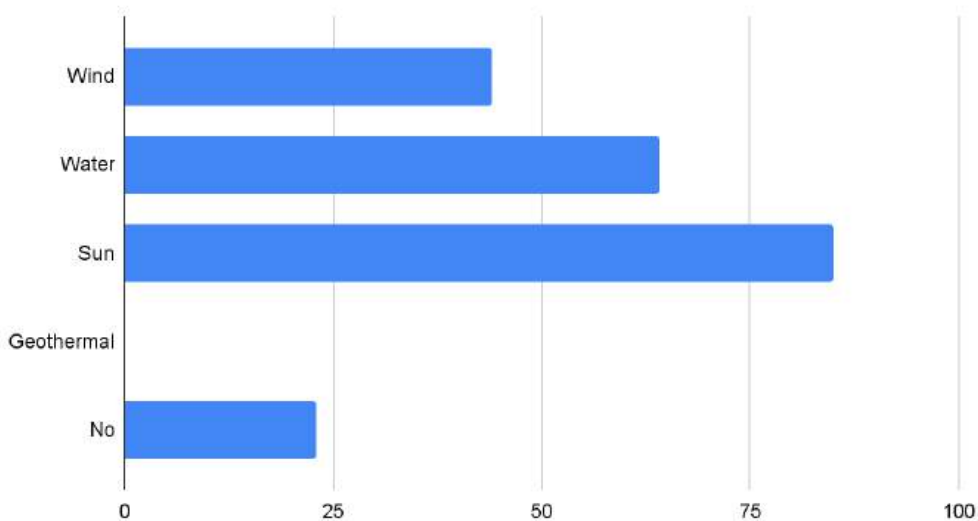

Figure 3: Types of green energy utilized

4. Economic Impact Perception

Respondents have varied views on the economic benefits of alternative energy:Respondents have varied views on the economic benefits of alternative energy: It's noteworthy that 45% of the participants are convinced that the process will create economic benefits. 25.8% percent of the respondents believe that outsourcing will not pose a major impact to the economy. 22.5% say that it may have risks which may incur losses. 6.7% of surveyed people stated that they have difficulties with it. This spectrum of thinking can be caused by the tendencies to be optimistic in terms of economical contributions of alternative energy to Kazakhstan.
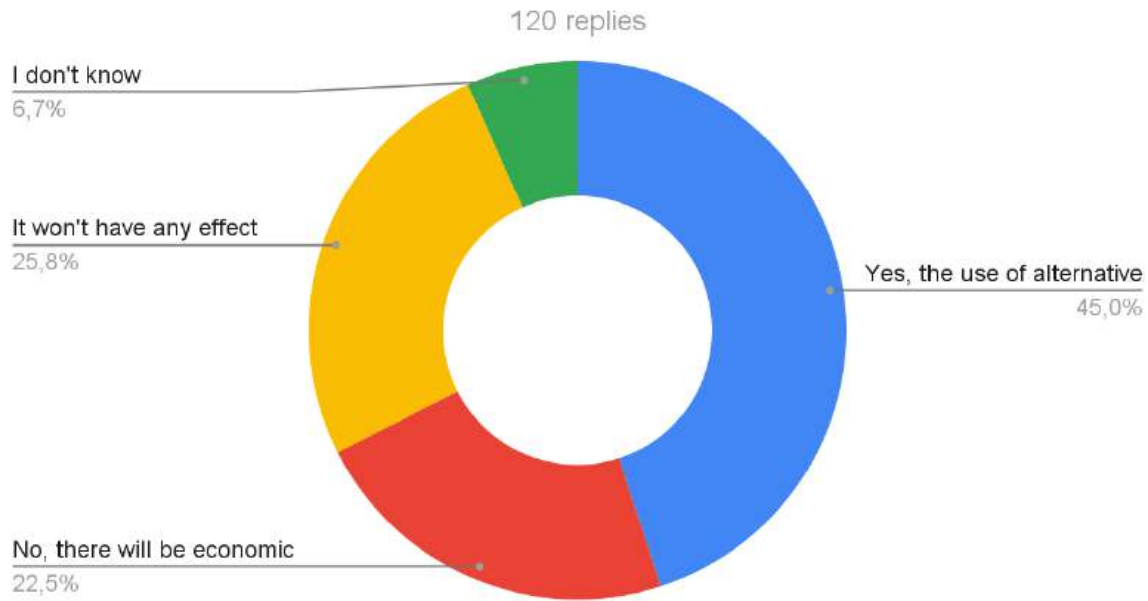
Figure 4: Opinion on the impact on the economy

5. Initial Investment Assessment

      Opinions on the justification of initial investments in alternative energy are diverse: 11.7% view high initial costs as justified in the long term. 30.8% feel the costs are high and not justifiable. 29.2% think the costs are sufficient. 18.3% consider the costs unreasonably low. 10% believe the costs are justifiably low. This spread indicates significant concern over the financial burden of transitioning to alternative energy compared to traditional sources.
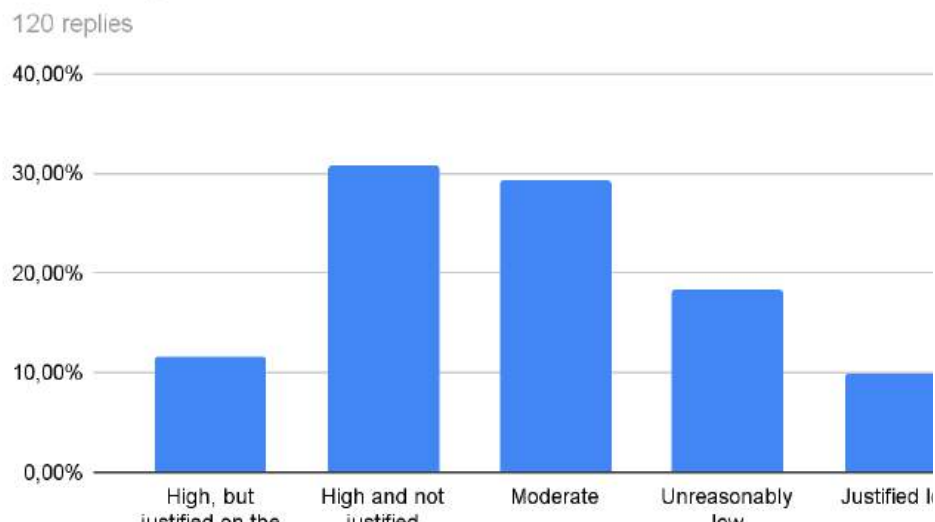

Figure 5: Initial Investment Assessment

6. Job Creation Potential

There is a generally positive view on job creation related to alternative energy: 28.3% completely agree that it can create new jobs. 40.8% partially agree. 18.3% disagree. 12.5% find it difficult to answer. This reflects a broadly favorable perspective on how alternative energy might contribute to employment.
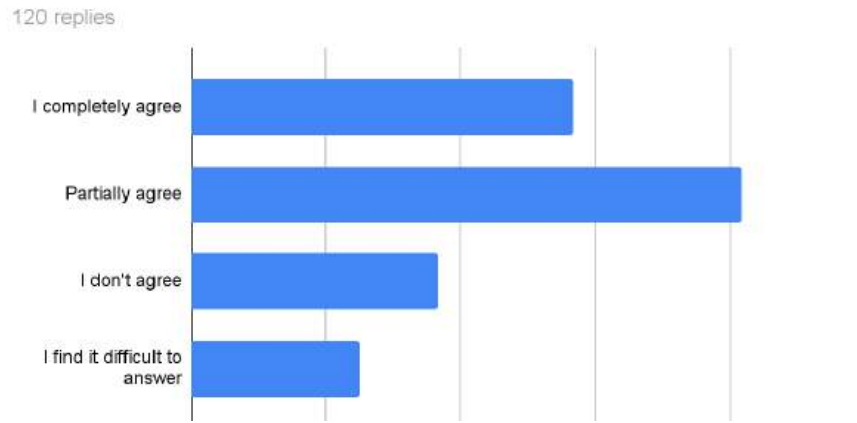
Figure 6: Job Creation Potential

7. Barriers to Development

The main barriers to the development of alternative energy in Kazakhstan are: Low awareness of the population (45%). Lack of technology and infrastructure (29.2%). High initial costs (19.2%). Political and legislative barriers (6.7%). Addressing the low awareness and infrastructure challenges could be crucial in advancing alternative energy in the country.

Figure 7: Barriers to Development

8. Future Economic Impact

Looking to the future, respondents have diverse expectations for the economic impact of alternative energy: 20% anticipate a strong positive influence. 33.3% expect a weakly positive effect. 17.5% foresee a weakly unprofitable impact. 6.7% think it will be highly unprofitable. 12.5% believe it will have a minor impact.

Figure 8: Future Economic Impact

Analysis of Survey Results on Alternative Energy in Kazakhstan
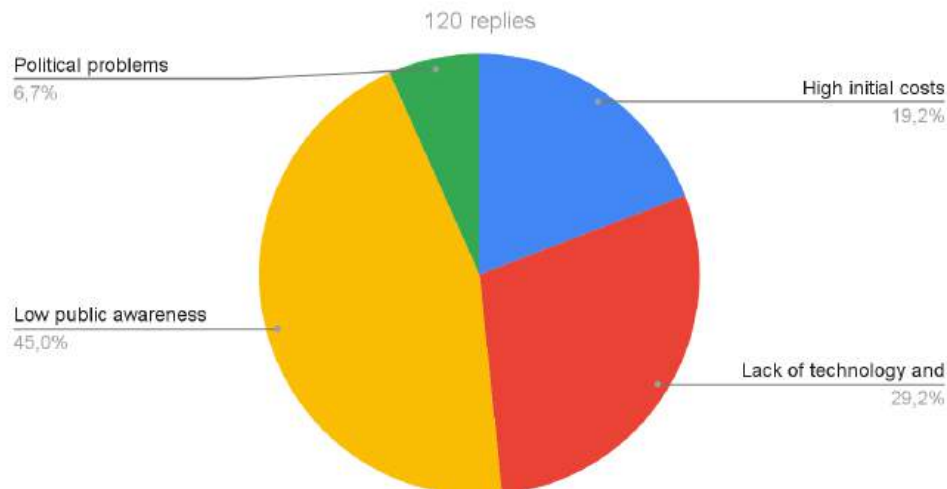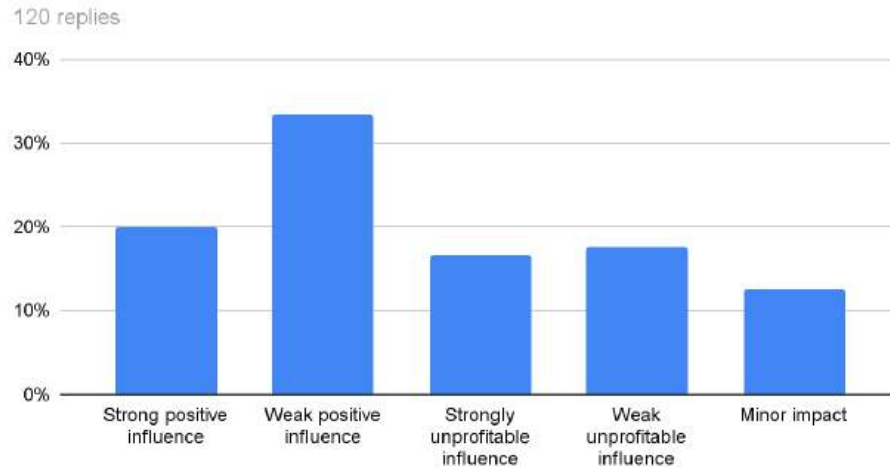
The survey on alternative energy in Kazakhstan offers a glimpse into how people across different regions and age groups perceive the future of energy in their country. Here's a more personal take on the findings:

1. Who Took the Survey?

Most of the survey participants are young, with 35.8% between 18 and 27 years old. This suggests that younger people are really paying attention to the future of energy in Kazakhstan. It's worth noting that there weren't any respondents over 60, so we might be missing some valuable insights from older generations who have seen the country's energy landscape evolve over time.

2. Where Are They From?

A significant portion of respondents come from South Kazakhstan (35%) and Northern Kazakhstan (29.2%). This could mean that people in these areas are more aware of or interested in alternative energy. Meanwhile, only 8.3% of the respondents are from Western Kazakhstan, which might suggest that either alternative energy isn't as big of a topic there or it simply hasn't gained as much traction yet. Central and East Kazakhstan also have their voices represented, but to a lesser extent.

3. What Energy Sources Are Available?

Solar energy seems to be shining the brightest, with 70.8% of respondents reporting its availability in their regions. Hydro power is also fairly common, with 53.3% of people saying it's an option where they live, and 36.7% have access to wind power. Geothermal energy, on the other hand, hasn't made any headway—nobody reported its availability. Alarmingly, 19.2% of respondents said they have no alternative energy sources at all, highlighting a significant gap that needs to be addressed.

4. How Do People View the Economic Impact?

Opinions on whether alternative energy will benefit Kazakhstan's economy are pretty mixed: 45% are optimistic, believing it will bring economic benefits; 25.8% think it won't make much of a difference; 22.5% are worried it could actually lead to economic losses; 6.7% aren't sure what to

think. This range of opinions shows that while many are hopeful, there's still a lot of uncertainty and concern about the economic implications.

5. What About the Costs?

When it comes to the initial costs of investing in alternative energy, people have different views: 11.7% think the high costs are worth it in the long run; 30.8% feel that these costs are too high and not justified; 29.2% believe the costs are about right; 18.3% actually think the costs are unreasonably low; 10% consider the costs justifiably low. This spread of opinions suggests that many are concerned about the financial burden of switching to alternative energy, especially when compared to traditional sources like coal, oil, and gas.

6. Can Alternative Energy Create Jobs?

The idea that alternative energy could lead to new job opportunities is generally well-received: 28.3% fully agree that it can create new jobs; 40.8% partially agree, seeing some potential; 18.3% don't think it will make a difference in job creation; 12.5% are unsure; overall, there's a positive outlook on the potential for job creation in the alternative energy sector, which could be a big plus for the economy.

7. What Are the Main Barriers?

The biggest challenge to developing alternative energy in Kazakhstan seems to be a lack of public awareness, with 45% of respondents citing this as a major issue. The next big hurdle is the lack of technology and infrastructure (29.2%), followed by high initial costs (19.2%). Political and legislative barriers are less of a concern, with only 6.7% seeing them as a major obstacle. This suggests that improving education and building the necessary infrastructure could make a big difference.

8. What Does the Future Hold?

Looking ahead, people have mixed expectations about how alternative energy will impact Kazakhstan's economy:

20% are optimistic, expecting a strong positive influence; 33.3% think it will have a mildly positive effect; 17.5% worry it could have a weakly negative impact; 6.7% believe it could be highly unprofitable; 12.5% think it will only have a minor impact.

This mix of views shows that while many people see potential benefits, there's also a fair amount of uncertainty about what the future holds.

Steps to Assess and Calculate the Economic Benefit or Loss:

1. Current Energy Profile and Costs:

Determine Kazakhstan's current energy mix, including the proportion of energy generated from fossil fuels versus renewable sources.

Analyze the costs associated with current fossil fuel-based energy production, including fuel costs, operation and maintenance, and environmental costs.

2. Investment in Alternative Energy:

Estimate the capital investment required to transition to alternative energy sources such as wind, solar, hydro, and biomass.

Consider the costs of building new infrastructure, integrating renewable energy into the grid, and potential subsidies or incentives.

3.   Cost of Renewable Energy:

Calculate the levelized cost of electricity (LCOE) for various renewable energy sources in Kazakhstan. The LCOE includes capital costs, operation and maintenance costs, and the cost of capital over the life of the energy plant.

Compare the LCOE of renewable energy sources with that of traditional fossil fuels.

4.   Economic Benefits:

Cost Savings: Estimate the potential savings from reduced reliance on imported fossil fuels and the reduced environmental and health costs associated with lower emissions.

Job Creation: Analyze the potential for job creation in the renewable energy sector, including manufacturing, installation, and maintenance of renewable energy infrastructure.

Energy Security: Assess the impact on energy security and the stability of energy prices due to diversification of energy sources.

5.   Environmental and Social Impact:

Quantify the reduction in greenhouse gas emissions and other pollutants as a result of switching to renewable energy.

Assess the long-term benefits related to public health and the environment, which might translate into economic benefits through reduced healthcare costs and improved quality of life.

6.   Scenario Analysis:

Conduct a scenario analysis comparing different levels of investment in renewable energy (e.g., low, medium, and high investment scenarios).

Calculate the net present value (NPV) and the internal rate of return (IRR) for these scenarios to assess the long-term economic impact.

To illustrate, let's assume:

Current energy mix: 70% fossil fuels, 30% renewable energy.

Investment requirement: $10 billion over 10 years to increase renewable energy to 50% of the energy mix.

LCOE for renewable energy: $0.06 per kWh.

LCOE for fossil fuels: $0.08 per kWh.

Annual energy demand: 100 TWh.

Reduction in healthcare costs due to lower emissions: $1 billion annually.

Cost Comparison:

Current fossil fuel energy cost: 70 TWh * $0.08/kWh = $5.6 billion annually.

Future renewable energy cost: 50 TWh * $0.06/kWh = $3 billion annually.

Savings in energy production: $5.6 billion - $3 billion = $2.6 billion annually.

Total Benefits:

Annual savings from energy production: $2.6 billion.
Reduction in healthcare costs: $1 billion.
Total annual economic benefit: $2.6 billion + $1 billion = $3.6 billion.

Investment Analysis:

Total investment: $10 billion.
Payback period: $10 billion / $3.6 billion ≈ 2.8 years.

This simplified analysis suggests that Kazakhstan could experience significant economic benefits from increasing its investment in renewable energy. The actual benefits would depend on various factors such as the rate of technological advancements, global energy prices, and government policies.

DISCUSSION

The survey data on alternative energy in Kazakhstan provides a comprehensive look at the economic benefits and challenges associated with transitioning to renewable energy sources. The results highlight key factors such as demographic engagement, regional distribution, energy accessibility, and perceptions of economic impact, all of which play crucial roles in shaping the potential economic outcomes of adopting alternative energy.

A significant finding is the high level of engagement among younger demographics, with 35% of respondents between the ages of 20 and 30, and 8% between 18 and 27. This suggests that the younger population is actively participating in debates around renewable energy, which bodes well for the future. Their interest and involvement could drive demand for alternative energy solutions, leading to increased support for policies and investments in this sector. This demographic's enthusiasm can be a catalyst for economic growth, as they are likely to advocate for and adopt renewable energy, contributing to a more sustainable energy market.

Regionally, the data shows that South Kazakhstan (35%) and North Kazakhstan (29.2%) have the highest number of respondents, indicating a greater interest in or access to alternative energy resources in these areas. In contrast, Western Kazakhstan, with only 8.3% of respondents, appears less engaged or has fewer resources available for alternative energy development. This disparity suggests that economic benefits from alternative energy might be concentrated in regions with higher engagement and better infrastructure. These regions could attract more investment and development, leading to regional economic growth driven by the renewable energy sector.

In terms of energy accessibility, solar energy emerges as the most available and preferred option, with 70% of respondents identifying it as the top alternative energy source. Hydropower follows with 53.3%, while coal remains in use by 20.7% of respondents. The absence of geothermal

energy use may indicate either a lack of natural resources or insufficient investment in this area. The popularity and accessibility of solar energy suggest that it could be a primary focus for economic benefits, helping to reduce energy costs and reliance on fossil fuels. This shift could lead to substantial savings for both consumers and the economy at large.

The perception of economic impact is varied among respondents. While 45% believe that alternative energy will bring economic benefits, 25.8% think it will have little impact, and 22.5% foresee potential risks that could lead to losses. This spectrum of opinions reflects both optimism and caution regarding the economic contributions of alternative energy to Kazakhstan. The significant portion of optimistic respondents suggests a strong belief in the potential for positive economic outcomes, which could drive further investment and policy support in the renewable energy sector.

However, opinions on the justification of initial investments in alternative energy are mixed. Only 11.7% of respondents view high initial costs as justified in the long term, while 30.8% feel these costs are too high and unjustifiable. This concern over financial burdens presents a potential barrier to widespread adoption. Addressing these concerns through financial incentives, subsidies, or technological advancements could make alternative energy more financially viable and unlock significant economic benefits.

The potential for job creation in the renewable energy sector is another positive economic aspect, with 28.3% of respondents completely agreeing and 40.8% partially agreeing that alternative energy can create new jobs. This positive outlook on employment opportunities suggests that the transition to renewable energy could stimulate local economies, particularly in regions where traditional energy sources are being phased out.

Despite the positive aspects, several barriers to the development of alternative energy in Kazakhstan remain. The survey identifies low awareness among the population (45%), lack of technology and infrastructure (29.2%), and high initial costs (19.2%) as the main challenges. Overcoming these barriers, particularly by increasing public awareness and developing necessary infrastructure, is crucial for advancing the alternative energy sector. Doing so could lead to significant economic benefits, including job creation, reduced energy costs, and increased energy security.

Looking to the future, respondents have mixed expectations for the economic impact of alternative energy. While 20% anticipate a strong positive influence, 33.3% expect only a weakly positive effect, and smaller percentages foresee negative impacts. This uncertainty highlights the need for careful management and strategic planning to ensure that the transition to alternative energy yields the maximum economic benefits.

CONCLUSION

In conclusion, the economic benefits of using alternative energy sources in Kazakhstan are significant and multifaceted, with the potential to create substantial long-term advantages for the country. As global demand for renewable energy continues to rise due to environmental, economic, and social factors, Kazakhstan stands at a pivotal moment to capitalize on this shift. The growing

awareness of climate change, the depletion of fossil fuel reserves, and the increasing efficiency and affordability of alternative energy technologies all point toward the urgent need for Kazakhstan to transition to cleaner, more sustainable energy solutions.

The environmental benefits of renewable energy are clear. Fossil fuels such as coal, oil, and gas are finite resources that contribute heavily to greenhouse gas emissions and pollution, both of which exacerbate climate change and environmental degradation. In contrast, alternative energy sources like solar and wind power produce far fewer carbon emissions and have a much smaller impact on ecosystems. These sources of energy are not only more sustainable but also more abundant and reliable in the long term, positioning Kazakhstan to reduce its reliance on traditional energy sources and mitigate the environmental costs associated with fossil fuel consumption.

From an economic perspective, the shift toward renewable energy presents numerous opportunities for Kazakhstan. As evidenced by successful projects like Bakhtiyar Yusupov's solar-powered greenhouse and the medium-sized sugar refinery in Baskuduk, renewable energy has the potential to create new revenue streams and improve the livelihoods of local businesses and communities. By reducing reliance on imported energy carriers and fossil fuels, Kazakhstan can improve its energy security and stabilize its economy in the face of fluctuating oil and gas prices. Moreover, renewable energy projects can generate significant job creation, particularly in regions with high interest and accessibility to these technologies. This not only supports economic growth but also contributes to social development by engaging the younger population and building a workforce skilled in green technologies.

Despite these benefits, Kazakhstan faces several challenges in its transition to renewable energy. The high initial costs of installation and maintenance, combined with infrastructure limitations, represent significant financial hurdles. Renewable energy production can be unstable, and additional investments are required to develop the grids and energy storage systems necessary to support a fully integrated renewable energy infrastructure. The economic risks associated with these investments are further complicated by Kazakhstan's reliance on more developed countries like China and Russia for technological advancements and subsidies. Corruption and inefficient use of budgets also pose barriers to achieving economic sustainability and long-term competitiveness in the renewable energy sector.

Nevertheless, these challenges are not insurmountable. By addressing financial and infrastructural barriers and strategically managing the transition, Kazakhstan can unlock the full economic potential of alternative energy sources. This will require a coordinated effort to leverage job creation opportunities, foster international partnerships, and ensure that renewable energy projects are implemented in regions where they are most viable. Engaging the younger population and promoting education and training in renewable energy technologies will be crucial to building a skilled workforce capable of driving the country's transition to a sustainable energy system.

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Economic Analysis of a Simplified Model of a D-T Fusion Reactor's Breeder Blanket
By Elijah Roller

Abstract

Studies have explored the different materials that have a high enough TBR, or Tritium Breeding Ratio, to be used in a Deuterium-Tritium Reactor's breeding blanket, which has the goal of "breeding" tritium, the rarest component of the reactor, also of which is fuel alongside deuterium. In this report we find using a very basic spherical model what material is the most efficient economically. We first find the TBR of the 5 different materials we are testing, after which we find the price of what the breeder blanket should cost given a specific radius and compare the two. Following this we then analyze any other qualities of the material, after which we determine which is the best material from an economical standpoint. We determined in this that the material most likely to be the most economically efficient out of the selected 5 was lithium titanate.

1. Introduction

In this work, we determine the material for a tritium breeding blanket that over a deuterium-tritium (DT) reactor's lifetime will be the most efficient in terms of cost while not greatly affecting its tritium breeding rate (TBR).

Using OpenMC's Monte Carlo simulations, we calculate the TBR of various materials. Using this, we estimate the cost of TBR of materials, for a D-T reactor over an assumed 30-year lifetime, assuming a breeder blanket lifespan of 10 years.

The purpose of this work is to determine which material would keep costs down the most without sacrificing TBR, not what design of a D-T reactor would be best. In some cases, being economically efficient outweighs TBR, and in some TBR outweighs economic efficiency. Ensuring that tritium self sufficiency is always possible is most important, due to how rare tritium is and how it and deuterium are fuel for the reactor.

2. Background on Fusion Reactors

2.1. Nuclear Fusion

Nuclear fusion is where two atomic nuclei combine together, as opposed to nuclear fission where an atomic nucleus splits into two. Both nuclear fusion and nuclear fission produce large amounts of energy, however nuclear fusion can produce four times as much as fission does [1]. D-T reactors use Deuterium-Tritium (D-T) reactions, which have the following formula [2]:

$$^2H + {}^3H \rightarrow {}^4He + n + 17.6 \text{ MeV*}$$
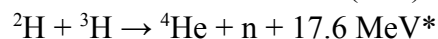
*the neutron created by the reaction carries out 14 MeV

In order for D-T reactors to produce energy, the rate of energy being generated by fusion reactions must surpass the rate of energy losses to the environment as indicated by the Lawson

criterion. In the figure below, we can see that D-T reactions have both the minimum temperature (in million Kelvin) and atm*sec resulting in them being the most viable in terms of meeting the Lawson criterion requirements [3]:
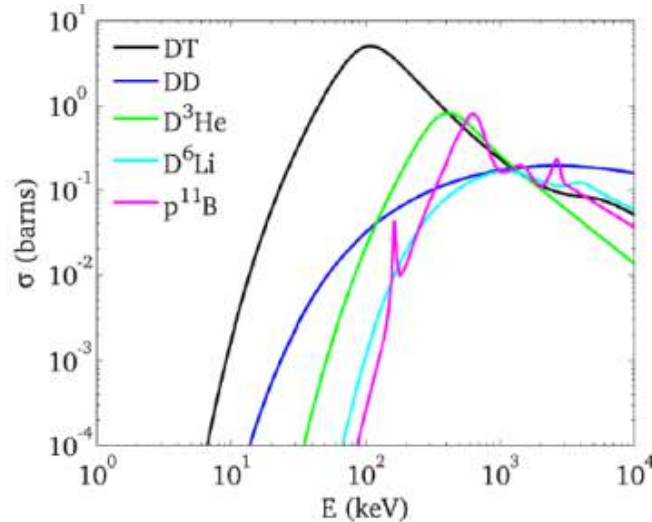

Fig 1: The likelihood of different fusion reactions producing certain amounts of energy in barns. D-T reactions have the highest likelihood to produce the most energy up to ~$10^{2.5}$ keV.

2.2. Tritium Rarity

D-T reactors will use deuterium-tritium reactions to produce energy. While obtaining enough deuterium to run the reactor is not of concern, the supply of tritium, due to how it is only ~1×10^{-18} % of hydrogen and its half-life of 12.33 years, poses a larger issue [4]. The artificial production of tritium has been accomplished in the past, however the supply of tritium is continuing to decrease due to how only 23 places produce tritium now [5]. The current price of tritium is $30,000 per gram, with it expected to increase to $100,000 to $200,000 per gram [6].

2.3. The Importance of the Breeding Blanket in a D-T Reactor

To counteract the current short supply and short half-life of Tritium, D-T reactors will use a breeding blanket to produce tritium using the spare neutron produced from a DT reaction. The breeding blanket materials considered are all lithium compounds or lithium, as the reactions for producing tritium are:

$^{6}Li + n_{slow} \rightarrow {}^{4}He + T + 4.8$ MeV,

$^{7}Li + n_{fast} \rightarrow {}^{4}He + T + n_{slow} + 2.5$ MeV
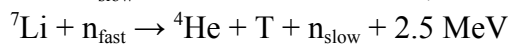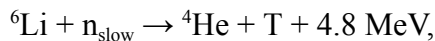
where n_{slow} and n_{fast} are low and high energy neutrons respectively [2].

This tritium can then be reused in DT reactions to not only produce more power but also through the produced neutron even more tritium. Due to how lithium based compounds have preferable TBR's, many D-T reactor designs use said compounds. The materials that will be investigated in this paper are lithium, lithium-lead, lithium titanate, Flibe, and lithium orthosilicate, all using natural lithium. Alongside this, ReBCO magnets will be included in

modeling and cost calculations as well, as the width of the breeding blanket will affect the cost for ReBCO magnets, which can cost ~$50 million [7].

3. Methodology

The neutronics analysis for this research paper was completed with OpenMC. OpenMC is an open-source Monte-Carlo radiation transport code.

3.1. Model

First we developed a simplified spherical model of a D-T reactor. This consists of an internal wall of steel beginning at a radius of 50 cm from the center of the model that is 3 cm thick, then immediately after the breeder blanket. The breeder blanket will have variable radius and material, and thus the starting radius of any following layers is affected by such. The layer following the breeder blanket is an outer wall of borated steel that is 3 cm thick. The last layer is a 3 cm thick layer of ReBCO.

The model's TBR is then calculated with the neutron source defined as a point centered at the very center of the model, at 14MeV. We assume that this remains constant. For every material being investigated, five batches of 10,000 particles are used. By doing multiple samples, we can ensure accuracy and reduce error. While we do not increase accuracy and reduce error for each individual particle, we do increase the average taken from them. This is repeated for the breeder layer thicknesses of 10, 50, 75, 100, 125, 150, and 200 cm.

The reason for the simplicity of the model is so that it can be applied generally. Because of this, the results from this paper should be able to aid in determining the material for a breeding blanket and its radius regardless of model. However, this simplicity is at the cost of certainty, and as the model used here does not directly reflect any planned design of a D-T reactor.

3.2. Materials Tested

The materials being tested (as previously mentioned) are lithium, lithium-lead, Flibe, lithium titanate, and lithium orthosilicate. All these materials will use 99% enrichment for lithium-6, with their compositions (by percent) being determined by their chemical formula. The lithium being used for simulating the breeder blanket has a density of 0.534g/cm^3 [8]. The lithium-lead (sometimes called 16Li-Pb, due to its composition) being tested consists of 84.2% lead and 15.8% lithium, and has a density of 9.64 g/cm^3 [8]. The material Flibe (2LiF-BeF_2) has a composition of 14.0381% Lithium, 9.1135% beryllium, and 76.8483% fluorine and a density of 1.94 g/cm^3 [8]. The lithium titanate being used has a composition of 12.6491% lithium, 43.6157% titanium, and 43.7352% oxygen, and a density of 3.43 g/cm^3 [9]. Finally, the lithium orthosilicate has a composition of 13.1005% lithium, 26.5045% silicon, and 60.3950% oxygen and a density of 2.39 g/cm^3 [10].

4. Results from Model

4.1. TBR
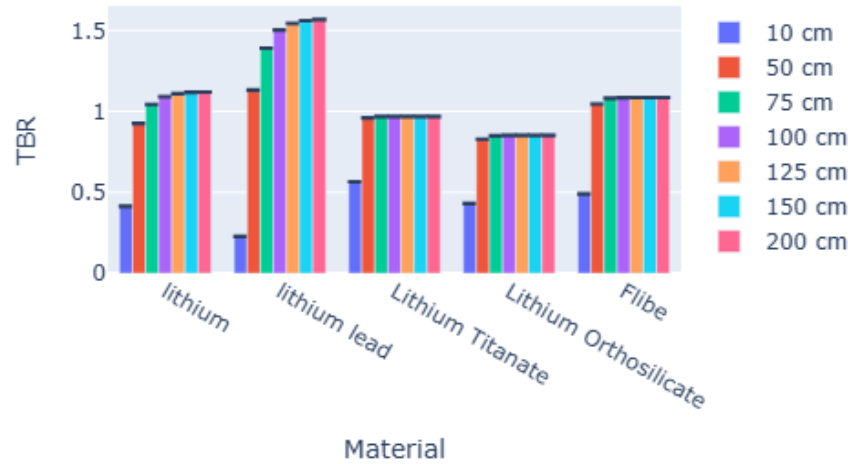
Fig 2: TBR of tested materials, error bars by standard error. A width of 10cm is included to show the general trend of TBR in the materials tested, but is not considered in.

Breeder thickness	Lithium (enriched, 99%)	Lithium lead	Lithium Titanate*	Lithium Orthosilicate*	Flibe (LiF-BeF2)*
10cm**	$0.415 \pm 695\mu$	$0.227 \pm 446\mu$	0.565 ± 0.0012	$0.431 \pm 966\mu$	$0.490 \pm 681\mu$
50cm	0.926 ± 0.0011	$1.132 \pm 792\mu$	0.960 ± 0.0014	0.828 ± 0.0010	1.046 ± 0.0011
75cm	1.043 ± 0.0011	$1.340 \pm 852\mu$	0.967 ± 0.0014	0.850 ± 0.0011	1.080 ± 0.0011
100cm	1.091 ± 0.0011	1.502 ± 0.0010	0.968 ± 0.0014	0.853 ± 0.0011	1.084 ± 0.0012
125cm	1.110 ± 0.0011	$1.543 \pm 942\mu$	0.968 ± 0.0014	0.853 ± 0.0011	1.085 ± 0.0012
150cm	$1.117 \pm 978\mu$	$1.559 \pm 884\mu$	0.968 ± 0.0014	0.853 ± 0.0011	1.085 ± 0.0012
200cm	1.120 ± 0.0001	$1.567 \pm 863\mu$	0.968 ± 0.0014	0.853 ± 0.0011	1.085 ± 0.0012

Fig 3: TBR of tested materials in table form, with error range by standard error.
Due to TBR being rounded, changes in TBR may not show at higher radii, though it should be noted it still marginally increases.
**Included to show general trend of TBR across materials*

In order for a D-T reactor to have net positive Tritium, it's TBR needs to be greater than 1. Tritium self-sufficiency, which is being able to produce more tritium than what is used or has been decayed over time, is crucial for D-T reactors, as without such they would not only lack the commercial feasibility necessary due to how the tritium fuel supply would slowly dwindle until there is no tritium left to use. The model used to find these numbers does not use a neutron multiplier, and as such TBR could be increased from these numbers. Thus, while in the table and graph above Lithium Titanate and Orthosilicate do not reach the minimum TBR of 1, they are still worthwhile, but it should be noted that designs using such would be required to have a neutron multiplier, which is a layer that has the goal of increasing the TBR of following materials [11]. The Lithium Titanate and Orthosilicate's TBR increase by minimal amounts in the model (less than 0.01) after a thickness of 75 cm, which may seem irregular. However, considering there is no neutron multiplier, it can be reasonably assumed that by that thickness the majority of neutrons had been absorbed at that point.

In order to determine the cost of the breeding blanket, we need to first know what the volume of the blanket is and what the cost of the material is.

The way cost per kilogram was calculated here was by calculating the cost of raw materials, and for materials with prices not readily available through calculating the cost of the base raw materials and using the percentages used in the material to calculate cost.

Material	Cost per kg*	kg/m^3	Lifetime Cost/ m^3 (Assuming lifetime is 30 years)***	Reference
Lithium	$15,000/kg	534 kg/m^3	$24,030,000/m^3	[8] [13][22]
Lithium-Lead	$2,373/kg	9,635 kg/m^3**	$68,587,113/m^3	[8] [18]
Flibe	$3,479/kg	1,940 kg/m^3	$20,250,030/m^3	[8] [13]
Lithium Orthosilicate	$2,728/kg	2,390 kg/m^3	$19,560,489/m^3	[10] [13]
Lithium Titanate	$2,414/kg	3,430 kg/m^3	$24,845,022/m^3	[9] [13] [17] [23]

Fig 4: Prices and densities of materials tested
*first price of raw materials, then uses the percent lithium, original cost of material from source and lithium cost to estimate price with lithium enrichment.
**Rough estimation from multiple sources
***Assuming the blanket needs to be replaced every 10 years

Given the width of the breeder blanket, the volume of the breeder blanket in cubic meters can be found using the following formula:

$$\frac{\frac{4}{3}\pi\left((53+w)^3 - 53^3\right)}{1,000,000}$$

This formula takes the outer sphere's volume and subtracts the inner sphere's volume from it to obtain the volume in cm^3, after which is converted to m^3 by dividing by 1000000.

Using this formula, we see that the needed amount of a breeder blanket material of width 50, 65, 75, 100, 125, 150, and 200 cm are 3.954 m^3, 6.259 m^3, 8.161 m^3, 14.379 m^3, 23.000 m^3, 34.417 m^3, and 67.211 m^3 respectively. By using the previously mentioned prices per m^3 and these volumes, we can derive the following table for the estimate prices of breeding blankets given a material and width:

Width	50 cm	75 cm	100 cm	125 cm	150 cm	200 cm
Lithium	$95.00 Million	$196.11 Million	$345.52 Million	$552.69 Million	$827.05 Million	$1.62 Billion
Lithium Lead	$271.17 Million	$559.73 Million	$986.20 Million	$1.58 Billion	$2.36 Billion	$4.61 Billion
Flibe	$80.06 Million	$165.26 Million	$291.17 Million	$465.75 Million	$696.95 Million	$1.36 Billion
Lithium Orthosilicate	$77.33 Million	$159.63 Million	$281.26 Million	$449.89 Million	$673.22 Million	$1.31 Billion
Lithium Titanate	$98.23 Million	$202.76 Million	$357.24 Million	$571.44 Million	$855.10 Million	$1.67 Billion

Fig 5: Estimated lifetime costs for different breeder blanket materials at thicknesses ranging from 50cm to 200cm.

Breeder Material	Positives	Challenges	Who is using it?	Ref.
Lithium (enriched, 99%)	easily accessible	Extremely high cost ($15000/kg)	General Fusion	[20] [13] [14]
Lithium Lead	High strength (1.132 TBR at 50 cm, 1.567 TBR at 200 cm)	Magnetohydrodynamic effects have to be accounted for Li loss from operating temperatures	ITER, in a WCLL design CIEMAT in a DCLL design	[15] [16] [13] [17]
Lithium Titanate	Lower cost ($2414/kg)	Difficult to obtain high purity	Tokamak Energy	[9] [14] [13] [24]
Lithium Orthosilicate	Has desirable properties, including thermal stability and mechanical strength	High Rengeneration temperature Prone to Sintering	Tokamak Energy	[10] [19] [14] [13] [25]
Flibe	Very heat resistant, storing more heat in its volume than water Resistant to radiation damage	Difficult chemistry to work with Supply chain issues	Commonwealth Fusion Systems (CFS)	[20] [21] [13]

Fig 6: Positives and Challenges of the different materials being tested, along with groups that are using them in designs.

5. Discussion of Results and Conclusion

There are many reactor designs that still have the same general breeder widths but vastly different volumes. For example, the DEMO reactor's breeder blanket will have a volume of about 1700 m^3 [26]. However, the goal of this paper is not to directly study what material a specific design's breeder blanket should be, rather to study under a general model that could be applied in a general fashion to multiple models.

In figure 6 we can see that every material has its upsides and downsides. Using these alongside the prices in figure 5, we can come to a conclusion on what material is likely to be the most economically efficient. Both lithium lead and lithium orthosilicate are likely less economically efficient than the rest, due to how the general use of the fusion reactor will cause wear on the material. We can also see from the pricing of 99% enriched lithium that it is not a good candidate for the most economically efficient material from the ones tested. Due to how Flibe has a hard chemistry to work with, through process of elimination we can see that lithium titanate is likely the most economically efficient material for a DT-reactor's breeder blanket based off of a general model.

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2024.

The Roles of *CDKN2A/B* in Tumorigenicity By Krish Konda

Abstract

The primary purpose of this literature review is to summarize the roles of *CDKN2A* and *CDKN2B* in the tumorigenicity of somatic and stem cells. This review identified that *CDKN2A* strongly influences tumorigenicity in cancers such as melanoma and pancreatic cancer. *CDKN2B* was also found to affect the tumorigenicity of FReP cells which may point to effects in induced pluripotent cells (iPSCs). The mechanisms of downregulation and upregulation of these genes were examined to identify why they may be out of balance within the cell. The findings indicate that *CDKN2A/B*'s role on CDK4/6 must be examined more closely within iPSCs so that steps can be taken to lower tumorigenicity in these cells.

Introduction

Understanding the mechanisms that can regulate the tumorigenicity of stem cells is crucial to effectively find a solution to make stem cells safer and more widely available (Lee et al., 2013). Stem cells are capable of multiplying indefinitely and being differentiated into almost any type of cell. However, these same processes can also backfire and cause problems for the cell, such as tumorigenicity. Examples of this are uncontrolled proliferation, tumor/teratoma formation, and dysregulation of their natural cell cycles. Stem cells have a high risk of tumorigenicity because of their high proliferative capability, differentiation potential, and epigenetic memory. These are also all reasons why stem cells are not yet widely available for people who need them, because along with their benefits, possible tumor/teratoma formation from factors such as incomplete reprogramming, genomic instability, or more, can pose a significant risk to patients (Blum & Benvenisty, 2008).

Some extremely important genes that could be a solution to this problem, or possibly a part of the problem if mutated, are the *CDKN2A* and *CDKN2B* genes (Sherr, 2001). These two genes are both tumor suppressor genes, so the key to solving the tumorigenicity problem may lie within them (Foulkes et al., 1997). The *CDKN2A* gene regulates the cell cycle by serving as a checkpoint, however, it also serves the critical role of activating p53, another crucial tumor suppressor that is known to be mutated often in many types of cancers (Merkle et al., 2017). The *CDKN2B* gene is primarily a cell cycle regulator gene, which is an important function so that cells do not uncontrollably proliferate. In addition to this, it frequently interacts with the *CDKN2A* gene and is also mutated homozygously with this gene due to its proximity (Wach et al., 2023).

Although the roles of *CDKN2A* and *CDKN2B* are well known in cancer cells, there is still a significant gap in information on their role within stem cells. This could prove to be a problem because even though stem cells and somatic cells share some similarities such as common signaling pathways and transcription factors, stem cells are unique in the way that they can proliferate indefinitely and have the capability to differentiate into most types of cells, possibly altering the roles of *CDKN2A/B* (Rossi et al., 2020; Bradley, 1991). While they control the cell

cycle in somatic cells and lower proliferation, if deletion of these genes occurs, the already enhanced proliferative abilities of stem cells could potentially lead to uncontrolled proliferation due to lower regulation of the cell cycle. It is important to bridge this gap in knowledge because it could lead to new therapeutic strategies that can lower the tumorigenic risk and make stem cells safer overall.

This article aims to understand how the genes *CDKN2A* and *CDKN2B* can impact the tumorigenicity of stem cells. More specifically, the effects of *CDKN2A/B* on tumor suppression of cancer cells, stem cell regulation, epigenetic regulation, and the effect of the upregulation and downregulation of these genes were examined.

Methods

The primary website used to source most of the articles used in this paper was Google Scholar, because of its efficient and easy-to-understand search engine, as well as its ability to provide consistent formatting of citations; however, other sources and search engines such as MDPI, Springer Link, Pubmed, NCBI, and especially JCI were used. To find information on the genes *CDKN2A* and *CDKN2B*, I used Genecards, Uniprot, NCBI Genome Viewer, Alpha Fold, and String. These websites were chosen for their comprehensive information on genes and their ability to generate a structure for the genes in a way that typical research articles cannot.

The main inclusion criteria were based on an article's relevance to the *CDKN2A/B* genes, although I picked a few subtopics like cancer and stem cells that related to the genes so that I had enough background information to fill in any gaps. Keywords used in the search were "*CDKN2A*", "*CDKN2B*", "stem cells", "cancer", and "melanoma".

Articles were initially screened by reading their titles and abstracts. Any articles that were not relevant to the topic were discarded, and the remainder were read fully so that I was able to accurately assess their value towards the research.

What are *CDKN2A* and *CDKN2B* and what are their functions

CDKN2A is a vital tumor suppressor gene that codes for two proteins, p16^INK4a (p16), and p14^ARF (p14), that help regulate the cell cycle and are involved in tumor suppression. The loss of this gene is an important link to many different types of cancers and could be the main cause of the uncontrolled proliferation that characterizes cancer. Because of this gene's relevance to cell cycle regulation, loss of the gene could lead to uncontrolled proliferation due to p16's role in acting as a checkpoint. p14 also plays a significant role in tumor suppression because it helps to stabilize the p53 gene, another vital tumor suppressor that is responsible for cell cycle arrest when the cell's DNA is damaged. If the cell is damaged but continues to grow through the cell cycle, it could cause much larger problems (Foulkes et al., 1997).

Similar to *CDKN2A*, *CDKN2B* codes for a protein that is a cell cycle regulator and helps to prevent a cell from becoming cancerous. The protein is called p15^INK4b (p15), which is a crucial checkpoint before the cell enters the S phase of the cell cycle. This is important, because after the cell has begun to grow, it will start preparing to replicate itself, and the first stage of that

is the S stage, in which the cell creates copies of DNA. By successfully blocking the cell cycle from continuing if something goes wrong in the growth phase, this protein can prevent future problems from occurring later on (Chang et al., 2013). In melanoma, *CDKN2B* is an essential gene, as p15 was found to have no expression whereas p16 retained expression (Foulkes et al., 1997). However C*DKN2A* is still a massive contributor to melanoma, in one study it was found that about 15% of subjects had germline *CDKN2A* mutations (Monzon et al., 1998). In addition, *CDKN2B* also plays a role in cellular senescence, when the cell cycle is arrested and is no longer allowed to grow due to damage, age, and type of cell, among other factors (Kumari et al., 2021).

Tumor suppression in cancer cells

The role of these genes is primarily tumor suppression, especially *CDKN2A*. They do this through a variety of mechanisms through the proteins that they create, p14, p16, and p15. One of the main ways that they stop tumors from forming is by halting the cell cycle as soon as there is any damage to the cell (Drexler, 1998). This can be through stopping the cell cycle for long enough so that the cell can repair damage; if the cell is damaged beyond repair, certain genes such as p53 (regulated by CDKN2A) will promote apoptosis so that the cell will die. This will prevent potential tumors from forming before they get too large and become a problem. Another way that they can stop tumors from forming is through supporting other vital tumor suppressors so that they can do their job more easily (Amaral et al., 2010).

CDKN2A's role in tumor suppression starts with its two proteins, p14 and p16. p16 mainly works to stop tumor growth by binding to CDK4 and CDK6, inhibiting their activity (Fig. 1). CDK4/6 are vital enzymes that help to progress the cell cycle from the G1 to the S phase. These enzymes are responsible for the phosphorylation (inactivation) of the retinoblastoma protein (pRb) within the cell. When the pRb is in its active state, it will bind to E2F transcription factors, preventing the transcription of genes that will cause the cell cycle to move from the G1 to the S phase. Without p16 to inhibit CDK4/6, the pRb will be inactive, allowing the cell cycle to keep moving forward, preventing proliferation if the cell is damaged (Goel et al., 2022). This is directly related to tumor suppression because stopping damaged cells from proliferating will help to prevent oncogenesis (Corn & El-Deiry, 2002).
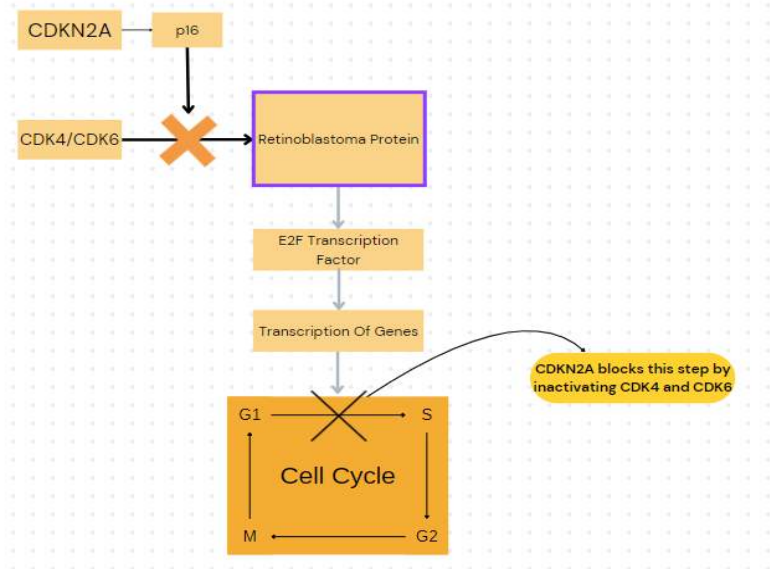
Fig 1: P16's role in the cell cycle

P15, which is a subunit of *CDKN2B*, also plays a very similar role in cell cycle regulation as p16. They both have overlapping functions in their function in inhibiting CDK4 and CDK6. But unlike p16, p15 has a more narrow role because its only job is to inhibit CDK4/6, however, p16 has a broader role (Latres, 2000). Some of these other roles are related to cellular senescence and oncogenetic stress. Its role in cellular senescence is significant because it can allow the cell to permanently stop proliferating and arrest the cell cycle so that tumorigenic cells do not uncontrollably proliferate (Rayess et al., 2011).

However, p14 has a different role in terms of tumor suppression, because it will mainly support other tumor suppressor genes to halt the cell cycle rather than do it directly. *P53*, another important tumor suppressor gene, supports the cell cycle and can temporarily stop it so that damaged DNA can be repaired, or in some cases, it can cause apoptosis, or programmed cell death, because there is too much damage. One of the regulators of this gene is the MDM2 regulator, which will lower the levels of *p53* within a cell and keep it inactive. p14 will trap the MDM2 inside of the nucleus, not allowing it to interact with *p53* so that its levels can rise enough for it to become an active transcription factor (Bates et al., 1998). When *p53* is activated, it will bind to DNA and promote the transcription of inhibitors and genes that will stop the cell cycle. One of its main targets is *p21*, which can stop the cell cycle for long enough to repair any damage done to the DNA (Firas Aljabery et al., 2018). If there is too much damage to repair, it will promote the expression of genes that are pro-apoptotic like BAX, PUMA, and NOXA, eliminating cells that could potentially become cancerous (Gartel & Tyner, 2002; Polyak et al., 1997).

Loss of these genes could tremendously impact the tumorigenicity of cells, causing many different types of cancer. Loss of *CDKN2A/B* will, in turn, lead to the loss of p14, p15, and p16, leaving the cell cycle unchecked and possibly allowing a much higher chance of tumorigenic

characteristics to appear. These genes are crucial to cancer prevention, but what about stem cells? While these genes are known to be essential tumor suppressors in differentiated somatic cells, their role in stem cells is less well-defined.

Role of *CDKN2A* and *CDKN2B* in Stem Cells

Unlike typical cells in the body, stem cells are different in the way that they can proliferate indefinitely and can differentiate into almost any type of cell. (Induced pluripotent stem cells) iPSCs; somatic cells that have been reprogrammed into stem cells; open up a world of possibilities now that some ethical issues can be avoided and stem cells are more widely available (Takahashi et al., 2007; Inoue et al., 2014). Previous to the development of these cells, the natural version of these cells, (embryonic stem cells) ESCs could only be collected from embryos, posing a challenging ethical concern. Because iPSCs are freed from most ethical restraints, many new possibilities can be explored as well as more testing and experiments because they are much easier to harvest. Because of the large difference between iPSCs and somatic cells, a much smaller amount of literature has been written about the specific role of these genes and their effects on stem cells.

iPSCs are an important advancement in the field of stem cells, first created in a lab by using human skin fibroblasts and reprogramming them to become pluripotent, credited to Shinya Yamanaka after his and many other researchers' findings (Malik & Rao, 2013). These remarkable cells are almost the same as embryonic stem cells, with the ability to proliferate indefinitely and differentiate into all different types of cells. These cells are capable of regenerating and repairing damaged tissue caused by injuries or diseases (Inoue et al., 2014). One of the biggest roadblocks limiting the availability of iPSCs is the high tumorigenicity of the undifferentiated versions of these cells (Yasuda et al., 2018). *CDKN2A/B*, if appropriately leveraged, could lower the tumorigenicity to a safe enough level that it can be safely used for patients because they are already key tumor suppressor genes in somatic cells.

CDKN2A in Stem Cells

Because *CDKN2A* plays such a large role in cell cycle regulation in somatic cells, it is believed to impact the cell cycle of stem cells too. With p16, controlling the CDK4/6 enzymes is important so that the natural stem cells do not proliferate uncontrollably, however, miR-302 can also fulfill this role in stem cells (Lin et al., 2010)However, iPSCs/ESCs have far fewer checks on their proliferation than natural stem cells and are more likely to apoptose when they are not in the correct environment, whereas tissue stem cells will simply slow down their division when they are crowded. Many mutations occur in iPSCs because of fewer checkpoints in the G1 and S phase of the cell cycle, which is typically p16's role in somatic cells (Araki et al., 2020). However, in the context of iPSCs elevated levels of p16 can lead to lowered efficiency in the reprogramming, because proliferation is required for a successful transition into a pluripotent state. P16 interferes in the reprogramming process because it can cause cell cycle arrest, thereby reducing the proliferative abilities of iPSCs (Haridhasapavalan et al., 2019). Currently, strategies

are being researched to find a way to balance p16, so that iPSCs can become more efficient and successful, and at the same time reduce the risk of tumorigenicity (Hayashi et al., 2016). I hypothesize that the inhibition of p16 so that the iPSC can be reprogrammed is causing the mutations in stem cells due to not having p16 to regulate the G1 and S phases.

P14's ability to activate and support *p53* is important in stem cells because by causing cell cycle arrest, it ensures that only healthy cells will be allowed to proliferate. This also prevents the formation of cancer stem cells, leading to tumor formation (Bates et al., 1998). Although this gene is typically considered a tumor suppressor, new studies are coming out that show that p14 could contribute to the progression of tumors in certain situations such as lung cancer. In addition, it is also beginning to be recognized as a possible target for lung cancer treatment (Vashi & Patel, 2021).

CDKN2B in Stem Cells

We have a deeper understanding of the role of *CDKN2B* rather than *CDKN2A* because of an important article," CDKN2B upregulation prevents teratoma formation in multipotent fibromodulin-reprogrammed cells". This study is about how *CDKN2B* affects FReP (Fibroblast-like Reticular progenitor cells), which is similar to iPSCs in most ways except in the fact that FReP cells are most suited for regenerative medicine, while iPSCs have broader uses. FReP cells are also reprogrammed a different way, as FReP cells are reprogrammed from human dermal fibroblasts with stimulation from FMOD, recombinant human fibromodulin, while iPSCs are derived from adult somatic cells that are then reprogrammed back into a state of pluripotency (Zheng et al., 2019). However, we can still hypothesize about the role of *CDKN2B* in iPSCs because FReP cells and stem cells are very similar. However, more research relevant to *CDKN2B* is needed to fill out the huge gap in understanding its role in stem cells.

Sustained suppression of *CDKN2B* caused teratomas to occur in multipotent FReP cells that are the same as the teratomas that were found in iPSCs. An important part of the reprogramming process for FReP cells is the upregulation of *CDKN2B*, which causes reduced tumorigenicity in these cells. The suppression of *CDKN2B* during reprogramming was a large factor in causing non-tumorigenic somatic cells into tumorigenic pluripotent cells, again highlighting the impact of *CDKN2B* (Zheng et al., 2019).

Mutations and abnormalities in this gene have been associated with different types of cancers, including melanomas, leukemias, and carcinomas (Platz et al., 1997; Jang et al., 201; Jafri et al., 2015). However, it is hypothesized that *CDKN2A* is often more important in cell cycle regulation and the deletion of *CDKN2A* usually has a greater impact on the cell than the deletion of *CDKN2B*. On the other hand, in FReP reprogramming it was found that *CDKN2B* plays the largest role in the increase and decrease of tumorigenicity (Zheng et al., 2019). Overall, there appears to be a need for an in-depth exploration of the roles of *CDKN2A* and *CDKN2B*.

Upregulation versus Downregulation

Another aspect to consider with these genes is their over and under-expression. The mechanisms in which the upregulation or downregulation seem to occur mainly because of damage to DNA, oncogenic stress, and mutations, although there are a variety of other ways that it can happen in a lab. Because of their pivotal role in cell cycle regulation, changes in the normal levels of *CDKN2A* and *CDKN2B* can heavily impact the function of cells.

Upregulation

The chief causes of upregulation naturally for *CDKN2A/B* are DNA damage and oncogenic stress. When the DNA of a cell gets damaged, *p53* becomes activated and will upregulate p14, which in turn will help to stabilize *p53*. The cell does this so that *p53* can cause cell cycle arrest or apoptosis depending on which is necessary so that genomic integrity is preserved (Sherr, 2002). Oncogenic stress can also cause upregulation, because after oncogenes such as RAS and MYC are activated, cellular stress increases, upregulating *CDKN2A/B* (Hunter et al., 2012; Gołąbek et al., 2022). The upregulation is a failsafe to ensure that the cell is protected from the uncontrolled proliferation that is typical of oncogenically mutated cells. The cell specifically upregulates these genes because they can help cause cellular senescence so that cancerous tumors are prevented. Other ways that upregulation can occur are through transcription factors. Scientists typically use these to cause upregulation in a lab, but on some occasions, they also occur naturally. One of the most common transcription factors is the E2f transcription factor. It directly upregulates p16 so that the cell cycle can be arrested in case of oncogenic stress (Agata Świętek et al., 2023; Gołąbek et al., 2022).

Downregulation

The downregulation of *CDKN2A/B* mainly occurs because of mutations like deletions or insertions, or promoter hypermethylation. Deletions and insertions impact the coding of *CDKN2A/B*. Deletions of these genes are common in many types of cancers because without them, the cell is significantly less protected from tumor formation and the cell cycle could be disrupted (Sievers et al., 2020). Without *CDKN2A/B* which supports cell senescence and cell cycle arrest, it will be much harder to control the cell and it may transition into a tumorigenic cell. Promoter hypermethylation will also cause the downregulation and even silence the gene. When the promoter region of the cell is hypermethylated, it often inhibits the transcription and binding of proteins. Hypermethylation in the *CDKN2A* promoter region will prevent the transcription of the gene, which will cause p14 and p16 to not be expressed (Arya et al., 2017).

Discussion

The purpose of the literature review was to explore and analyze current literature on the subject of *CDKN2A* and *CDKN2B*, and how it connects to the topic of stem cells and tumorigenicity. Some important themes that came into view were how the genes affected tumorigenicity, and effects on stem cells, as well as the mechanisms of upregulation and

downregulation in the cell. In the discussion, connections between different articles will be revealed, possible future implications of this research will be discussed, and current knowledge gaps on the subject will be identified.

Connections

Some consistent findings in different literature are the relationships between *CDKN2A* and familial melanoma, as well as the role of CDK4/6. Some articles disagree about whether *CDKN2B* must be deleted in order for pancreatic cancer to develop.

CDKN2A and familial melanoma have been found to be related to each other by at least 4 different research articles. In individuals who inherit a mutation in the *CDKN2A* gene, there was an increased risk of melanoma as the cell cycle was less regulated thereby elevating the probability of tumor formation (Zocchi et al., 2021). Specifically, familial melanomas were formed with an increased percentage because of a genetic history mutation in the *CDKN2A* gene, and in multiple studies, there was a high chance that other people in the subject's family had the same disease (Lal et al., 200). This points to the conclusion that *CDKN2A* is critical in cancer causation because a mutation in it can cause entire families to have increased chances of cancer (Jeong et al., 2022; Walker et al., 1998).

Another vital connection is the role of CDK4 and CDK6. Both *CDKN2A* and *B* are related in the fact that they inhibit these enzymes so that they can regulate the cell cycle. This places greater importance on CDK4/6 because if 2 tumor suppressor genes both target the same enzymes, it must be vital in the formation of tumors. They are also targeted by drugs such as palbociclib aimed to stop or slow down cancer, further increasing their importance, as these enzymes may be the key to tumorigenicity (Finn et al., 2016). Further research should be conducted on these enzymes so that they can be understood in the context of stem cells.

Along with these significant connections, two articles were identified showing progression in research while studying the cancer aspect of these genes. Pancreatic cancer develops as a direct result of *CDKN2B* deletion rather than just playing a secondary effect due to its position near *CDKN2A (Tu et al., 2017)*. In many mutations, the two tumor suppressor genes *CDKN2A* and *CDKN2B* get deleted together (AKA co-deletion), which may lead to the assumption that *CDKN2A* is the main driver of cancer, with *CDKN2B* being a side effect. However, this article shows that *CDKN2B* deletion alone plays a significant role in the development of cancer, implying that further is needed to study the role of this gene in treating cancer. However, another study found that *CDKN2B's* role in pancreatic cancer development can be substituted with *Smad4*, another tumor suppressor gene that is mainly responsible for regulating other genes (Jia et al., 2021). The loss of this gene can work in combination with other genes like *CDKN2A* to induce pancreatic cancer without requiring the loss of *CDKN2B*, which is logically compatible with the other article and shows the progress done with this gene compared to the first article. The first article talks about how *CDKN2B* was essential for pancreatic cancer, but the second article, written 3 years later, discovered a new pathway for pancreatic cancer.

Future Implications and Research Gaps

      This research has huge potential to help people because of its implications for cancer. There is substantial evidence already that *CDKN2A/B* are key tumor suppressors and as the topic gets further research, more compelling evidence may arise. There are already drugs like palbociclib, among others, that replicate the activities of *CDKN2A* to prevent further progression of cancer. Similarly to *CDKN2A*, it targets CDK4 and CDK6 to prevent the phosphorylation of pRb (Goel et al., 2022). By doing this it will effectively halt the cell cycle and the cell will cease to proliferate. So far, it can only be used for a very specific type of metastatic breast cancer, in which it has shown effectiveness in combination with endocrine-based therapy (Diéras et al., 2018). Drugs like these will surely create more interest in *CDKN2A/B* because of the proven effectiveness of the drugs, and because there is only a narrow range of cancers that they can currently treat, there is much more room to grow. This will ensure that a greater amount of research will be done.

      Cancer is a very well-known problem, with 6% of the world having it, and because many types of cancers are very specific, if a solution for one is created there are still many different types remaining. With most of the treatments being very expensive and cancer having such a high fatality rate and fast mutations, it means that these treatments are often the only option. Upregulating *CDKN2A/B* or replicating their effects with drugs is a more affordable option, and as more drugs like this come out, they will add to the armamentarium of cancer-fighting therapies.

      It is believed that stem cells have similarities to somatic cells in terms of gene expression and cell cycle progression, the above research applies to the control of tumorigenicity in stem cells.

Conclusion

      Along with the future progression of research on *CDKN2A/B* in somatic cells, its possibility for growth in stem cells is many times larger. Since these genes have shown promise in reducing tumorigenicity in somatic cells, there is a likely chance that the tumorigenicity in stem cells could be reduced. The effects of CDKN2A/B on CDK4/6 specifically in iPSCs must be looked into because they may play a critical role in the tumorigenicity of those types of cells, similar to how they have played a critical role in somatic cells. However, there exist large gaps of information that are needed to provide concrete evidence for this hypothesis. The faster more research is published on this topic, the faster stem cells could become more available to the public to help change lives.

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Cows, Clovers, and Carbon: Economic Winners and Losers in Irish Sustainable Dairy Agriculture By Cooper Schirmeier

Abstract

Agriculture stands at the heart of modern civilization, shaping economies, sustaining communities, and, more recently, balancing food production demands with environmental concerns. In Ireland, dairy farming is particularly significant, contributing €18.98 billion to the economy in 2022. Nevertheless, the increasing pressure to adopt sustainable practices has reshaped the sector due to the increased involvement of national and international policymakers. This study investigates the rise of sustainability practices in Irish dairy farming and their implications for farmers. It focuses on their perspectives on sustainability measures, the abolishment of milk quotas, the challenges of family farming, and the tensions between Irish government regulations and EU agricultural policies. In order to probe these issues, semi-structured interviews were conducted with three dairy farmers in the West of Ireland. Recurring themes emerged from the analysis that showcases the interplay between economic viability and environmental responsibility, underscoring that while some farmers benefit from sustainable practices, others struggle with the variability of success and external pressures. The study points to the need for policy support that aligns with the diverse conditions of individual farms to ensure more consistent economic stability and environmental progress.

Context/Intro

Agriculture plays a vital role in global economics, influencing food security, rural development, and environmental sustainability. Common agriculture systems vary, from mixed farming practices, where farmers grow crops and keep animals on the same land, to subsistence farming, where farmers cultivate small areas primarily for personal use, to plantation farming, where a farmer grows a single crop on a large piece of land (McConnell & Dillon). Each system has a unique set of practices and outputs, resulting in differences in economic stability and environmental impact. For instance, while mixed farm systems often provide a buffer against market volatility and offer a diversified income stream for farmers, specialized monoculture practices instead yield higher efficiency while experiencing an increased risk of market fluctuations (Bell et al.).

Income variety in agriculture is substantial and commonly influenced by factors such as farm size, crop type, market access, and government policies. Further, income volatility is equally significant, and a study from the United States Department of Agriculture found that every year, farmers experienced a median change in income eight times as great as nonfarmers (Key et al. 1). Issues of income disparity are intensified with farm classifications. Smallholder farms, prevalent in many parts of the world, often rely on diverse income sources such as off-farm employment and government subsidies to manage economic risk. In contrast, larger

commercial farms may have more consistent income streams but face significant investment and operational costs. Government interventions, including many incentives to ensure all agri-demands are met, play a crucial role in stabilizing farm incomes and promoting increasingly sustainable practices (Stringer et al.).

Agriculture is a vital economic sector, contributing significantly to global economic growth. It supports millions of jobs in farming, food processing, distribution, and retail at the EU level. The EU has an estimated 10.6 billion farms, and the larger agri-food industry represents a significant portion of many countries' GDP and export earnings (*EU Agricultural, 1*). In Ireland, for instance, agriculture and food production across dairy and tilling industries account for a substantial proportion of the national economy. The estimated value of total agri-production was €18.98 billion in 2022 (*Overview of the Irish*). The value of the industry even extends beyond economic metrics and can influence social and environmental outcomes. Further, recently, there has been a global shift towards more sustainable consumption and production practices. As a result, countries like Ireland, alongside various organizations, have shifted their focus to more environmentally conscious methods of operations, and governments have begun incentivizing utilizing practices such as organic farming, limiting waste, and striving for clean water (Finnegan & Goggins).

Agriculture in Ireland

Agriculture has long been a notable part of Ireland's economy and cultural identity. With its lush landscapes and temperate climate, the country is ideally suited for agricultural activities, particularly dairy farming. Ireland has roughly 127,000 active farmers, of which over 18,000 are dairy farmers (*Dairy*, Teagasc). The suitability of the environment allows an estimated 64% of the land to be utilized for agriculture operations. More recently, Ireland's agriculture sector has seen significant evolution, driven by initiatives and technological advances targeted at improving socio-economic conditions in rural areas and enhancing competitiveness while prioritizing the promotion of sustainable development (*Ireland – CAP Strategic*).

The Irish government's strategic direction has influenced the country's agriculture landscape, particularly through the Food Harvest 2020 and Food Vision 2030 initiatives. Launched in 2010, the Food Harvest 2020 strategy aimed to increase the value of agricultural output by 33% and dairy production by 50% by 2020. Adopting key technologies and practices enabled this change and helped improve technical efficiency while reducing the environmental impact of farming. As a result, Irish dairy farmers not only boosted production but also enhanced profitability and reduced emissions (*Ireland – CAP Strategic*). In the case of Food Vision 2030, the adoption of the strategy is still underway. Some of the initiative's key goals include enhanced animal well-being, a climate-smart and environmentally sustainable agri-sector, trusted, safe, and nutritious food, and an innovative and competitive agri-sector driven by technology (*Food Vision*).

Despite the positive developments, the Irish agriculture industry still faces several notable challenges. One of the most pressing is the economic viability of many farms, particularly those

involved in cattle and sheep farming. Approximately one-third of all Irish farms are considered economically vulnerable and heavily reliant on direct payments to remain viable. To showcase the extent to which farmer's economic viability is threatened, the 2022 Teagasc National Farm Survey found the average yearly income for a family sheep farm was €16,300, and the average for a cattle rearing farm was reported as €8,300 (*Teagasc National*). Low profitability in these sectors poses a continual threat, as evidenced by cattle farms often generating a farm income that is less than direct payment support, indicating operational losses.

Furthermore, Brexit represents a considerable risk, potentially leading to disruptions in trade and increased costs, which would disproportionately affect regions more dependent on low-margin beef farming, such as the West, Mid-West, and Midlands. The sector also grapples with aligning agricultural expansion with environmental sustainability goals. Agriculture contributes significantly to Ireland's greenhouse gas emissions, and meeting national climate targets requires substantial changes. Moreover, potential reforms in the Common Agricultural Policy (CAP) and further trade liberalization could introduce additional uncertainties, compelling the industry to navigate an increasingly complex landscape while striving for economic and environmental sustainability (Conefrey).

Policy

Implementing effective policy is crucial for advancing sustainable agriculture, providing a baseline that aligns economic incentives with environmental goals. In Europe broadly, policy is constantly introduced to keep member countries collectively within specific sustainability parameters and to ensure the production of sufficient goods. In Ireland, the introduction of strategic policies has aimed to promote sustainable farming practices, balancing agricultural productivity needs with ecological preservation. This section will discuss key initiatives, including the Common Agricultural Policy (CAP), the policy behind the Teagasc Marginal Abatement Cost Curve (MACC), and the Nitrates Action Programme (NAP), highlighting their respective roles in shaping a sustainable agriculture landscape.

Initially, the main objective of the Common Agricultural Policy (CAP) was to "increase agricultural productivity by ensuring technical progress, the rational development of agriculture production and the optimum utilization of the factors of production". More recently, the policy's main objectives have evolved and been modernized to address society's new demand regarding prevalent issues concerning environmental conservation and product quality (Czyżewski et al. 1). According to the European Commission, the Irish CAP strategic plan aims to promote "the sustainable development of the farming and food sector by supporting viable farm incomes and enhancing competitiveness". The European Commission also highlights Ireland's commitment to contributing to achieving climate objectives at national and EU levels, striving to improve socio-economic conditions across rural areas. To achieve success in some of Ireland's goals, which include reducing the income gap between farming and other economic sectors, supporting the development of arable farms, and investing in the modernization of holdings such as digital farming technology, Ireland plans to dedicate €590 million to support small and medium-sized

farms. Furthermore, to secure the long-term economic viability of the agricultural industry, Ireland intends to allocate an additional €180 million as complementary funding to promote young farmers (*Ireland – CAP Strategic*).

The Teagasc Marginal Abatement Cost Curve (MACC) aims to identify "the most cost-effective pathway to reduce greenhouse gas emissions and enhance carbon sequestration in the Agricultural, Land-Use, Land-Use Change, and Forestry sectors (LULUCF)". A MACC itself is a graph visualizing the abatement potential of greenhouse gas mitigation measures while taking into account economic risks associated with said measures (*Marginal Abatement*). To better understand Teagasc's MACC, it's important to understand the policy context. One primary policy that informs the potential reduction of greenhouse gas emissions is the Climate Action and Low Carbon Development Act. This act legally binds Ireland with the target of achieving a climate-neutral economy by 2050, in addition to a reduction in emissions of 51% by 2030 (compared to 2018 levels). Furthermore, policy is also implemented on a broader EU scale. Proposals for a regulation amending the EU LULUCF regulation, for instance, highlight one example of an effort introduced targeted at increasing carbon removals and achieving climate neutrality in agriculture, forestry, and other land-use sectors. This amendment aims to achieve these goals by 2035 at the EU level, exemplifying the importance of Ireland's pro-agriculture sustainability initiatives (Lanigan et al.).

Finally, the Nitrates Action Programme (NAP) introduces measures intended to address significant issues concerning climate, biodiversity, and water quality targets set at national and EU levels. Ireland first adopted the NAP in 2006, and has been supported by successive regulations. The program primarily targets the prevention of water pollution from agricultural sources and protecting and improving water quality throughout the country. At present, the fifth and most recent edition of the NAP hopes to bring more attention to controlling nutrient and sediment losses from agriculture through a new holistic approach (*An Overview*).

Dairy Farming

Ireland's dairy sector plays a substantial role in the nation's agriculture, utilizing modern practices and evolving technology to reap the benefits of sustainable agriculture most effectively. Irish dairy competitiveness primarily stems from its favorable agronomic and weather conditions, which allow for a grass-based, spring calving milk production system in addition to an extended grazing period lasting from early Spring to late Autumn (Läpple et al. 5). Teagasc is Ireland's agriculture and food development authority. Their remit includes research, advisory, and education services, which enable Irish dairy farmers to be "among the most competitive on the world stage" (*Dairy, Teagasc*).

While the sector has experienced success, it's important to understand the beginnings of the industry's recent profitability. The industry experienced a 54% increase in milk production between 2005 and 2018. A pivotal moment in Irish agricultural history came with the abolition of the European Union milk quotas in 2015. The quotas were part of the EU's Common Agricultural Policy and limited the amount of milk farmers could produce to stabilize the market

and mitigate overproduction. This policy change allowed Irish dairy farmers to expand milk production significantly for the first time since the quotas were imposed in 1984 because farmers were no longer subject to financial penalties for exceeding quotas. This expansion required a substantial investment in farm infrastructure, increased specialization, and a greater emphasis on efficiency and sustainability (Kelly et al.). In addition, a significant growth in cow numbers was observed, with the national herd expanding by 377,600 heads between 2014 and 2021 (*Statistics Point*). According to Teagasc's 2022 National Farm Survey, a dairy farm's average family farm income is €148,600, the highest income of any farm type. The second most profitable sector in 2022 was tillage, with an average family farm income of €76,000, showcasing the drastic difference between agricultural sectors (*Teagasc National* 7).

Sustainability in dairy farming

Increases in milk production, together with a growing demand for operational efficiency, have spurred the need for technological innovation and operational solutions for the promotion of sustainable practices (Finnegan et al.). The National Economic & Social Council found that the dairy sector while having the highest level of economic viability at 85%, the highest average farm income, and the lowest reliance on direct payments, was responsible for an estimated 40% of total agricultural emissions, at 608 tonnes of CO_2 in 2021 (*Just Transition* 22). Nevertheless, the National Dairy Council says Irish dairy producers have already committed to reducing emissions by 25% by 2030. Additionally, Irish dairy farmers and Irish agricultural scientists have taken action on climate change, adapting to new standards, embracing new practices, and developing better technology to consider environmental impact more effectively. For instance, incorporating clover and other plants into pastures is one method of reducing chemical fertilizer use, lowering emissions, and reducing dangerous run-off into waterways. Moreover, breeding strategies have also been adopted, which allow farmers to improve cattle genetics to create a lower-emission cow. Institutions in Ireland are researching many additional ways to implement more sustainable methods, such as developing superior feed supplements showcasing Ireland's commitment to the future of sustainable agriculture practices (*Sustainable Irish*).

Economic Breeding Index

The Economic Breeding Index (EBI) is a program launched in November 2000 that aims to serve as a selection tool for realizing Irish dairy cow breeding objectives (Berry et al. 6). The EBI is a single-figure profit index that enables farmers to identify the most profitable bulls and cows for breeding. EBI comprises information on seven related sub-indexes, including milk production, fertility, calving performance, beef carcass, cow maintenance, cow management, and health. DNA profiles of individual cows can be analyzed and compared to the DNA profiles of proven animals within the reference population to accurately predict the animal's genetic makeup and corresponding traits (*Understanding the Economic* 1). While EBI can be effectively utilized to engineer and produce the most economically viable specimens genetically, the genetic technology of EBI can also be used to promote the most sustainable genetic profiles. The

introduction of EBI as a sustainability measure will enable farmers to breed a more profitable dairy cow with lower greenhouse gas emissions. Research by Teagasc has shown, "for each €10 gain in herd EBI, there has been a gain of €20 in terms of additional net profit per cow per year while leading a 3% reduction in the carbon footprint" (*Sustainable Breeding*). This practice is sustainable because of numerous factors, including improved fertility, which reduces calving interval and replacement rates; increased milk yield, which contributes to production efficiency; and improved health, as lower disease rates lead to lower replacement rates. Further, benefits additionally include younger age at first calving and a pattern of compact calving, which maximizes the proportion of grass in a cow's diet to reduce culling (*Sustainable Breeding*).

White Clover

Another sustainability strategy that farmers have recently implemented is white clover. The temperate Irish conditions enable white clover to grow well with perennial ryegrass. The legume itself can improve sward quality and, in turn, improve the diet of grazing cattle. Research has shown that utilizing a sward with a white clover content of at least 20% results in a positive impact on animal performance and can lead to increased profitability by upwards of 10%. Furthermore, Teagasc's MACC has identified the incorporation of white clover into pastures as a notable greenhouse gas emission reduction and mitigation measure. Past use of synthetic fertilizers has been reported as a principal source of nitrous oxide emissions, a potent greenhouse gas with a global warming risk 265 times stronger than that of CO_2. White clover can potentially replace these harmful fertilizers while benefiting cattle health (*Sustainable Dairy*).

Water Quality

According to the Environmental Protection Agency's (EPA) Water Quality in Ireland 2016-2021 report, 43% of river sites have high nitrate concentrations, while an additional 30% of river sites and 33% of lakes have high phosphate levels. In addition to these statistics, the EPA declared that 54% of surface waters are in good ecological condition, meaning that nearly half, 46%, are considered unsatisfactory (*Smart Farming*). The EPA recently released its "Water Quality in 2023" indicators report. Regarding river nitrate quality, 42% of rivers were considered unsatisfactory, 18% were considered good, and 40% were considered high (Figure 1). Furthermore, it is essential to note that a majority of dairy farms can be found in the southern and eastern parts of the country, which may contribute to the worsening river quality in those areas. Additionally, in this report, the EPA made comparisons between its findings, starting with its 2007-2009 report and ending with its 2021-2023 report, which collectively showcases that there has been a notable decline in lakes with high biological quality (Table 1). While numerous factors may contribute to declining water quality, Ireland's agriculture industry plays a role. Namely, unrestricted cattle access to rivers and streams with free grazing represents a significant localized pressure on freshwater systems. Cattle access to these water systems can impact aquatic ecology, sediment ingress, the integrity of riparian zones, which refer to the lands along the edges of water bodies, and general water quality. One issue with cattle grazing and movement

near riparian zones includes reduced plant cover and vitality of rivers, leading to soil erosion and elevated sediment inputs, which commonly impairs water quality. Other issues include cattle trampling on river banks and riverbeds, soil detachment impacting water quality, and other geomorphic impacts (Conroy et al.). Nevertheless, another significant issue surrounds large quantities of slurry and manure produced annually. While having practical uses as a source of organic matter for agriculture, the benefits of waste recycling have been offset by water pollution risks due to runoff from fields where slurry or manure has been applied (Ramos et al. 1).
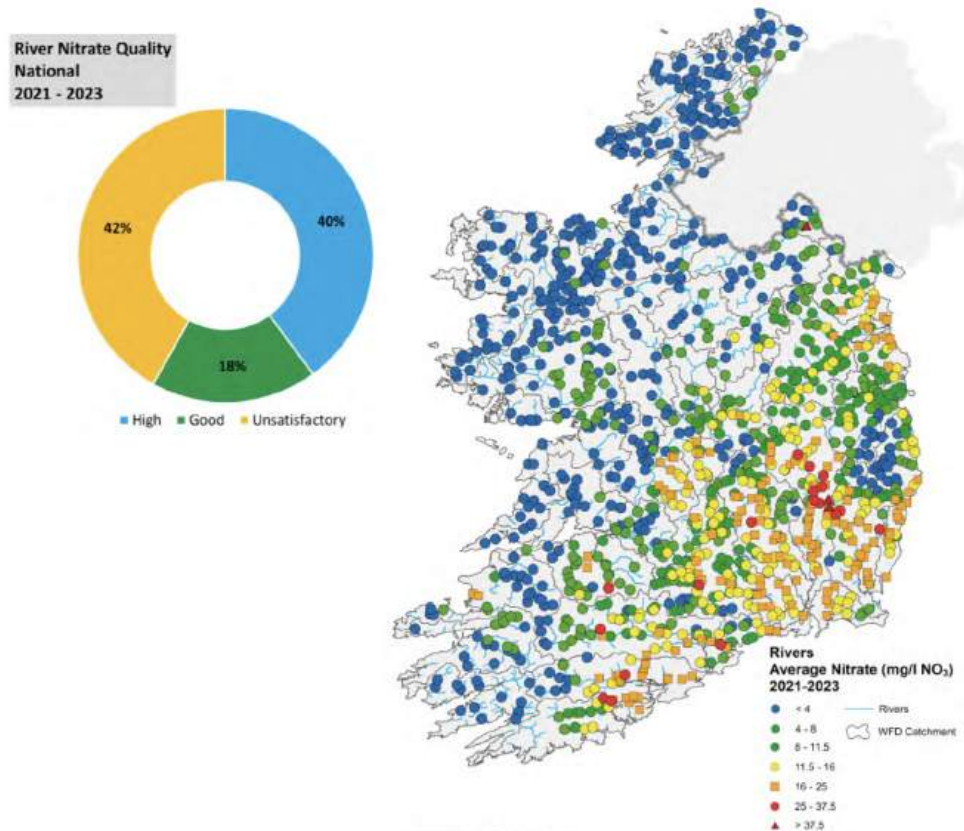

Figure 1: River Nitrate Quality Data from EPA's 2021-2023 Report (*Water Quality* 5)
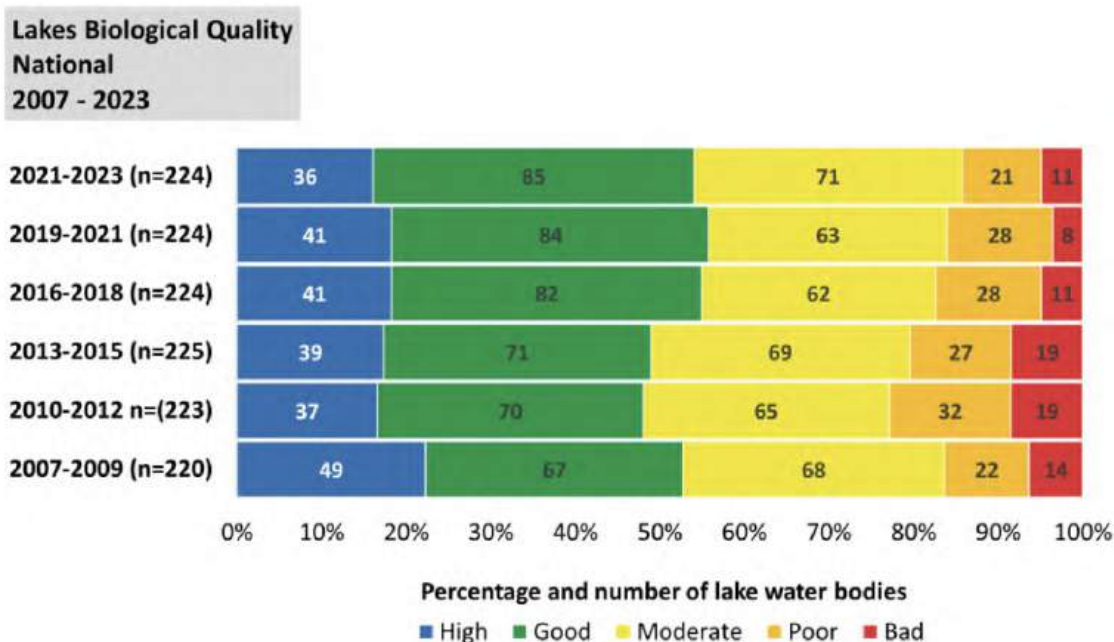
Lakes Biological Quality National 2007 - 2023

Period	High	Good	Moderate	Poor	Bad
2021-2023 (n=224)	36	85	71	21	11
2019-2021 (n=224)	41	84	63	28	8
2016-2018 (n=224)	41	82	62	28	11
2013-2015 (n=225)	39	71	69	27	19
2010-2012 n=(223)	37	70	65	32	19
2007-2009 (n=220)	49	67	68	22	14

Percentage and number of lake water bodies
■ High ■ Good ■ Moderate ■ Poor ■ Bad

Table 1: EPA's Lake Biological Quality Data Over the Past 16 Years (*Water Quality* 4)

With concerns about the quality of water in Ireland, specifically as a result of agricultural-based risks, EU and national policies have been introduced to guide agricultural activity and ensure clean water sources. The Water Framework Directive (WFD) establishes a framework for protecting all waters, including rivers, lakes, estuaries, coastal waters, and groundwater. The legislation additionally includes the protection of any dependent wildlife habitats. The WFD is also related to several EU directives on protecting biodiversity, general water use, and soil health. Under the WFD, the Minister for Housing, Local Government and Heritage published its second River Basin Management Plan for Ireland (RBMP) in 2018, aiming to improve water quality and achieve "good" ecological status in the near future. The final plan for the third cycle of RBMP was published in 2022, addressing pressures on Irish water bodies from different sectors, including agriculture. The Nitrates Action Programme is a related piece of legislation that is a key measure for mitigating agricultural pressures (*An Overview*). This legislation will be addressed in the next section.

Nitrates Action Programme

The Nitrates Action Programme (NAP) is Ireland's primary strategy for implementing the Nitrates Directive to reduce and prevent water pollution caused by agricultural activities. Introduced to address the adverse impacts of nitrates from agricultural sources on water quality, the NAP outlines various measures and regulations to promote sustainable farming practices and protect water resources. These measures help ensure that agricultural activities are conducted in an environmentally responsible manner to safeguard Ireland's landscape and public health (*6 Key Changes*). Furthermore, agriculture in the EU contributes 40 to 80 percent of the nitrogen and 20

to 40 percent of the phosphorus that enters surface waters. The Nitrates Directive, a precursor of the Water Framework Directive, aims to minimize agriculturally produced surplus phosphorus and nitrogen from entering aquatic environments. The Nitrates Directive requires each member state to introduce its program to combat the issue of corrupted waters. Despite introducing the Nitrates Directive in 1991, it wasn't until 2006 that the Irish NAP was transposed into legislation. Nevertheless, the policy has been subject to a periodic 4-year update and review (Buckley 1).

Ireland is on its fifth edition of the NAP and is still committed to preventing the pollution of surface waters and groundwater from agricultural sources. This new edition was effective beginning in March 2022 and will continue to be in effect until 2025 (*Information Note*). The continuation and evolution of the NAP highlights the importance of adapting and improving environmental policies to address ongoing and emerging challenges. The fifth edition underscores Ireland's dedication to protecting its water resources, reflecting a proactive approach to environmental concerns and public health protection. By continually refining the NAP and utilizing new research and data to inform new objectives and reforms, Ireland complies with EU directives and promotes its own sustainable development.

Ireland's fifth NAP

To focus on the most recent edition, some new measures will focus on slurry storage and management, soiled water storage and management, livestock excretion rates, and chemical fertilizer control. Managing organic manure, especially slurry, is crucial for reducing environmental nutrient loss. Inspection statistics indicate that inadequate slurry storage is a primary non-compliance issue on farms. To address this, new regulations hope to increase farm storage capacity and mandate specific dates within which slurry can't be spread to reduce the risk of nutrient loss during periods of high rainfall. From January 1st, 2023, all slurry must be applied by October 1st of that year. Soiled water management is another critical area. The addition of soiled water to slurry tanks has caused notable storage issues. To mitigate this, spreading soiled water is prohibited during specific periods to reduce potential runoff risk. These dates will eventually restrict the spreading of soiled water between December 1st and 31st. Moreover, livestock excretion rates are being revised to reflect current data on nutrient output. These measures ensure nutrient management plans are accurate and based on up-to-date information, which will facilitate better compliance with environmental standards and control the amount of nitrogen and phosphorus entering water bodies. Finally, new regulations include the introduction of a national register for chemical fertilizer sales to track sales against individual farmer's herd sizes. This initiative aims to improve the efficiency of fertilizer application and possibly mitigate future use (*An Overview*).

Methods

Approach

This study employed a qualitative approach, utilizing semi-structured interviews to gather insights into the perspectives of current and recently retired Irish dairy farmers. Qualitative research was chosen because it allows for collecting in-depth, nuanced data that might be overlooked in more extensive, more generalized surveys. Open-ended questions and flexible discussions allow semi-structured interviews to provide interviewees the opportunity to engage more personally (Busetto et al. 2-3). This method is particularly valuable in agri-research as context-specific knowledge and lived experience can significantly influence perspectives and individual practices. The interview questions focused on three primary topics: sustainability, policy, and governmental intervention.

Sampling

The study sample consisted of dairy farmers (n = 3) across Ireland who currently engage in dairy farming or have recently retired. Participants were contacted through familial connections, ensuring a level of trust and openness during the interviews. The interviews were conducted over the phone and on Zoom, and recordings were transcribed using Microsoft Word transcription software and edited for accuracy.

Data Collection

The interview process began with an introduction to the study's topic and objectives. Participants were informed that the interviews would be recorded for data analysis purposes, with assurances that all recordings would be deleted upon completion of the write-up and would not be shared beyond the researchers. Verbal consent was given by all participants to be recorded. To begin the interviews, baseline questions were asked to determine herd size (number of cows), farm size (hectares), and whether or not a body of water was present on their farmlands. A series of questions followed targeting perspectives on sustainability (namely the implementation of sustainability measures), policy change (the abolishment of the milk quotas in 2015 and the Nitrates Action Programme), and governmental intervention (the importance and extent of government involvement in the sector).

Data Analysis

The recorded interviews were transcribed and analyzed using thematic analysis, which involves several stages to ensure a thorough examination of the data. Thematic analysis is a method for identifying, organizing, and offering insight into patterns of conclusions taken from a data set (Braun & Clarke 57).

The process began with familiarizing ourselves with the data by reading the interview transcripts. Next, we generated initial codes by systematically identifying and labeling relevant features. These codes served as the base for the next steps of our data analysis, where we searched for themes by grouping features into broader patterns that offered insights. Following this, we reviewed potential themes to ensure they accurately represented the data. Finally, we

defined and named themes. The report provided a comprehensive understanding of the similar and differing perspectives among Irish dairy farmers.

Limitations

This study has several limitations. First, the sample size is small, which may not provide a comprehensive representation of all Irish dairy farmers. Second, this study was conducted in specific parts of the country, which may impact the findings due to area-specific conditions. Third, the transcription software was not wholly accurate, but human verification was used to ensure relative accuracy. Nevertheless, despite the limitations, the insights gained from this study offer valuable contributions to understanding the challenges and perspectives of Irish dairy farmers.

Discussion

The discussion section delves into four key themes that emerged from interviews with Irish farmers: the implications of sustainability measures, the impact of the milk quota abolishment, the challenges facing family farming, and the tensions between Irish government regulations and EU agricultural policies. Through these themes, the section explores farmers' diverse perspectives and experiences, offering insights into the complexities and challenges of contemporary Irish agriculture. Each theme is analyzed in relation to existing literature, highlighting both the alignment and divergence of farmers' views with broader trends and research findings.

Sustainability Measures Implications

The implications of adopting sustainability measures in Irish farming are multifaceted, revealing a mixture of optimism and caution among farmers. Farmer 1 highlighted the financial benefits, stating, "*Your costs are going to come down because you won't be using multiple fertilizers*". This sentiment aligns with the findings of Teagasc's analysis of the impacts of fertilizer alternatives such as white clover, which emphasize the economic advantages of sustainable practices through reduced input costs (Sustainable Dairy). However, the complexity of implementing these measures became evident in Farmer 2's experience. While incorporating red clover and mixed species swards have been beneficial for nutritional value, Farmer 2 noted that "*what suits me here won't work 10 miles away*", emphasizing the variability of success depending on local soil conditions. This points to the importance of context-specific approaches to sustainability, reaffirming findings in Teagasc reports that underscore the need for tailored strategies targeted at different farm types to promote the most economically viable environment (Teagasc National, 2023). Farmer 3's perspective adds another layer, as they acknowledged the benefits but expressed concern over the broader sustainability of current practices, particularly given the pressure from co-ops and the government to adopt specific measures. The variation in these experiences suggests that while sustainability measures hold promise, their effectiveness is deeply influenced by individual farm conditions and broader industry pressures.

Abolishment of Milk Quotas

The removal of milk quotas has had significant economic and environmental impacts on Irish dairy farming, reflecting both opportunities and challenges. Farmer 1 expressed frustration, noting, "*People would have spent big money on quota over the years... and they just got rid of it*". This sentiment highlights the financial burden and sudden devaluation faced by many farmers. In contrast, Farmer 2 viewed the removal positively, linking it to increased land rental and expansion opportunities, stating, *"The milk quota removal has been very, very positive.*" This divergence of opinions underscores the literature's emphasis on the mixed impacts of quota abolishment, where larger farms benefited from expansion while smaller ones struggled with new pressures. Specifically, research in the International Journal of Dairy Technology points to broad benefits accompanying the quota abolishment in the form of resounding economic gain (Kelly et al.). Nevertheless, Farmer 1 highlighted that the quota systems didn't impact farmers equally. Those who had overinvested faced substantial negative implications from the policy change. Finally, Farmer 3 brought attention to the environmental repercussions, asserting that the quota removal "*has a massive impact on climate change... I don't think it's sustainable at the moment.*" Similarly, concerns have been raised by the Irish Climate Change Advisory Council concerning the intensification of farming and its environmental toll, suggesting that while economic gains were made, the long-term sustainability of such practices still needs to be improved. In its 2019 annual review, the advisory council noted, "*Emissions in Agriculture are projected to continue increasing to 2030 due to growing cattle numbers, increased fertilizer use and ongoing carbon losses from land. If allowed to proceed unchecked, this would seriously undermine our ability to meet our 2030 target for a reduction in national emissions" (Läpple et al. 1)*. Individual farms and the dairy industry can significantly expand production and herd size without herd and production limits, further ingraining sustainability issues with the sector's increased output.

Family Farming

The viability of family farming in Ireland is increasingly under threat, with farmers expressing concerns about economic sustainability and the future of small farms. Farmer 1 summarized the challenge: "*You wouldn't make a living off a small family farm anymore... it's not sustainable to raise a family or to pay a mortgage and things like that.*" This observation increases in relevance as the most recent Teagasc annual report points to a significant decrease in annual income for dairy farmers. In 2022, the average yearly income was 148,600 euros (*Teagasc National*, 2023), while in 2023, Teagasc reported a mean annual income of 49,400 euros (*Teagasc National*, 2024). The decline of family farms is inevitable, and larger, more industrialized farming operations will take hold in the sector. Farmer 2 advocated for support through technology rather than subsidies, suggesting that family farms "*should be supported... through improved technology*", highlighting a potential pathway for preserving these traditional operations. However, Farmer 3 was more pessimistic, stating, "*I think family farms are gone. Just the nature, the climate around the whole lot has changed"*, supporting certain concerns

about family farms' declining cultural, economic significance, and general prevalence (Galeski). The differing perspectives reveal a complex picture where the future of family farming may depend on both technological innovation and policy support.

Irish Government vs. EU Policy

The relationship between Irish government regulations and EU agricultural policies is a source of tension and uncertainty for farmers. Farmer 1 expressed frustration with the lack of national control, stating, "*The Irish government have no control. It's all based on a common agricultural policy now from Europe.*" This reflects a broader distrust, highlighted by the European Commission's address of CAP-related concerns that speaks to the loss of national sovereignty in agricultural policymaking. Some concerns addressed included overregulating farmers, the EU policy's harm to agriculture in developing countries, and neglecting environmental concerns (*The Common*). Farmer 2 highlighted the benefits and drawbacks of EU membership, noting that "*the disadvantage is that you're treated the same as the rest of the countries... whenever your climate is completely different*", underscoring the challenge of applying uniform policies across diverse agricultural environments. Farmer 3 echoed this sentiment, adding that farmers "*have no voice anymore*", suggesting a disconnect between policymakers and those on the ground. These quotes illustrate the complexities and frustrations that arise when broader, more generalized policies overshadow local conditions. The CAP is a policy created by the EU and partially adapted to each member state (*Ireland – CAP Strategic*). Yet, a disconnect stems from countries' vastly differing landscapes and climates. So, a possible solution may be to better differentiate different member countries' sustainability responsibilities to suit respective conditions.

Conclusion

While Ireland's dairy industry has undergone significant expansion in recent decades, the increasing focus on sustainability in all forms has created a scenario of incongruence between policy and practice. The results attained as part of this research highlight this, with farmers noting the impact of policy change at the farm level and the challenges they face while implementing new technologies. Themes of sustainability, economic viability, and regulatory tensions were explored, with a sense of uncertainty surrounding the future of small-scale family farms coming to the fore. Farmers expressed a shared concern over the economic implications of sustainability transitions, which, while undeniably beneficial for some, are not universally adaptable to all farms. Additionally, abolishing milk quotas has allowed for significant expansion but introduced new environmental and financial pressures. Finally, the disconnect between Irish government regulations and EU agricultural plans complicates farmers' efforts to align with sustainability goals relative to their farm environment, as some broader politics often fail to account for varying local farm conditions. While progress has been made, future efforts should focus on aligning policy with local farming realities to target sustainability within the dairy sector.

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Entering the Global Market: The Cases of Two Chinese Cosmetic Brands By Zihao Zhao

Abstract

This paper examines the global expansion strategies of two prominent Chinese cosmetic brands, Herborist and Florasis, focusing on their approach to balancing cultural authenticity with strategic adaptation in diverse international markets. Through case study methodology, the research analyzes the brands' use of cultural storytelling, localized marketing, and product innovation to navigate challenges such as cultural differences and regulatory barriers. Results indicate that cultural integration, combined with strategic localization, is crucial for success in global markets. The study highlights the importance of maintaining brand identity while adapting to local demands, with limitations discussed in the context of market-specific challenges.

1. Introduction

The global beauty industry is a dynamic and rapidly evolving sector, driven by continuous innovation, shifting consumer preferences, and the growing influence of cultural narratives (Cosmoprof, 2024). As the market becomes increasingly globalized, brands from diverse regions seek to expand their presence beyond domestic borders. Chinese cosmetic brands, in particular, are increasingly making their mark on the global stage. This expansion offers unique insights into the interplay between cultural heritage and international business strategies.

The journey of Chinese cosmetic brands like Herborist and Florasis into global markets is particularly compelling. These brands offer a rich case study in balancing the preservation of cultural authenticity with the need to adapt to diverse consumer preferences and regulatory environments. The success or failure of such brands in international markets hinges not only on product quality but also on their ability to navigate the complexities of cultural differences, regulatory barriers, and fierce competition (Keillor, 2013).

Understanding the strategies employed by these brands is critical not just for other Chinese companies, but for any brand aiming to expand globally. The aim of this study is to analyze the internationalization strategies of Herborist and Florasis, exploring how they have leveraged cultural storytelling and strategic marketing to achieve success, as well as the challenges they have faced. The hypothesis driving this research is that a brand's ability to maintain cultural authenticity while strategically adapting to local markets is a key determinant of its success in global expansion.

By examining these cases, this study contributes to a broader understanding of how brands can effectively enter and thrive in diverse global markets, providing valuable lessons for future internationalization efforts across industries.

2. Literature Review

Benefits and Strategies of Global Expansion

The international expansion of indigenous cosmetics brands has become increasingly significant in the context of globalization. The cosmetic product industry is experiencing exceptional growth and holds a substantial global market share. Technological advancements, consumer purchasing power in numerous countries, and increased globalization have created substantial opportunities for market penetration and business expansion (Saleh & Rasyidin, 2024). Continuous product innovation, intense competition among prominent brands, and increasing consumer demand are among the characteristics (Putri & Dimyati, 2024). Diverse product categories that cater to a broad market segment are offered by prominent companies such as L'Oréal, Estée Lauder, Procter & Gamble, Shiseido, and Revlon (Putri & Dimyati, 2024). Riyadi et al. (2024) highlighted three key benefits for cosmetic companies to expand internationally. First of all, beauty companies can access a broader consumer base and realize a higher sales potential by entering the global market. The global market provides access to millions of new potential consumers with a wide range of preferences, requirements, and habits in the context of beauty products (Maulidya et al., 2023). In addition, in the international market, globally recognized beauty brands frequently play a critical role in satisfying consumer requirements and expectations. Beauty companies can increase their market share and competitiveness by enhancing brand recognition and trust among international consumers through global expansion. Last but not least, the cosmetics industry is constantly introducing new trends and innovations. Beauty companies are able to introduce the most recent trends and innovative products in a variety of countries around the globe as a result of global market expansion. This establishes them as trendsetters and sources of inspiration for local brands in various markets (Armiani et al., 2024; Ariawa et al., 2024).

Several global expansion strategies have been extensively discussed in the literature. Riyadi et al. (2024) reviewed strategies for new market penetration in beauty products, highlighting the need for a deep understanding of local consumer preferences and behaviors. Brands like L'Oréal have successfully adapted their products and marketing strategies to resonate with local consumers while maintaining a global identity (He et al., 2024). For instance, L'Oréal's success in China can be attributed to their tailored marketing campaigns and product adaptations to suit local preferences, such as formulating products specifically for Asian skin types and using Chinese celebrities in advertisements.

Another strategy involves leveraging digital marketing and e-commerce platforms to reach global audiences. Brands like Estée Lauder have used social media and online influencers to create a strong presence in international markets, which has been crucial in engaging younger consumers and building brand loyalty across different regions (Hassan et al., 2021).

Challenges in Global Expansion

The current literature acknowledges that cultural differences, regulatory barriers, fierce competition, and logistical concerns are significant challenges for local cosmetics brands expanding internationally. Brands need to deeply understand local cultural norms and consumer

preferences to achieve success (Alden et al., 1999). For instance, beauty standards can vary dramatically between regions, influencing product formulations, packaging, and marketing strategies. What is considered attractive or desirable in one culture may not resonate in another, requiring brands to tailor their offerings to meet diverse consumer expectations.

Regulatory barriers pose another significant hurdle (Vogel, 2010). Countries have different product safety standards, ingredient regulations, and import restrictions that brands must meticulously navigate. Compliance with these regulations often involves extensive documentation, product testing, and potential reformulation, which can be both time-consuming and costly. Additionally, regulatory changes can occur, necessitating ongoing vigilance and adaptability to ensure continuous market access (Cardoza et al. 2015).

Fierce competition from both local and global brands further complicates international expansion (Porter, 1986). Established local brands often have strong customer loyalty and deep market insights, making it challenging for new entrants to gain a foothold. Global brands with substantial resources and well-established reputations also present formidable competition. To stand out, brands must offer unique value propositions, whether through innovative products, superior quality, or exceptional customer service. Effective marketing strategies are crucial, leveraging digital platforms, social media influencers, and localized campaigns to build brand awareness and connect with consumers on a personal level (Johnson & Tellis, 2008; Zhou & Belk, 2004).

Furthermore, logistical challenges such as supply chain management and distribution networks are vital considerations (Arsova et al., 2019). Efficient logistics are essential to ensure product availability and maintain quality across different regions. Developing robust distribution networks can help brands reach a wider audience and enhance their market presence. Strategic partnerships with local distributors and retailers can facilitate smoother market entry and expansion, leveraging their local expertise and established channels.

In summary, understanding and addressing cultural differences, regulatory barriers, and fierce competition are essential for the successful international expansion of cosmetics brands. By focusing on these aspects and implementing tailored strategies, brands can navigate the complexities of global markets and achieve sustainable growth.

3. Method

This research employs a case study methodology, focusing on two prominent Chinese cosmetic brands—Herborist and Florasis—as representative examples to explore the dynamics of international business strategies in the cosmetics industry. The study gathers data from a variety of internet sources, including comprehensive market reports, industry analyses, and company financial statements, which provide a solid quantitative foundation for understanding the brands' market performance and financial health during their international expansion.

Moreover, the study reviews existing case studies of other cosmetic brands, both successful and unsuccessful, to draw parallels and contrast the strategies employed by Herborist and Florasis. This comparative analysis helps to identify the key factors that have contributed to

their success or presented challenges during their international ventures. By synthesizing insights from both practical industry data and academic theories, the research aims to provide a comprehensive understanding of how different strategies influence the success of cosmetic brands in global markets.

4. Herborist Case

Founded in 1998, Herborist quickly became a leading Chinese cosmetics brand by integrating traditional Chinese medicine (TCM) with modern skincare technology. Initially focused on the domestic market, Herborist began exploring international opportunities in the mid-2000s. Despite its strong cultural heritage and unique product offerings, the brand encountered significant challenges in its global expansion, including adapting to different regulatory standards, understanding diverse consumer preferences, and building brand recognition in highly competitive markets.

In July 2001, Herborist made its first attempt at internationalization by entering the Hong Kong market. The company management believed that succeeding abroad meant adopting Western standards. Consequently, they altered product packaging to feature English prominently and minimized Chinese cultural elements, which were relegated to mere product descriptions. Herborist opened two stores in prime locations, Mong Kok and Causeway Bay, and directly managed them from mainland China, deploying high-cost management staff and salespeople. However, this strategy proved ineffective. Herborist did not collaborate with local distributors or conduct thorough market research, instead relying on a single advertising agency to execute a marketing plan devised by headquarters. This plan failed to resonate with Hong Kong consumers, who were more accustomed to established international brands. The superficial approach to internationalization, combined with high rental costs and poor market understanding, led to low sales performance. By 2003, Herborist was forced to withdraw from the Hong Kong market.

This failure prompted deep reflection within Herborist. The management realized that their lack of confidence in their Chinese cultural heritage and the decision to Westernize the brand had eroded its differentiation. By stripping away the core Chinese elements, Herborist had positioned itself as a second-rate Western brand, which did not appeal to consumers. Learning from this experience, Herborist shifted its strategy. In 2007, the company re-entered the Hong Kong market, this time through a partnership with Mannings, a large local health and beauty chain. Rather than operating their own stores, Herborist placed its products in select Mannings outlets to test the market. They fully embraced their Chinese heritage in marketing materials, emphasizing the TCM roots of their products. This strategic shift proved successful, leading to improved sales and a gradual expansion of Herborist's presence in Hong Kong. The lessons learned in Hong Kong provided Herborist with valuable insights that they applied in other international markets. By acknowledging the importance of their cultural identity and adapting their strategy to local market needs, Herborist managed to turn previous failures into a foundation for future success.

In 2008, Herborist entered the European market through a strategic partnership with Sephora, a luxury beauty retailer owned by LVMH. This move began with Herborist products being introduced in Sephora's flagship store on the Champs-Elysées in Paris. The entry into Europe was challenging, as Sephora initially hesitated due to Herborist's lack of brand recognition in France. However, the brand's unique selling point—cosmetics infused with traditional Chinese herbs—eventually persuaded Sephora to give it a chance. This partnership marked the beginning of Herborist's expansion across Europe, including markets in Italy, Spain, Germany, and Poland (Cosmetics Business, 2013; Global Times, 2014).

Herborist's success in Europe was further bolstered by its emphasis on Chinese culture, which was presented as a key selling point alongside modern scientific research. This approach helped the brand resonate with European consumers who were increasingly seeking natural and traditional skincare solutions (Global Cosmetics News, 2015).

Strategic Adaptations for Global Success

Herborist's global expansion strategy involved a meticulous approach to adapting its operations to meet the needs of diverse international markets. The brand established R&D centers in key locations to better understand and respond to local skincare preferences, enabling the development of products tailored to specific markets, such as lighter formulations and fragrances that appealed to European consumers while maintaining the essence of TCM.

To ensure broad market reach, Herborist employed a multi-channel distribution strategy. This included forming strategic partnerships with local retailers, leveraging e-commerce platforms, and establishing flagship stores in prominent global cities. Their advertising efforts were carefully crafted to align with the cultural values of their target markets. Herborist utilized global celebrities and influencers in their campaigns to highlight the brand's unique blend of TCM and modern skincare science. Moreover, digital marketing and social media engagement played a crucial role in Herborist's international strategy, allowing the brand to directly connect with consumers, gather insights, and create marketing campaigns tailored to different cultural contexts.

This combination of localized product adaptation, strategic distribution, and culturally attuned marketing helped Herborist navigate the challenges of international expansion. While the brand's success was driven by its unique product offerings, effective localization strategies, and strong digital presence, it also faced challenges such as regulatory hurdles, intense competition, and the need for continuous innovation to stay relevant in the global market.

5. Florasis Case

Florasis, founded in 2017, has quickly emerged as a distinctive player in the global cosmetics industry, known for its innovative blend of traditional Chinese cultural elements with modern beauty techniques. The brand's commitment to integrating Chinese aesthetics and heritage into its product lines, including intricate packaging and formulations inspired by traditional Chinese medicine (TCM), has resonated deeply with both domestic and international

consumers. Florasis's rapid rise in popularity can be attributed to its innovative products, cultural storytelling, and strategic marketing efforts.

Cultural Integration Strategy

Florasis incorporates a rich array of traditional Chinese cultural elements into its products, using ancient styles in both packaging and advertising. This approach is designed to captivate both domestic consumers, who feel a strong connection to their cultural roots, and international consumers, who are drawn to the exotic and authentic aspects of Chinese culture. For instance, the brand's lipstick packaging is intricately designed with traditional Chinese patterns, offering not just a product but an experience steeped in cultural heritage. These designs serve to elevate the visual appeal of the products while also embedding a profound sense of Chinese identity and history.

Florasis excels in weaving cultural narratives into its brand identity, creating emotional connections with consumers through stories rooted in ancient Chinese aesthetics and philosophies. This storytelling approach adds layers of depth to the brand, making it more than just a cosmetics line. By integrating quotes from ancient Chinese poetry and drawing on classical themes, Florasis crafts an elegant and mysterious brand image that resonates deeply with consumers, helping them to better understand and embrace the brand's cultural essence.

Localized Marketing

Florasis tailors its advertisements to align with the cultural preferences and consumer habits of different international markets. In Japan, for example, the brand merges local aesthetic preferences with traditional Japanese cultural elements to create advertisements that resonate strongly with Japanese consumers. This localized approach not only enhances brand recognition but also fosters a deeper connection with the local audience, making the brand more relatable and desirable.

Florasis maintains an active presence on social media platforms, where it engages directly with consumers, gathers feedback, and extends its brand influence through strategic influencer marketing. Regular content updates and interactions on platforms like Instagram and YouTube, particularly through collaborations with beauty bloggers, have significantly boosted Florasis's global visibility. This strategy not only increases brand exposure but also builds a community of loyal followers who are invested in the brand's story and products.

Product Innovation

Florasis continually innovates by developing products that cater to the diverse needs of international markets. For instance, the brand customizes products to suit different skin types and beauty standards across various regions, ensuring that their offerings remain relevant and appealing to a global audience. This focus on differentiation not only meets the specific demands of consumers but also strengthens Florasis's competitive position in the global beauty market.

The brand places a strong emphasis on transparency regarding its use of natural and traditional Chinese medicinal ingredients. This approach appeals particularly to health-conscious consumers worldwide, who appreciate the detailed explanations of ingredients and their benefits. By educating consumers on the unique aspects of its offerings, Florasis builds trust and establishes itself as a credible and reliable brand.

Florasis is committed to sustainability, both in its product development and packaging practices. The brand uses eco-friendly materials and promotes recycling initiatives, aligning with the global trend toward sustainability in the beauty industry. This commitment not only enhances Florasis's brand image but also attracts consumers who prioritize environmental responsibility in their purchasing decisions.

Florasis's success in both domestic and international markets can be attributed to its strategic integration of traditional Chinese cultural elements, innovative product offerings, and targeted marketing efforts. By embracing and promoting its cultural heritage, Florasis has carved out a unique niche in the global beauty industry, appealing to consumers seeking authenticity and cultural richness. Through localized marketing and a commitment to sustainability, Florasis continues to expand its global footprint, solidifying its position as a leader in the modern cosmetics market.

6. General Discussion

Market Potential

The majority of Asian cosmetic brands tend to first expand to other countries within Asia due to their geographical proximity, similarities in skin tone and type, cultural commonalities, and comparable beauty trends followed by consumers. This strategic choice allows these brands to integrate more smoothly into new markets.

For instance, in 2019, several leading Japanese beauty influencers discovered Chinese makeup styles through the social media platform Xiaohongshu. They began creating imitation tutorials, which quickly garnered significant attention. Since then, "Chinese-style makeup" has gained traction in the Japanese consumer market, characterized by the pursuit of fairness, prominent lip color, mature beauty, and sophisticated makeup. These features have become notable in the eyes of some Japanese consumers. Seizing this opportunity, numerous Chinese beauty brands signed contracts with Japanese idols and collaborated with Japanese television dramas to dominate social media and capture local consumer interest.

The increasing number of Asian brands expanding within the region has significantly heightened competition. Consequently, expanding further into Europe and North America becomes an attractive next step for these brands. However, it is crucial for brands to recognize the differences in consumer preferences when planning to enter these markets.

Cultural Difference

Cultural differences pose a significant challenge for cosmetic brands aiming to expand globally. In the United States, young female consumers generally prefer a "realistic" skin appearance, which drives the popularity of foundation products that create a "natural" makeup effect. The American market is highly concentrated, with established brands like L'Oréal dominating the space. However, new brands consistently disrupt the market through innovative and aggressive marketing strategies.

For Asian cosmetic brands, understanding these cultural nuances is essential. Beauty standards in Asia, which often emphasize fair skin and youthful appearances, contrast sharply with Western preferences. This necessitates a tailored approach in product development and marketing. Brands must also navigate cultural nuances in communication, symbolism, and consumer behavior to ensure their marketing messages resonate with the target audience without causing offense. This requires a deep understanding of local consumer preferences and trends, enabling brands to navigate the competitive landscape effectively and establish a strong presence in diverse global markets.

By integrating this cultural understanding into their strategies, Asian cosmetic brands can better adapt their offerings to meet the unique needs of Western consumers, ultimately enhancing their competitiveness and success in these markets.

Lessons Learned from the Cases

The contrasting experiences of Herborist and Florasis offer valuable insights into the complexities of international expansion. Herborist's initial failure in North America underscores the risk of losing cultural authenticity by attempting to Westernize too aggressively, which diluted its unique identity and lessened its appeal. In contrast, Florasis successfully leveraged its cultural heritage by integrating traditional Chinese aesthetics into its branding and products, preserving its identity while differentiating itself in a crowded market, demonstrating the power of cultural storytelling in global branding.

Key lessons include the importance of regulatory compliance, which entails understanding and adhering to the target market's standards for product formulation, safety, and labeling. Comprehensive market research is essential to grasp consumer preferences and cultural nuances, enabling brands to craft tailored products and messages. Establishing strong local partnerships is also crucial, as these partners provide market insights and help navigate regulatory and logistical challenges. Additionally, effective brand messaging involves more than just translation—it requires adapting the brand story to align with the cultural values of the target market, ensuring resonance and authenticity.

In summary, successful international expansion requires a careful balance of cultural authenticity, strategic adaptation, and local partnership, all underpinned by thorough market research and regulatory compliance.

Conclusions

The international expansion of cosmetic brands like Herborist and Florasis illustrates the complexities and opportunities within the global beauty market. Success is rooted in the ability to balance cultural authenticity with strategic localization. Herborist's initial missteps and eventual adaptation underscore the importance of understanding and embracing cultural heritage while adapting to local consumer preferences and regulatory environments. Florasis, on the other hand, exemplifies the power of cultural storytelling and innovative marketing in establishing a global presence. Ultimately, the key to successful global expansion lies in a brand's ability to remain true to its core identity while thoughtfully navigating the diverse landscapes of international markets.

Limitations and Future Research

While this study provides valuable insights into the international strategies of Herborist and Florasis, there are limitations that suggest avenues for future research. Firstly, the focus on two Chinese brands limits the generalizability of the findings to other regions and industries. Future research could explore a broader range of brands and markets to offer more comprehensive insights. Additionally, the rapidly evolving nature of digital marketing and e-commerce suggests a need for ongoing research into how these tools can be leveraged for international expansion. Finally, further investigation into consumer perceptions of cultural authenticity versus adaptation in global branding would provide a deeper understanding of the balance required for successful international market entry.

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The Evolution of Kurdophobia in Turkey and Iran from the Early 20th Century into the Modern Day By Alan Mehmetoglu

Introduction

According to the Daily Sabah, on November 25th, 2020, Turkish President and leader of the ruling AK Party, Recep Tayyip Erdogan addressed his party's parliamentarians. Regarding the Kurdish issue, he proclaimed, "I've said this dozens of times before and will say it again: There is no Kurdish issue in Turkey[...]We cannot ignore the fact that it is the separatist terrorist organization's (PKK) armed and political representatives that are the biggest enemy of our Kurdish brothers." The apparent shift from former explicit kurdophobia to simple criticism of the Kurdistan Workers' Party (PKK) in Turkish rhetoric, has become a superficial reality of the Turkish-Kurdish conflict in the wake of the former PKK-Turkey peace process.[9] Similar surface-level change has also occurred in Iran. Kurdophobia has taken form throughout the region of Kurdistan[10] in various forms: Ranging violent massacres such as the Dersim and Zilan Massacres killing tens of thousands of Kurds in Turkey and Kurds being discriminated against, stereotyped, and had their language denied and censored in both of these nations. Hence, given both of these countries' history with cultural and violent kurdophobia it is appropriate to ask the following question: How have the methods as well as the rhetoric used by the aforementioned states and their residents evolved from the 20th and early 21st century into the present day? For the purpose of this research paper, I have analyzed individual accounts of kurdophobia presented by journalists and human rights organizations, academic works on kurdophobia from the fields of sociology and political science, and social media threats on the Kurdish issue. Said sources show that although the rhetoric used by the state has changed somewhat, acknowledging and even occasionally pandering towards Kurds, the methods and rhetoric of kurdophobia have remained the same.

Background

Turkey has made surface-level changes which give its government plausible deniability of kurdophobia. For example, in the mid-2010s Turkey allowed for heritage-based language education in schools. In theory, this policy allows for students belonging to groups not legally considered minorities in Turkey such as the Kurds, Laz, and Circassians, to take their mother tongue as an elective in school. However, the reality in schools is far different. Minority Rights Group states, "There is still no right to mother tongue education at schools[...]students and parents do not know how they can apply for these courses. These courses are not run due to ` lack of enough students` as an official explanation." Essentially the state does not allow Kurds to take these courses. The change for supposed greater acceptance of Kurds is mostly superficial, with people in wider society still being discriminated against for speaking Kurdish. However,

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[9]Chaliand, Gérard, and Abdul Rahman Ghassemlou. *A People without a Country : the Kurds and Kurdistan*. Rev. and upd. ed ed., London, Zed Press, 1993.

[10] Henceforth, Kurdistan will be used to refer to the areas of Turkey, Iran, Iraq, Syria traditionally seen as populated by Kurds

said shift from the policies of former governments which saw activities as simple as even speaking Kurdish as a dissident and seperatsit behavior, making them illegal. In an effort to garner sympathy from Kurdish voters, President Erdogan even apologized for Kemalist massacres against Kurds. However, seeing that the AKP has allied with the virulently, anti-Kurdish MHP (National Movement Party) these words seem to be empty as well. In fact, with the aforementioned massacres also came deportations eerily similar to current shifts in population in the region with the large-scale displacements of Kurds occurring in Afrin at the hands of its Syrian proxies. The methodology below will reveal whether or not the Turkish and Iranian goevrnments' public rhetoric is the only element of kurdophobia which have evolved.

Methodology

Considering the state of the Kurds' geopolitical situation, one cannot rely on Tehran or Ankara to publish reliable information regarding the kurdophobia that is present within their borders or practiced by their governments. Although detailed journalistic coverage can also serve as a satisfactory source of information, it is important to only include extremely well-substantiated news reports to avoid allowing a certain journalistic bias to disproportionately impact research. Hence, analyzing the statements of its victims proponents, or instigants themselves is the most effective manner of examining contemporary kurdophobia, allowing social media such as Reddit and Twitter to be perfect mediums.

In the case of Reddit, popular subreddits in which the Kurdish issue is often discussed such as 'r/Kurdistan', 'r/Turkey', or 'r/Iran', were sought out. In these subreddits, popular threads where posts that elicited anti-Kurdish sentiment were identified. Posts that have been deleted by moderators, were excluded from the data. In addition, posts that criticized the original comment, or did not pertain to the Kurdish issue were excluded from the research. All other replies to a post, including those made by moderators, were included. The remaining posts were then sorted into three categories, some being classified as belonging to more than one of them. The first category includes comments that deny Kurdish history, identity, or the current geopolitical situation. The second category includes comments that blame Kurds for social problems within Turkey and stereotype Kurds. The third category includes comments that advocate for genocide or assimilation. Some of the classifications that were identified as part of the same category are listed together since they are mostly combined within singular examples of kurdophobic language both in the comments examined and in everyday societal interaction. On the other hand, certain classifications are identified as part of separate categories because they pertain to very different kurdophobic sentiments, even though they both signify extremely racist and kurdophobic intent. For example, someone advocating for the killing of Kurdish people through genocide is very different in his rhetoric than someone who denies Kurdish historical claims over Kurdistan.

For the social media analysis focusing on a Reddit post on Iran there are four categories: 1.Comments that allude to the notion that Kurds are a part of and should therefore defer to a central Iranian entity; 2. comments that express historical denialism including such sentiment

and other forms of such denialism; 3. comments that promote genocide or removal; 4. comments that expressed general racism such as stereotyping or racialized insults.

Regarding the Turkish language data found on Twitter, the methodology slightly differed when compared to Reddit. The keyword that was employed in finding tweets was 'Kürtler,' meaning 'Kurds' in Turkish. I selected one of the Twitter posts with an official count of 200-600 comments so that the research could be completed in the most time-efficient manner possible. In all threads analyzed, comments celebrating the original post are categorized under the tags by which the original post would be identified.

Despite both Turkish and Iranian societies being quite restrictive in terms of freedom of expression, netizens and activists outside of Kurdistan have been able to create primary sources on kurdophobia. Journalists and researchers have typically collected primary experiences of kurdophobia through interviews with victims themselves. While online, videos of perpetrators themselves expressing kurdophia can also easily be located. Taking this into account, Reddit and Twitter were also searched for both types of aforementioned sources.This was done using keywords such as 'Kurds,' or searching accounts or subreddits that seemed to frequently discuss Kurd and the Kurdish issue. Including said findings is vital in maintaining the objectivity of this research study. With them, one can ensure that this studies results is not overwhelmingly influenced by the fact that racism and prejudice is present in rgeater quntities thn average on sical media, but are in fact representative of real societal trends.

Literature review

Since its rise near the 20th century, kurdophobia has manifested itself in a plethora of different methods. In Turkey, kurdophobic behavior began during the Ottoman Era when Kurdish populations were viewed as an obstacle to the demographic homogeneity desired by the Young Turks as they deemed such homogeneity necessary for the sociopolitcal unity of a future nation state. According to Üngör, "The CUP elite had ostensibly agreed upon first destroying the 'zo' (the Armenians), whereupon they would proceed to annihilate the 'lo' (the Kurds)" (The Making of Modern Turkey, 115). In line with the Young Turks desire for demographic homogeneity, it was decided that many Kurds were to be deported from Kurdistan to Western Anatolia. In 1916 alone, 750,000 to 1,000,000 Kurds were deported in said fashion with approximately half of them perishing during the journey.

After Mustafa Kemal Ataturk came to power, such kurdophobia in a genocidal form increased in its intensity, especially as Kurds also opposed secularism. David McDowall, a historian, remarks upon the nature of Turkey's demographic politics,

No one could mistake the intention to destroy Kurdish identity[...]. Today such legislation seems wholly repugnant, yet one must remember that Turkey was practicing the crude ideas of social engineering which had currency not only in Nazi Germany but among many European intellectuals.

Only the impracticability of transferring and assimilating up to three million
people prevented the law from being implemented.

The Kurdophobia seen during the Kemalist era climaxed in the massacres witnessed in Zilan and Dersim. McDowall describes, "These [Turkish forces] traversed the whole of Dersim[...]rounding up rebels, burning villages and declaring as 'uninhabitable zones' all those areas, for example with caves, which favored guerrilla warfare" (A Modern History of the Kurds: Third Edition, 209). Kurdophobia in the form of dehumanization and anaimalization was also present during this time. Üngör writes,

From the authorities' point of view, this 'civilization process' required a twofold assault on Kurdish children's identities. On the one hand, the school needed to strip away all outward signs of the children's identification with tribal and rural life, that is to say, their 'savage' ways. On the other hand, the children needed to be instructed in the principles, values, ideas, and behaviors of Turkish 'civilization'.

Unfortunately, the Kemalst methods depicted here are continued today in some regions of Kurdistan such as Afrin, as subsequently discussed in this research paper. Furthermore, the systematic, kurdophobic denial of Kurdish history and culture continued into the far-right dictatorship can also be seen during the 1990s. Human Righs Watch recounts, "In May 1990, Ms. Fugan Ok, head of the human rights department of the Foreign Ministry, told Eric Siesby of the Danish Helsinki Committee that[...]there is no discrimination against Kurds, but that such discrimination would exist if the Kurds insisted upon a separate language and a separate culture" (Destroying Ethnic Identity: The Kurds of Turkey, 2). In addition, kurdophobic behavior also manifests itself in Turkish society. Gullistan Yarkin, a sociologist claims, "Kurdish inhabitants in Zeytinburnu have been subjected to many racist slurs, such as 'dirty Kurds', 'bigot Kurds', 'terrorist;", "Armenians", 'kıro' , "keko', "Go back to where you came from!", 'Don't speak Kurdish here!' and 'The best Kurd is a dead Kurd'" (Fighting Racism in Turkey: Kurdish Homeownership as an Anti-racist Practice, 11).

Turning to Iran, Amnesty International also provides valuable insights on the impact that kurdophobia has on local Kurds. Amnesty states, "Kurds in Iran have long suffered deep-rooted discrimination. Their social, political and cultural rights have been repressed, as have their economic aspirations. Kurdish regions have been economically neglected, resulting in entrenched poverty. " The Washington Kurdish Institute continues to describe kurdophobia acted on Kurds as political discrimination: "Kurds are often detained for merely being a member of a Kurdish political party and as of January 2018, 45% of recorded political prisoners were Kurds." Although this picture may be bleak, the modern day realities of kurdophobia are questioned by genuine skeptics and facetious interlocutors alike. Therefore, it is important to conduct a research study, like this one, that analyzes the evolution of kurdophobia.

Results

The first English language Reddit thread analyzed in this study was started by a post from someone who is supposedly a person of Turkish descent living in the Netherlands. This post was made in r/Turkey. Their post exhibits a slew of kurdophobic stereotypes and expresses racist messaging, although they themselves claim to not be racist. Besides the comments previously categorzied as excluded from the study for research purposes, there are 126 comments in the thread. The following pie chart shows which categories these posts fall into:
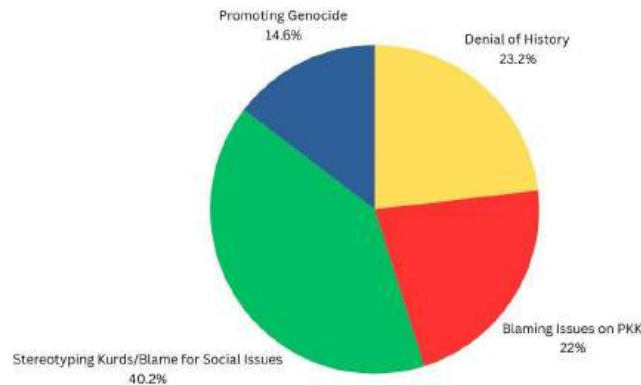
The second English language Reddit thread analyzed in this study was taken from r/Iran. The comments are responses elicited by a screenshot taken by a community member of a thread displaying a discussion on Kurdish nationalism. Excluding the comments that were part of the categories excluded in the methodology section, 33 comments will be analyzed for the purposes of this research study. The next pie chart shows the distribution of the Reddit replies within the categories previously mentioned.

The Turkish language post extracted from Twitter contains a number of racial insults towards Kurds. It complains of what certain ultranationalist groups believe to be a supposed 'occupation' of Turkish beaches by who they claim are Kurdish businessmen and companies. It calls for Turks to take action and insinuates the need for a genocide of Kurdish people. For research purposes, 41 comments have been analyzed. The following pie chart shows the categorization of these comments.
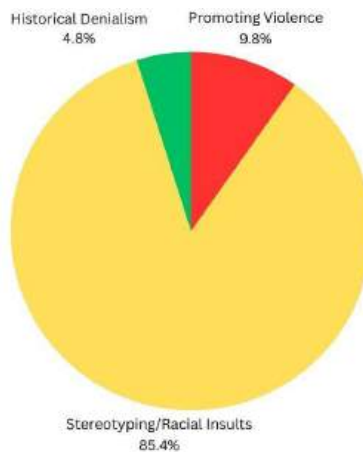
One more source of material found is an instagram post discovered by means of the pro-Kurdish Reddit community r/Kurdistan. It depicts a group of Turkish men rallying on a road, presumably in Turkey. They are shouting, "Kerkuk will become the grave of the Kurds," in apparent reference to the ethnically Kurdish majority province that, although disputed between Iraq's Federal Government and its Kurdistan Region, is also inhabited by Turkish speakers. The statement that they uttered infers that if the Kurds do not stop attempting to enforce their claims over Kerkuk, then they deserve to be genocided. What is interesting here is that later their slogan is changed to, "Kurds and Turks are brothers. The PKK is the enemy," most probably for optical purposes. More evidence of Kurdish language oppression has also been found using the resources of the 'Respond: Crisis Translation,' an international initiative that focuses on providing linguistic support and language-focused awareness in regions around the World, including Palestine, Ukraine, and Kurdistan. Their project on the Kurdish language has examined modern language discrimination during the 2023 earthquakes, as well as discrimination in everyday life, including by the Turkish State. Further examples of kurdophobia can be seen in areas under Turkish control in Syria and Iraq. The full range of kurdophobic tactics taking place in Aleppo's Afrin district, which has been under the occupation of the Turkish and Syrian National Army since 2018. According to a report conducted by Ceasefire and YASA, since the takeover, the formerly Kurdish-majority region has undergone a "complete restructuring of the political and security landscape in Afrin" (Escalating Human Rights Violations in Syria's Afrin: 2024 Update, 1)) Kurdish residents live under constant threat of violence at the hands of the Turkish Military and Intelligence operatives and their Syrian henchmen. Both frequently expose Kurds in Afrin to torture, looting, summary executions, beatings, extortion, sexual assault, and dehumanization. Kurdish detainees, some of which are minors or elderly people, are transferred to prisons under the control of the Turkish military, where they are rarely tried. Many Kurds have been forced out of their homes, have had their property confiscated, and crops destroyed. The Kurdish names of important streets and roundabouts as well as those of entire towns and villages have been Replaced in all of Turkish-controlled Syria. According to HRW, Turkey is also attempting to demographically de-Kurdify the region by resettling Arab refugees there from mainland Turkey, granting them ownership over previously Kurdish homes, helping Afrin's Kurdish population drop from over 90% to 35% of the city's population since 2018. With the departure of much of the Kurdish population came a complete overhaul of Afrin's educational system. Although Afrin was previously a Kurdish majority town, Kurdish children in Afrin are not accredited for Kurdish language classes if they choose to take them, and the number of Kurdish language classes is limited to four hours per week or abolished in some schools. This echoes Turkey's previous abolition of Kurdish language educational institutions during the founding of the Republic. In Afrin and other areas of Northern Syria controlled by Turkey, violent tactics such as torture and village displacement like those used during the 20th century can still be clearly observed. On the other hand, in Iran, in the aftermath of the killing of Zhina Amini, violence against Kurds sharply increased. Besides physical and political violence, violence against Kurdish culture and language has remained strong, with Kurdish language

teachers being imprisoned simply for teaching the language. Kurdish parents are prohibited from utilizing certain Kurdish names in naming their children as well. Also, Kurdish access to religious and educational equity, mainly in the lack of a sufficient number of mosques and local schools, is hindered by the government due to most Kurds being Sunni. Furthermore, the system by which the Government of Iran selects its employees, known as Gozinesh, is also discriminatory to Kurds. It evaluates employees' eligibility for state employment based on their perceived loyalty to the state and its version of Islam. Since Kurds are mostly non-Shia and belong to a minority group often viewed as dissident, this system prevents them from attaining such employment. The inability to do so is far more significant than it may initially seem. As Amnesty International states, "Gozinesh is used to select successful candidates for any state sector job, whether as a teacher, factory employee, shop worker or parliamentary candidate. The state is by far the main employer in Iran" (Iran: Human Rights Abuses Against the Kurdish Minority, 9) In addition, Iranian Kurdistan, although situated on Iran's overland trade routes, is chronically underdeveloped, which Kurdish activists claim is an intentional policy on the part of the Iranian State. The said underdevelopment not only denies Kurds the same economic opportunities as other Iranians but also access to other services such as healthcare. Kurdish language journalists are also frequently unfairly imprisoned and fined simply for writing in Kurdish. Further considering the Iranian justice system, Kurdish people are disproportionately sentenced to death in unfair trials as well. According to Hengaw, a Kurdish human rights organization, Kurds were the most likely to be executed in the first half of 2024, with 72 executions taking place in total. To this day, the Iranian state is also known to brutally torture Kurdish prisoners inside of its prisons due to their ethnic identity. One torture victim recounted to Amnesty International, "While they were writing down my details, they asked me of my origins as soon as I said, 'Kurd' they flogged me all over my body with a hose-looking whip" (Amnesty International, 52). The Iranian state also frequently abuses Kolbars, typically young Kurds who are forced to smuggle across Iran's borders to make ends meet. Some estimates stipulate that Iranian persecution causes 90% of Kolbar deaths. Seeing many continuities between the Kurdophobia present in the region today and that present historically, it is clear that although there is some change in Kurdophobic language, the methods still remain the same.

Analysis

In order to be able to realize the extent of the overwhelming continuities when it comes to kurdophobia, this research paper discusses social media posts previously mentioned. In the English-language thread on r/Turkey, 78% of the posts echoed kurdophobic language present in the 20th century as opposed to more contemporary language present in Turkey surrounding the Kurdish issue which became more popular after Turkey aspired to join the European Union. As Reddit most accurately represents the views of the citizenry of a given community rather than those of governmental officials or politicians, the fact that 40.2% of the comments in this thread are composed of stereotypes or blame Kurds for sociological issues is to be expected. This is because stereotypes and scapegoating, mainly emerge from perceptions that groups have

regarding each other within a society. However, it is quite surprising that comments expounding historical denialism, composed 23.2% of the thread, while justifying discrimination against Kurds using Turkey's conflict with the PKK only made up 22%. These statistics show a significant continuum in kurdophobia within Turkish society in the methods of kurdophobia before the peace process becauseKurds were widely viewed as officially non existent within Turkey, especially in the 1990s. Showing how despite the rhetoric of the Turkish government having changed, the modus-operandi of Kurdoophobia on the ground remains largely a continuum as far back as the Kemalist period can be seen in the fact that 14.6% of respondents promoted genocide or removal, as was common during the Kemalist period. Said continuum can be seen in how regular netizens discuss the resettlement of entire ethnic groups as a viable government policy. One Reddit user writes, "Can you guys take [the Kurds] and give us the azeris? This way, both pan-Turkists and pan-Iranists can be satisfied." The fact that a similar population transfer, as previously explained, was also promoted by the Turkish government during the 1920s. The only difference is that said policy called for a transfer of Kurdish and Turkish populations within Turkey rather than one across international borders, which is what the user calls for.

The presence of genocidal sentiment in Turkey as a whole can be further backed up by the footage from the Turkish rally concerning the demographic future in Kirkuk, as well as clear and popular governmental support for policies in Afrin. In the case of the Kirkuk-related rally, the blue flags present in the video indicate that the men are also affiliated with the ultranationalist MHP, which is influential within the Turkish Government. One can therefore infer that the government also subtly supports or at least tolerates the MHP's genocidal desires while also using anti-PKK rhetoric to obfuscate their true desire as the men in the video do. The said id inference further signals a continuity in kurdophobic methods among Turkish society. Coincidentally, the largely insignificant change in rhetoric on the part of the Turkish government is also reflected through its cronies in the video. They only change what they are saying due to visibly literal exterior pressure by the journalists filming the event.

The second piece of analysis taken from the Turkish language is even more telling. From among all of the comments analyzed, not a single one even mentioned the PKK, while 85.4% of the comments partook in racial insults and stereotypes. Although the state cloaks anti-Kurdish attacks under the pretense of combatting the PKK, kurdophobic actors in public places of discussion, such as Twitter, do not hide their intentions. Scholarly research, such as a 2010-study presented by Yarkin shows that generally racist attitudes such as those used in the Reddit posts were also present before the peace process of 2013-2015 between the Turkish government and the PKK. Yarkin writes, "According to the research conducted in different parts of Turkey in 2010 by KONDA, a survey company, 62.2 percent of Turks do not want to have a Kurdish work partner, 47.4 percent of Turks do not want to have a Kurdish neighbor, and 57.6 percent of Turks do not want to have a Kurdish bride/wife" (Yarkin, 8). Such racist attitudes are also reflected in

Kurdish stereotypes. Kurds are often thought of as criminals and terrorists in Turkish society.[11] Many anti-kurdophobic netizens seem to agree. The whole focus of the Twitter thread centers around a notion, included without evidence in the post, that a 'Kurdish mafia' was responsible for restricting access to Turkey's beaches. Another common stereotype is that Kurds 'breed quickly,' referring to the fact that, on average, they have more children than Turks. This stereotype is echoed by a Reddit user on r/Turkey who is sympathetic to the Azerbaijanis of Iran. The user writes, "We have a similar "Kurdish" problem in Iran as well. Western Azerbaijan province used to be 80% Azeri and now it's 40-50% Kurdish. Why? Excessive breeding! A typical Kurdish household in that province produces no less than 3 kids per family. Azeri population growth is the same as Persians. 2 kids per family." The fact that stereotypes such as the one documented by Yarkin are still present in forums of discourse on social media, further shows a strong continuity between old and recent kurdophobia.

More specifically, despite the superficial change in the language applied in Turkey and Turkish society as a whole, not much has changed in terms of kurdophobia's everyday application. When considering the Iranian Reddit post analyzed, strong consistencies between former and present discrimination are also present. The Iranian constitution allows for so-called 'tribal and regional languages in schools,' as well as their limited societal use such as in media. The use of such nomenclature with regard to languages such as Kurdish in Iran's constitution shows what the Iranian State considers Kurdish to be not only in the modern day but since its founding in 1979, namely, a 'tribal or regional' language subordinate to that of a greater Iranian nation whose singular official language is Farsi. The view that the Kurds are a tribal group within Iran manifests itself in a discriminatory fashion present within Iran by means of institutions such as Iranian schools. Gordyaen Jermayi, a Kurdish language activist who spoke to the Respond Crisis translation, describes the violence currently taking place against the Kurdish language in Iranian schools:

> The ongoing violence extends beyond suppressing the Kurdish language to portraying it and other non-Persian languages as 'uncivilized.' Authorities push for perfect Persian in schools, equating proficiency with education.[...]I encountered Persian language oppression in first grade when the teacher punished us for not speaking it fluently. Non-Persian-speaking children face linguistic barriers imposed by teachers, hindering their academic performance. This challenge often leads to high dropout rates. The exclusion of these languages in education jeopardizes their survival.[12]

[11] Yarkin, Gullistan. "Fighting Racism in Turkey: Kurdish Homeownership as an Anti-racist Practice." *Ethnic and Racial Studies*, vol. 43, no. 15, 5 Nov. 2019, pp. 2705-23, https://doi.org/10.1080/01419870.2019.1685116. Accessed 11 Aug. 2024.

[12] Respond Crisis Translation. "Ant-Kurdish Language Violence in Schools." *Respondcrisistranslation.org*, Respond Crisis Translation, 6 Feb. 2024, respondcrisistranslation.org/en/newsb/ks-anti-kurdish-language-violence-in-schools. Accessed 8 Aug. 2024.

Unfortunately, the notion that Kurds are part of a greater Iranian entity rather than their own group is reflected in 46.8% of posts examined, the most common categorization. In addition, historical denialism, another form of kurdophobia also along the lines of trivializing Kurdish identity, is also noticeably present. Said manifestation of kurdophobic sentiment was observed in 31.3% of all comments analyzed. Furthermore, the founder of the Islamic Republic himself, Ayatollah Khomeini considered the separate existence of ethnic minorities in violation of so-called 'Islamic beliefs'. Further signaling continuity with the Khomeini era, threats of violence are also seen in this post. After Khomeini ordered Kurdish opposition to be eliminated following the Iranian Revolution, approximately 10,000 Kurds were killed and many Kurdish settlements were destroyed by Iranian security forces. This history of state violence helps explain why 15.6% of the comments contain threats of violence or genocide, followed by stereotyping Kurds, which made up 6.3% percent of them. These results further signal towards greater amounts of continuity among everyday Iranian society, despite slight regime reform.

Regarding linguistic and cultural oppression, what is being seen now in Afrin is quite similar to Mustafa Kemal Ataturk's policies at the beginning of the Turkish Republic, starting with the renaming of Kurdish villages to Turkish ones. Ugur Ümit Üngör, a historian and professor of Holocaust Genocide Studies at the University of Amsterdam, recalls, "Even the name of the Tigris ('Dicle') was Turkified: according to official texts, the name emanated from the 'Akkadian Turks' who had given the river this name. Those who did not believe this were urged to look it up 'in the first volume of the Great History Book that the Turkish Historical Association had published'". Geography was thus stripped of its Ottoman, Armenian, and Kurdish connotations." Like in Eastern Anatolia in the 1920s and 1930s, Turkey and its Syrian proxies are currently changing Kurdish place names, and generally attempting to erase Kurdish culture from Afrin. Hence another continuity has been established between older and modern Turkish discriminations. In further detail, despite the Turkish government somewhat withdrawing from all out kurdophobic rhetoric, its policies and methods regarding Kurdish culture and language show strong continuities to the starkly anti-Kurdish Kemalist era. In the past, Turkish military officials have even publicly posted maps of a greater Turkey, stretching beyond its current borders and into waste swathes of Syria, Iraq, and other nations. The ultimate goal of the nationalists in Turkey's governmental and military institutions is clear, namely, to form a Turkic state spanning what they see as Turkish land, without any rights for Kurdish populations, which may obstruct their plan. In other words, their ultimate goal has remained the same, but its rhetoric due to a need to conform to a new era, one where they achieve already established supposed goodwill with the Kurds, blaming the need to expand on the PKK, rather than an aim motivated by Turkey's own ambitions.

Conclusion

Although the Turkish and Iranian government have made superficial strides regarding their rhetoric concerning the Kurdish people, this is far from being reflected in their actual

policy. In addition, the very same kurdophobic behaviors formerly found in these societies and indisputably confirmed to be practiced by these governments have been found to be acting within these societies. After having examined sources regarding current affairs, first hand reports of kurdophobia, and extensive social media study, it is clear that although kurdophobic rhetoric has minimally transformed, kurdophobic methods, attitudes, and the general nature of anti-Kurdish sentiment has remained the same throughout the 20th and 21st centuries at least in intensity. The results of this research should not be taken lightly. This research study proves to Western actors that negative attitudes towards Kurds in the region have effectively remained unchanged. And, hence, firm pressure must be exerted on host states of Kurds in order to preserve their millenia old culture and tradition.

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Determining Affected Genetic Biomarkers within Hyperglycemic C. elegans As a Model Organism for Type II Diabetes Through qPCR Methods By

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ABSTRACT

Type II Diabetes (T2D) is a complex metabolic disorder characterized by hyperglycemia and is associated with increases in insulin resistance and oxidative stress. The nematode Caenorhabditis elegans has emerged as a valuable model organism for studying T2D, due to its genetic similarity to humans. This study aimed to investigate the effects of hyperglycemia on the genes superoxide dismutase 1 (SOD-1) and dauer formation protein 2 (DAF-2) as potential biomarkers for T2D. The SOD-1 gene is used to measure oxidative stress while the DAF-2 gene is used to measure insulin resistance. Wild-type C. elegans were cultured on plates containing three levels of glucose concentrations modeled after prediabetic (125 mg/dl) and diabetic blood sugar levels (500 mg/dl) blood sugar levels. Gene expression levels of SOD-1 and DAF-2 were measured after a 4-day incubation period. Our findings revealed that DAF-2 expression was most upregulated in C. elegans exposed to "normal" glucose levels and less so among the "high" glucose levels. Similarly, C. elegans samples exposed to normal-level glucose conditions exhibited the largest SOD-1 gene upregulation, yet there was less variability across glucose concentrations. These results indicate an increase in insulin resistance among lower glucose levels in C. elegans and less variation in the C. elegans response to oxidative stress among differing glucose levels. The outcomes of this experiment highlight the need for further investigation and independent confirmation of SOD-1 and DAF-2 as biomarkers for T2D in both C. elegans and humans.

INTRODUCTION

In the field of genomics, much research has been done on the various genetic biomarkers for Type I Diabetes, as it is a genetic condition and therefore easier to identify genetic mutations in genes of affected organisms. However, fewer studies investigated Type II Diabetes, as it is not a genetic condition, and instead requires researchers to focus on the metabolism and oxidative stress of affected organisms. Hence, much less research concerning the genetic biomarkers of Type II Diabetes has been carried out, although it impacts 6.28% of the global population (Khan et al., 2020), making the illness an increasingly apparent health issue, especially in populations with sedentary lifestyles and unhealthy diets. Research on more extensive diagnostic methods of Type II, such as identifying genetic biomarkers, could aid with the diagnostic process, and potentially help millions of cases be caught in earlier stages of the disease and thus provide more effective treatment and reduce the health care cost.

A study done by Alcántar-Fernández et al. found that glucose-fed wildtype C. elegans have shorter lifespans and more oxidative stress. Wild-type C. elegans were cultured on Nematode Growth Agar with Escherichia coli and kept at room temperature. The researchers mixed 20, 40, 80, and 100 mM glucose into the NGM agar. The C. elegans grown with glucose

at the levels of 80 and 100 mM were larger and thicker compared to the control group, but all of the glucose-fed worms had shorter lifespans and a decreased reproduction rate.

Similarly, a study done by Hashmi et al. found glucose-fed C. elegans to have a decreased life span through increased reactive oxygen species (ROS) formation. The researchers included a control group, a "normal" glucose level group, and a "high" glucose level group (14 mmol glucose/l). The study found that high glucose reduces the activity of glyoxalase-1, an enzyme that detoxifies methylglyoxal, a harmful byproduct of glucose metabolism. Increased methylglyoxal led to more advanced glycation end products (AGEs) accumulating in mitochondria, which increased the formation of ROS. Another experiment by Zhu et al. found hyperglycemia to shorten lifespan and increase oxidative stress and fat storage by using a microfluidic device to expose C. elegans to controlled glucose concentrations. The glucose-fed worms were found to have elevated GST-4 expression, indicating increased oxidative stress, and an upregulation of fat metabolism genes SBP-1, NHR-49, and FAT-6.

In the human body, loss of insulin signaling is most commonly associated with insulin resistance, and eventually, Type II Diabetes. Under these conditions, the DAF-2 gene, which is a homolog of the human insulin/IGF-1 receptor, becomes upregulated. Typically, the upregulation of the IGF-1 receptor gene is caused by insulin resistance (Boucher et al., 2010) in which the human body is exposed to an excessive amount of blood sugar, prompting an increase in insulin generation. This leads to cells developing a resistance and becoming less responsive to insulin. In an attempt to override this insulin resistance, the body produces large quantities of insulin, which leads to increased signaling to the insulin receptors and subsequently upregulates the IGF-1 receptor and other genes related to insulin signaling.

Our work aimed to determine affected genes and changes in population rates within C. elegans when administered with hyperglycemic diets, simulating Type II Diabetes. C. elegans has proved as an extremely efficient model organism for studying human growth and development (Roussos et al., 2023). According to a study by Zhang et al. (2014), over 70% of C. elegans genes involved in glucose or lipid metabolism have human orthologs, and of these, 94 genes have human orthologs associated with metabolic disease. This makes C. elegans a good model organism to study human metabolic disease due to its similarities with the human genome. Additionally, we chose to work with C. elegans due to their relatively short lifespan. C. elegans completes its life cycle within 3-4 days, which is an ideal population doubling rate to produce sufficient worms during the time span of our experiment.

SOD-1 is the gene that codes for the enzyme superoxide dismutase, which is responsible for converting superoxide into hydrogen peroxide and oxygen (Horspool & Chang et al., 2018). SOD-1 is implicated in glucose metabolism disease and has been used to measure oxidative stress, which is why we tested the gene in our experiment. Cells convert glucose into energy using oxygen. During aerobic respiration, cells naturally produce reactive oxygen species (ROS) as a byproduct. Excess ROS leads to oxidative stress that damages cells. Hyperglycemic conditions promote ROS production, thereby increasing oxidative stress (González, Patricia et

al). By inducing hyperglycemic conditions in C. elegans, we expected to observe an upregulation of the SOD-1 gene, indicating an increase in oxidative stress.

In addition to these two genes, we utilized the Ribosomal Protein S23 (RPS-23) coding gene for normalization. RPS-23 is a part of the 40S subunit found in ribosomes. It is often expressed in abundant, and most importantly, consistent quantities, making it a suitable housekeeping "baseline" gene in qPCR experiments.

In this experiment, we used slightly different glucose concentrations from the studies described in the introduction in order to effectively model C. elegans after prediabetic and diabetic conditions in humans. We hypothesized that we would observe a drastic upregulation of the abnormal dauer formation protein 2 (DAF-2) and the superoxide dismutase 1 (SOD-1) gene in the C. elegans group that was administered the highest level of glucose. DAF-2 and SOD-1 genes have associated human homologs, potentially allowing us to extrapolate our results to humans.

METHODS

This experiment was conducted over 4 days, in accordance with the average life cycle of C. elegans (Ridder et al., 1997). Glucose concentrations were modeled after Type II diabetic conditions in humans. A blood sugar value of 200 mg/dL following a random blood sugar test indicates diabetes. After a fasting blood sugar test, a blood sugar value of 100 to 125 mg/dL indicates prediabetes, while a value of over 125 mg/dL suggests diabetes ("Type 2 Diabetes"). 0.056 g glucose ("normal") and 0.225 g glucose ("high") per 45 ml Nematode Growth Agar respectively mimicked the 125 mg/dL prediabetic and 500 mg/dL diabetic blood sugar levels.

One plate of Caenorhabditis elegans, living, culture sample from the Carolina Biological Supply was stored at room temperature (20-25°C). We created one control condition and two hyperglycemic conditions. We mixed, under sterile conditions, 0.0 g, 0.056 g, and 0.225 g of ALDON Innovating Science Laboratory-Grade Anhydrous glucose, respectively, with 45 ml freshly autoclaved Nematode Growth Agar. Half of the content from each tube was added to a sterile 9 cm diameter United Scientific Petri dish, resulting in two plates per growth condition. Plates solidified within 15 minutes at room temperature and were stored at 4℃ until use.

We inoculated approximately 20 ml LB broth in a 50 ml tube with Escherichia coli OP50 from a living culture plate, obtained from Carolina Biological Supply. The liquid culture was grown on a bacterial shaker at 37 C for approximately 7 hours, at which point significant growth was observed. 250 µl of the E. coli culture were spread on the nematode growth agar plates with a sterilized glass rod and incubated at 37°C overnight. The next morning we observed an even bacterial lawn of E. coli on the surface of the agar plates.

We then transferred the C. elegans from the original plate to the new plate by cutting out six 2cm x 3cm agar pieces from the original C. elegans plate and used these to inoculate our experimental plates by placing these sections in the center of the six experimental petri dishes. We left these plates at room temperature overnight to allow for the migration of the C. elegans

into the experimental plates. The next day, we removed the original agar pieces from each of the experimental plates.

After allowing the C. elegans to incubate at room temperature for four days, we extracted the worms from the plate by adding 1.5 mL of DEPC-treated water to each of the six agar plates. We left the plates with water for approximately one hour to allow the C. elegans to migrate out of the agar into the water. The supernatant from each plate containing C. elegans was transferred to separate tubes. We repeated this process 2-3 times to maximize the yield of C. elegans.

We set an Eppendorf Centrifuge 5427R to 650 rpm to pellet the worms at the bottom of the tubes and excess water was carefully removed with a pipet tip. We immediately froze the worms at -80°C.

We followed the protocol in the Bio-Rad Aurum™ Total RNA Mini Kit (Cat #1701598) with modifications outlined below to extract the RNA from the C. elegans. C. elegans has a tough cuticle (Ly et al., 2015) which needs to be broken up before RNA can be efficiently extracted. We implemented several freeze-thaw cycles to assist in breaking up the cuticle. We froze the worms in a -80°C freezer and left them for two hours, then thawed them for fifteen minutes and repeated this three times. We homogenized the worms in the tube using a pestle working over liquid nitrogen to ensure that the tissue stayed frozen. After adding 350 µl of lysis buffer to the tube, we continued to crush the worms with the pestle for two minutes, then used a 15-gauge syringe to shear the worms by sucking the solution up and down for another two minutes. After extraction, the purity and yield of the samples were determined using a Thermo Scientific™ Invitrogen™ Nanodrop™ One Spectrophotometer.

We generated cDNA using the reverse transcriptase instructions SuperScript™ III First-Strand Synthesis SuperMix kit (Cat #18080400) from Invitrogen™ to convert total RNA into stable cDNA, which was stored in a -80°C freezer.

Using Primer Express Software version 3.0 (Thermo Scientific), and mRNA sequences derived from NCBI, we designed forward and reverse primers for SOD-1, DAF-2, and RPS-23. Primers were designed to have a melting temp of 60℃ and the resulting amplicon had a length of approximately 120 base pairs. At least one primer was designed to stretch across exon-exon junctions to increase specificity.

SOD-1 Gene
Forward Primer: 5'-ATTTCTGCCGGTCCACACTT-3'
Reverse Primer: 5'-ACTCCATCGGCTCAGCTT-3'

DAF-2 Gene
Forward primer: 5'-TCAGCTCTGGCATTGGATAATAGTTA-3'
Reverse primer: 5'-GATGGGATATTGAGCAAGATGCT-3'

RPS-23 Gene
Forward primer: 5'-CCGCCTTCGTCCCAAAT-3'
Reverse primer: 5'-AGCACTCGTGGTTTTCTTCAAC-3'

Figure 1: Primer sequences for gene expression analysis

      Before analyzing gene expression, we tested the specificity and efficiency of the primers to ensure that we could perform relative quantification experiments to analyze gene expression in our different experimental conditions. We used a Thermofisher ABI qS6Pro qPCR instrument for our qPCR experiments with the following conditions: 2 min at 50 ℃, 2 min at 95 ℃, 40 cycles of 95 ℃ for 15 sec and 60 ℃ for one min. Additionally, we utilized the SYBR™ Green Universal Master Mix (catalog number 4309155).

Primer Specificity and Efficiency Testing

      Due to the abundant cDNA material available, we used one of our high-glucose cDNA samples to test the primer efficiency of the three primer pairs we used in our study. We used a negative control for each primer pair plus the following dilution (DIL) amounts: 100 ng (DIL 1), 40 ng (DIL 2), 4 ng (DIL 3), 0.4 ng (DIL 4), 0.04 ng (DIL 5), 0.004 ng (DIL 6), and 0.2 ng (DIL 7).
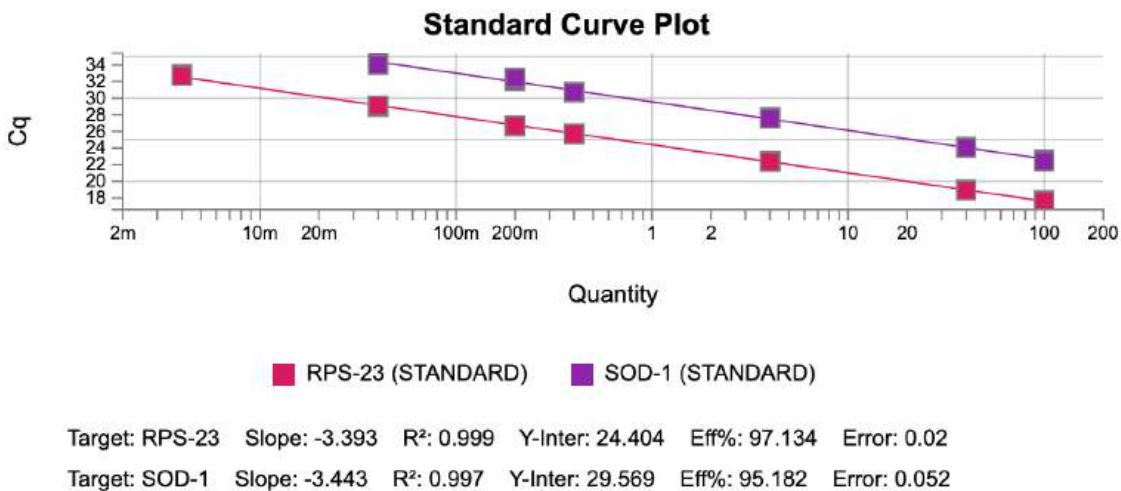

Target: RPS-23   Slope: -3.393   R²: 0.999   Y-Inter: 24.404   Eff%: 97.134   Error: 0.02

Target: SOD-1   Slope: -3.443   R²: 0.997   Y-Inter: 29.569   Eff%: 95.182   Error: 0.052

Figure 3: qPCR primer   testing showing efficiency of RPS-23, and SOD-1 primers

      Our efficiency testing demonstrated that all three primer pairs performed within the expected efficiency range of 90-110 % and therefore were usable in relative quantification experiments. The standard curves for RPS 23 and SOD-1 are shown in figure and for DAF-2 in figure 4. . Melt curve analysis (data not shown) demonstrated specific single amplicon PCR amplification.
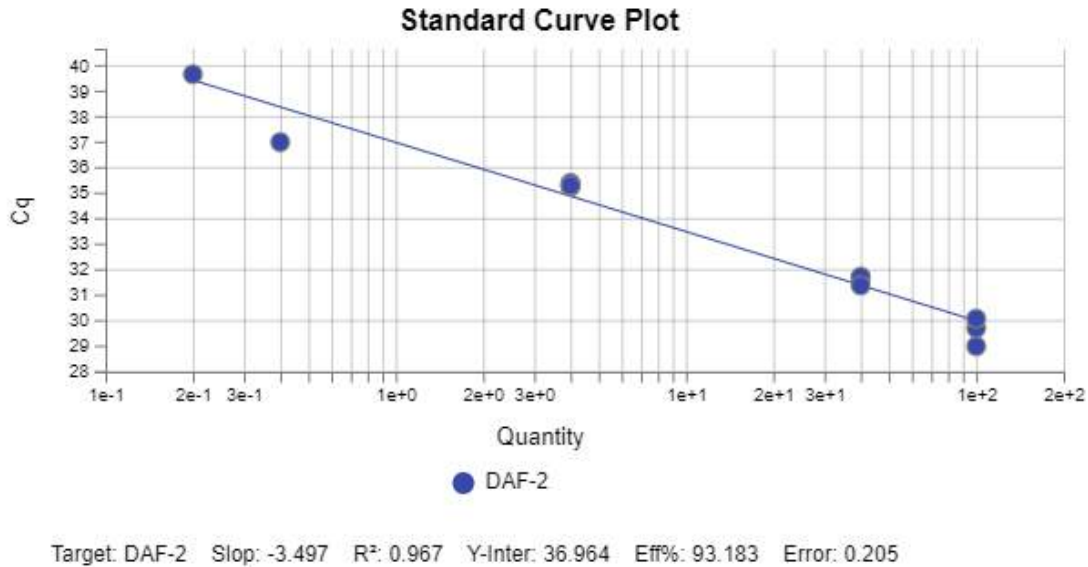
Standard Curve Plot

Target: DAF-2   Slop: -3.497   R²: 0.967   Y-Inter: 36.964   Eff%: 93.183   Error: 0.205

Figure 4: qPCR primer testing showing efficiency of DAF-2 primer of 93.183 %.

      In order to test different C.elegans growth conditions we also used supraphysiological glucose concentrations of 0.562g and 2.25g, respectively, and we incubated the C. elegans at room temperature for three days instead of four. When extracting C. elegans from thist experiment, we observed significantly more C. elegans on the control plate compared to the normal and high-level glucose plates. Interestingly, the normal-level glucose plates produced the least amount of worms, followed by the high-glucose plate.
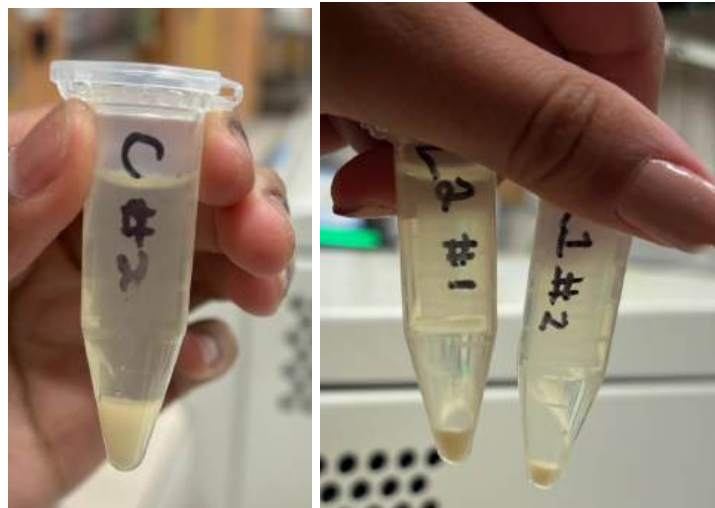
RESULTS

Figure 5: C. elegans yield extracted from plates, 7/19/24. From left to right: control, high glucose, normal glucose plates.

      When we first extracted RNA from C. elegans, we found low purity 260/230 ratios and low RNA yields. The inadequate amount of RNA was likely a result of the C. elegans cuticle not

being broken up completely. Subsequently, we implemented several freeze-thaw cycles as well as the use of liquid nitrogen to crush the worms more efficiently. In addition, we used a smaller amount of animal tissue (40-50 mg per column) to prevent clogging of the spin columns used in the RNA extraction process. This led to adequate 260/230 ratios and higher RNA yields.

After four days of incubation, the C. elegans on one of the normal glucose plates were observed to be slow-moving. This plate was also the most crowded out of the six plates. The slow movement of the worms was likely a result of overcrowding, and the worms may not have had enough food. Interestingly, this was only the case for one of the normal glucose plates, Additionally, there were more clumps of breeding C. elegans on the high glucose plates compared to both the normal and control plates.

After confirming that our primers worked as expected with regard to efficiency and specificity, we then performed qPCR experiments using the C. elegans RNA samples we collected.

We used one of the control sample (C#1, no glucose) as the baseline sample to which we compared all other samples. The fold change of the regulation of genes DAF-2 and SOD-1 are calculated relative to C#1 and are normalized to the housekeeping gene, RPS-23. We used the Delta-Delta Ct method to calculate fold changes. "H#1" was obtained from the "high glucose" plate 1, "H#2" was obtained from the "high glucose" plate 2, "N#1" was obtained from the "normal glucose" plate 1, and both $N\#2_1$ and $N\#2_2$ samples were both obtained from the "normal glucose" plate 2. We obtained two samples from plate N2 in case of inconsistencies with the slow-moving worms extracted from this plate. Observed variation between the Trials of qPCR testing is likely due to pipetting and or quantification inaccuracies

Fold change DAF-2 Expression

Sample	Trial 1: Fold change (relative to C#1 and normalized to RPS-23)	Trial 2: Fold change (relative to C#1 and normalized to RPS-23)
C#1	1.0	1.0
H#1	2.7	1.0
H#2	1.7	2.1
$N\#2_1$	70.1	54.8
$N\#2_2$	53.4	53.4
N#1	44.6	37.8

Table 1 DAF-2 expression changes samples and fold changes relative to C#1 and normalized to RPS-23.

In the table above, "Trial 1" and "Trial 2" refer to two different qPCR tests on the same samples.

In trial 1, sample "N#2$_1$" had the most upregulation of DAF-2 with a fold change of 70.1, followed by sample "N#2$_2$" with a fold change of 53.4. However, in the second trial, the fold change of N#2$_2$ was much closer to N#2$_1$, suggesting that the value of 70.1 could be an outlier. Confoundingly, H#2 had the least upregulation with a fold change of 1.7.

In trial 2, sample "N#2$_1$" again had the most upregulation of DAF-2 with a fold change of 54.8, followed by sample "N#2$_2$" with a fold change of 53.4. Surprisingly, H#1 had no upregulation of SOD-1 when compared to the control and normalized to RPS-23.
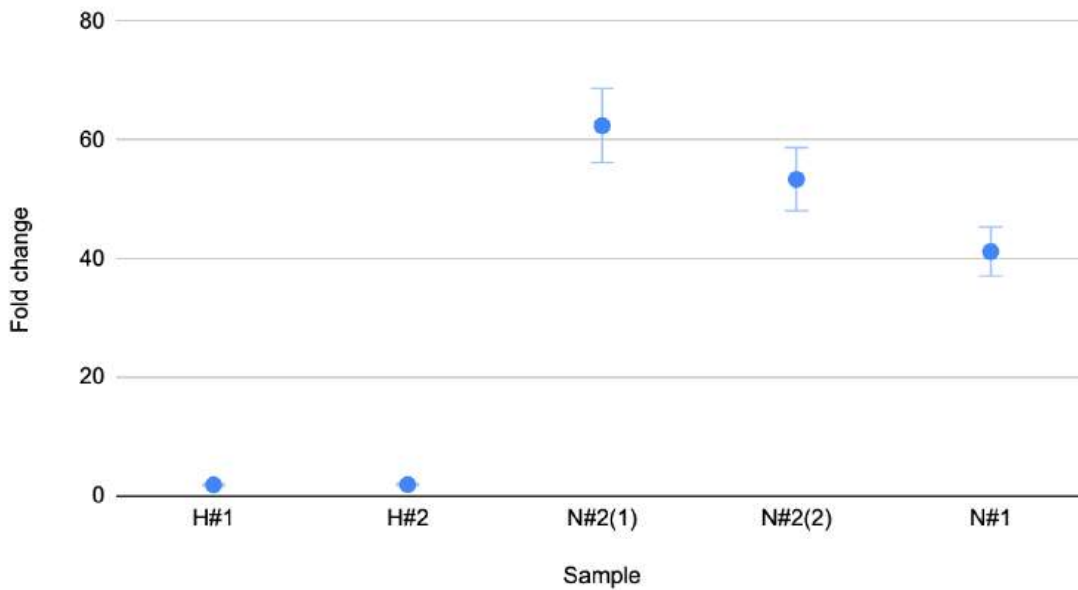

Figure 8: Scatterplot, fold-change of DAF-2 gene in C. elegans grown in different glucose concentrations, averaged across both trials.

Fold change SOD-1 Expression

Sample	Trial 1: Fold change (relative to C#1 and normalized to RPS-23)	Trial 2: Fold change (relative to C#1 and normalized to RPS-23)
C#1	1.0	1.0
H#1	5.3	5.1
H#2	5.7	6.1
N#2$_1$	10.2	10.1
N#2$_2$	10.0	9.3
N#1	6.5	8.1

Figure 8: Table from SOD-1 qPCR experiment; samples and fold-changes relative to C1E4 and normalized to RPS-23

There was much less variation in the fold change of SOD-1 than in the fold change of DAF-2. In trial 1, overall fold-change values ranged between 5.3 (H#1) and 10.2 (N#2$_1$). Similar to the DAF-2 results, sample "N#2$_1$" had the most upregulation of SOD-1 with a fold change of 10.2. H#1 had the least upregulation with a fold change of 5.3. Again, sample "N#2$_1$" had the most upregulation of SOD-1 with a fold change of 10.2, followed by sample "N#2$_2$" with a fold change of 9.2. H#1 again had the least upregulation with a fold change of 5.1.
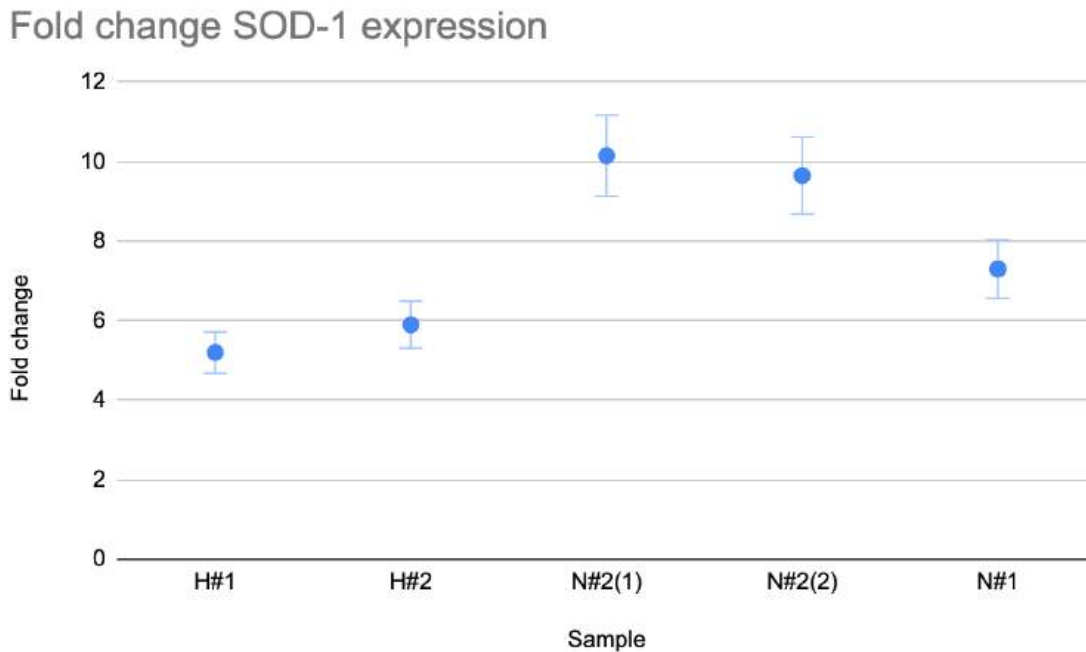

Figure 10: Scatterplot, fold-change of SOD-1 gene in C. elegans grown in different glucose concentrations, averaged across both trials.

There are slight variabilities between the fold changes in each trial, which may be due to uneven pipetting. Yet, trends still emerge. There is more variability in the fold changes of the DAF-2 gene, with the "normal glucose" C. elegans showing the most upregulation of the gene. The fold changes for the SOD-1 gene are closer in value across both the normal and high glucose plates (ranging between fold changes of 1.0 and 10.2), yet the "normal glucose" samples still had the greatest fold change values. In the second qPCR experiment, there was no upregulation of SOD-1 in sample H#1.

STATISTICAL ANALYSIS

For our statistical analyses, we compared the two genes, SOD-1 and DAF-2, across two different experimental groups through a 2-sample t-test. Here, we calculated both p-values and t-values to evaluate statistical significance, specifically whether or not the fold-changes observed are truly due to the changes in glucose level, or if they are attributed to random change. The two

groups were "Control vs. Normal" and "Control vs. High.", using the control as a baseline to compare the gene expression through the two experimental glucose levels. We generated corresponding p-values and t-values to evaluate statistical significance.

For the SOD-1 fold-change data, the Control vs. Normal group showed a high significance, with a p-value of <0.00001, which is well below the 0.05 significance level, and the corresponding t-value was 13.86574. The comparison between the SOD-1 Control vs. High group, however, was not statistically significant, with a p-value of 0.96656, much higher than the significance level of 0.05. Additionally, the t-value was relatively low, with a value of 1.56203. This indicates that the control and high groups are not significantly different for the SOD-1 gene, and gene expression did not vary with or without the glucose treatment.

For the DAF-2 fold-change data, the Control vs. Normal group also showed high significance, similar to the SOD-1 data. The p-value was <0.00001, and the t-value was even larger than the SOD-1 Control vs. Normal group, with a value of 19.95704. However, there was once again no significant difference between the Control and High experimental group, with a p-value of 0.448457. Additionally, the t-value is -0.13799, signifying that the control and high glucose groups are not significantly different for the DAF-2 gene either, and can be considered statistically indistinguishable.

DISCUSSION

DAF-2 is the C. elegans homolog of the human insulin/IGF-1 receptor. When the human body is exposed to an excess amount of sugar, even in healthy individuals, it increases its generation of insulin, as the sugar is sensed by pancreatic beta cells. In the case that insulin is overproduced, molecular insulin resistance occurs, in which cells have a reduced ability to respond to insulin regulation, disrupting metabolism and glucose intake. As cells develop insulin resistance, the body produces more insulin to override this effect, leading to more insulin signaling and an upregulation of the IFG-R gene. Both humans and C. elegans share this gene. The qPCR results indicate the most upregulation of the DAF-2 gene for the C. elegans in the normal glucose plates, but smaller to insignificant upregulation of DAF-2 in the C. elegans in the high-level glucose plates. We observed modest upregulation of DAF-2 in one of our experiments and no upregulation when we run a technical replciate experiment. This could be due to technical problems and repeat the experiment with RNA obtained from an independent biological experiment would be required to clearly distinguish between biological effects and possible technical issues. . Nevertheless, our results differ from our hypothesis. We hypothesized that the upregulation of DAF-2 would be the greatest in the C. elegans exposed to the highest amounts of glucose, followed by the C. elegans exposed to the normal glucose level. However, our results indicate that the C. elegans exposed to normal-level glucose conditions experienced the most upregulation of the DAF-2 gene. The expression of this gene varied greatly between the samples of C. elegans exposed to different levels of glucose (on average x-fold for normal and y-fold for high glucose) . This could indicate that the C. elegans exposure to the normal level of glucose activated DAF-2 expression - (do these worms have blood??) - which would lead to a greater

increase in insulin generation. The normal glucose level in this experiment was designed to replicate the glucose levels in prediabetic humans. Since the DAF-2 gene in C. elegans is a homolog to the human IGF-R gene, our results suggest that upregulation of the IGF-R gene in prediabetic humans could also occur.

On the other hand, the SOD-1 gene had less variation between the normal and high glucose exposed C. elegans. Again, both of the normal samples had the most upregulation of the gene. While the upregulation of DAF-2 was much higher among the C. elegans samples with normal glucose, this was not the case for the SOD-1 gene. The normal-level glucose samples had the greatest fold-change values (ranging from 6.5 to 10.2), but they were not as varied when compared to the high-glucose samples (where fold-change values ranged from 5.1 to 6.1). This was not in line with our hypothesis that the upregulation of SOD-1 would increase based on the amount of glucose added to the C. elegans diet. This could indicate that a smaller amount of glucose in the normal-level plates can still lead to excess ROS production, which damages cells and increases oxidative stress. The SOD-1 gene in C. elegans is a homolog to the human SOD-1 gene, and these results may be translated to oxidative stress in prediabetic and diabetic humans.

SOD-1 and DAF-2 have different functions with varying regulatory mechanisms and behaviors in response to glucose level changes. Since DAF-2 corresponds to insulin signaling, it will have a more apparent 'spike' in upregulation levels. Therefore, higher glucose concentrations should cause more apparent increases in DAF-2 upregulation, causing many varying data points. Interestingly, our data contrasts this theory. The C. elegans exposed to the normal-level glucose conditions had the greatest fold change in the upregulation of the DAF-2 gene.

SOD-1 corresponds to oxidative stress, which has a more indirect relationship to changes in glucose levels than DAF-2 does. This means that SOD-1 gene expression would not show as much variation, since oxidative stress is associated with many other underlying variables, and could be impacted by even the smallest increase in glucose levels. Additionally, recent research has concluded that C. elegans may be more sensitive to oxidative stress. This would mean that SOD-1 expression could be upregulated regardless of what the glucose concentration may be. As a result, less variation in the SOD-1 results in comparison to the DAF-2 results is because the C. elegans oxidative stress pathways are always being 'triggered,' even at very low glucose levels.

To get a clearer idea as to why there was more variability in the upregulation of DAF-2 versus SOD-1 at different levels of glucose in C. elegans, we would repeat this experiment, changing a few variables. To prevent overcrowding on the plates, we would use a significantly smaller piece of agar from the original plate to seed the experimental plates. Increasing the incubation time (2 weeks) would allow the worms to better adapt to the experimental conditions (this may also require transferring the worms onto new experimental plates to prevent overcrowding and lack of nutrients). Additionally, we would create more variability in the levels of glucose in the agar by including experimental plates with higher and lower concentrations of glucose to see if a trend emerges with the upregulation of SOD-1 versus the level of blood sugar in C. elegans. Due to time restrictions, we are unable to implement these variations in this

experiment, but the experiment could be replicated to gain more insight into the affected biomarkers of hyperglycemic C. elegans. In short, our experiment suggests trends to be explored through repeated trials and further experimentation.

CONCLUSION

This study on hyperglycemic C. elegans aimed to investigate the different genetic biomarkers that are linked to Type II Diabetes, specifically, SOD-1 (superoxide dismutase 1) and DAF-2 (abnormal dauer formation protein 2). As shown in our findings, we observed that the DAF-2 gene displayed the most upregulation in response to the normal-level glucose concentration. This does not correspond to its normal function of insulin signaling pathway regulation, where in human Type II Diabetes symptoms, increased insulin resistance and production should coincide with DAF-2 upregulation. We also observed that the SOD-1 gene had less variability in its upregulation across the two glucose levels. This may be due to the fact that oxidative stress pathways are more sensitive within C. elegans, and may be triggered at low glucose levels as well as high levels. Our study indicates that C. elegans could be used as a model organism for human Type II Diabetes, and could be applied to studying other genetic biomarkers of metabolic conditions. However, we do acknowledge the need for further research for precise results, including adding more glucose concentration levels or extending incubation periods and feeding cycles. Our experiment yielded interesting results which need independent confirmation through repetition. This information could contribute to the current understanding of Type II Diabetes, and could benefit research concerning genetic therapies to target this condition.

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Anti-Heroes of the Cold War: Black Panthers and the Viet Cong By Ava Francis

Introduction

On March 17, 1966, co-founder of the Black Panther Party (BPP),[13] Bobby Seale, then a scrappy Merritt College student obsessed with dreams of a fully realized Black Liberation Movement, stood proudly on a hastily acquired chair, to an audience of two, and performed Ronald Stone's infamous black anti-war poem, "Uncle Sam Call Me Fulla Lucifer",

> *You school my naive heart to sing*
> *Red-white-and-blue-stars-and-stripes songs and at pledge eternal*
> *allegiance to all things blue, true,*
> *blue-eyed-blond, blond-haired,*
> *white chalk white skin with U.S.A.*
> *tattooed all over…*
> *I will not serve.*

While his audience started off small, Seale's emotional recitation quickly drew the attention of other equally-frustrated students, creating an impressively-sized crowd of disillusioned young Americans. Throughout them, an energy grew. The anti-war rhetoric of Stone's poem and Seale's impassioned delivery struck a chord.[14]

At the time, the Vietnam War[15] was escalating, and many were becoming less accepting of the American government's justification for the war. This situation demonstrates the ability of the Black Panthers to garner attention for their cause by capitalizing off of the nation's disapproval of the war in Vietnam. It also highlights a communist aspect of the Panther's ideology. While they were a militant organization themselves and were frequently involved in armed confrontations with the police, they were still against conflict if they felt the justifications for it were weak. Like many other communist organizations, the only army the BPP supported was the "people's army".

These communist roots inspired the BPP to form alliances with similarly-minded groups. One such group that they specifically cultivated a relationship with was the Viet Cong, or as they're also known, the National Liberation Front of South Vietnam (NLF), a communist organization that sought to overthrow the South Vietnamese government and reunite North and

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[13] The Black Panther Party (BPP) is an African American revolutionary party that was founded in 1966 in Oakland, California. Created with the intent of protecting local black neighborhoods from police brutality, the BPP is known for supporting Black nationalism and socialism at a time when both ideologies (and the Panthers themselves) were considered contentious issues.

[14] Bloom, Joshua, and Waldo E. Martin. *Black against Empire: The History and Politics of the Black Panther Party, with a New Preface*. University of California Press, 2016.

[15] The Vietnam War was a brutal and expensive conflict between the communist government of North Vietnam and South Vietnam, who had the aid of its principal ally, the United States.

South Vietnam.[16] A quote from NLF Minister M. Hoang Minh Giam is a superb representation of their relationship,[17]

> *You are Black Panthers.*
> *We are Yellow Panthers!*

Precisely, the Black Panther Party and NLF were similar in many ways. For one, they were both militant organizations driven to oftentimes extreme measures in order to protect their own, both being proponents of armed struggles against oppression. This reliance on militia and violence as a way of advancing their platforms was oftentimes a source of hefty criticism, but nearly everything the BPP and Viet Cong did was scrutinized by the mainstream media. After all, they both held communist ideologies in the midst of the ongoing Cold War,[18] a time when the term "communism" was nearly synonymous with "malignant". In fact, their alliance in general was heavily condemned. When Eldrige Cleaver, the Black Panther Party's Minister of Information, who was extremely vocal about his alignment with communist causes and opposition to U.S foreign policy, met with members of the Viet Cong in Algeria, Cleaver was met with severe criticism from anti-communist and conservative groups in the United States, who viewed his actions as unpatriotic.

Eldrige Cleaver (second to right) meets with representatives of the National Liberation Front for South Vietnam and a translator in the Vietnamese embassy in Algiers.

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[16] Canton, Trevor, et al. "Vietnamese National Liberation Front." *The Black Panther Party History and Theory*, 2021, wp.nyu.edu/gallatin-bpparchive2021/international-branches/vietnamese-national-liberation-front/.

[17] Bloom and Martin, *Black Against Empire*, 310.

[18] The Cold War was a period of tension between the United States and the Soviet Union that started in 1947 and lasted until 1991.

Nonetheless, the pair's alliance remained strong. Like the Black Panther Party, the NLF sought to free their people from the control of colonialist and imperialist forces, specifically the American government. In fact, their connection initially came about because of their shared anti-imperialist identities. While the Viet Cong fought against the cruel hand of the United States alongside the North Vietnamese Army in the Vietnam War, the Black Panther Party also believed they were engaged in a war of sorts against American imperialism. As Seale's co-founder Huey P. Newton describes,[19]

> *In America, black people are treated very much as the Vietnamese people or any other colonized people because we're used, we're brutalized, the police in our community occupy our area, our community, as a foreign troop occupies territory.*

While Newton's assertion may seem markedly justified from the lenses of today's standards, in the late 1960s, the notion that Black Americans were oppressed to the extent that the American government was interfering with their way of life or "colonizing" them, was unpopular to say the least. Coupled with the Party's ties to communism and groups like the NLF, the BPP was constantly the target of criticism and denunciation from the American public. Moreover, while disapproval of a communist organization is usually supported by the traditional American viewpoint, such dissension was certainly heightened by the anti-communist fervor of the Cold War.

Indeed, during the Cold War, the United States' global fight against communist movements greatly impacted the American psyche. Many Americans feared that socialists, radicals, and labor organizers, like the Black Panther Party, were certainly inspired, if not led, by Communists who wanted to subvert American society.[20] This fear greatly influenced the way that the Black Panther's have been immortalized, and the same can surely be said for the Viet Cong. In fact, this fear of communism was, at times, borderline paranoia, with citizens questioning anyone or anything that was "different", assuming that such differences were a sign of communist sympathies.[21] While Americans feared that communism was subverting the authority of "traditional" American life, this apprehension to the thought of anything remotely communist was just as dangerous to the ideals on which this country was founded- with domestic groups like the BPP being targeted as "un-American" and foreign groups like the NLF considered pawns of the Soviet Union.[22] Both instances are a clear infringement on the intellectual freedoms supposedly provided by the idealized United States anti-communists sought to protect.

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[19] Abdelfatah, Rund, and Ramtin Arablouei. The Real Black Panthers. Other. *NPR*, April 23, 2021.

[20] SIRACUSA, JOSEPH M. "REFLECTIONS ON THE COLD WAR." *Australasian Journal of American Studies* 28, no. 2 (2009): 1–16.

[21] BRENNAN, MARY C. "THE COLD WAR WORLD." In *Wives, Mothers, and the Red Menace: Conservative Women and the Crusade against Communism*, 13–30. University Press of Colorado, 2008.

[22] Though many Americans believed that the NLF had ties to the Soviet Union, no such evidence exists that pinpoints any direct relationship between the two.

Considering the substantial impact the Cold War had on the characterization of the Black Panthers and the Viet Cong, it can be argued that both groups would have had completely different trajectories if not for the frenzied anti-communism of the period.

Yet, when setting out to conduct research on the extent to which the Black Panther Party and National Liberation Front were similarly and differently treated for their shared anti-imperialist ideologies- no existing evidence can be found that compares the two in the context of the Cold War. This exclusion of the Cold War in research regarding the BPP and NLF is a considerable gap. While we already know that both the Panthers and the Viet Cong were targeted by the anti-communist mob of the Cold War, we don't know what methodologies this group used to target them or what tactics proved most effective. Without a comprehensive report on how the Black Panthers and NLF were vilified in the context of the Cold War, our understanding of their relationship is extremely lacking in nuance. Which is a shame considering the plethora of information that can be gained from their relationship on how strict definitions of what is and isn't American can be weaponized against groups that are considered "different"- an issue that is undeniably still relevant today.

To address this gap, and add a new perspective to the catalog of existing research on the BPP and Viet Cong, the question that drives the research presented in this paper is *"How were the Black Panther Party and National Liberation Front similarly and differently villainized in the context of the Cold War's anti-communist fervor?"*.

Literature Review

Currently, while a handful of existing research briefly chronicles interactions between the Black Panthers and the Viet Cong, only three major case studies actively analyze their similarities, differences, and the nature of their relationship as the principal purpose of their research.

The first, entitled *"Ho Chi Minh, the Black Panther Party, and the Struggle for Self Determination"*, conducted by University of Kansas alum Sophia Southard in 2020, was part of an exhibit hosted by the university's Kenneth Spencer Research Library. Southard describes her research as a reflection on the links connecting members of the Black Panther Party to Ho Chi Minh[23] and the Democratic Republic of Vietnam, as well as African American anti-war sentiment.[24]

In her research, Southard's foremost conclusion is that the BPP and Viet Cong held each other in high regard and shared a profound mutual respect. Southard maintains that this reverence is attributed to the near-identical cycles of persecution and exploitation the two groups endured from the same oppressor.

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[23] Ho Chi Minh was the President of North Vietnam from 1945-1969 and spearheaded the movement for Vietnamese independence from colonial powers. He was a beloved leader and is responsible for the creation of the National Liberation Front.

[24] Southard, Sophia. Rep. *Ho Chi Minh, the Black Panther Party, and the Struggle for Self-Determination*, January 15, 2020.

To defend this assertion, Southard presents various pieces of evidence spanning the entirety of the pair's relationship and beyond. Of these, two primary references support the bulk of Southard's argument.

The first are two essays penned by Ho Chi Minh in 1924, titled *"Lycnhing"* and *"the Ku Klux Klan"*, which detail the violence and racism African Americans faced in the United States.[25] Ho Chi Minh expresses his disdain for the oppression of African Americans,[26]

> *After sixty-five years of so-called emancipation, American Negroes still endure atrocious moral and material sufferings, of which the most cruel and horrible is the custom of lynching.*

Being that these essays were written in 1924, Southard makes the argument that *"Lynching"* and *"the Ku Klux Klan"* represent the long-standing support that Ho Chi Minh, and subsequently the NLF, offered to Black America's fight against systemic racism. Southard also concludes that the atrocities Ho Chi Minh speaks of in America mirror the equally turbulent period of history in 1920s Vietnam, which saw the cruel colonialist rule of France[27] and the fight for Vietnamese independence.

Here, Southard establishes clear similarities between the struggle for Black liberation and the struggle for Vietnamese liberation. By doing so, she furthers her point that the eventual relationship between the Panthers and Viet Cong stemmed from such similarities.

The second of Southard's key pieces of evidence is *Vietnam: An Anti-War Comic Book* by Julian Bond, a founder of the Atlanta sit-in movement and of the Student Nonviolent Coordinating Committee. The comic book is a piece of anti-war propaganda that highlights the connections between the struggles of African Americans and Vietnamese people during the 1970s.[28]
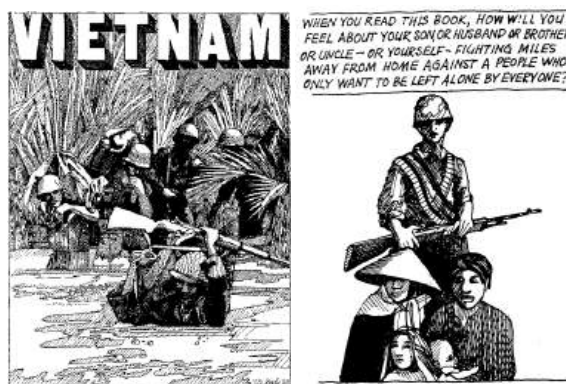
The cover of *Vietnam: An Anti-War Comic Book* by Julian Bond (left). An excerpt from the comic book reads "When you read this book, how will you feel about your son, or

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[25] Southard, *Ho Chi Minh, the Black Panther Party.*
[26] Idib.
[27] The French colonization of Vietnam began in the 1880s and lasted for six decades.
[28] Southard, *Ho Chi Minh, the Black Panther Party.*

husband, or brother, or uncle- or yourself- fighting miles away from home against a people who only want to be left alone by everyone?" (right).

As Southard states, this comic is an example of the ties between the Black Liberation Movement and the opposition to the Vietnam War in America. Because the draft[29] was unpopular in the U.S. (particularly in black communities)[30], the BPP pushed propaganda like Bond's comic to feed the growing anti-war sentiments. The comic's characterization of the Vietnamese as an oppressed people who only wanted to be left alone reaffirms Southard's logic that the BPP felt sympathy for the Viet Cong, especially considering the fact that the Black Panthers viewed themselves in a similar manner.

Jana Cary-Alvarez comes to a similar conclusion in her research paper, *Revolution or Reform: Contradictions Within the Ideology and Actions of the Black Panther Party, 1969-1970,* in which she highlights the unification of the Black Panthers and NLF against a common enemy. Cary-Alvarez claims,[31]

> *Blacks were united with Third World nations, yet it was a unity not primarily by cultural ties but by political repression – that is, by a common enemy.*

This assertion is supported by Cary-Alvarez through the reference of a photo published in the March 16, 1969 issue of the Black Panther's newspaper, *The Black Panther*. The photo depicts a group of soldiers racing forwards while a second group, crouched in the left foreground of the photograph, hold machine guns at the ready.[32] Cary-Alvarez claims the photo's caption, which reads, "South Vietnamese Liberation Fighters Launch An Attack On the Enemy.",[33] is likening the United States to "the Enemy". By referring to America as the antagonist, she argues, the caption and photograph serve to unite the Black Panther Party with international socialists and communists against a common "enemy".[34]

Cary-Alvarez's sentiments here are nearly identical to the conclusions established by Southard. In fact, both are making the same argument.

While Cary-Alvarez believes that the BPP and Viet Cong are united by their common enemy, American imperialist forces, Southard believes that the BPP and the Viet Cong are united by their similar experiences of oppression.

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[29] During the Vietnam War era, between 1964 and 1973, the U.S. military drafted 2.2 million American men out of an eligible pool of 27 million. This was the first time the draft was used since 1942 and it was quite unpopular.
[30] Black Americans were more likely to be drafted in the Vietnam War than White Americans. Though Black Americans comprised 11% of the U.S population in 1967, African Americans were 16.3% of draftees. This continued for nearly a decade and infuriated the black community. The Black Panther Party in particular were vocal on the issue, leveraging the issue to justify their relationship with the Viet Cong.
[31] Cary-Alvarez, Jana. *Revolution or Reform: Contradictions Within the Ideology and Actions of the Black Panther Party, 1969-1970*, April 13, 2014. https://soundideas.pugetsound.edu/cgi/viewcontent.cgi?article=1011&context=honors_program_theses.
[32] Idib.
[33] The term "South Vietnamese Liberation Fighters" is referring to the National Liberation Front.
[34] Cary-Alvarez, *Revolution or Reform*.

When considering the fact that the "similar experiences" Southard touches on were brought about, or at least heightened, by the common enemy Cary-Alvarez refers to, we can see that the pair's research works in conjunction with each other to establish the validity of the claim that BPP and NLF were not only allies for political reasons, but also developed a strong emotional connection as a result of of shared, intense, generational experiences of subjugation.

The third research paper, conducted by Yudi Feng, a member of a group or researchers from NYU, entitled *"The Black Panther Party: History & Theory: Vietnamese National Liberation Front"*, exists as a part of a larger research project on the history of the Panthers. In it, Feng focuses on how the BPP's connections to third-world communist organizations like the NLF affected their long-term development in America. Feng outlines the clear benefits both groups got out of the alliance. As Feng describes, by gaining the support of an American organization, the NLF signaled to the global community the importance of their cause beyond the confines of national identity, further strengthening the bounds for their argument. Her research asserts an additional benefit of the alliance for the NLF: because of the Panthers' extremely vocal support for the Viet Cong in the states, the anti-war movement in the United States was able to grow.

This sentiment is echoed in both Southard's and Carey-Alvarez's research, with Southard referencing Bond's *Vietnam: An Anti-War Comic Book* and Carey-Alvarez referencing editions of the *The Black Panther* that addressed the Vietnam War explicitly as examples of the Black Panther's vocal support of the NLF.

Feng furthers her claim of the mutually-beneficial nature of the pair's alliance by referencing the benefits the Black Panther Party received from the Viet Cong's support. According to Feng, the Black Panthers recognized the advantage of having "strength in numbers", meaning that the BPP pursued an alliance with the Viet Cong in order to expand their influence, promote their cause, and gain supporters from similarly-minded groups that could be swayed by the NLF's endorsement.[35] Feng frames the Panther's intentions in all of this as tactical, suggesting that the BPP stayed in constant communication with the NLF because they recognized the advantage of this union beyond their genuine similarities.[36]

By analyzing Southard's, Cary-Alvarez's, and Feng's existing research, we can establish two distinct truths of the nature of the BPP and NLF's relationship.

For one, the pair shared a deep emotional connection that stemmed from the comparable systems of oppression they encountered due to the torment they faced from their "common enemy" (American imperialist forces).

Still, a second truth simultaneously exists, that the BPP and NLF were aligned for strategic and calculated reasons as well, and both parties were able to benefit their respective causes by wielding the others' endorsement.

By combining these two conjectures, we can establish an overarching theme of all three papers: that the Black Panthers and Viet Cong had a relationship that was mutually-beneficial,

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[35] Feng, Yudi. "Vietnamese National Liberation Front." *The Black Panther Party History and Theory*, 2021, wp.nyu.edu/gallatin-bpparchive2021/international-branches/vietnamese-national-liberation-front/.
[36] Idib.

both on a political and empathetic level, suggesting that the two found solace in their partnership despite the turbulence of the systems of oppression they were fighting.

What is notably missing from the conclusion gained from these existing scholarly works is that Southard, Cary-Alvarez, and Feng all fail to define what this "turbulent system of oppression" looked like- something this research paper and the developed methodology intends to address.

Method

To answer the research question: *"How were the Black Panther Party and National Liberation Front similarly and differently villainized in the context of the Cold War's anti-communist fervor?"*, the following methodology was developed.

The chosen research method was content analysis. Content analysis, a research tool used to determine the presence of certain words or concepts within some given qualitative data,[37] was essential to answering the research question because it helped define the themes of the anti-communist fervor during the Cold War. This examination of the Cold War and the tactics anti-communists used to attack groups like the BPP and Viet Cong was essential to this research paper because the inclusion of this step is what clearly separates this research from the existing scholarly works.

Using content analysis, interviews, speeches, essays, books, newspaper headlines, media, and historical documents, all related to the Cold War and the anti-communist movement during that time period, were examined to determine the characteristics of this chaotic time period. Following the process outlined by content analysis, all of the examined data was then broken down into categories that indicated the definitive concepts of the anti-communist movement. These "definitive concepts" will be referred to as "codes"[38] for the purpose of this research paper. There are seven codes in total.

Each code was established as a result of the thorough research required by content analysis, with each code having several analyzed documents supporting their validity. Furthermore, each code is an interpretation of the tactics used by the anti-communist mob against dissident groups (these tactics are similar to those that can be assumed were used against the BPP and NLF). It is important to recognize the significant assumption made here, that the Panthers and Viet Cong were the victims of the tactics these codes define in the first place, when, in general, it is quite possible that neither the BPP or NLF were affected by these codes at all.

The first code is called, "Anti-American Dream", meaning that anti-communist groups would frame communists as a threat to the American Dream, even when these groups only held communist ideologies and were not overt allies of the Soviet Union (as was the case for both the

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[37] "Content Analysis Method and Examples: Columbia Public Health." Columbia University Mailman School of Public Health, March 30, 2023. https://www.publichealth.columbia.edu/research/population-health-methods/content-analysis#:~:text=Content%20an alysis%20is%20a%20research,words%2C%20themes%2C%20or%20concepts.

[38] The term "codes" is the standard when using content analysis.

BPP and NLF). It is important to note that the concept of the "American Dream" was created in 1931 by James Truslow Adams. He described it as,[39]

>*That dream of a land in which life should be better and richer and fuller for everyone, with opportunity for each according to ability or*
>*achievement*

While Adams' sentiments are certainly admirable, such a reality was not the case for Black Americans, who were the constant victims of America's cruel system of oppression, or the Vietnamese, who were being ruthlessly attacked by these so-called forebears of opportunity in the Vietnam War.

Nonetheless, this code asserts that the anti-communist crowd misconstrued Adams' American Dream to further their cause and presented evidence against communist groups fabricating an attack on American patriotism and freedoms. Using content analysis, this code was determined by collecting research like National Commander of the American Legion James F. O'Neil's 1948 address to Congress in which he foreshadows that communist revolutions in far-off places could occur in the "good old United States" if Americans did not open their eyes to the foreign agents in their midst[40]

Another piece of evidence that led to the "Anti-American Dream" code was a quote from President Herbert Hoover about the potential impacts of communism on American life,[41]

>*Not only would Americans lose their everyday freedoms, but their families would be destroyed as well.*

Both O'Neil's and Hoover's remarks are examples of the kinds of rhetoric this first code represents. They also serve as guidelines for the kind of evidence needed to establish a code as outlined by this study's methodology.

The second code, "Exaggeration of Opponent's Strength", chronicles the over-estimation of communist forces and minimization of America's power. This code was determined by evidence such as another of Hoover's testifications. Given before the House Un-American Activities Committee[42] in 1947, Hoover outlined communism's goal as the ultimate world revolution.[43]

The next code, "Frightening the Public", was a tactic typically used by the American government. This study developed this third code largely because of tactics used by President Harry S. Truman's administration. In order to convince Congress and the public to support the Truman doctrine, an anti-communist take on foreign policy that sought to support other

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[39] Adams, James Truslow. *The Epic of America*. Boston: Little Brown, 1931.
[40] Brennan, *The Red Menace.*
[41] Idib.
[42] The House Un-American Activities Committee was a committee of the U.S House of Representatives that investigated allegations of communist activity in the U.S. during the early years of the Cold War (1945-1991).
[43] Brennan, *The Red Menace.*

democratic nations fighting communism, Truman and his advisors decided to frighten the public into accepting the legislation.

The fourth code, "Omission of Nuance", touches on the fact that the situation of the Cold War was more complex than anti-communists claimed. While the politics of the Cold War and whether communism was *good* or *bad* was an overwhelmingly complicated matter, the average American interpretation of these situations was shallow and close-minded.

The fifth code, "Omission of Facts", details the anti-communist mob's tendency to sector off information from the general public, which led the majority of Americans to be misled on the goals and philosophies of communist groups like the Black Panthers and Viet Cong. Most Americans sensed that communism was bad, but, if prompted, could not have defined the philosophy of communism,

The sixth code, the "Us Against Them" mentality, was enforced to frame anti-communism as a fight the U.S. was engaged in that relied on societal divisions like race, class, and nationality. Americans were encouraged to stay in clearly defined societal groups. Even being friends with someone of a different race was suspicious behavior and raised concerns that one was a potential communist. Wealthy white Americans who came from traditional backgrounds were seen as the "good guys" and anyone who did not fit these descriptions were seen as the "bad guys". One either agreed with the good guys or was one of the bad guys.[44]

The seventh and final code, "Utilizing Partisan Issues", saw influential political figures divide the American public, playing off of the existing divisions created by political parties, in order to further their own anti-communsit political agendas. Increasingly, the seemingly genuine support of anticommunism, took on a partisan flavor.

By utilizing content analysis, a clear definition of what the Cold War's anti-communist fervor looked like has been set, and an analysis of how these themes impacted the NLF and BPP can now begin.

The next step was creating a system in which these codes could be used to compare their impact on the Black Panthers and Viet Cong. The following system was developed: firstly, for both the BPP and NLF, considerable research was done (similar to the initial research that was conducted when creating the codes) going through texts of various natures that documented the characterization of the BPP and NLF during the Cold War; from there, a tally was kept each time a new piece of information was found that aligned with a theme established by one of the codes. This was considered "affirming" a code.

To briefly explain the process of affirming a code, when examining Eric S. McDufffie's essay *"Black and Red: Black Liberation, the Cold War, and the Horne Thesis"* that details the similarities between white supremacist and anti-communsit rhetoric, it was found that during Ronald Reagan's 1966 gubernatorial[45] campaign in California, Reagan oftentimes relied on characterizing the Black Panther Party as a serious threat to California's law and order so that he

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[44] Idib.
[45] relating to a state governor or the office of state governor

could present himself as a patriot ready to destroy the ill intentions of the BPP.[46] This evidence stands as an affirmation of the third code, *Frightening the Public*, because it depicts the tactic of scaring Americans, in this case into voting, so that Reagan, a devout anti-communist, could further his agenda.

This logic was used for the rest of the study and each affirmation of the code needed a substantial occurrence like Reagan's gubernatorial campaign messaging in order to be considered for the purposes of this paper.

Once this had been done for both the BPP and NLF, it was time to analyze the data. To do so, a chi-square test was utilized. A chi-square test is a statistical test used to compare observed results with expected results. This test helps better explain and interpret the relationship between two variables.[47] For the purpose of this study, the chi-square test will help determine whether or not the BPP and NLF have a statistically proven relation based on the way they were misrepresented by anti-communists during the Cold War. In order to complete the chi-square test the following null hypothesis was developed,

There is no significant difference between the frequencies related to the Black Panther Party and the National Liberation Front.

To determine whether the above hypothesis was accepted or rejected, the following data was obtained using the explained methodology.

Findings

This study analyzed over 60 different interviews, speeches, essays, books, newspaper headlines, media, and historical documents, each with varying interpretations of the Black Panther Party and/or National Liberation Front, as influenced by the politics of the Cold War.

Table 1 depicts the results of the section that records the amount of times the seven codes were recorded in regards to the Black Panther Party.

Table 1: Black Panther Party

Codes	Number of occurrences
Anti-American Dream	10
Exaggeration of Opponent's Strength	5
Frightening the Public	25

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[46] Erik S. McDuffie. "BLACK AND RED: BLACK LIBERATION, THE COLD WAR, AND THE HORNE THESIS." *The Journal of African American History* 96, no. 2 (2011): 236–47. https://doi.org/10.5323/jafriamerhist.96.2.0236.

[47] "Chi Square." Chi Square | Practical Applications of Statistics in the Social Sciences | University of Southampton, 2024. https://www.southampton.ac.uk/passs/full_time_education/bivariate_analysis/chi_square.page.

Omission of Nuance	16
Omission of Facts	14
"Us Against Them" Mentality	17
Utilizing Partisan Issues	11

Data Set 1 represents the results of Table 1 as a bar graph.
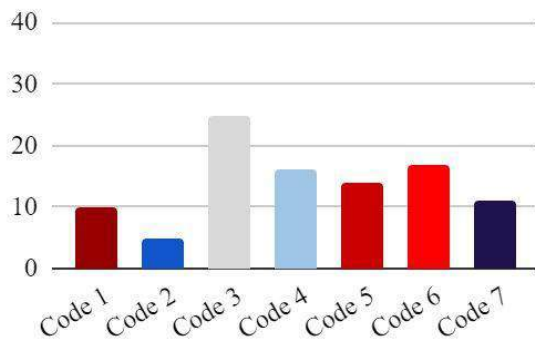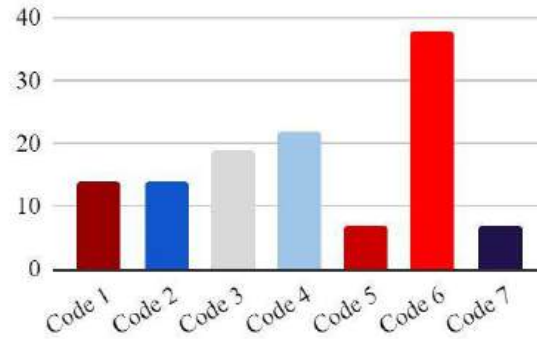
Data Set 1: Black Panther Party

Table 2 depicts the results of the section that records the amount of times the seven codes were recorded in regards to the National Liberation Front.

Table 2: National Liberation Front

Codes	Number of occurrences
Anti-American Dream	14
Exaggeration of Opponent's Strength	14
Frightening the Public	19
Omission of Nuance	22
Omission of Facts	7
"Us Against Them" Mentality	38
Utilizing Partisan Issues	7

Data Set 2 represents the results of Table 2 as a bar graph.

Data Set 2: National Liberation Front

Table 3 is a contingency table that will be used to interpret the results through a chi-square test.

Table 3: Contingency Table

Codes	Black Panther Party	Viet Cong
Anti-American Dream	10	14
Exaggeration of Opponent's Strength	5	14
Frightening the Public	25	19
Omission of Nuance	16	22
Omission of Facts	14	7
"Us Against Them" Mentality	17	38
Utilizing Partisan Issues	11	7

Data Set 3 compares the results of Data Set 1 and Data Set 2.
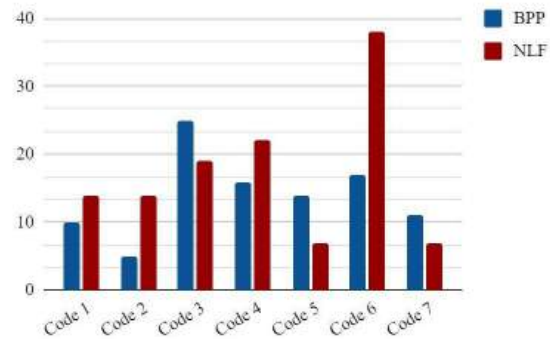
Data Set 3: Black Panther Party vs. National Liberation Front

From the above data, the chi-square test was conducted.

First, a contingency table[48] was created that compared the given data for the Panthers and Viet Cong. In this case, that would be Table 3, replicated below,

Table 3: Contingency Table

Codes	Black Panther Party	Viet Cong
Anti-American Dream	10	14
Exaggeration of Opponent's Strength	5	14
Frightening the Public	25	19
Omission of Nuance	16	22
Omission of Facts	14	7
"Us Against Them" Mentality	17	38
Utilizing Partisan Issues	11	7

From there, the traditional methodology required of a chi-square test was followed, which involved calculating the expected frequencies and then calculating the chi-square statistic using the following formula,

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[48] A contingency table is a table that is used to study the association between the two variables.

$$X^2 = \sum \frac{(Observed - Expected)^2}{Expected} = \sum \frac{(O-E)^2}{E} \cdot df = k - 1$$

The calculated expected frequencies can be best interpreted by looking at the below table,

Table 4: Expected Frequencies

Codes	BPP	NLF	BPP Expected Frequencies	NLF Expected Frequencies
Code 1	10	14	1.905	3.555
Code 2	5	14	2.008	3.752
Code 3	25	19	4.157	7.782
Code 4	16	22	3.537	6.615
Code 5	14	7	2.077	3.882
Code 6	17	38	7.399	18.354
Code 7	11	7	1.818	3.4

Then, using the above formula, the chi-square statistic was found to be approximately 18.726.

After that, the degrees of freedom, the number of independent pieces of information used to calculate a statistic,[49] were determined based on the rows and column of the contingency table using this equation,

$$df = (r - 1) * (c - 1)$$

The degrees of freedom came out to be 6. Once they were found, the critical value from the chi-square statistical table was found based on the chosen significant value, 0.05.[50]

By referencing the below chi-square distribution table, we can see that the critical value when the degrees of freedom is 6 and the significant value is 0.05 is 12.59.

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[49] Turney, Shaun. "How to Find Degrees of Freedom: Definition & Formula." Scribbr, June 22, 2023. https://www.scribbr.com/statistics/degrees-of-freedom/.
[50] 0.05 is the typical significant value chosen when conducting a chi-square test.

Degrees of freedom	Probability (alpha) that the tabulated value is exceeded			
	0.10	0.05	0.01	0.001
1	2.71	3.84	6.63	10.83
2	4.61	5.99	9.21	13.82
3	6.25	7.81	11.34	16.27
4	7.78	9.49	13.28	18.47
5	9.24	11.07	15.09	20.52
6	10.64	12.59	16.81	22.46
7	12.02	14.07	18.48	24.32
8	13.36	15.51	20.09	26.13
9	14.68	16.92	21.67	27.88
10	15.99	18.31	23.21	29.59
11	17.28	19.68	24.73	31.26
12	18.55	21.03	26.22	32.91
13	19.81	22.36	27.69	34.53
14	21.06	23.68	29.14	36.12
15	22.31	25.00	30.58	37.70
16	23.54	26.30	32.00	39.25
17	24.77	27.59	33.41	40.79
18	25.99	28.87	34.81	42.31
19	27.20	30.14	36.19	43.82
20	28.41	31.41	37.57	45.32

Now, since the critical value has been determined (12.59), we can compare the calculated chi-square statistic to it (18.726) and see that the chi-square statistic is greater than the critical value, meaning the null hypothesis has been rejected and there is a definite, consequential relationship between the way the BPP was portrayed and the way the NLF was portrayed.

Discussion

From the above findings, we can see that the representations of the Black Panthers and Viet Cong during the Cold War era were significantly similar. These findings are notable for many reasons.

For one, it suggests that the argument developed in Southard and Cary-Alvarez's research that the BPP and Viet Cong cultivated an alliance based on their shared experiences of oppression is correct. In fact, it adds a new perspective to this claim, that these shared experiences also included the way the Black Panthers and NLF were villainized by the media, given that the ways in which the media terrorized them could certainly be considered oppressive.

For instance, Joseph L. Alito, the Mayor of San Francisco in 1969, dismissed the Panthers as "a bunch of hoodlums",[51] a clear case of racial discrimination *(Code 3: Frightening the Public)*. In the same vein, former Secretary of State Dean Acheson once declared the Viet Cong showed their "true colors as the mortal enemy"[52] *(Code 6: "Us Against Them" Mentality)*.

What's frustrating about both of these occurrences is that they are largely rooted in biases brought about by the very systems the Panthers and NLF were fighting. By characterizing the BPP as hoodlums and refusing to see the nationalist origins of the NLF's part in the Vietnamese revolution, American anti-communists, and the general American viewpoint, make it clear that they have no intentions of breaking from the repressive, undemocratic systems they created. This

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[51] Caldwell, Eric. "Declining Black Panthers Gather New Support From Repeated Clashes With Police," December 14, 1969.

[52] Herring, George C. "The Cold War and Vietnam." *OAH Magazine of History* 18, no. 5 (2004): 18–21. http://www.jstor.org/stable/25163717.

refusal from anti-communists to open their interpretation of Cold War politics certainly forced the BPP and Viet Cong to open their perspectives- causing them to unite against an enemy determined to crucify their good-name and shun them from society.

Furthermore, these findings suggest that the anti-communist fervor in the United States during the Cold War itself was so powerful *because* it was built on harmful over-exaggerations and falsifications. In a way, anti-communists united against a common enemy similar to how the BPP and NLF did. By making it clear who wasn't welcome in Cold War America, those who happened to fit in felt inspired to join the fight to protect their version of "human freedom".[53] By adding nuance to the existing understanding of the Cold War, we may better prepare ourselves for the political hostilities of the future, something many have been warning against since the dawn of man. Indeed, as Aristotle once asserted some 1,600 years before the Cold War began,

> *Tyranny preserve themselves by sowing fear and mistrust among the citizens by means of spies, by distracting them with foreign wars, by eliminating men of spirit who might lead a revolution, by humbling the people, and making them incapable of decisive action*

Implications

This study implies the potential dangers that can occur if the media continues to disallow for differing opinions. While the Black Panther Party and Viet Cong eventually lost their influence and power, largely due to the anti-communist portrayal of them, their respective fights and revolutionary spirits still remain as pertinent as ever. Eventually some other groups will arise and continue down the path carved out by the BPP and NLF, and when they do, the world must be ready to offer them the respect of painting them in an honest light.

Limitations

Before moving on to the conclusion, it is important to note certain limitations to this study. Perhaps the most significant limitation is the potential for human error. While the methodology of this research is ideal for this particular study, content analysis does come with the consideration that it relies heavily on humanistic decision-making- which isn't always correct. Another limitation is the amount of documents that were analyzed to collect the data. While scouring through 60 different reports of varying categorizations proved efficient for this study, if this research was to be replicated, a larger variety of sources would greatly improve the accuracy of its findings.

Conclusion

The research done in this paper will ultimately contribute to the existing research on the portrayal of revolutionary movements during the Cold War. As with any historical research

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[53] Alva, Chittaranjan. "Ideology and the Vietnam War." *Social Scientist* 1, no. 3 (1972): 68–75. https://doi.org/10.2307/3516400.

paper, scholars may gain insight into broader patterns and continuities that occur over time such as the weaponization of political discourse and corrupt propaganda strategies.

Further, this paper provides valuable findings on the exploitation of existing bigotry to advance certain "patriotic" and "real" American causes. This tactic is certainly something to be mindful of, as societal divisions become more stark, and more easily manipulatable. The foremost principle gained from this research is that society must learn to critically analyze the difference between the constructed historical narrative and what actually transpires. If no ulterior opinion is offered, one must take the initiative to question all existing narratives themselves. Otherwise, systemic biases and political schemes will continue to thrive.

When morals decline and good men do nothing, evil flourishes. A society unwilling to learn from past is doomed. We must never forget our history.

- J. Edgar Hoover

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Transformer-Based Analysis of Cancer Mutations in Underrepresented Asian Populations
By Nitza Kahlon

Abstract

This study investigates the application of machine learning, specifically transformers ([1]), to analyze genetic data from underrepresented Asian cancer patients. Our novel approach utilizes transformers to extract semantic meaning from tiered feature data, generating embeddings that capture relationships between gene expression for clustering. This method bypasses the need to explicitly differentiate between driver and passenger genes, while mitigating dimensionality challenges inherent in high-dimensional genomic data. By addressing overfitting and gene classification issues, our approach yields high prediction accuracy for the cancer site of origin on South Asian cancer patient data allowing oncologists to recommend therapies for cases when the primary site of cancer's origin was previously unknown.

Keywords Cancer, machine learning, sentence transformers, word embeddings, mutations, underrepresented population

Introduction

South Asian populations have historically been underrepresented in cancer mutation research due to limited data and associated factors ([2]). This study focuses on the development of innovative machine learning methodologies for analyzing cancer mutation data, with a specific emphasis on applying these techniques to gain insights into cancer mutations within South Asian populations. To facilitate this research, we established a partnership with 4baseCare ([3]), a provider of genetic sequencing services for South Asian cancer patients. This collaboration granted us access to their extensive repository of raw mutation datasets as well as expertise in validating our research findings.

Predicting cancers from genetic mutation data is a complex task with several key challenges:

1. *Distinguishing driver from passenger mutations*: Many mutations found in tumors are "passengers" that do not contribute to cancer development, adding noise to the data ([4, 5]).
2. *Accounting for mutational heterogeneity*: Tumors often harbor numerous mutations, which can influence disease progression ([6]).
3. *Lack of a comprehensive gold standard*: There is no universally accepted gold standard dataset to benchmark prediction tools ([5]).
4. *Overfitting and dataset biases*: Many prediction tools are trained on datasets enriched for *well-studied* cancer genes, limiting generalizability ([4, 5]).
5. *Accounting for mutation context*: The same mutation can have different effects depending on the tissue type, mutational burden, and disease stage ([5]).

Despite these challenges numerous computational methods and tools have been developed to analyze cancer data. These include frequency-based methods like MutSigCV, which look for genes that are mutated at significantly higher frequencies than expected by chance to identify potential driver genes. However, they struggle to detect infrequently mutated drivers ([5]). Many recent tools employ machine learning to integrate diverse data types to predict driver genes including random forest classifiers ([7]), multi-task neural networks ([7]) and deep learning models trained on mutation and gene expression data ([5]).

Additionally, when planning treatment for patients, oncologists need to understand the primary site of origin of the cancer. Thus, cancers of unknown primaries (CUP) pose a significant challenge since the ambiguity complicates treatment decisions and limits therapeutic options ([8]), leading to poor outcomes for patients with CUP compared to patients having cancers with an identified primary site. There is a critical need for tools that precisely predict cancer types to guide oncologists in identifying the cancer's site of origin for planning ideal treatment regimens for their patients.

In this study, our goal is to address this gap, providing a novel methodology for predicting cancer's site of origin based on patient genetic mutation data. This research addresses a critical need within the context of early detection and therapeutic intervention recommendation, particularly for under-represented populations. While cancers of unknown primary (CUP) account for approximately 2% of all cancers in the USA ([9]), they represent a significantly larger proportion in Asian countries due to limited access to advanced diagnostic techniques. Ren et al. ([10]), for instance, report a 49% CUP rate for adenocarcinoma among Chinese patients based on data from a single hospital. The scarcity of advanced diagnostic tools necessitates the development of cost-effective diagnostic technologies. Artificial Intelligence, coupled with high-quality genetic data, offers a promising solution. Cancer detection does not necessitate whole-genome sequencing, which is expensive. Instead, we can focus sequencing efforts on specific genes commonly associated with cancer-related mutations. This targeted approach is both scalable and cost-effective, as demonstrated by organizations such as 4basecare ([3]).

Our approach utilizes transformer models to extract semantic meaning from tiered feature data, generating embeddings that effectively capture relationships in gene expression for clustering. This method mitigates overfitting, circumvents the need to explicitly identify driver genes, and addresses limitations of existing techniques. Our new method demonstrates a high accuracy in predicting cancer site of origin on South Asian cancer patient data and offers a new approach to extract novel insights from complex genetic datasets.

Materials and Methods

Our research uses a rich dataset of cancer patient information from Asian populations including genetic mutations from sequencing for each patient. Despite the comprehensive genetic data from roughly 1400 patients, we faced two main challenges:

1. *High Mutation-to-Patient Ratio*: With over 1,700 distinct mutated genes across 1,400 patients, the dataset presented a high mutation burden relative to the cohort size.
2. *Data Skew Across Different Cancer Types*: The class imbalance (Figure 1) observed in our dataset, characterized by the overrepresentation of certain cancer types and underrepresentation of others, creates a data skew. This reflects the varying incidence rates of different cancers within a population.
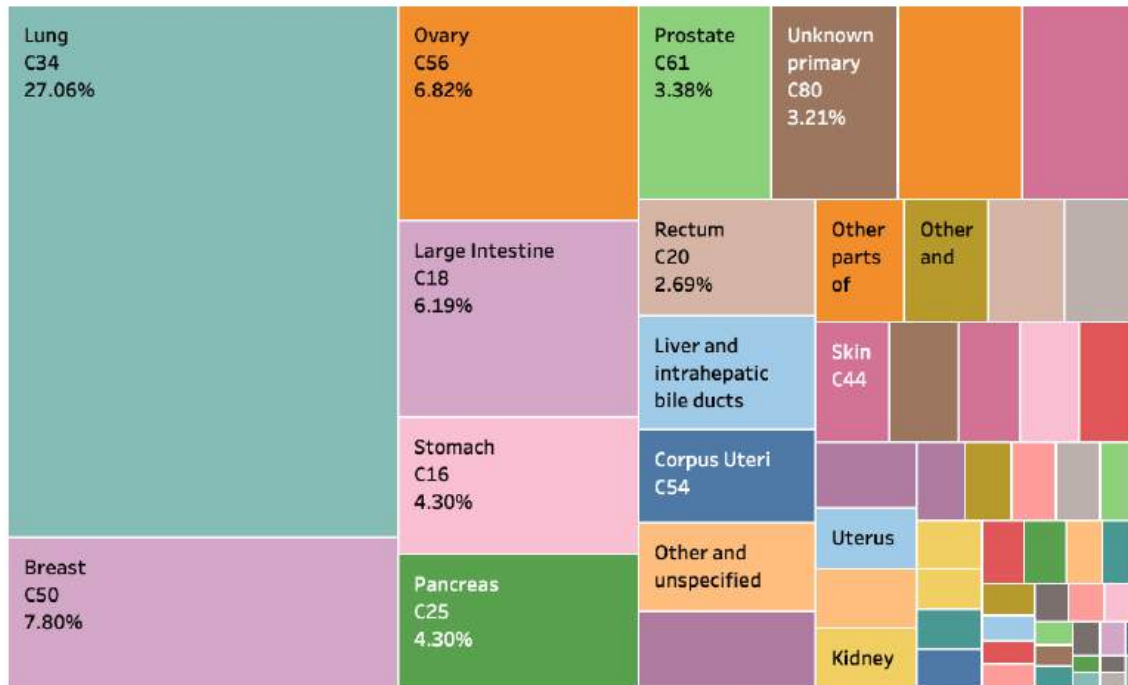

Figure 1: Distribution of Cancer Types Within the Patient Cohort

Transformers

Sentence transformers are designed to generate dense vector representations (embeddings) for sentences. These embeddings capture the semantic meaning of the input text in a high-dimensional vector space, allowing for efficient comparison and retrieval of similar texts using cosine similarity or other vector operations. During inference, the sentence transformer takes a sentence as input and outputs a fixed-length dense vector that encodes the semantic meaning of the sentence. These rich, semantic embeddings can then be used for performing text similarity operations, clustering etc.

A crucial feature is that the transformer generated embeddings take the order of words into account. These contextualized token embeddings capture both the semantic meaning of the token as well as its relationship and ordering with respect to other tokens in the sentence ([11]). This sentence embedding therefore encodes the semantic meanings of the individual words as

well as their order and relationships within the sentence context. Thus, sentence transformers can generate rich embeddings that go beyond just combining individual word vectors - they model the compositional meaning of words in the context and order they appear in the sentence.

Modeling Mutation Sequences using Transformers

We leverage the aforementioned attributes of transformers to address the three challenges outlined previously:

1. **Dimension reduction to reduce risk of overfitting:** We achieve dimensionality reduction by limiting the size of the embedding vectors generated by the transformer. This mitigates the risk of overfitting and enhances computational efficiency. Note that we do not limit the number of input mutations into the transformer - only the size of the output vector which is a tunable parameter.

2. **Capturing Gene Interaction:** The inherent heterogeneity of cancer genetics makes distinguishing driver mutations from passenger mutations challenging. Transformers, with their ability to consider context and extract semantic meaning, are employed to capture the intricate relationships between mutations and identify potential interactions and correlations between genes thereby obviating the need to identify driver and passenger mutations. This approach surpasses traditional frequency-based analyses, which treat mutations in isolation and may overlook context-dependent effects.

3. **Addressing Cancer Type Skew:** To account for the varying sample sizes across cancer types, we exploit the transformer's sensitivity to word order. Each patient is modeled as a sentence comprising concatenated features, where the weightage assigned to each feature depends on its position within the sentence. Features appearing earlier in the sentence receive greater emphasis. To minimize noise from passenger mutations, we sort mutations by decreasing frequency among patients, prioritizing more frequently occurring mutations. This enhances the stability of clustering as new patients are added to the corpus, as the distribution of mutations remains relatively consistent. By strategically leveraging word ordering and semantic extraction capabilities, we demonstrate the effectiveness of transformers in collectively analyzing pan-cancer data, even in the presence of skewed sample sizes and high dimensionality.

Algorithms

We present two algorithms, the first for clustering and the second for predicting cancer type of a patient using the generated clusters.

Clustering using Transformers

We sort the mutated genes across all patients by decreasing order of frequency of occurrence. Each patient is represented via a sentence of the form: *"CancerType {<CancerType>} CancerMorphology {<CancerMorpoholoy>} SortedGenes[0] : {MutatationStatus[0]} SortedGenes[1] : {MutatationStatus[1]}, …,"* The order in which we

append the features is the Cancer Type first, then Cancer Morphology, which is followed by the mutated genes in decreasing frequency of occurrence. As an example, a Lung cancer patient with morphology *8149/3* and the frequency-sorted list of genes *H2AFx, ZEB1, PIK3R1, CSF3R, SPRTN, …* is represented as follows: *CancerType: {Lung} Morph: {8149/3} H2AFX: {0} ZEB1: {0} PIK3R1: {0} CSF3R: {1} SPRTN: {0}*

Clustering Algorithm

1. *Feature Sorting*: Generate a vector SortedGenes of mutation across all patients sorted by frequency of occurrence
2. *Sentence Generation*: For each patient generate a feature vector of the following form: *CancerType {<CancerType>} CancerMorphology {<CancerMorpoholoy>} SortedGenes[0] : {MutatationStatus[0]} SortedGenes[1] : {MutatationStatus[1]}*.
3. *Embedding Generation*: Feed the input data into a sentence transformer to generate embeddings.
4. *Hierarchical Clustering*: Using the embeddings to generate a hierarchical clustering via Ward's ([12]) linkage algorithm.
5. *Flat Cluster Generation*: Using a distance threshold to generate flat clusters from the hierarchical clustering by grouping together patients that are a distance less than the given threshold with regard to each other.

Results

Clustering Precision Test

The most basic test of clustering precision is that all patients grouped in a cluster must have the same cancer type. We use this test to evaluate clustering quality as we vary the (i) feature order, and (ii) the threshold distance tuning parameter for flat cluster generation.

Feature Order Dependency

We used transformers to exploit word order by tiering features, placing cancer type first, followed by mutated genes in decreasing frequency. To validate this, we conducted a clustering precision test with three scenarios, hypothesizing that Sorted Features would perform best:

1. *Sorted Features*: Cancer type and morphology first, followed by mutated genes.
2. *Reverse Sorted Features*: Cancer type at the end.
3. *Mutations-only*: Only mutations data, without cancer type.

In our algorithm, the distance threshold employed for cluster generation serves as a tunable parameter that can be adjusted to regulate cluster size. We optimize this threshold by initiating the process with a high value, whereby all patients are aggregated into a single cluster, and then progressively decreasing it until each cluster encompasses only a single cancer type. Due to the

discrete nature of the data, only specific threshold values yield alterations in the generated clusters. Excessive reduction of the threshold leads to each cluster containing solely one patient, which is not conducive to modeling objectives. In instances where we are unable to attain clusters comprising exclusively one cancer type, we opt for the lowest threshold value preceding the isolation of each patient into their own cluster.

Employing this strategy, we generate histograms illustrating the distribution of cancer types per cluster for the three aforementioned scenarios (Fig. 2). Ideally, each cluster should contain exclusively one cancer type. It is evident that in the case of Sorted Features, we do indeed achieve a unique cancer type per cluster, whereas in the other scenarios, a cluster may encompass patients with multiple cancer types. Consequently, in Fig. 2 (a), we observe that if we position cancer type at the end, we obtain only 20 clusters with a unique cancer type, and there are nearly 80 clusters containing two cancer types. This does not constitute a useful clustering model for predicting cancer type. For a model to be effective, we require clusters to contain only one cancer type, so that when a new patient is presented and matched to a cluster, we can definitively isolate the predicted cancer type. This is clearly not feasible for scenarios 2 and 3, where the majority of clusters harbor more than one cancer type. This justifies our decision to use transformers with tiered features.

A crucial observation is that the clustering generated by our methodology can differentiate cancer subtypes. Notably, a cancer within a specific organ can manifest multiple subtypes and morphologies, each arising from distinct sets of mutations that activate various pathways. This genetic diversity underscores the complexity and heterogeneity of cancer, where different mutations can drive the same type of cancer in different patients ([13]). Consequently, for each cancer type classified by the affected organ, our methodology can categorize patients with different sets of mutations leading to a given cancer into distinct cancer subtypes. This has particularly valuable therapeutic implications, as different pathways may necessitate different treatment approaches. This is exemplified by the fact that, despite considering various cancer types based on the affected organ, we obtain over 300 clusters, with multiple clusters representing each set of mutations responsible for a specific cancer subtype.
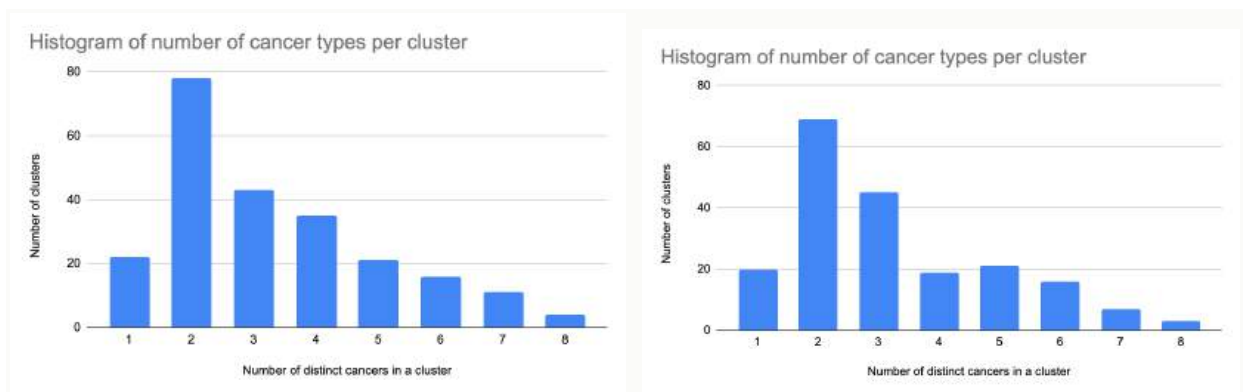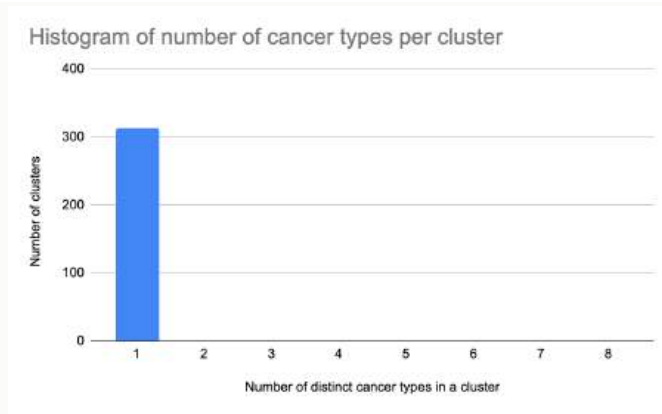
Figure 2: Histograms of the number of cancer types within a cluster for 3 different methods

Clusters depend on both cancer type and mutated genes

It is important to note that while partitioning data by cancer type and performing clustering on these partitions could ensure that patients within the same cluster share the same cancer type, this approach would preclude the analysis of pan-cancer mutations. Our transformer-based embedding clustering method, on the other hand, considers both cancer type and mutated genes, allowing for a more comprehensive analysis.

Indeed, when clustering is performed based on transformer-generated embeddings, we observe multiple clusters (Fig. 3) even within the same cancer type, suggesting that distinct genetic mutations can result in the same cancer. For instance, we identify 83 lung cancer clusters, underscoring the capability of our approach to capture nuanced relationships between mutations and cancer types, while still facilitating the identification of pan-cancer mutations. The various clusters represent different sets of mutations triggering distinct pathways, all culminating in lung cancer. However, these differences are crucial to identify, as they often necessitate different therapeutic interventions.

In essence, our transformer-based methodology offers a unique advantage in that it allows us to simultaneously analyze both cancer types and mutations, providing a more holistic view of the underlying genetic landscape while retaining the ability to identify potentially significant pan-cancer mutations.
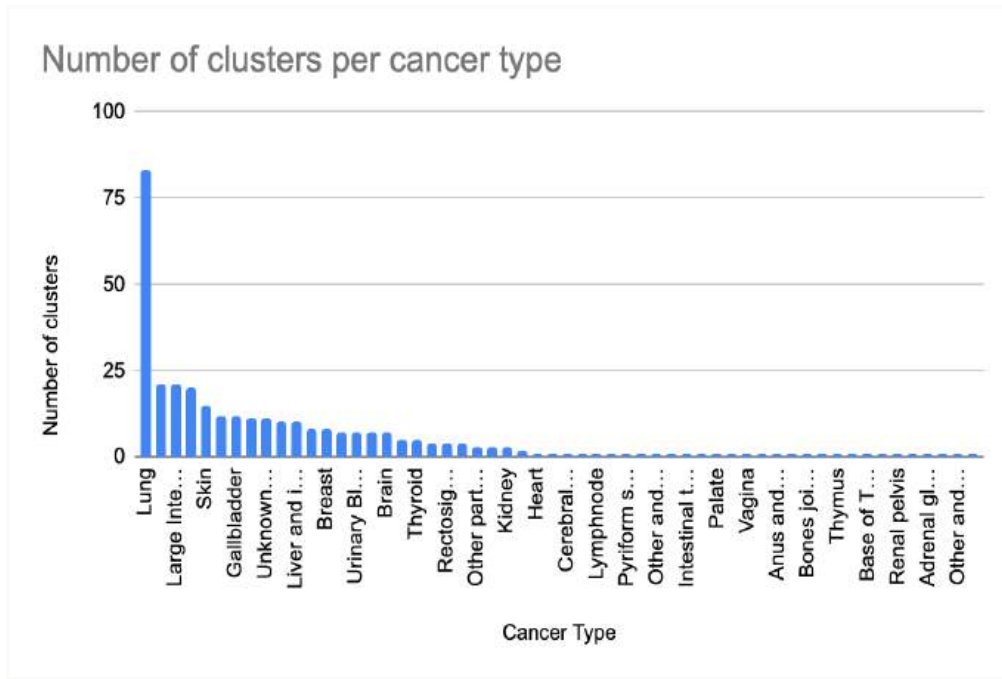
Figure 3: Number of patient clusters per cancer type

Tuning the Distance Threshold for Flat Clustering

We optimized the distance threshold employed in step 5 of the clustering process to achieve two primary objectives: ensuring homogeneity within each cluster, where all patients share the same cancer type, and maximizing cluster size as quantified by the number of patients within a cluster to enhance prediction accuracy. As previously mentioned, we optimize this threshold by commencing with a high value of the distance threshold, wherein all patients are grouped into a single cluster, and then progressively decreasing it until each cluster encompasses solely one cancer type. Due to the discrete nature of the data, only specific threshold values result in modifications to the generated clusters.

As we reduce the distance threshold, there is a gradual decrease in cluster size, evidenced by the diminishing number of clusters. A notable transition occurs between thresholds 1.1 and 1.2, wherein we begin generating clusters containing exclusively one cancer type. Thus, at a threshold of 1.2, all patients are aggregated into a single cluster, indicating that the distance between each pair of patients is less than 1.2 in our embedding space. When we proceed to a threshold of 1.1, the entire set of patients is partitioned into 313 distinct groups, with all patients within each group sharing the same cancer type. This suggests that the optimal threshold lies within the interval (1.1, 1.2].

To ascertain the precise threshold value, we examine the minimum distance between any pair of patients and utilize that value to incrementally traverse the interval, starting from 1.2, to identify the point at which we obtain the fewest number of clusters, such that all patients within each cluster exhibit the same cancer type. Interestingly, due to the discrete nature of the data, we

still end up with 313 clusters. These clusters can now be leveraged to predict not only the overall cancer type but also the different sets of mutations leading to a given cancer type, as evidenced by the presence of multiple clusters for a specific cancer type, e.g., 83 clusters for lung cancer.

Table 1: Optimization of clustering with different distance thresholds

Distance Threshold	Number. of Clusters	Percentage Clusters with multiple Cancer Types
0.9	434	100
1.0	384	100
1.1	313	100
1.2	1	0
1.3	1	0

We tested various thresholds and selected the highest one (1.1) that maintained cancer type homogeneity within clusters. This optimal threshold was then used to generate a hierarchical clustering dendrogram (Figure 4).
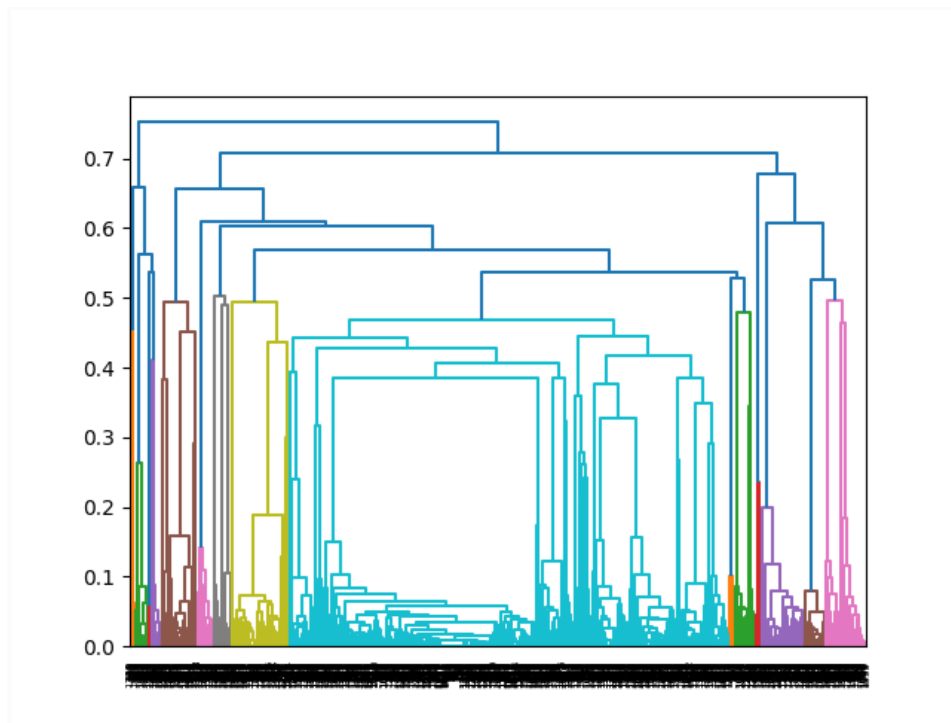

Figure 4: Hierarchical clustering with a distance threshold of 1.1

Isolating a predictive model

A key objective of our analysis is to predict the cancer type of a new patient based on their genetic mutations. To accomplish this, we aim to match a new patient's genetic profile to one of our established clusters. However, since our clusters are based on transformer-generated embeddings, directly matching raw genetic data to embeddings is not feasible.

To address this, we associate each cluster with a "canonical gene set," comprising the mutated genes most common within that cluster. This simplifies the matching process by enabling a comparison between the patient's mutated genes and the canonical gene sets associated with each cluster.

Cancer Prediction Algorithm

1. *Compute Canonical Gene Set*: For each cluster, determine a representative set of genes by identifying the set of mutated genes shared by a predetermined threshold percentage of patients within that cluster.
2. *Compute Cluster Distance*: We represent each patient as a binary vector where each dimension corresponds to a gene, with the corresponding coordinate being 1 if the gene is mutated and 0 otherwise. Using this vector representation, we calculate the distance between the patient's vector and the binary vector determined by the canonical set of genes associated with each cluster.
3. *Cluster Matching*: The cluster with the largest cosine distance (highest similarity) is matched with the patient
4. *Predicting Cancer Type*: The cancer type of the patient is then the unique cancer associated with patients of the matched cluster.

Analysis of Cancer Prediction Quality

In order to analyze the quality of our matching algorithm, we generate a randomly sampled set of roughly 20% patients which are not used in clustering. For these patients we then run the cancer prediction algorithm to gauge prediction accuracy. Below we plot the prediction accuracy of cancer type using clusters generated based on distance thresholds of 0.9, 1.0 and 1.1. The results, illustrated in the plot, demonstrate high prediction accuracy, which further improves with increasing distance thresholds, leading to larger clusters.

Table 2: Optimization of prediction accuracy with different distance thresholds

Distance Threshold	Prediction Accuracy
0.9	92.70
1.0	93.50
1.1	93.51

Discussion

We presented a novel methodology for cancer prediction leveraging patient genetic mutation data. Our approach harnesses the semantic extraction capabilities of transformer models applied to tiered feature data, generating embeddings that effectively capture relationships in gene expression.

A key distinction between our transformer-based method and existing statistical/ML approaches lies in addressing the dimensionality curse ([14]) which traditional methods address by limiting the number of input features, such as mutated genes per patient. This is typically carried out by first trying to distinguish driver from passenger mutations and focussing analysis on the driver mutations. Towards that end, these techniques look at the most frequently occurring mutations across a given cancer type and prioritize them as features for ML models. However the prediction quality of such approaches is not high due to the following reasons. First, simply looking at the mostly frequently mutated genes is not enough since some genes are frequently mutated across many disparate cancer types. For instance, BRCA2 mutations occur in high frequencies across many varied cancer types, i.e., melanoma, breast, prostate, and pancreatic cancer ([15]). Moreover, the occurrence of cancer at a specific site is typically driven by the interplay of multiple mutations, not just a few frequently occurring ones. Often, low-frequency mutations combine with high-frequency ones to trigger the development of distinct cancer types. Crucially these low frequency mutations are hard to identify statistically. This is where the weakness of ML based methods is exposed. Further adding all these low frequency mutations as inputs to ML models greatly increases the input feature dimensions rendering a lot of these techniques ineffective. The curse of dimensionality hits particularly hard in the context of cancer prediction where, due to privacy concerns, genetic data is available only for a very limited set of patients. To keep the ratio of number of training samples to input features manageable, ML based techniques are forced to reduce the set of input features, i.e., mutated genes, thereby impacting prediction quality.

Our technique bypasses the curse of dimensionality by leveraging the ability of transformer generated embeddings to capture the semantic meaning of the input sentence in a high-dimensional vector space. The input sentence is tokenized and passed through the transformer encoder layers, generating contextualized embeddings for each token while attending to the entire input sequence ([11]). This sentence embedding therefore encodes the semantic meanings of the individual words as well as their order and relationships within the sentence context. This ability of transformers to account for the relationship between words allows us to capture correlations between sets composed of both high and low frequency mutations that lead to a specific cancer type. In this way, transformers allow us to account for both high and low frequency mutations without incurring the dimensionality curse. This is the key reason for the enhanced precision of our methodology. Our technique leverages the transformer's sensitivity to word order to prioritize high-frequency mutations by placing them earlier in the input sequence. Simultaneously, we utilize the transformer's ability to capture contextual relationships to identify correlations involving both high and low-frequency

mutations. In this way, our approach allows us to retain all mutations while avoiding the dimensionality curse thereby contributing to the enhanced precision of our technique.

We validated the efficacy of our method by developing a highly accurate model for predicting cancer type solely based on a patient's set of mutations, a task previously considered challenging. This provides an extra tool in the hands of oncologists to plan ideal treatment regimens for patients by correctly identifying the cancer's site of origin.

Another key objective of this study was to determine the applicability of our methodology in uncovering insights into South Asia-specific cancer mutations. To this end, we examined clusters generated by our transformer-based model, focusing on frequently occurring mutations within each cluster. This analysis aimed to elucidate both known and novel associations between genes and cancer types in the South Asian population. For instance, a cluster representing biliary tract cancer patients exhibited mutations in several genes, including *APOBEC3H*, *CCT5*, *FES*, *HNF1A*, *LOC102724788*, and *SYNE1*. Notably, genes such as *CCT5* and *SYNE1* have been extensively documented in the literature as being associated with various cancers, including biliary tract cancer ([16, 17, 18, 19, 20]). This finding not only validates our methodology but also suggests that certain mutations prevalent in the South Asian population are shared with other populations, raising the possibility of utilizing existing therapies.

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Predicting Microplastic Concentrations in the Pacific Ocean and Pacific Coast Using Machine Learning By Carley Chen

Abstract

Microplastics pose severe threats to marine ecosystems and human health. As microplastic pollution continues to increase in the oceans, there is an urgent demand for efficient methods to both predict and alleviate its effects. This study uses machine learning models to predict microplastic concentrations in the Pacific Ocean and along the Pacific Coast based on geographic location. Utilizing the National Oceanic and Atmospheric Association's data, the research dives into predictive models trained on microplastic concentrations from various locations. Through a neural network, the models take longitude and latitude points as inputs to classify microplastic concentration levels into five groups: very low, low, medium, high, and very high. Separate models were applied for ocean and coastal data due to differences in data collection and microplastic types. These models both consistently achieved 70-75% accuracy. This study emphasizes machine learning's potential to provide direction for clean-up efforts and preventative policies regarding plastic pollution. The research emphasizes the importance of widespread data collection and collaboration between governments, corporations, and citizens to reduce the influx of microplastics into the oceans.

Intro

Plastics are present in virtually every part of human life. Water bottles, electronics, plumbing pipes, and thousands of other ubiquitous products are made of plastic. Many overlook the microscopic consequences that stem from plastic production: microplastics. Most microplastics originate from both industrial and household products, while others result from larger plastics degrading over time (Xu et al.). Common culprits include textiles, medicines, body scrubs, and manufactured pellets as primary sources and nets, tires, and films as secondary sources. The latter few are the leading cause of microplastic pollution. These minuscule particles, defined as being less than 5 mm in diameter, are a massive threat to aquatic life and human health due to our seafood consumption. The small size makes microplastics easy for marine life to consume, and the plastics also often absorb toxins from surrounding areas(*Effect of Microplastics in Water and Aquatic Systems*). Thus, microplastics function as transports that move harmful pollutants into important water systems.

Microplastic content reaches more than 36 particles per 100 grams in organisms like mussels and oysters, while the average fish carries 35 microplastic particles. Microplastics accumulate in the intestines, gills, and livers of fish, often decreasing their ability to swim and grow regularly. With microplastics in almost all shellfish and seafood, humans can ingest more than 50,000 particles annually. There is a clear motivation for dealing with this issue, as not only are millions of organisms in the oceans being negatively impacted, but human water sources are also being polluted, and the plastics are cycling back through the ingestion of seafood. However, the task of reducing microplastic pollution is challenging and complex. According to The United

Nations Educational, Scientific and Cultural Organization (UNESCO), approximately 8 to 10 million tons of plastics are released into the ocean annually, resulting in around 50-75 trillion pieces of microplastics in the ocean at this time (*World Ocean Day: How Much Plastic Is in Our Oceans?*). Solving this issue would not only require a cheap and effective clean-up effort but also waste management to stop the flow of plastics into the ocean in the first place.

Numerous organizations have conducted studies and collected substantial amounts of microplastic data, which can all be found at the National Oceanic and Atmospheric Administration's (NOAA) Center for Environmental Information (*Marine Microplastics | National Centers for Environmental Information (NCEI)*). For example, the Marine Science Institute at the University of Texas conducted an in-depth study of nurdle amounts on the coastlines of the United States (Tunnell et al.). Nurdles are small plastic pellets that serve as the raw materials for plastic products like grocery bags. They can reach the ocean in many ways but most commonly flow down the drains of industrial facilities. Their ability to absorb toxic compounds like pesticides and other toxins seriously threatens marine life and, ultimately, human health (*What Are Nurdles and What Are Nurdles Used For*). The primary method of data collection for nurdle concentration is citizen science (Tunnell et al.). Organizations can gather a consistent influx of data on microplastic pollution with the help of citizens trained through a well-developed data collection methodology.

With the rapid development of artificial intelligence, deep learning algorithms have become increasingly powerful and accessible. Several studies have been conducted on image processing and classification applications concerning microplastics. The results have been promising; the models have high accuracy and reliability (*Using Artificial Intelligence to Rapidly Identify Microplastics Pollution and Predict Microplastics Environmental Behaviors*). However, there has not been as much research on the predictive modeling of microplastic concentrations, which is the focus of this study (*A Critical Review on Artificial Intelligence-Based Microplastics Imaging Technology: Recent Advances, Hot-Spots and Challenges*). While using similar deep learning techniques, this model looks at the issue from a different angle in an attempt to curtail the microplastic challenge with a forward-looking predictive solution.

Methods

For this project, the data was sourced from the Marine Microplastic Concentrations map provided by the NOAA. The map contained a total of 22,266 data points, of which this project sampled around 2,500. Each data point includes the same information: data, longitude, latitude, ocean, unit, density range, concentration class, and references. Only the longitude, latitude, and concentration data were used to create a model that most concisely predicted the microplastic concentration. The concentration category was split into five distinct classes: very low, low, medium, high, and very high. The model inputs included longitude and latitude points, as well as output predicted concentration levels after training on existing data. If the model's output is "very low," it is less urgent to direct cleaning efforts to that area. If the output is "very high," on the other hand, that area would be an excellent place to target for cleanup. Thus, the model can

help streamline and optimize the efforts to reduce microplastic pollution by providing precise directions and locations.

The model's architecture falls under supervised learning; data is provided to train and test its accuracy before it is used to predict the concentrations at locations without recorded data. Two models were built, one modeling coastal data and the other modeling ocean data. This separation was done because the nature of the data differs, with the coastal data measuring the number of nurdles in an area of the coastline. In contrast, the ocean data collects and quantifies the number of microplastics differently. If the two methods were combined, the accuracy of the results would fall dramatically. In both datasets, data was first converted into a CSV file. This was inputted into the program and processed into categorical columns. Next, the categories were split into features and targets, with the former being the longitude and latitude points and the latter being the concentration class. The data was then split into training and testing sets at a 0.8 to 0.2 ratio. In other words, 80 percent of the data was used to train the model, while the remaining 20 percent was used to test the model's accuracy.

The model itself is a neural network built with TensorFlow. It has two dense hidden layers and one dense output layer. Each hidden layer has 16 nodes, which are components that place inputs through respective transfer functions to compute output values. The first two layers use "ReLU" activation, while the output layer uses "softmax." This is standard for basic neural networks. ReLU is computationally straightforward to implement, making it the ideal choice for hidden layers. Softmax is commonly used in output layers for non-binary classification problems. Subsequently, the optimizer, loss, and metrics were defined using the .compile() function. The Adam optimizer was chosen, with a learning rate of 0.001. The loss was defined as sparse categorical cross-entropy, which is often used for non-binary classification tasks. After testing several performance metrics, such as prediction, recall, and accuracy, accuracy remained the best choice for clarity and consistency. Lastly, the model was trained using the .fit() function. It trained over 100 epochs, meaning it iterated over the entire data set 100 different times. The batch size was set to 32, so the model processed 32 examples before updating the respective weights. There is a validation split set to 0.2, meaning that 20 percent of the data within the training data will be used as cross-validation to test the model's performance after each epoch.

Results

A confusion matrix was employed to display the accuracy of the model visually. One column represented the actual class of the data point, while the other displayed the model's prediction. For simplicity, if there were no results across the board for either the true or predicted label, the class would not appear on the confusion matrix.
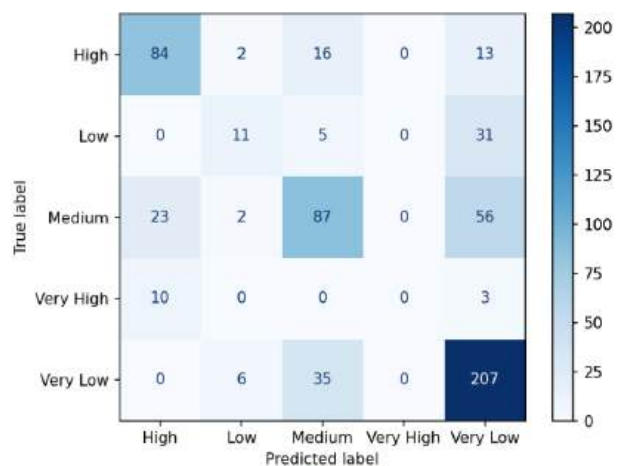

Figure 1.0

Figure 1.0 demonstrates the average results for a data set trained and tested on around 2000 points, sampling only ocean data from the Pacific Coast. As shown in Figure 1.0, the model predicted the classes "very low," "high," and "medium" the best. It commonly misclassified "medium" as "very low," with 56 data points falsely predicting "very low." Other misclassifications were less frequent, with 10 classified as "high" instead of "very high," 31 classified as "very low" instead of "low," and 23 classified as "high" instead of "medium." The final accuracy provided with this run was 72.86%.
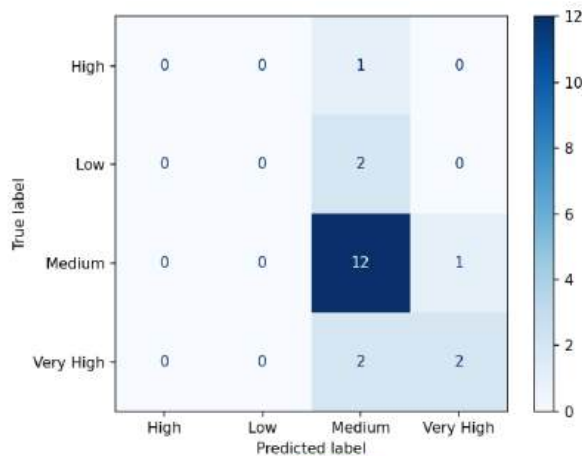
Figure 1.1 demonstrates the average results for a data set trained and tested on around 150 data points sampled from the Southern California Coast, starting at the Mexican border and extending to Santa Barbara. This data set included only nurdle data, a different type of pollution than was used in the ocean data in the previous example. The reason for separating the two was that the method in which the data was collected along the coastline was completely different from that within the ocean. Combining the two would not only dramatically decrease the performance of the predictive model but would also not be

Figure 1.1

as helpful. With them separated, different clean-up efforts could use each model for their respective purposes, depending on whether they are trying to tackle cleaning microplastics on the beaches or in the ocean. The accuracy remained similar, consistently staying in the 70-75% range. The confusion matrix reflects this by accurately predicting the "medium" class. No predictions fell very far out of line like that of the ocean model, but that was because most were grouped into the "medium" class rather than being correctly classified.

Figure 1.2 shows the same coast model as Figure 1.1, tested on approximately 200 data points from the Northern California Coast. Like the previous figure, the model most successfully predicted the "medium" and "very high" classes, with 12 and 8 correct labels, respectively. The "low" and "high" classes were not predicted correctly, with every example falling under the "medium" and "very high" columns. Only one example was misclassified as very
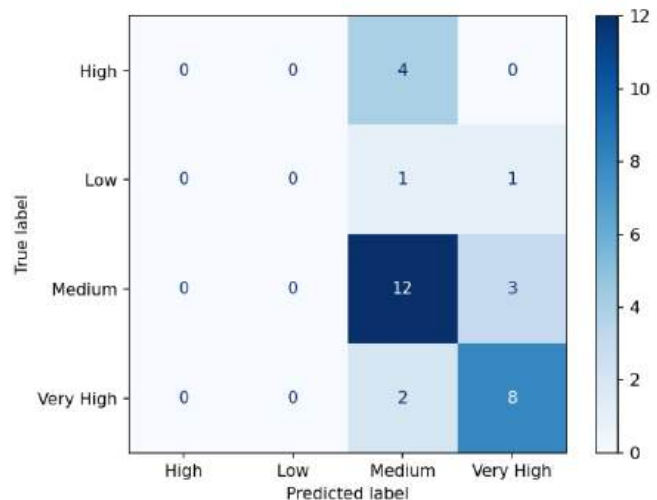

Figure 1.2

"high" when its true label was "low". The accuracy remained in the range of 70-75% with 32, 64, and 128 nodes. The lack of co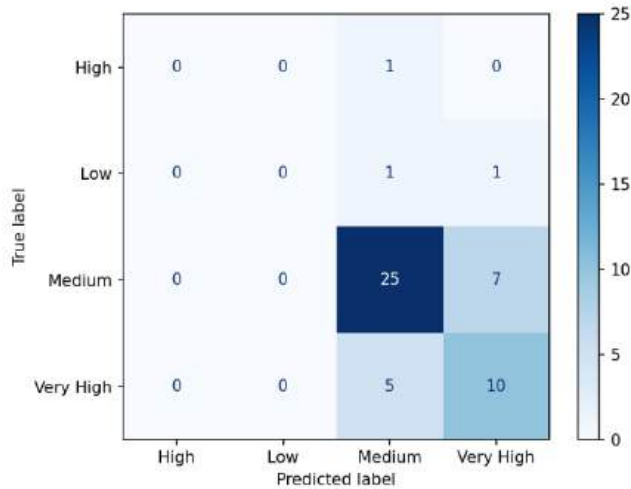astal data, with around 100 to 200 points available for each test, made it more challenging to increase the accuracy of the model. Therefore, another test was done using the coast model on all of the combined data points on the California Coast. **Figure 1.3** displays the results. The accuracy decreased compared to the previous two runs, staying at around 60-65%. However, the information given by the confusion matrix reveals the same trend as that of Figures 1.1 and 1.2, with all of the predictions falling in the "medium" and "very high" columns. When examining the original data, most of the points were in the "medium" or "very low" class, making it

Figure 1.3

surprising that the "very low" class did not even appear in the confusion matrix for all three runs. The bar graph in **Figure 2.0** demonstrates this disparity. Most of the data falls under the "medium" and "very low" columns, with the "very high" column being minimal. The results of the predictive model, therefore, do not make sense even if the accuracy seems to be reasonably high.
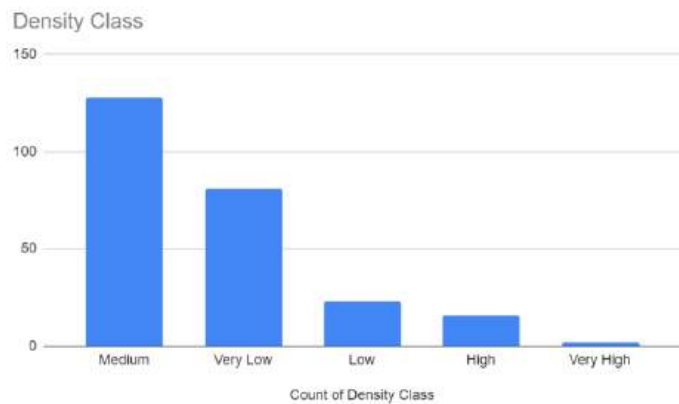
Testing the data on the same set but
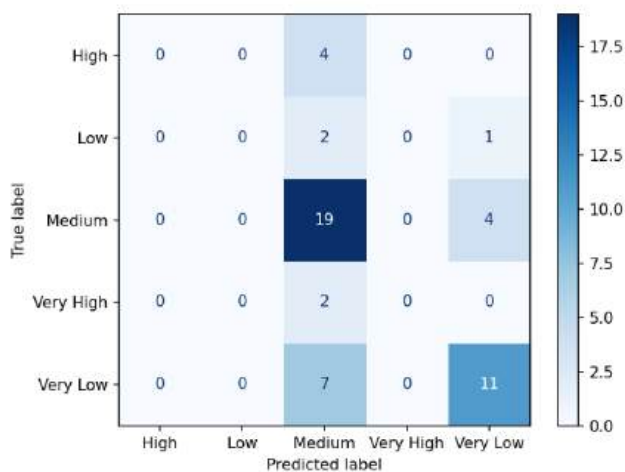
Figure 2.0

using 16 nodes for each layer helped to resolve this issue. **Figure 1.4** exhibits this, with the data falling under the "medium" and "very low" columns. Although the model struggles to successfully classify the "low" and "high" classes, often grouping them as "medium," the results make much more sense when looking at the original training data. The issue previously encountered in Figures 1.1, 1.2, and 1.3 was overfitting. Because the only two features used were

Figure 1.4

545

longitude and latitude, having a model with 64 or even 32 nodes was too complex. Using 16 nodes for each layer created results that made logical sense and had significantly better performance.

Figure 3.0

A map of the California Coast was employed to better visualize the effectiveness of the model (**Figure 3.0)**. The collected nu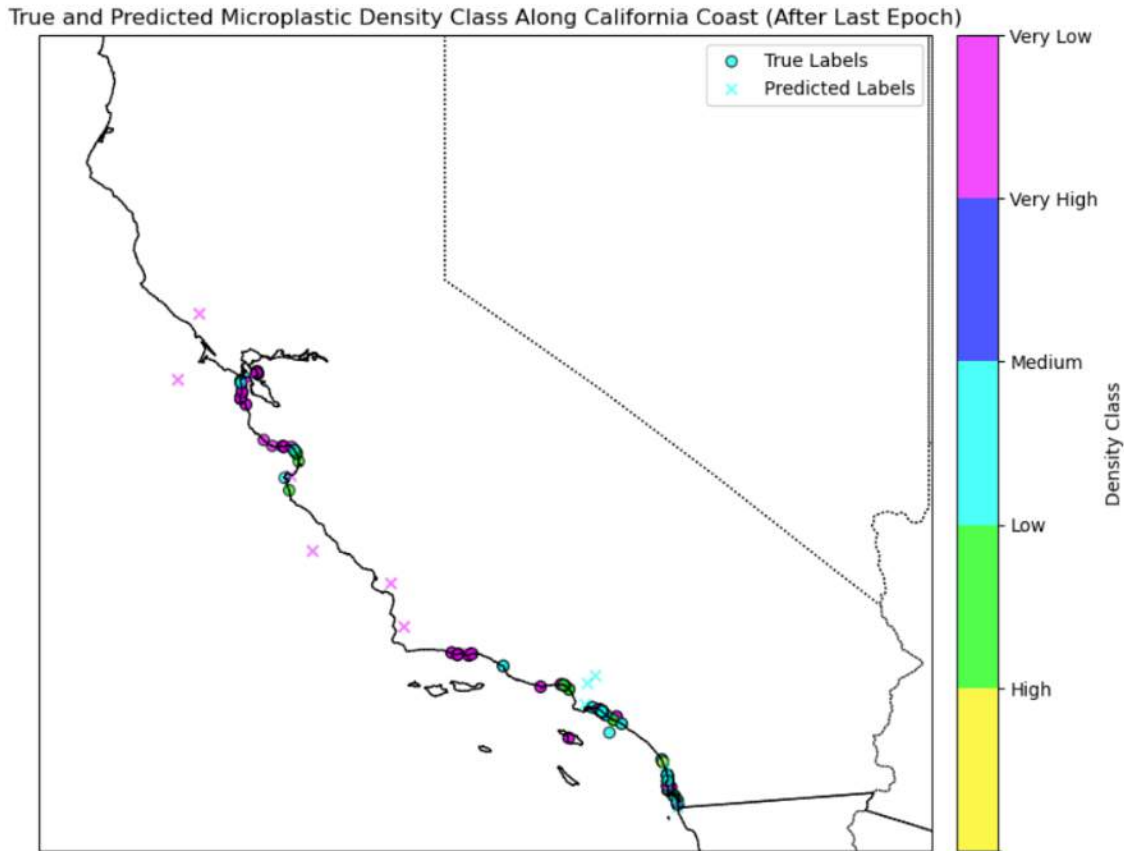rdle data only ran up to the Bay Area, so the points selected as tests also stayed within that range. The circular points are the data used to train the model, plotted by longitude and latitude and colored by density class. The predicted labels, marked by X's, are similarly plotted and colored. The cities used for predictions run along the coastline, including San Diego, La Jolla, Long Beach, Los Angeles, Pasadena, Santa Barbara, Lompoc, San Luis Obispo, Monterey, Salinas, San Francisco, Half Moon Bay, and Sonoma. Near Los Angeles, the X's are consistently light blue, matching with the majority of light blue circles surrounding them. On the other hand, the X's are magenta near San Francisco and above, which also matches the majority of magenta circles surrounding them. Between the two highly populated sections of the state, such as San Luis Obispo, the Xs are also magenta, and there is no supplemental data to affirm or deny the accuracy of the predictions. However, it makes sense that those areas would

be labeled as magenta, the color code for the density class very low, because the lower populations would logically lead to less microplastic pollution.

Discussion

It is possible to use AI algorithms to create useful models for various applications. In this case, a classification algorithm successfully predicted the density of microplastics in areas along the Pacific Coastline based solely on their longitude and latitude points. This information will be extremely useful in both preventative and restorative efforts. If a governing body or organization is looking for areas that are consistently outputting nurdles and microplastics into the ocean and neighboring bodies of water, they can employ the algorithm and test locations such as specific parts of major cities or places close to industrial factories. On the flip side, if the goal is to clean up microplastics already polluting the waters, the algorithm can be used to ensure efforts are not misdirected. For example, it would be much more effective to target areas with very high microplastic concentrations instead of unintentionally heading to areas with very low concentrations. Given the magnitude of microplastic pollution, it is crucial to focus resources in the areas where they will make the most significant impact rather than mindlessly diving into large-scale clean-ups.

Government policies and funding for studies like the Nurdle Patrol to encourage annual and uniform data collection of microplastic concentrations can also be beneficial from several fronts. The updated data can enhance the predictive model's performance and be a good benchmark to see if the situation is improving or worsening. Even when modeling only the Pacific Coast along California, there were significant gaps in the NOAA's data set—most of the collected data congregated around San Diego, Los Angeles, and San Francisco. The area between the latter two had close to no data points. Above San Francisco, there was only one data point to Oregon. These inconsistencies made it difficult to raise the model's accuracy above 80%. With a more standardized data collection strategy and government support, the path to solving microplastic pollution becomes much more possible.

With this said, just an algorithm is not nearly enough to solve this massive problem. Citizens, corporations, and government bodies must work together. To stop the continuous influx of new microplastics into the ocean, individuals and companies must be mindful of the materials they release daily. Small actions like recycling, using reusable water bottles and bags, and picking up trash can make a significant difference over time. Companies need to be regulated, especially those that continue releasing raw materials like nurdles from their factories, without considering the environmental consequences. More than anything, being conscious of the damage microplastics have on the ecosystem and humans is critical. Without this awareness, no action will be taken. Manufacturers must be held accountable for the harm they do when releasing, whether intentionally or unintentionally, nurdles and other plastics into the environment.

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Educational Inequality, Expectancy Value Theory and Academic Achievement
By Rosella Liu

Abstract

This literature review analyzes the relationship between educational inequality, student motivation, and academic achievement. It discusses different forms of educational inequalities: gender, race, and income inequalities. The subject of educational inequality has widely been discussed from the sociological and economic angle because it is an area that requires policy intervention. However, the purpose of this study is to examine it from a psychological perspective through the theoretical framework of expectancy-value theory (EVT). It has been found that EVT is linked strongly with academic success because students' intrinsic beliefs can affect the value attributed to a particular academic task, which in turn can affect their eventual performance. There are limited studies that examine how educational inequality can affect a student's success through the lens of motivational theories in education. This literature review will attempt to close this knowledge gap by establishing a relationship between educational inequality, student motivation, and academic achievement.

Key Words: Expectancy value theory, educational inequality, student motivation, academic achievement

Introduction

Outliers by Malcolm Gladwell was a very thought-provoking book that I recently had the chance to read. It is a book about the factors for success, explaining how even the seemingly smallest details, such as being born earlier in the year, can compound to affect an individual's success. A myriad of different factors come together to make people successful. For example, Bill Gates would not have been nearly as successful if he didn't have rich parents backing him. The fact that he had access to one of the very first computers at Lakeside, and subsequently used it for hours on end was because he was at the right place at the right time.

This book inspired me to start thinking about other factors of success and how they are applicable to the field of education. Many different factors can influence educational success, but a large part of it is the different inequalities students around the world face. Educational inequality is a global issue, and while different countries may experience it to different degrees, it exists everywhere. In fact, the United Nations (UN) is working to combat gender inequality and poverty in its 17 goals. This paper will try to analyze the links between educational inequality and adolescents' academic attainment, including insights into the practical implications of the expectancy-value theory. The paper will conclude with some recommendations for schools.

Methodology

To research this topic as in-depth as possible, I collected research papers from Google Scholar, using keywords such as "Educational Inequality", "Expectancy Value theory", "Gender inequality in Education" and "Racial inequality in Education". I then read the abstract to determine the relevance of the paper to the current study. If I determined the paper to be valuable, I analyzed it critically, paying close attention to key findings and conclusions. This paper is a literature review given limited resources for collecting empirical data.

After doing a broad search, I tried to narrow it down to the sphere of educational inequality in the United States (US). This was due to the fact that the US is the most relevant country-context to me as someone who has grown up in the American society and experienced the education system. This enabled me to support the theoretical standpoint of this paper with practical insights as a present-day adolescent and student in America. However, this paper includes some references to other countries, as educational inequality is a global issue. This paper will discuss the gender, income and racial inequality, and its relationship to academic attainment using EVT, as well as concluding with recommendations.

Gender Inequality in Education

Gender inequality is discrimination on the basis of sex. In the educational context, this can range from different cultural or social norms, but ultimately it is the different opportunities given based on gender. Historically, women have been subject to higher gender inequality, not having equal opportunity to pursue education the same way men have. The first schools opened in the United States were created for men, only allowing men to teach while women fell into the domestic worker roles. Historically, women have been subject to comparatively higher gender inequality; not having equal opportunities to pursue education the same way men have due to the strong patriarchal society engrained in American society. Even in modern times, fewer women make it to the top of the career ladder due to a lack of mentoring, lack of interest, and familial responsibilities in countries such as Nigeria (Ogbogu).

As American history progressed, many led the way for feminist movements, which eventually led to men and women having equal rights in the face of the government. However, some cultures have preserved the patriarchal structure. For example, in Nigeria, men are typically in jobs of higher positions and power due to the lack of opportunity and expected cultural roles of women, such as marriage (Ogbogu). As a result, women typically get jobs that are low paying, such as elementary school teachers (Kuchynka et al). Since some women today have restricted access to higher education as a result of historical traditions and practices, the different cultural norms influencing adolescent girls may result in them not attaching much value to education, possibly resulting in poor academic results in the future.

When discussing gender inequality, many papers I reviewed did not include theoretical frameworks. They focused more on the practicality and effects of gender inequality from an economic or cultural perspective.

Jacobs found that in the United States the gender gap was closing, and many women were found going to college after high school to receive their bachelors. However, women were

discovered to be underrepresented at elite colleges, compared to being slightly overpopulated at lower-ranking institutions. This was mainly because among the students enrolled in engineering, it was primarily male-dominated, and many women were enrolling part-time (Jacobs). Women are still underrepresented in competitive learning environments and have other responsibilities such as familial ones, which leads to part-time enrollment. This reinforces the idea that men have the responsibility to be educated for a job, especially in technical majors such as Engineering, while women are not competitive at the top level and take on college as a secondary responsibility. Hence, they are less likely to commit as much time and resources as men, further perpetuating the male dominance in "hard" jobs.

Although this disparity is decreasing, women today are still underrepresented in STEM fields historically dominated by men. Women make up roughly 35% of the STEM field, but the gap between men and women representation is much higher in Engineering and Computer Science (Deitz). The historical domination perpetuates the gender-STEM stereotype that men do more masculine work, even though data indicates that women exhibit stronger STEM performances than men (Kuchynka et al.).

However, there is also "hostile" and "benevolent" sexism present in learning environments, which justify stereotypical gender expectations. Benevolent sexism reflects the patronizing treatment of women but is damaging because it communicates that women are incompetent. (Kuchynka et al.). This is associated with longer-lasting physiological stress response and impairs cognitive performance (Kuchyka et al.).

Income Inequality in Education

Income inequality is the different resources and opportunities given based on income. It is a heavily studied topic due to the lasting effects it has on individuals' future outcomes and the prevalence of income inequality in the world. It is easier for families with more income to provide their children or wards with better education. For example, parents with more money are able to send their children to private schools, where a better quality of teaching and learning experience and resources for both the students and the teachers is more guaranteed than in public schools (Achinewhu-Nworgu). Teachers are incentivized to teach at schools where they are respected and valued. Schools with sufficient funding can pay teachers better, while schools with poor funding struggle to recruit highly qualified teachers, which in turn affects the quality of education students receive. Also, the degree of funding available to schools influences the quality of the curriculum. Some high schools in the US do not offer a more advanced curriculum (ie. AP, IB)[54], because they do not have the resources to do so.

Many underfunded US districts do not have the same financial resources as others. This can reflect in the degree of computer technology, software advancements, and the standard of school conditions and clubs. The most prevalent being computers—poorly funded schools may

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[54] AP stands for Advanced Placement. The AP Program offers college-level courses and exams that students can take in high school (College Board). IB stands for International Baccalaureate. "The International Baccalaureate (IB) is a global leader in international education - developing inquiring, knowledgeable, confident, and caring young people. IB programmes empower school-aged students to take ownership in their own learning and help them develop future-ready skills to make a difference and thrive in a world that changes fast" (IBO).

not have access to a lot of computers, especially one-to-one technology. In the age of digital technology, many teachers choose to post their curriculum online for ease of access and a centralized system. Computers offer many benefits, such as easily accessing information online. Still, some students cannot access the internet at home or on a personal device, and underfunded schools struggle to bridge this digital gap by providing access, hindering educational quality and equality.

On the other hand, wealthy families have better resources to provide their children with access to computers, private tutors, counselors, and high-end schools. These resources culminate and can elevate a student's academic performance and future path to success.

The COVID-19 highlighted digital disparity based on income inequality. For example, in Pakistan, the majority of students are enrolled in public schools (Ullah et al.). When Covid hit, and all schools were closed, many students enrolled in public schools were unable to continue learning. However, richer kids enrolled in private schools were able to do online learning, while many of their less advantaged peers did not learn at all. Instead, they were either mostly playing or helping their families with agricultural work (Ullah et al.).

Poverty sometimes serves as an obstacle to achieving personal success. In addition, children and adolescents living in poverty are often delayed in their cognitive, language, and social-emotional growth (Dearing). Early developmental growths contribute to crime or poor mental health across life (Dearing). Adolescents who grow up poor tend to externalize their internal problems and display them in forms of aggression, destructive behavior, and hyperactivity. They also have a harder time socializing with peers and adults (Dearing 2008). Although this does not necessarily result in an unsuccessful life, it shows that those who grow up impoverished struggle to build healthy relationships, but rather develop a strain on their mental health. In addition, poverty leads to parental mental health issues and influences a child's social-emotional functioning (Dearing). Consequently, poverty acts as a direct factor in disadvantaging those with underdeveloped childhoods, as they must work harder to thrive in society.

Racial Inequality in Education

Historically, America has been a very unequal society; segregation did not end until 1964. Although the Civil Rights Act legally ended discrimination on all accounts, the lasting effects are still prevalent.

Koenig et al. conducted a study in the greater Chicago area. Surveyors randomly asked people who appeared at least 18 years old to answer a short questionnaire. It was found in student samples (from Midwestern University) that Black women were perceived as occupying jobs that were low in competence, such as food service or cleaning service workers, while more STEM jobs were perceived as more common for Asian or Arab women (Kuchynka et al.). The high occurrence of Black women in "low competency" jobs perpetuates the stereotypes and reinforces the racial and gender inequality in society.

Due to historical and systemic racism, income inequality is a notable issue in the United States. White parents typically have higher-paying jobs and more education than Black parents (Gamoran). The disparities in parents' income and education status between racial groups can cross over to children's learning opportunities. A major instance of this is exemplified by summertime learning. Studies that examined test scores in the fall and spring found that most differences between Black and White students lie in the summer (Gamoran). While White students continue to improve, Black students typically do not. However, during the school year, they showed similar rates of improvement (Gamoran). No race is inherently better at learning than another, but rather have different accessible opportunities. Racial inequality can also manifest itself in the classroom. Teachers may have either an unconscious or conscious bias in terms of race or gender, which shapes their expectations of the children they teach.

Fig 1: Proposed theoretical model showing the effects of social inequality dimensions in education
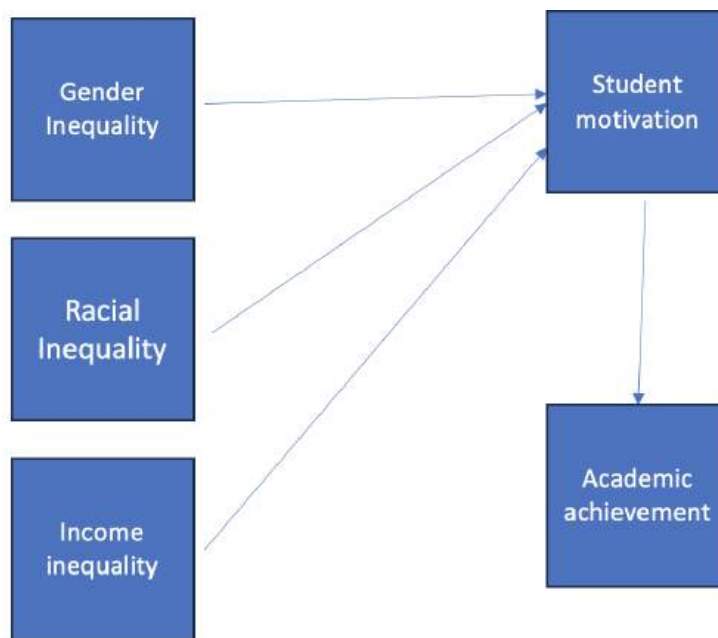
Linking Educational Inequality, Expectancy Value Theory, and Academic Achievement

EVT proposes that a child's effort and performance on an upcoming task is dependent on their beliefs about how well they will perform and the value they place on the task. For instance, if a child has negative beliefs toward math and positive feelings toward English, they will place significantly more value on math compared to English, thus shifting their effort. This value will dictate their future class choices and further education (Wigfield). If a student believes themselves to be poor at math, they are likely to either avoid it or take the easiest math courses. Inevitably, students with these mindsets almost never challenge themselves to improve on the neglected subject.

In particular, gender-STEM stereotypes reinforce the idea that boys are naturally more talented in STEM than girls, who are expected to not do as well as boys in STEM. If a girl does better in STEM, it is usually attributed to external factors such as working hard, while if boys do well in STEM it is attributed to natural gifts (Kuchynka et al.). As a result, women are less likely to pursue STEM courses because they believe they cannot do well unless they work very hard, for they lack the "natural gifts" men hold. In addition, adolescents from ethnic minority groups often face a double standard, as working hard is seen as a threat, while not working hard enough is seen as being lazy or incompetent. This leads to the increased stress of failure when taking math tests (Kuchynka et al.) and reduces their own motivation to keep persisting when the pressure worsens.

Eccles et al. showed that even as early as first grade, children have their own different perceptions of their competency in different tasks and, subsequently, success. The study found that as their age increased, so did their pessimism about different academic abilities (Eccles et al. 1994). In addition, boys valued their competence higher for math and sports, while girls valued their competence higher for music (Eccles et al.). This furthers the stereotype of boys being good in relatively difficult and physical subjects while girls are good in the sphere of domesticity—the more liberal arts and not the science subjects. If girls do not place much value on STEM, or they believe not being competent enough, it can result in poor academic achievement in that area (Kuchynka et al.).

A student with a poor socioeconomic background will likely not place as much value on their education compared to a child from a wealthy background due to their decreased motivation from the numerous factors against them. In the case of some cultures valuing marriage over education, a child is likely not to be motivated to do well in school if they believe that higher education or working is not in their future. Naturally, they will put less value on it. This means they will be unlikely to pursue it further because they do not value it as highly.

In general, people who grow up impoverished or less empowered to aspire have to create opportunities and motivation to succeed, working much harder in order to close the gap. Socioeconomic status is not absolute, but it provides much-needed resources for an individual's development. When adolescents don't take advantage of those resources, it is sometimes because they don't trust that education will make them successful. The knowledge and awareness of how students' motivational beliefs affect their behavior towards educational tasks is vital for better effectiveness of policies aimed at improving students' academic achievement. Economic and sociological interpretations of educational inequality are helpful but do not provide the full picture. Understanding the psychological implications of educational inequality is equally important because it helps to *explain* the predictors and consequences of students' expectancy beliefs on their academic success.

Recommendations for Schools and Educators

It is crucial to look at a student holistically, and not just categorize them as low or high achievers to determine their future success. Education stakeholders must take into consideration

how background experiences can shape academic performance and identity. They also need to try and resolve any existing social factors, like gender stereotypes, that restrict a child from performing at their best. It is, as such, not realistic to hold students to a standard while isolating them from their social context.

Motivation comes from both internal and external sources. For example, some students may be motivated by good grades or parents, while others may be motivated by their own internal aspirations and self-worth. It is important to support students while giving them a sense of control. There needs to be a balance between emphasizing students' personal responsibility and extending academic support. Helping students set achievable goals for themselves and taking the time to understand and provide support for a child is important to their development. It is not necessarily the teacher's job to be a therapist for a student, but if schools can provide resources, it may help alleviate anxiety among adolescents.

De-emphasizing grades is crucial because many students feel the stress of grades, even more so when they do not receive a good grade. Teachers should build incentives while emphasizing the relevance of knowledge and not just good grades. This is why grade recovery can be valuable, because having the pressure to do well the first time leads to other issues, like academic dishonesty. If students are pressured to get an A on an exam, perhaps from their environmental factors, such as their parents or friends, then it can lead to cheating. This may lead to a dangerous cycle of consistent cheating because not getting caught consequently reinforces the idea that cheating is acceptable, losing guilt and relying on others for knowledge. Academic competition drives academic dishonesty. A study found that perceptions of academic competitiveness raised the probability of anxiety by 70% and depression by 40% (Ou et al. 2023).

A way to alleviate academic pressure is through meditation. Studies have found that meditating helps alleviate anxiety as well as improve executive functioning, ie self-awareness (Spitzer et al.). Implementation of "Quiet Time", where students spend 15 minutes at the beginning and end of the day meditating in Visitacion Valley Middle School, led to dramatic drops in suspension and increases in academic achievement (Spitzer et al.). In general, "Quiet Time" induced a more peaceful environment. Meditation can be used to calm the mind and perform better in school.

Investments in education should be supported with job creation. Schools should ensure that they help students develop the practical skills needed to boost their chances for employment. For example, by providing good career advice and support in school. While more education usually corresponds to better pay, due to uncertain job prospects, newer generations are considerably wary of investing in longer periods of learning. Many older people are in jobs they are overqualified for, but the cycle of costly higher education and uncertain future prospects continues (Green et al.). In the UK, many older generations are working in occupational-specific jobs (Green et al.). Since it is harder to fire older workers due to their experience and knowledge, a large number of youth are unable to take up jobs they are qualified for leading to them working

for less pay. Thus, uncertainty for the future has caused a significant decrease in spending for education.

I believe it is important for educators to keep encouraging students because while everybody has the ability to succeed, some lose hope. It may seem that a student is lagging behind because they keep failing, but on the other end, it is very easy to become discouraged after getting a bad test result or grade. This does not mean that they are doomed to fail or are not smart; a little encouragement and acknowledging students' broader social contexts and experiences can go a long way.

Conclusion

Educational inequality has been reduced throughout the years but is still widely prevalent today in different forms. Many different factors can be attributed to academic success, but I suggest that there is a need for further research and studies investigating the impact of students' backgrounds on their academic achievement based on the expectancy-value theory. Expectancy theory is not highly researched in the sphere of educational inequality. Constant motivation is difficult to attain on a daily basis due to uncontrollable inequalities such as gender. Also, some people find it harder than others to keep persisting. Expectancy-value emphasizes the consideration of how we encourage students to get up every day and persevere.

There are many issues regarding the quality of teaching in schools, and that is not easy to change. But there should be standards for teachers to reach and schools to achieve. Adequate funding should also be prioritized to help more impoverished districts. The position of this paper is that every young person deserves to have a quality education despite their background. Even though individual determination plays a role in one's success, students should have access to equal opportunity that gives them a fighting chance.

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Breast Cancer Tumor Identification Using Deep Learning By Daniel Xu

Abstract/Summary

According to the NIH, Histopathology reports are time consuming and tedious since they have a high average Turn Around Time (TAT). Analytical TAT is around 3.6 ± 2 days and most reports have a TAT of around 5 working days (Atanda et al., 2017). With the advancement of digitalization of modern medicine, implementations of Artificial Intelligence (AI) in the application domain of Histopathology could potentially assist doctors in the process of generating the diagnostic reports. There have been numerous papers in past literature that explore the application of AI in Histopathology. For example, in *"Rotation Equivariant CNNs for Digital Pathology"*, a variant of a Convolutional Neural Network (CNN) architecture was used to identify locations where cancerous cells may be (Veeling et al., 2018). In this research, I used a 19 layer VGG (Visual Geometry Group) CNN model to create an image recognition algorithm that classifies whether or not an image given to it contains cancerous cells. This research could potentially help histopathologists in their work by making their work more efficient and less time consuming.

Introduction

Histopathology is the term for visually recognizing tissues that are cancerous from whole slide images and characterizing the nature of the tissue. Histology images in comparison to radiology images have a higher magnification which allows doctors to examine the patients' samples at a tissue level. Traditionally, these complicated diagnoses were done using the help of chemical stains of H&E staining (He et al., 2012), which stains the tissues and cells into a color that's easier for the human eye to identify cancerous tissue. These stains make the cells a deeper color and thus enhance their details(NIH Dictionary of Cancer Terms). However, it is a time-consuming and tedious process for the doctors to go through each and every image, zooming in and out, to see if a tissue is cancerous. The purpose of this project is in hopes of using AI and computer vision to help speed up the doctor's processes in cancer diagnostics, providing results to the patients sooner and relieving part of the load for the doctors.

Computer Vision is a form of AI that enables the computer to see, observe, and improve (Raval, Prateek. 2018). It's generally used to tell one object apart from another, which in this case, is to distinguish normal tissues from cancerous tissues. Through massive amounts of data, the algorithm can learn to differentiate between these two types of images. In our case, we're going to use a CNN trained through backpropagation, which is a self-adjusting mathematical algorithm that will adjust the weights of different nodes in the CNN layers to produce a better classifier to predict the class of each image.

In the past, there has been research done by other researchers in this field of medical science where there were CNN Computer Vision models that were made for applications in histopathology. In 2017, for instance, in the research paper "Diagnostic Assessment of Deep Learning Algorithms for Detection of Lymph Node Metastases in Women With Breast Cancer"

(Ehteshami et al., 2017). Here, machine learning was used for Lymph Node detection in a slide image for breast cancer. In another study, "Rotation Equivariant CNNs for Digital Pathology"(Veeling, Bastiaan S., et al., 2018) researchers elaborated on how as the medical field becomes increasingly more digitized, and modernized, an implementation of AI trained for accurate histopathology using slide images could be beneficial to not only the doctors but perhaps also the public. The authors train a better performing AI algorithm through methods using a Rotational Group CNN, by modifying images through rotation and flipping, as well as combining results from different CNN groups and creating a deeper convolution layer to achieve a more accurate result.

In this study, we aim to create a CNN model to achieve a relatively high accuracy in classifying tissue sample images as containing cancer cells or not. This will be achieved using a multi-layer CNN visual recognition network.

3. Methods

Data set and Data Processing

The dataset that was used for this project is from the Kaggle database, originally from a research project in breast cancer from the CAMELYON16 database, for a competition(originally 399 slide images from 399 patients), which the images are then cropped for this set of training data. The data set from Kaggle that came from Camelyon-16 was cropped into smaller pieces and became 220K+ stained colored slide images in the training data and around 56K+ in the testing data. The images were stained through H&E staining, which is a commonly used staining method in cancer research.

All of the data are image-based data stored in ".tif" format and the testing folder contains an Excel file containing all the correct labels which tells us which of the specific slide images contains at least 1 pixel of cancer cells and which one is free of cancer cells. Through a basic algorithm, I converted all of these images into numerical data by taking the average RGB values of all of these images and plotting them on 3 separate graphs, red vs blue, red vs green, and green vs blue. We then used the graphs to see if there were any correlations between the positive slide images and the negative slide images and how their color data appears on plotted graphs. Because if there is a certain pattern, the algorithm for finding the cancerous cells could become simplified.

In the Exploratory Data Analysis, we first created a library that associated each image with their given label from the CSV file in the training dataset: Class 1 (images that are positive for cancer cells presence), and Class 0 (images that are negative for cancer cells presence). This allows us to pull out an image and link the image with what label this image is, enabling us to analyze what's the difference between the 2 classes of images. We then wrote an algorithm that'll link each image with their average RGB data to see if there's any difference between Class 1 and Class 0. This was an attempt to see if a classifier can be made with a simpler algorithm that doesn't involve a multi-layer Machine Learning network. The comparison is: Red vs Blue; Red
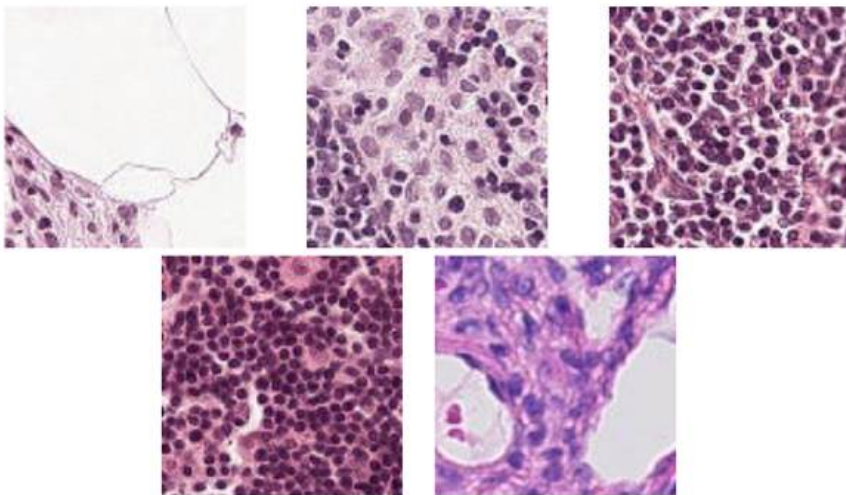
vs Green; and Green vs Blue.

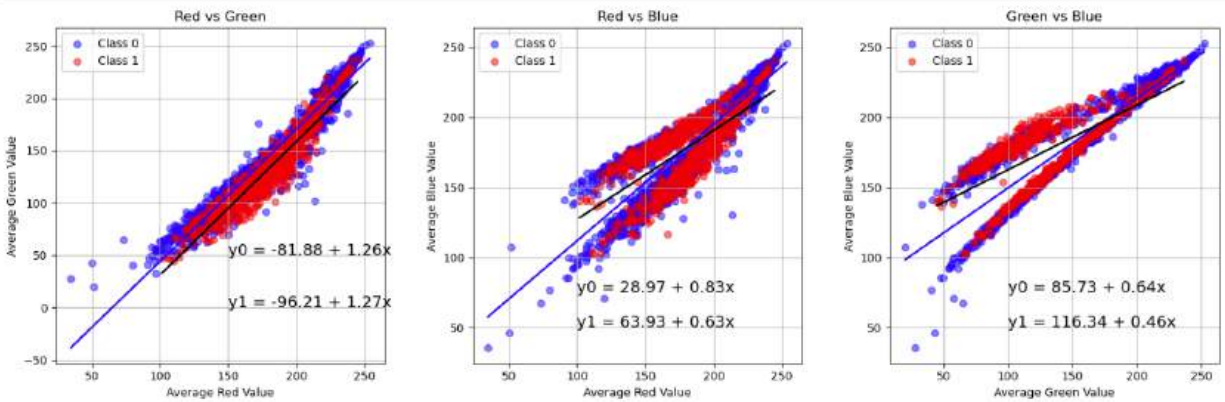Here's the Class 1 sample images:
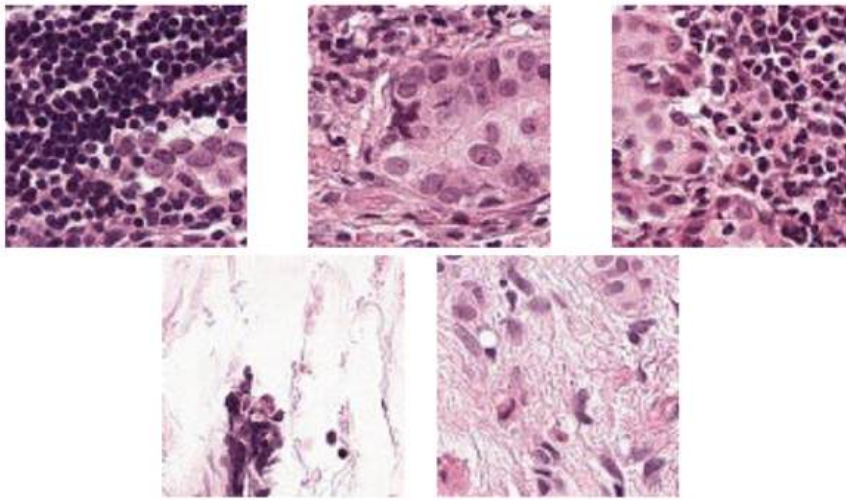
Data Sample Picture (With Cancerous Cells, Class 1)

And here's the Class 0 sample images:

Data Sample Picture (Without Cancerous Cells, Class 0)

Here's the Plot of the Class 1 vs Class 0 images (y0 = line of best fit for Class 0) (y1 = line of best fit for class 1):

Red vs Green	Red vs Blue	Green vs Blue
y0 = -81.88 + 1.26x	y0 = 28.97 + 0.83x	y0 = 85.73 + 0.64x
y1 = -96.21 + 1.27x	y1 = 63.93 + 0.63x	y1 = 116.34 + 0.46x

First, I analyzed the graph and plotted the line of best fit for each of the graphs, as well as found the mean and standard deviation for each graph. A need for a more complicated algorithm is introduced because as you can see, the difference between Class 0 and Class 1 images are almost indistinguishable, and the line of best fit shows us that. We've concluded that a more sophisticated algorithm is needed for the identification between Class 1, and Class 0. In our case, we resorted to using a Deep Learning computer vision algorithm to learn and later classify whether or not an image has a cancer cell within the sample image.

AI Model

At first, I was using a shallow 4-layer CNN model, which consists of 2 convolutional layers, one which has a 2x2 filter and a stride of 2; a ReLu (Rectified Linear Unit) layer; and a softmax output classifier layer. It's a simple model for adjusting and for the beginning should do the job of recognizing cancer cells within a slide image. I chose this model due to the simplistic and stable structure this training method provides, we then will determine if any more complicated models are necessary. I used Pytorch's back-propagation algorithm for the CNN training model. And used data downloaded from a Kaggle dataset of the Digital Vision regarding Histopathology, titled "Histopathologic Cancer Detection".

My current code is based on an existing data structure from Kaggle made by Naveen Kumar Ravella (Owner), Abdul Wahab Syed (Editor), and Dakshender Peddapalli (Editor). I altered their code by incorporating Accelerated Linear Algebra as well as changing the data induction channel to better fit my needs. I also changed the learning rate as well as the batch size to utilize more of my computer's memory, and I wanted to experiment with different learning rates to see if results were changing for the better or worse. I also attempted to make this code compatible with my GPU. Unfortunately the CUDA driver supported is out of date with my computer's current CUDA driver and therefore can't be utilized.

Later I decided that a more complicated model is indeed necessary to run this task of classification, so I resorted to using the VGG19 model which consists of Convolutional layers, which is a 3x3 filter with a stride of 1 and padding of 1 to preserve resolution; Activation Function, ReLu is applied after each convolutional layer to introduce non-linearity; Pooling Layers, Max pooling with a 2x2 filter with a stride of 2 to reduce spatial dimension; Fully

Connected Layers, 3 fully connected layer for classification purposes at the end; and Softmax Layers, which gives us the output of the possibilities for the classes.

Here's a diagram for what I had just described:
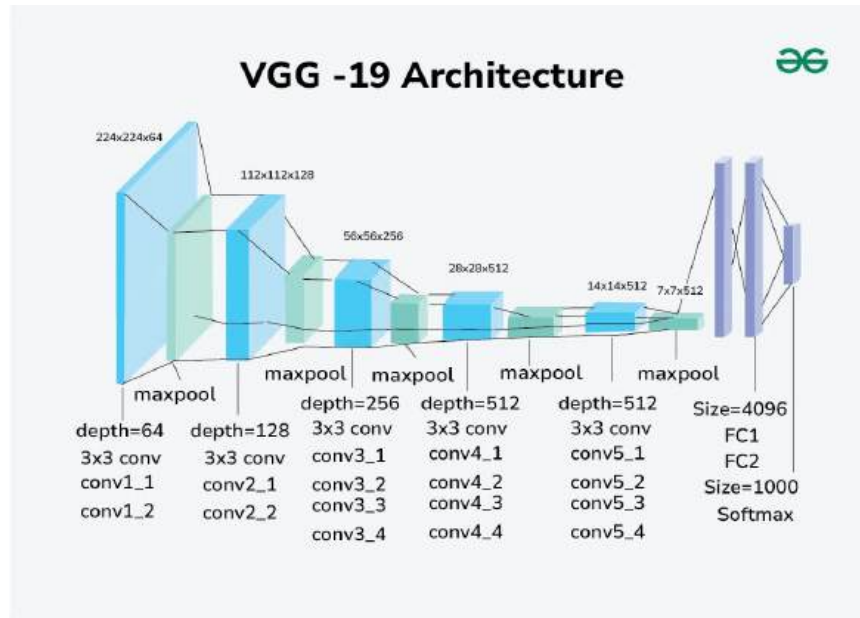
<p align="center">(Geeks for geeks)</p>

This model is more mature and stable in comparison to my model, which only contains 2 convolutional layers, 1 ReLU layer, and 1 softmax classifier layer. However, this model does take up a lot of processing power as even with an Intel i9, with 100% of the CPU being used, the steps were still around 1 second, and it takes around 5 hours to go through 10 epochs of 2750 steps. If there is a GPU involved the results could potentially be achieved faster.

While making this model, I also decided to use accelerated linear algebra to optimize the data movement, and to use parallel processing, using all the cores in my CPU (CPU usage up to 100%).

However, due to TensorFlow only supporting up to CUDA 11.2, I unfortunately wasn't able to use my GPU in this specific example. In the future, I potentially would use a CNN structure sustained by more recent software and GPU drivers available and then there can be better calculations and data usage to achieve the result.

4. Results
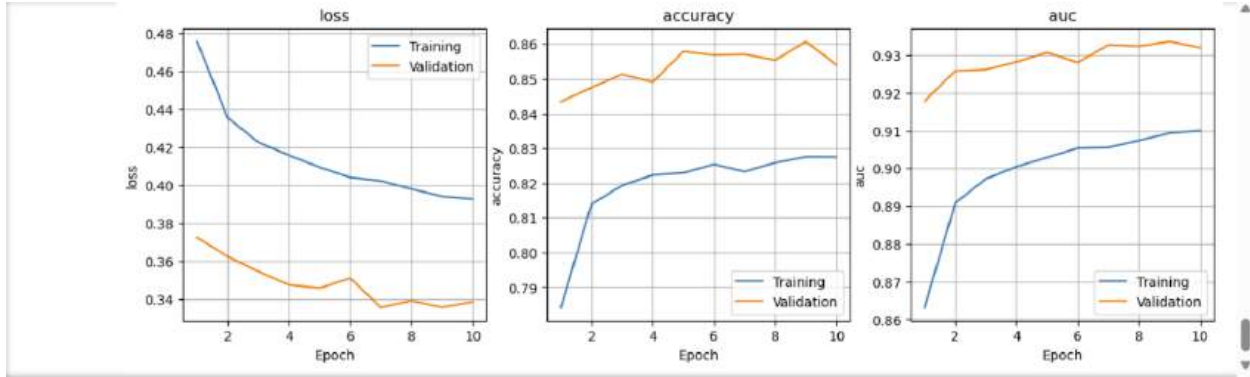
(EPOCH 10 RESULT: loss: 0.3926 - accuracy: 0.8275 - auc: 0.9100 - val_loss: 0.3383 - val_accuracy: 0.8540 - val_auc: 0.9320)

This was run on a VGG-19 model which consists of 19 layers – 3 fully connected layers and 16 convolutional layers, as I described in the methods section above.

What I found interesting in this graph is that the training data group has a lower accuracy and loss rate in comparison to the validation group, which usually is the other way around. In the end, we were able to achieve an accuracy of ~83% in training and ~85% in the validation set; an AUC value of 91% in training and ~93% in validation; and a loss rate of ~39% in training and ~33% in validation.

The result was achieved with 10 epochs of the dataset with access to all images from the Kaggle database. With Google Charts we can find that the line of best fit of logarithm for accuracy would be the equation of

f(epoch) = 0.795 + 0.0159 ln(epoch)

Which if we sample an (epoch) value from f(20) we'd get 84.26%.

If we calculate the line of best fit for Validation accuracy and make a prediction according to the equation

f(epoch) = 0.8436 + 0.0064×ln(Epoch)

We can get a prediction for f(20) for 86.28% for validation accuracy. However, this is just a prediction according to the logarithmic line of best fit, and the actual results of 20 epochs for the model may vary.

5. Discussion

As I mentioned in the results, with enough time and energy spent on a CNN model there may be a viable solution to the slow processing of histopathology image slides, which may shorten the time of patient getting results, as well as ease up the work for the doctors working within the field of histopathology.

The data from the resulting models support my hypothesis of the possibility of the introduction of AI in Histopathology. My findings would be consistent with other research papers concerning this similar topic. For instance, "Diagnostic Assessment of Deep Learning

Algorithms for Detection of Lymph Node Metastases in Women With Breast Cancer"(Ehteshami, et al., 2017) showed similar results in their algorithmic parts of the results.

The limitations that I've encountered include the lack of resources available for me to run this model through more epochs, as well as the limitation of my inexperience in AI programming that may have hindered my process in creating this model. I believe this experience refreshed my knowledge of what can be achieved by computer vision and machine learning.

In the future, if I have time, I may experiment with different CNN models and architecture to see if a different model could achieve a better result in perhaps a shorter time. In the future, I'd also like to use a newer GPU programming driver that'll allow me to utilize my GPU when training it, which would speed up the process significantly and would allow me to train a more accurate model to identify the different classes because there can be more epochs trained within the same amount of time.

If there is enough time or resources there could even be a model that's trained to not only determine a slide image to be positive or negative with cancer cells, but perhaps can be implemented with another model that can also identify the different types of cancerous tissues and even produce an output of suggestions of possible diagnoses, as well as the location of the site.

6. Conclusion

In conclusion, there was a successful and running CNN model with a relatively high accuracy in identifying cancer cells' existence in different images. This can be used in a hospital or a lab for researchers or doctors to quicken their process of finding cancer cells within an image by giving them suggestions of which slide images may contain cancerous tissues. This can increase the efficiency of the cancer diagnosis process and can speed up the turnover time for the patients to receive a report. With further research, this model can potentially do a lot more than just saying if it has cancer cells within a tissue or not. In the future, I'd imagine this technology to be used more conventionally as it can speed up the process of cancer diagnosis massively and perhaps earn more time for the patients than the current conventional methods does.

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Accurate News Reporting Is a Public Good. Does It Follow That News Agencies Should be Funded from Taxation? By Fay Ma

ABSTRACT

This essay argues that accurate news reporting is a public good requiring government intervention, particularly through tax-funded support for news agencies. It explores how such funding can address market failures in news provision and reduce information inequality. The paper examines the characteristics of news as a public good, the economic rationale for government intervention, and the potential benefits of subsidizing news agencies. However, it also acknowledges concerns such as the risk of censorship, opportunity costs, and policy conflicts associated with tax-based funding. The essay suggests that a combination of approaches, including tax incentives and innovative business models like non-profit journalism, may be necessary to sustainably support accurate news reporting. It concludes by emphasizing the need for adaptive policies in the face of evolving technological challenges, such as the impact of artificial intelligence on information accuracy and verifiability.

Introduction

The insidious spread of misinformation on social media platforms appeared as a threat to the public in various aspects. According to one of the World Health Organization's reports, inaccurate information surrounding COVID-19 led to the "infodemic" problem, which posed significant risks of hampering effective pandemic response efforts. Similarly, the integrity of democratic elections has been compromised by the proliferation of false information, notably during the 2016 U.S. presidential election where fake news potentially influenced voter perceptions and decisions(Allcott & Gentzkow, 2017). Amidst this backdrop, the role of accurate news reporting became more apparent than ever(Managing the COVID-19 Infodemic: Promoting Healthy Behaviours and Mitigating the Harm from Misinformation and Disinformation, n.d.).

Thesis statement

This essay argues that accurate news reporting is a public good that requires government intervention. Allocating tax revenue to support news agencies is beneficial beyond solving market failures. Yet using tax money should not be the sole method due to various limitations.

Accurate news as a public good

Public goods are both non-excludable and non-rival in consumption. It is not possible to prevent consumption of the good by people who do not pay for it and more than one person can consume the same unit of the good at the same time without diminishing benefits(Ray et al., n.d.). Accurate news reports arguably can have these characteristics. Information spreads rapidly through social media and word-of-mouth, making it hard to restrict access(Yochai Benkler, 2006). Even if news is behind a paywall, summaries or key points often become available through other channels. Moreover, public spaces like libraries often provide free access to new

sources, further reducing excludability. In terms of non-rivalry, especially in the digital era, news can be accessed simultaneously by countless users without degradation (Hal R. Varian, 1998).

Analysis of the taxation funding method

Since the free markets fail to provide public goods, it is rational for the government to intervene in the news industry. Due to its non-excludability, news agencies struggle to prevent non-payers from accessing information once it's published, leading to a free-rider problem where individuals benefit without contributing (James T. Hamilton, 2006). This situation creates a lack of profit for news organizations, as people prefer others to pay for the service (Kaye & Stephen, 2010). Even if some media has some subscription fees to exclude others, it is still hard to prevent the spread of information to non-payers so that free riders still exist. As a result, the free market tends to under-provide or not provide accurate news due to insufficient financial incentives (McChesney & Nichols, 2010). The resulting scarcity of reliable information creates a vacuum often filled with misinformation and fake news and continues to harm the economy and society as mentioned in the beginning of this essay.

However, market failure is not the sole reason for government interventions, using tax revenue to fund accurate news agencies can play a crucial role in reducing inequality since the dissemination of accurate news may only reach a portion of the population.

Theoretically, subsidies for news agencies will lower the cost of production and shift the supply curve of news to the right, increasing the equilibrium quantity and reducing the price as we can see from Figure 1(Subsidies, 2020). This improves broader access to accurate news in society which helps to reduce inequality.
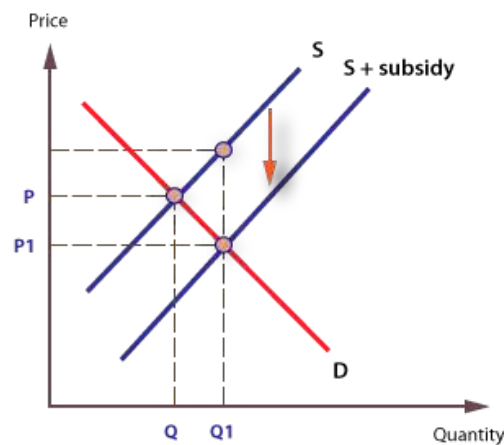

Figure 1. market of accurate news with government funding

For instance, accurate weather forecasts are crucial for small-scale farmers to make decisions about planting and harvesting their crops in rural India (energy policy institute at the university of Chicago, 2024). On days with extreme weather like flood and heat stress, poor rural households lose 2.4% of their on-farm incomes, 1.1% of the value of their crops, and 1.5% of their off-farm income compared to non-poor households in India and 23 other low-and-middle-income-countries without accurate weather information. However, India's main weather forecast company, Skymet Weather Services, is privately held (Traxn, 2024). According to the India Internet 2019 report, while internet usage with the supply of accurate news and weather forecasts in urban India was 97%, it was only 25% in rural areas (Has Digital Illiteracy, Particularly in Rural Areas, Coupled with Lack Of Information And Communication Technology (ICT) Accessibility Hindered Socio-Economic Development? Examine With Justification. (150 Words, 10 Marks) - PWOnlyIAS, n.d.). If the subsidy from the government can be implemented, the rural-urban gap can be narrowed.

Besides, tax-funded news agencies can prioritize coverage of issues affecting marginalized communities, which are often overlooked by commercial media (Rodney, 2018). Commercial media outlets are primarily motivated by profit, which can lead to prioritizing content that attracts the largest audience or the most lucrative revenue, resulting in catering to mainstream interests (Elia & Magda, 2016). For instance, government-funded media BBC is allowed to allocate resources to stories and perspectives that are crucial for public understanding and representation of marginalized groups due to public funding, reflecting its character of "reflect, represent and serve the diverse communities of all of the United Kingdom's nations and regions." (BBC Mid-Term Review 2024, n.d.). In particular, there are also attempts to reduce gender inequality by increasing the appearance of female characters in the news. There is a "100 Women" initiative that focuses on the experiences and challenges faced by women around the world, especially in marginalized groups.

Despite all these justifications, one of the biggest concerns with government interventions in news is censorship which brings negative economic consequences. Some critics' concern is that financial reliance on the state may create pressure for news organizations to avoid criticizing government policies or investigating political corruption. Weder (2003) found that press freedom's one standard deviation improvement could help to lower corruption between 0.4 and 0.9 points (on the 0 to 6 scale), indicating a strong negative correlation between press freedom and corruption levels across countries (Brunetti & Weder, 2003). Corruption increases income inequality and poverty through lower economic growth. According to research that investigated the impact of corruption on poverty done by Gupta, an increase in the growth rate of corruption by one standard deviation (a 0.78 percentage point decrease) is correlated to a 1.6 percentage point decrease in annual income growth for the poorest 20% of the population. This shows that higher growth in corruption is associated with lower income growth of the poor, accompanied by higher education inequality and lower real per capita GDP (Sanjeev Gupta et al., 2002).

However, there is no solid evidence that government subsidy on media in a well-functioning democracy can lead to corrupted media. Instead, some argue that government

subsidies can enhance journalistic independence by reducing their reliance on commercial interests and advertising revenue. This allows news organizations to focus on in-depth reporting and cover important, less profitable topics (Nielsen, R & Linnebank, G, 2011). Finland provides a strong example of how public funding can enhance journalistic independence. Yleisradio, which is the country's main broadcaster, is primarily funded through a dedicated tax, which accounts for about 80% of its budget in 2021(Financial Figures 2021, n.d.). The utilization of this funding strategy has enabled Yleisradio to maintain exceptional journalism quality without becoming overly dependent on advertising income. Therefore, Finland consistently ranks among the top countries in the World Press Freedom Index, winning the 5th position in 2023 and 2024(Finland | RSF, 2024).

Yet, making government subsidy from tax money the sole method can face serious opportunity costs. Diverting funds to media could detract from other high-priority areas that directly impact economic and social well-being, such as publicly subsidized economic development and municipal projects in developing countries. For developing countries such as Nigeria, its budget was approximately 35 trillion naira in 2021, with only about 24% allocated to infrastructure development (YourBudgIT, 2021). In this tight budgetary environment, key development initiatives like the Lagos-Ibadan railway project are already facing financial pressures. Meanwhile, establishing an effective public broadcasting system is estimated to require at least $500 million in annual investment (businessofnews, 2023). Diverting tax revenue to support media organizations could severely impact the funding available for these crucial infrastructure projects, hurting long-run economic growth.

Although the government can increase taxes to increase its budget, such a policy could lead to policy conflicts. Higher direct taxes reduce disposable income, which in turn can decrease citizens' overall consumption and investment, leading to a leftward shift in the aggregate demand curve (Figure 2) (Ray et al., n.d.). The result will be a lower GDP and higher cyclical unemployment. If the tax revenue is raised from indirect tax, this leads to an increase in
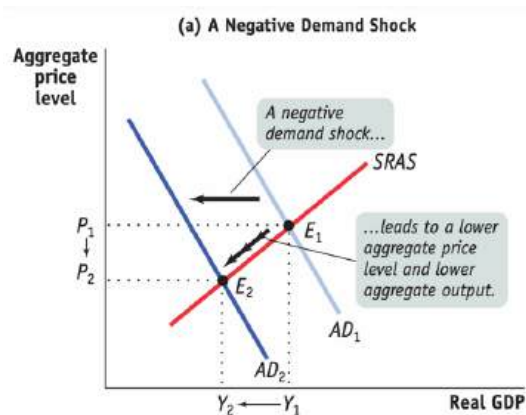
inequality due to its regressive nature.

Figure 2. A negative demand shock of accurate news after funding with tax

For instance, in 2023, the annual budget for the BBC was approximately £600 million, and the majority of this came from license fees (around £3,740 million) which is regressive (BBC Group Annual Report and Accounts 2022/23, n.d.). Moreover, in the long run, the negative impact on the economy may reduce the consumption of accurate news. As disposable income decreases, individuals may cut back on subscriptions to quality news sources or reduce their consumption of paid news content, thus decreasing the demand for accurate news. Lower demand for news can result in reduced revenue for news agencies, potentially leading to budget cuts, layoffs, and a decrease in the quality and quantity of news production potentially leading to more inaccurate but profitable news coverage (Blanchard & Sheen, 2013).

What is worse, this funding model may not be sustainable. According to the Laffer Curve model (Figure 3) (Ray et al., n.d.). increasing taxes over an optimal point can lead to decreased government revenue due to decreases in economic activities, making funding more and more difficult.
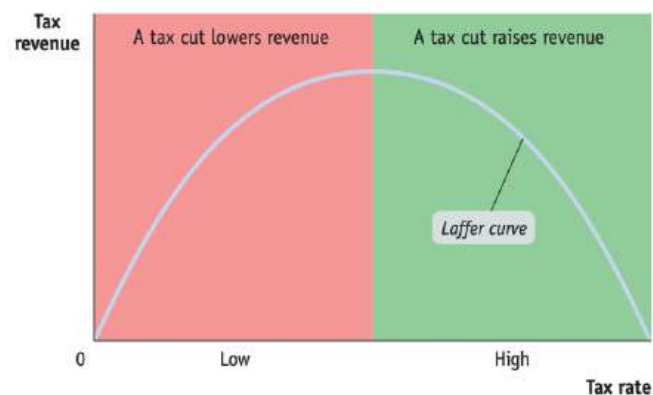
Figure 3. Laffer Curve model

Discussion

Therefore, alternative methods such as tax incentives and innovative business models may be combined to subsidize news agencies.

Sales tax reliefs of accurate news can be an alternative support for news. Newspapers in many countries receive sales tax relief, which is now transitioning towards digital news subscriptions. In 2020, the United Kingdom's government budget eliminated the sales tax on e-books and digital print subscriptions. The Local Journalism Sustainability Act, filed in Congress in 2021, is a proposed bill in the United States that would let individuals receive an income tax credit of up to $250 for subscribing to a local newspaper. The bill also provides payroll tax credits to local newspapers to cover journalist salaries, all avoiding problems of policy conflicts (UNESCO, 2022).

Another way to support accurate news is using the non-profit model, which relies on philanthropic support, and membership contributions to support and maintain the accuracy of news while ensuring economic sustainability, reducing opportunity cost, and preventing

censorship. The success of ProPublica, a Pulitzer Prize-winning investigative newsroom, demonstrates the viability of this model (Rodney, 2018). Since its founding in 2007, ProPublica has produced high-impact journalism while relying primarily on philanthropic donations and small individual contributions (Elia & Magda, 2016). The Guardian's shift to a reader-supported model has also shown promise, with over one million readers contributing financially in 2018, allowing the newspaper to break even for the first time in two decades (The Guardian & Viner, 2018). These examples suggest that reader revenue, coupled with foundation support, can create a sustainable funding model for quality journalism.

Conclusion

In all, funding accurate news with taxes by the government can be an effective approach to intervene in accurate news. Firstly, it can negotiate the market failure of accurate news due to its non-excludability and non-rivalry. Secondly, tax-funded news helps reduce information inequality by improving broader access to accurate news in society and prioritizing coverage of issues affecting marginalized groups. In addition, government subsidies may strengthen journalistic independence by diminishing their dependence on commercial interests, thereby enabling news organizations to prioritize comprehensive reporting. However, some problems such as high opportunity costs, policy conflicts, and censorship are brought about by funding with tax. Therefore, other strategies could be employed to ensure adequate accurate news. In some cases, sales tax relief and a non-profit model that mainly depends on philanthropic support may be alternative ways. Note that due to the limited length of this essay, many unsolved questions still exist. For example, how exactly should accurate news be defined, and as technology advances, the emergence of artificial intelligence has led to information that is harder to distinguish as true or false. Hence, the government must adapt its news policies to keep pace with the changing times, and these forthcoming issues warrant additional research.

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Post-Covid Consumer Confidence and Spending Power Shifts in East Asia
By Jaeheon Lee
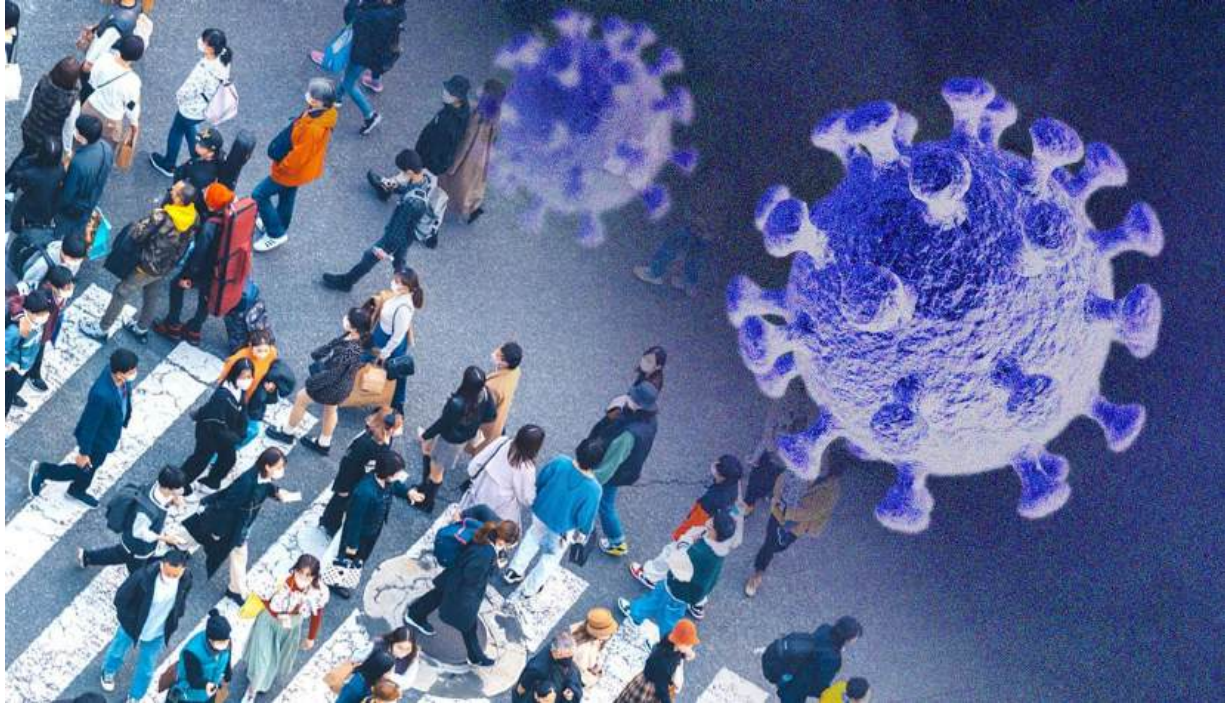
Abstract

   COVID-19 brought a global outbreak of a respiratory disease. This pandemic has led to government interventions, and subsequent personal preference changes in different parts of the world. This paper was approached in a diversified manner, first informing what revenge spending is, then sharing original data from 27 respondents, all residents of East-Asia, along with an in-depth secondary analysis on economic reports from organizations and news articles from China, Japan, and South Korea. Long-term implications and government intervention tactics are the central focus to this study, sharing procedures and trends across East-Asia under the branch of one cohesive topic of consumer behavior. In contrast to published research papers in behavioral economics, this paper examines long-term economic shifts in East Asia as they stabilize. To condense the findings, it can be said that there was a marked increase in luxury sectors that include cars and traveling. In short, this notion implies that while spending power had positive change, a similar practical effect in consumer confidence is questionable, which will be discussed later.

Keywords: COVID-19, East Asia, consumer confidence, revenge spending, economic recovery, & luxury sector

Materials and Methods

The overall structure of the study is experimental research and desk-research. An original data collection was facilitated with responses from 27 respondents specifically from South Korea, Japan, Philippines, and China. A survey was utilized for original data collecting purposes, yet most importantly, I wanted to address the lack of anecdotes in existing research, while customizing the focus specifically on my paper. In regards to desk-research, extensive research was conducted on different nations published in news articles. More specifically I used information from Lotte Mart, a Korean supermarket, for South Korean analysis, Nikkei Asia for Japanese analysis, and South China Morning Post for Chinese analysis. Concerning ethical considerations, all data responder information is kept confidential as emails were not purposefully not tracked to optimize legitimacy, and existing information studied were cited appropriately. This ensures the integrity and reliability of our research.

Introduction

In December 2019, a contagious respiratory disease known today as the coronavirus was discovered in Wuhan, China. By March 2020, the spreading through droplets released from infectious coughs and sneezes exponentially grew, prompting combative government intervention such as prolonged lockdowns and aggressive measures to retain physical interactions outdoors. COVID-19 has led to economically detrimental impacts, especially when factoring consumer confidence and purchasing power into respect. At variance with other behavioral economics papers, this research is oriented towards exhibiting the long-term shifts in the global event in the scope of East Asia as the economy gradually stabilizes. Understanding the long-term impacts of COVID-19 may lead to more effective policy making and future shock management. The study is primarily in Japan, China, and South Korea with an emphasis on spending and consumer confidence, thus does not necessarily provide a comprehensive analysis on a global scale. Additionally, there are challenges in maintaining a controlled experiment, thus the assumption behind the paper is that COVID-19 is the major factor influencing concurrent economics trends. Elements of policy and behavioral economics are covered in this paper through an original survey from a selected East-Asian population, an explanation of revenge spending, and an analysis on three different countries in an attempt to answer the following research question.

Research Question: How Have Consumer Confidence and Spending Power Shifted As a Result of the COVID-19 Pandemic in East Asia, and What Are the Long-Term Implications of Such Changes?

Immediate Shifts in Consumer Behavior: First of all, the foundation in conceiving the long-term ramifications is a brief account into the immediate shifts in consumer behavior. The emergence of COVID-19 resulted in a transformation of consumer spending behaviors, influenced by factors such as uncertainty, apprehension, and governmental measures

implemented to mitigate the transmission of the virus. Essential goods, stockpiling food, and healthcare products were prioritized, diminishing discretionary spending ((Statista, 2024)). On a global scope, local supermarkets experienced panic bulk-buying. In Japan, Minister of Agriculture, Forestry and Fisheries Taku Eto reassured the public, urging them to purchase only what they need, emphasizing that the food supply is adequate. He said, "There is sufficient food supply" ((NHK, 2023)). He observed a reassuring absence of any signs that grain imports, a vital lifeline for Japan, were facing interruptions ((NHK, 2023). Meanwhile, the closure of brick-and-mortar shops has sparked a surge in online shopping, as consumers flock to the digital marketplace. Initially, these changes seemed like mere temporary adjustments to a sudden outbreak. Yet, COVID-19 persisted much longer than anticipated, with such behavioral changes solidifying.

Results

Revenge Spending:

Figure 1: Post-Covid saving habits pie chart categorized into improved, worsened, and stayed the same.

Revenge Spending emerges as a curious phenomenon, marked by a notable uptick in consumer expenditure following an unexpected economic downturn. This behavior can often be seen as impulsive and financially detrimental. In line with this notion, a recent survey focusing on the East-Asian demographic unveiled a troubling trend: their spending habits have deteriorated in the aftermath of the Covid pandemic (Jennings, 2024). From 27 responses, 44.4% (12) answered "worsened" to the question, "Would you say your saving habits improved, worsened, or stayed the same after Covid?" (Deng, 2024). Accordingly, 33.3% (9) said it stayed the same, and only 22.2% (6) people said it got better. This spending surge is most notable in luxury goods sectors where individuals value their wants over needs to compensate for the lost time and experiences during the extensive restriction period. Specifically, one responder unconsciously paraphrased the definition of revenge spending while providing his input on post-covid spending asserting, "After the pandemic, people went to places more because they

were deprived of that [pre-Covid] feeling for a while, making spending more enticing" (Deng, 2024).

Regional Differences in Consumer Behavior: Japan, South Korea, and China

While having experienced the similar detriments of the pandemic, distinct economic landscapes of Japan, South Korea, and China have led to divergent behavioral patterns. In China, the government response of removing COVID-19 restrictions had led to a rapid economic rebound, with a noticeable uptick in spending on luxury goods, real estate, and technology, suggesting its post-pandemic spending power growth (Deng, 2024). South China Morning Post underscored in the article, "Huawei's 2023 profit more than doubles, as a sales rebound helps tech giant hack a profitable path out of US sanctions." Huawei recorded a 9.63 percent increase in revenue to US$97 billion in 2023, while profits surged 144.5 percent year on year (Deng, 2024). Additionally, the Electric Vehicle Sector faced market share expansion, where Nio reported delivering 15,620 vehicles in April, marking an impressive 134.6% increase from the previous year. This total included 8,817 premium smart electric SUVs and 6,803 premium smart electric sedans. So far this year, Nio has delivered 45,673 vehicles, which represents a 21.2% increase from the same period last year. Moreover, as a means to solidify its position in the EV market ecosystem, it aimed at enhancing its battery swap partnerships. These initiatives are designed to alleviate growing consumer concerns about driving range. To push this idea further, according to a report from McKinsey, travel and auto spending have surged notably (Zipser, 2024). More specifically, from 2023 to 2024, there has been a 37% increase in electric vehicle purchases and a 44% increase in air passengers (Jennings, 2024). In 2014, Lunar Holiday domestic travel was said to have reached over 19% since 2019. In accordance with these statistics, recent insights from Global Blue demonstrate that the average Chinese travel expenditure has soared since 2019. Specifically, those venturing to Italy are spending 14 percent more, while those exploring the enchanting landscapes of France are indulging 20 percent more than before (Jennings, 2024). A recent report from China Daily provides a more accurate representation of China's current economic climate. In 2023, China's GDP grew by 5.2%, with a significant 83% of this growth driven by a surge in consumption (Deng, 2024). Early 2024 data further highlights this trend, with retail sales increasing by 5.5% year-on-year, including a 4.6% rise in goods sales. Additionally, food service sales saw a notable jump of 12.5%. Lastly, a 44.4% increase is underscored in air passenger numbers, reflecting a strong recovery in travel, alongside significant expansion in the automotive industry, particularly with a surge in electric vehicle sales (Jennings, 2024).
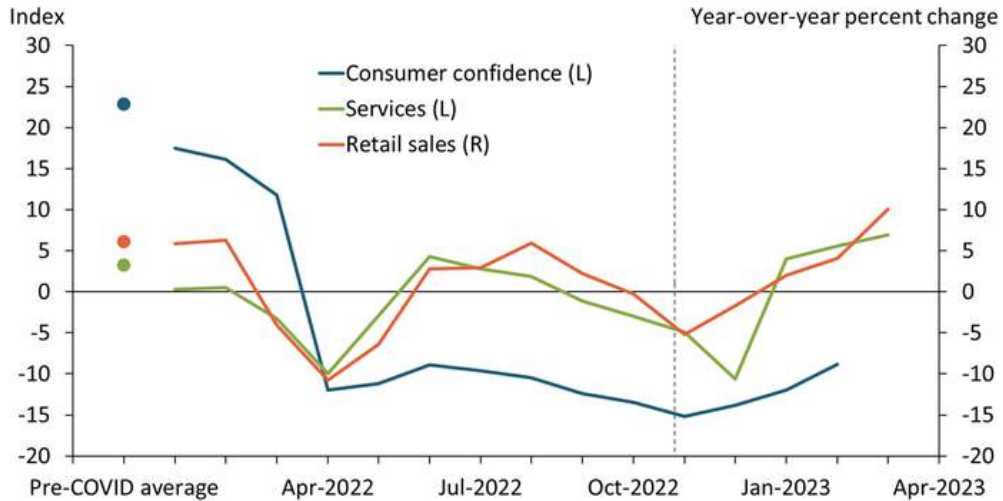
Figure 2:. Compared to rebounding rates of retail sales and service, consumer confidence has been stagnant.
(Source: Federal Reserve Bank of Kansas City)

However, consumer confidence results are a little different. A report from South China Morning Post asserted that, "China's consumer confidence index hit 86 in July [of 2024], according to investment bank Nomura, just above the all-time low of 85.5 in November 2022" (Deng, 2024). Economists reporting to the South China Morning Post believe that the property sector is the root of this phenomenon, since housing prices adversely impact financial statements. Statistics from the Chinese National Bureau of Statistics (CNBS) and the China Federation of Logistics and Purchasing show that the consumer confidence index is negative (Deng, 2024). The graph demonstrates the degree of confidence on a scale of 0 to 200, utilizing 100 as a neutral indication. The National Bureau of Statistics accumulated responses from a total of 6,480 individuals from 15 provinces. Nikkei Asia reports that China Overseas Land & Investment (COLI), a Hong Kong-listed subsidiary of China State Construction Engineering Corp., saw its net profit drop by 23.5% in the first half of the year to 10.31 billion yuan, an estimated value of $1.45 billion (Nikkei Asia, 2024). Revenue fell by 2.5% to 86.93 billion yuan, and the value of its investment properties decreased by 99.5%. The significant sales decline among state-owned companies highlights the severity of the crisis and the need for more government intervention (Nikkei Asia, 2024).
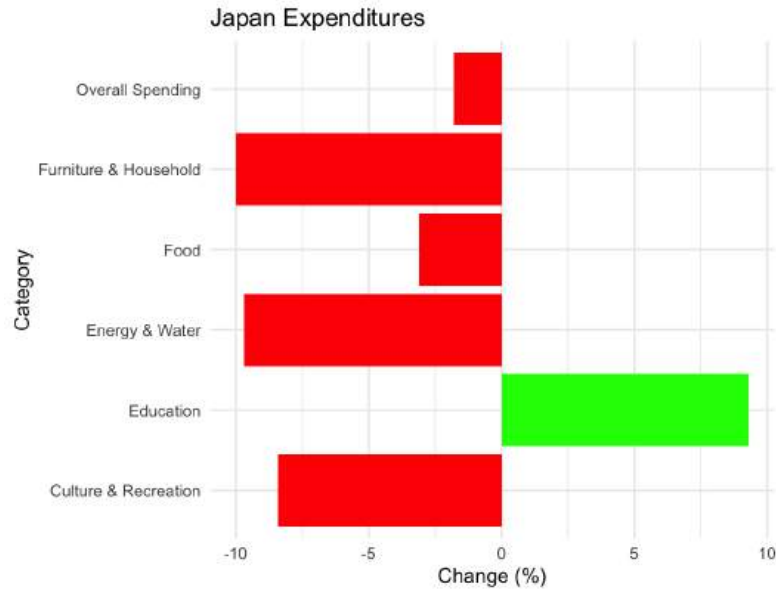
Figure 3: Japan's post-Covid expenditure changes in percentage organized into different categories.

In Japan, the pandemic exacerbated existing economic challenges, leading to a more conservative approach to spending. Japanese consumers have preferred saving over spending, a trend that has persisted even as restrictions have eased. This cautiousness reflects a broader cultural emphasis on financial security and stability, reinforced by the pandemic. Nikkei Asia insists that household spending in 2024 has dropped 1.8% from the previous year, and the first increase between months was in May, which is the first increase recorded in 14 months (Nikkei Asia, 2024). The general public may gauge private consumption stats through data from household spending, as household spending is essentially half of Japan's GDP. Additionally, food spendings, which constituted about 30% of total expenses, decreased by 3.1% as people reduced their purchases of vegetables due to raised prices (Nikkei Asia, 2024). Expenditures on culture and recreation fell by 8.4%, primarily driven by reduced spending on overseas travel, impacted by the yen's ongoing depreciation against major currencies (Nikkei Asia, 2024). There was a 9.7% decrease in spending on energy and water bills, and a 10% decline in spending on furniture and household items, reflecting a shift back to office work compared to the previous year (Nikkei Asia, 2024). Conversely, spending on education increased by 9.3%, attributed to higher tuition fees at private universities after pandemic-related exemptions and waivers ended (Nikkei Asia, 2024). All things considered, the decline in spending in different sectors reveals a dip in purchasing power, while consumer confidence is characterized by cautiousness, a Japanese traditional cultural value, to maintain financial security.
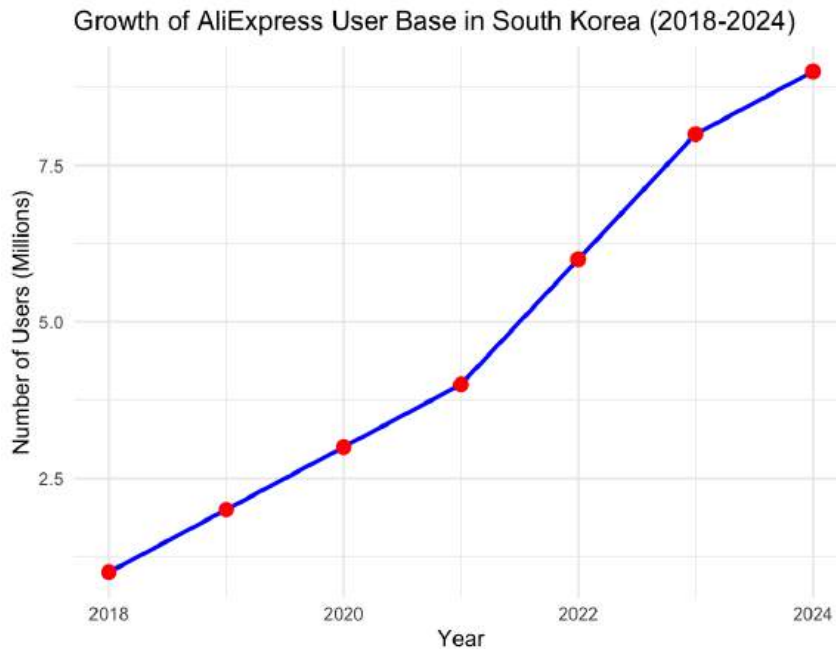
Figure 4: Growth of AliExpress user number in millions in the span of 2018 through 2024.

Korea presents a middle ground, with consumers gradually returning to pre-pandemic spending patterns but with a heightened emphasis on health and well-being. The pandemic has accelerated the adoption of e-commerce and digital payments in Korea, and trends will likely persist in the long term. AliExpress and Temu are currently the leading Chinese-affiliated e-commerce platforms used by South Korean consumers for cross-border shopping. Both platforms operate on a marketplace model, allowing third-party sellers from China to sell directly to consumers. Although AliExpress entered the South Korean market in 2018, the use of C-commerce platforms was limited due to long delivery times, often extending over several months (AliExpress, 2018). However, in June 2023, AliExpress established dedicated logistics centers in Weihai and Yantai in Shandong Province, close to Pyeongtaek Port in South Korea. This development allowed for faster delivery of Ali-Choice-branded products and other popular items, with shipments arriving in South Korea within a week. In April 2024, a combination of improved delivery pace coupled with a strong marketing scheme translated to the national AliExpress user base reaching nine million (AliExpress, 2024). South Korean consumers have embraced cross-border e-commerce, and the market, including imports from China, is anticipated to keep expanding. Nonetheless, as cross-border e-commerce transactions rise, so do related challenges. Consequently, there is increasing agreement on the need for government regulation concerning the sale of electronics and products containing potentially harmful chemicals. Additionally, Korean consumers have grown interested in sustainable and ethical products, reflecting a broader global shift towards conscious consumption. The food sector has seen a surge in demand for health-related products, with consumers prioritizing organic and locally sourced foods (Korean Consumer Trends, 2023). Today in South Korean media, health and

welfare are key focal points, thus health-conscious consumption initiatives are likely to leave permanent traces. Lotte Mart, one of the leading supermarkets in South Korea, has increased sales of organic food by 10–20% in 2023 compared to the previous year. Vegan products grew by five times more than 2022 in 2023 (Lotte Mart, 2023). The electronics sector has benefited from increased spending on home entertainment and work-from-home setups, a trend that has been particularly strong in China (Consumer Electronics Sector, 2024). The travel industry, one of the hardest hit by the pandemic, is gradually recovering. However, consumer preferences have shifted towards domestic and short-haul travel, emphasizing safety and hygiene. This trend is expected to persist long-term, particularly in Japan and Korea, where cautious consumer behavior will likely influence travel choices.

In the wake of the COVID-19 pandemic, the landscape of consumer behavior in East Asia has been altered. To sum up, the pandemic has accelerated contemporary trends, the emergence of revenge spending and a cautious approach to consumption. We survey these trends today to conjecture that the changes will not be fleeting anytime soon. They will likely redefine East Asia's socioeconomic conditions in the coming years. As consumers navigate this post-pandemic terrain, businesses must don their thinking caps, adapting to these evolving preferences of East Asian consumers.

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Why does Having An Older Maternal Age Affect the Frequency of Miscarriages in Pregnancy; How Significant are External Factors? By Aarishi Gali

Key Words: advanced maternal age, miscarriages, external risk factors, internal risk factors

Abstract

Advanced maternal age significantly impacts pregnancy outcomes, and also causes increased risks such as ADHD, Down syndrome, stillbirths, and miscarriages. This article goes into the basic aspects of pregnancy, focusing on the effects of maternal age on miscarriage percentages. Pregnancy, a complex process, is divided into three trimesters, which involves tremendous changes in the mother, including increased risk for heart attacks and unexpected hormones. As maternal age advances, fertility goes down, and the possibility of genetic defects in eggs increases, leading to higher miscarriage risks. Advanced maternal age often comes with complications such as gestational diabetes and hypertension, miscarriages, occurring in about 15% of pregnancies. Miscarriages can stem from various factors which include chromosomal abnormalities of the egg, uncontrolled diabetes, obesity, and infections. While advanced maternal age is a significant factor, external factors such as medication use, environmental pollution, and lifestyle choices also contribute to miscarriage risks. This review goes into the complexities of an older maternal age and miscarriages. It highlights the importance of also considering external factors when studying the connection between advanced maternal age and miscarriages.

Introduction

Having an older maternal age has significant effects on the baby. Many of these include ADHD, down syndrome, stillbirths…etc. Attention-deficit/hyperactivity disorder, or also known as ADHD, is a condition that refers to impulsiveness and hyperactivity in people. Stillbirths are when a baby dies while in the womb and is older than 20 weeks (Molnar & Gair, 2024). Miscarriages are also commonly seen throughout women with an older maternal age. Miscarriages is when a baby is lost before 20 weeks. This can happen because of various reasons, and recent studies have also shown that maybe an older maternal age is not the only reason these women are having miscarriages (Molnar & Gair, 2024) . This article will go through the basics of pregnancy, having an older maternal age, miscarriages, connecting an older maternal age with miscarriages, and what other underlying causes might be causing these miscarriages to happen.

Basics of pregnancy

Motherhood is an amazing journey that first starts when an egg is fertilized. At this time, the egg is referred to as a zygote (Pascaual & Langaker, 2024). The zygote proceeds into the uterus, and the embryo attaches itself to the wall.The next periods of time are divided into 3 trimesters, consisting of 3 months each. In the first trimester many vital internal organs start to form. By the fifth week the eyes, heart, and liver of the baby have formed (Pascaual & Langaker,

2024). At 8 weeks, the baby is then called a fetus. Its body is mostly formed, although most of the organs do not function properly yet. In the second trimester the fetus starts moving slightly. The baby grows to around 12 inches long and the organs continue to grow throughout this trimester (Pascaual & Langaker, 2024) . The third trimester is when the mother feels the most discomfort. There is a lot of pressure on her bladder during this period. The fetus will grow rapidly, and many organs will continue developing. The development of a baby is a complex process and a lot can go wrong (Pascaual & Langaker, 2024).

During pregnancy many organs/organ systems in the mother go through huge changes to accommodate the baby. The cardiovascular system increases its output by 45% during the first trimester, and this is kept until delivery (Willcox & Weinberg, 2019). Both systolic and diastolic blood pressure decrease and the position of the heart changes slightly. Hormones such as estrogen and progesterone increase, often causing nausea. The red blood cell count will increase by 25% and the plasma volume increases by 50% (Willcox & Weinberg, 2019) . White blood cell counts will also increase. Overall, many changes occur in the human body during pregnancy and the mother will go through lots of discomfort (Willcox & Weinberg, 2019) . This is a very demanding process for the mother, and while difficult, can successfully be tackled by a healthy body.

Pregnancy in women with an older maternal age

Over the past few decades there has been an increase in mothers having an advanced maternal age. Advanced maternal age is a term often used to describe someone who is pregnant and is over 35 years old (Advanced Maternal Age, 2024). These pregnancies are often considered more dangerous and have higher risks for genetic diseases, miscarriages, high blood pressure…etc. These complications happen because as one gets older, the amount of eggs decreases overall (Advanced Maternal Age, 20244) . As these decrease, these leftover eggs will tend to have genetic defects, and therefore the baby might have complications. Since there are less eggs, the chances of also getting pregnant each menstrual cycle also decrease (Advanced Maternal Age, 20244) . This leads many couples to choose alternative options such as IVF. IVF, or in vitro fertilization, is a process when an egg is fertilized in a laboratory and then transferred into a uterus. There it will attach to a wall and grow as normal (In Vitro Fertilization (IVF, 2024).).

As one gets older, one's body also responds to pregnancy differently than it would have before. Increased blood pressure is a huge risk to look out for. Gestational diabetes also has higher risks of appearing in women with an older maternal age (Pregnancy after 35: Healthy pregnancies, healthy babies, 2022). Gestational diabetes can only occur when pregnant and if left untreated will cause the baby to grow bigger, causing many problems during delivery (Pregnancy after 35: Healthy pregnancies, healthy babies, 2022) . The change of having a c-section also skyrockets. There are often more complications in the pregnancy, and therefore the chance of having a c-section is very high (Pregnancy after 35: Healthy pregnancies, healthy babies, 2022) .

Miscarriages in women with an advanced maternal age

A miscarriage is a scary experience for a mother. It is often defined as the spontaneous loss of a baby who is younger than 20 weeks old (Dekker et. al, 2016). Around 15% of pregnancies end up in a miscarriage although many go unseen as this happens so early on in the pregnancy (Dekker et. al, 2016) . Some might not even know they are pregnant when a miscarriage happens. The unborn baby often does not develop properly and this causes it to not be able to sustain (Dekker et. al, 2016) .

Although many miscarriages happen unexpectedly with no signs, some pregnancies do show some symptoms. Often, mothers experience bleeding from the vagina, and it varies from very painful to painless. It all depends on how the mothers body reacts to the miscarriage (Dekker et. al, 2016) . There is often pain near the pelvis and fluid/tissue passing from the vagina. Certain health conditions of the mother can also lead to having a miscarriage. Uncontrolled diabetes, obesity, infections, hormonal problems, and having malformations in the uterus/cervix are also common cases (Dekker et. al, 2016) . Most miscarriages happen because the baby does not develop properly. This could mean the fetus is missing some chromosomes or even has extra chromosomes (Dekker et. al, 2016) . Chromosomes are what contain a person's genes, and they get 23 from the mother and 23 from the father, resulting in 46 chromosomes in total. Many things lead up to miscarriages, and they are a very trauma induced event for both the mother and the father (Dekker et. al, 2016) .

Concludingly, many studies have shown that having an older maternal age also leads to a higher risk of having a miscarriage (Female Age and Miscarriage and Fertility , 2024). As said before, when an egg's quality decreases it will cause the fetus to have genetic defects. These defects often leave the fetus struggling to survive (Female Age and Miscarriage and Fertility , 2024) . While, in some cases the fetus might survive, in most cases it ends up in a miscarriage (Female Age and Miscarriage and Fertility , 2024) .

Pie chart showing miscarriage chances in women with a younger maternal age vs women with an older maternal age.

Miscarriage percentages in older maternal groups

non-miscarriage pregnanices
47%

miscarriage pregnancie
53%

Figure 1a

Miscarriage percentages in average maternal groups

miscarriage pregnancies
7.9%

non-miscarriage pregnanices
92.1%

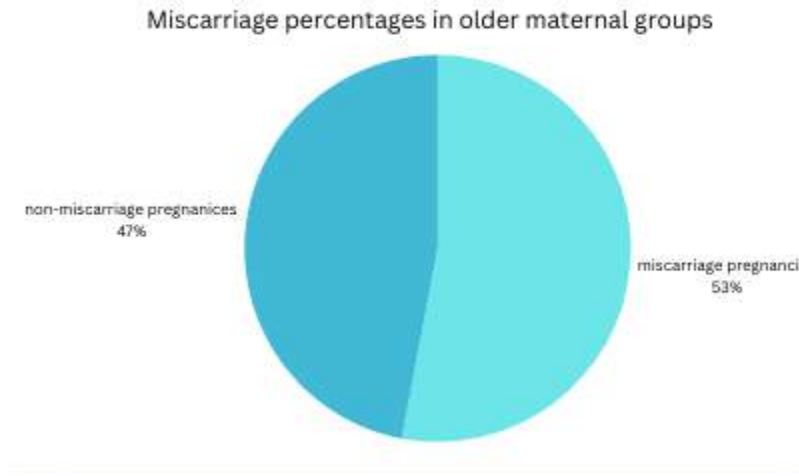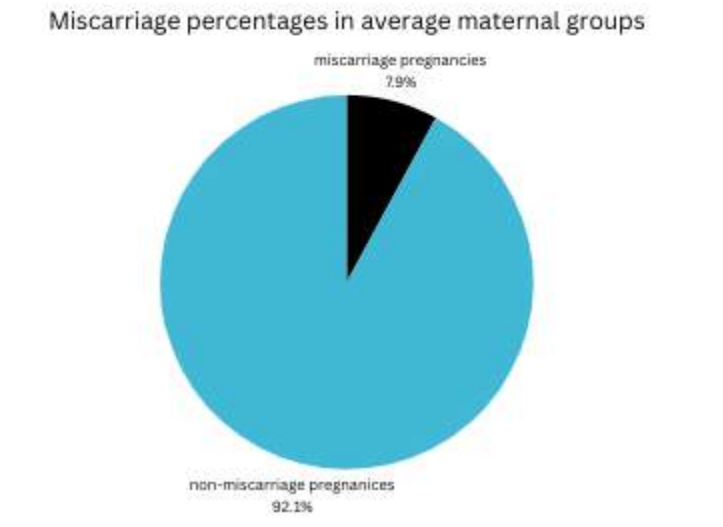**Figure 1b**

Description

These figures show a pie chart showing miscarriage chances in women with a younger maternal age vs women with an older maternal age. In figure 1a there is miscarriage percentages in older maternal groups shown. In figure 1b there is miscarriage percentages in average age maternal groups (Female Age and Miscarriage and Fertility , 2024) .

What external factors can play a role in miscarriages?

It has been shown that advanced maternal age plays a role in miscarriages, but other research has also said that other factors may play a role in miscarriages (Causes of Miscarriage , 2021).

Taking certain medications while pregnant can put a fetus in higher risk for miscarriages. These medicines include ibuprofen, isotretinoin, ergotamine, and methysergide. Isotretinoin is often used to treat acne and ergotamine and methysergide are used for headaches (Causes of Miscarriage , 2021) . If these medicines are used a lot in a pregnancy then they can lead to miscarriages. It is also shown that having a medical condition prior to or during the pregnancy can also increase chances of miscarriages. This includes infections, such as HIV, malaria, and syphilis (Causes of Miscarriage , 2021) .

Many environmental and lifestyle factors are to be looked at as well. Using any kind of tobacco products, alcoholic products, and drugs are huge reasons as to why miscarriages happen (Causes of Miscarriage , 2021) . All of these should be avoided before and during pregnancy. Metals such as lead, which can be found in some types of fish, and nickel can also play a role. These metals have shown to affect the mothers body and often lead to miscarriages of the baby (Causes of Miscarriage , 2021) . High levels of pollution have shown to affect the fetus and eventually lead to miscarriages if exposed to it for too long. Often fruits and vegetables which have been grown using pesticides can also lead to miscarriages (Causes of Miscarriage , 2021) .

Conclusion

In conclusion, having an advanced maternal age causes higher chances of miscarriages. While this might be because of many reasons, the most common cause is genetic defects in the fetus. These defects often happen because the egg has defects in it. While maternal age and miscarriages are linked together, it is not the only reason. Often, other external factors play a huge role in pregnancies. While little research has been done on this, the research so far says that external factors should also be taken into account.

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What impact does the thickness and material of the wire have on the thermoelectric effect in copper, constantan, and iron.

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Abstract
The goal of this project is to identify cheap, easily available materials with good thermoelectric properties for use in renewable energy applications. The experiment shows what impact does the thickness and material of the wire have on the thermoelectric effect in copper, constantan, and iron. Before the experiment, the author made the hypotheses: the thermoelectric effect will be more significant with the increasing of the thickness of the wire; different materials will cause the thermoelectric effect to be different. To create the experimental setup, the author made thermoelectric couples using copper, constantan, and iron wires, setup a temperature difference and then measure the voltage with a multimeter. After doing the experiment, the author found that the thickness of the wire has little effect on the thermoelectric effect, but the material of the wire does influence the voltages that were measured. During the experiment, the author found another variable: time. The author measured the time it takes the voltage to change when the temperature difference changes immediately. The author recorded the voltage change over time and use the data to made line charts. As the conclusion of the work, conductor materials can be chosen based on the specific situation, allowing for optimal performance in different scenarios. For example, if you want to achieve high voltage, you can choose a thermocouple composed of copper and iron wires; if a rapid rate of voltage change is critical, thermocouples made of constantan and iron wire become the first choice.

INTRODUCTION
The Seebeck effect is when electricity is created between a thermocouple when the ends are subjected to a temperature difference between them. (1)The effect results from the response of charge carriers to temperature differences. When one joint is exposed to a higher temperature and the other is at a lower temperature, an electrical potential difference is created between the two joints. At the atomic level, temperature differences cause charge carriers in the material to experience varying degrees of thermal excitation. This causes charge carriers to migrate from the hot joint to the cold joint, attracted by the equilibrium energy level. Therefore, an electric field is created, which creates an electric potential difference.

In the field of thermoelectric materials, numerous remarkable application

examples have emerged. Here are some instances from different domains:

The first one is temperature measurement and sensors：thermocouples based on the Seebeck effect can be used to measure temperature. The potential difference caused by the temperature difference can be measured and proportional to the temperature. This principle is widely used in temperature sensors and measuring instruments in industrial processes, vehicle emission systems, etc., there is a large amount of waste heat.(2)

The second one is energy harvesting: the utilization of the Seebeck effect presents a transformative approach in the domain of energy harvesting. In this context, the substantial waste heat generated during industrial processes or from other sources can be harnessed and transformed into a valuable resource — electricity. The Seebeck effect, which involves the conversion of a thermal gradient into an electric voltage, serves as the foundation for this conversion process.(3)

The last one is thermoelectric generators: thermal batteries based on the Seebeck effect can convert the temperature difference between the Earth's surface and space into electricity, providing a continuous power source for space vehicles and deep space probes.(4)

Since there are plenty of applications for the Seebeck effect, it is crucial to find both cheap and efficient materials to make thermocouple. This paper studies thickness, materials, and other properties of the wire to find different materials to choose under different circumstances. The hypotheses are the thermoelectric effect will be more significant with the increasing of the thickness of the wire; different materials will cause the thermoelectric effect to be different. The result from the experiment shows that if we need to achieve high voltage, we can choose a thermocouple composed of copper and iron wires; If we want to achieve a fast rate of voltage change, we can choose constantan and iron wires to make thermocouples.

RESULTS

In this section, the author present the outcomes of the experiments involving thermocouples, which are devices known for generating voltage from temperature differences. The magnitude of the generated voltage is influenced by two key factors: the temperature difference and the choice of conductor materials. These factors can be strategically selected to optimize performance for specific applications.

Influence of Temperature Difference
From the data of the experiment, there is a direct relationship between the magnitude of the temperature difference and the voltage generated by the thermocouple. As the temperature difference increased, so did the generated

voltage. This finding confirms the fundamental principle of thermocouples, where a temperature gradient across the junctions results in voltage production.

The data collected in the experiment agree with the Seebeck effect(a temperature difference between two dissimilar electrical conductors or semiconductors produces a voltage difference between the two substances), and voltage is proportional to the temperature difference. The data is presented in Table 1.

Influence of Thickness

The variations in wire thickness have a negligible impact on voltage. The data are presented in table 2 and 3. This observation can be attributed to the predominant influence of wire thickness on the propagation of heat within the material. When the material thickness increases, the heat propagation rate within the wire tends to slow down, resulting in a temperature differential. However, this subtle temperature difference has a minimal effect on the magnitude of the potential difference measured.

Influence of Conductor Materials

Conductor materials play a crucial role in determining the performance of thermocouples. To investigate this aspect, The author tested different thermocouple configurations.

In scenarios where achieving the highest maximum voltage is of paramount importance, the author found that selecting a thermocouple composed of copper and iron wires yielded advantageous results. The copper-iron thermocouple consistently generated higher maximum voltages compared to other configurations. The data is presented in Table 5.

Conversely, when a rapid rate of change in voltage is crucial, the author found that the thermocouple made of constantan and copper wires outperformed other combinations. This configuration exhibited a more rapid response to temperature fluctuations, making it the preferred choice for applications requiring quick voltage changes. The data is presented in Table 4.

The flexibility in material selection, as demonstrated by our experiments, highlights the adaptability of thermocouples to meet the unique requirements of various applications.

These results underscore the importance of considering both temperature differences and conductor materials when designing and utilizing thermocouples. The ability to tailor thermocouples to specific scenarios allows for optimal performance across a wide range of applications. Detailed experimental methods and data are provided in the "Materials and Methods" section.

DISCUSSION

The data in Table 1 agree with the Seebeck effect(a temperature difference

between two dissimilar electrical conductors or semiconductors produces a voltage difference between the two substances).

The data of Table 2 and 3 show the thickness of the wire does not influence the voltage: when the temperature difference is constant, the voltage produced hardly changes with the thickness of the material. The reason is the thickness mainly affects the propagation of heat within the material. If the material is thicker, the heat may travel more slowly through the interior, resulting in a less noticeable temperature difference, which in turn affects the magnitude of the potential difference, but this effect is usually very small.

The data of Table 4 shows that when a rapid rate of change in voltage is needed, the thermocouple made of constantan and copper wires outperformed other combinations.

Figure 1 shows the voltage change over time for thermocouple made of different materials of wires. Table 5 made a summary for the data presented in figure 1.

There are several limitations to this experiment
1. Equipment limitations: There is no professional experimental equipment, such as accurate temperature controllers, high-precision measuring instruments, etc., which may affect the accuracy and repeatability of the experiment.
2. Material selection: The variety of materials is very limited, and the final material selected may not be the best material for applying the Seebeck effect.
3. Temperature control: In the experiment, it is necessary to accurately control the ambient temperature to remain unchanged, but in my experimental environment, the temperature control may not be accurate enough, which may affect the reliability and accuracy of the experiment.

METHODS

To create the experimental setup in figure 2, the author prepared copper, constantan, and iron wires of varying thicknesses, a thermometer, and a multimeter. The author tied two wires together in pairs and taped them to form a thermocouple. The author put the thermocouple in water at 0 degree Celsius, 50 degree Celsius, 100 degree Celsius. The ends of the thermocouple were connected to a multimeter with a measuring range of 200 mV. The data are presented in Table 1.

As my research question, the author took the thickness of the wire as the independent variable and observe the change in voltage. The data are

presented in table 2 and 3. The author also took time as the independent variable. The author measured the time it takes the voltage to change when the temperature difference changes from 75°C(boiling water) to -25°C(ice water). The author also performed the experiment in the reverse direction. The data are presented in table 4.

The author recorded the voltage change over time and made line charts (the author switch the wires from the boiling water to the ice water at t=0; the red circle shows the point in time when the wires are moved from the ice water into the boiling water). The charts are presented in Figure 1. The author looked for the key points on the graph and then put them in table 5.

ACKNOWLEDGMENTS

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Figures and Figure Captions

Temporal Voltage Variations in Thermocouples with Different Wire Materials during Ice-to- Boiling Water Transition
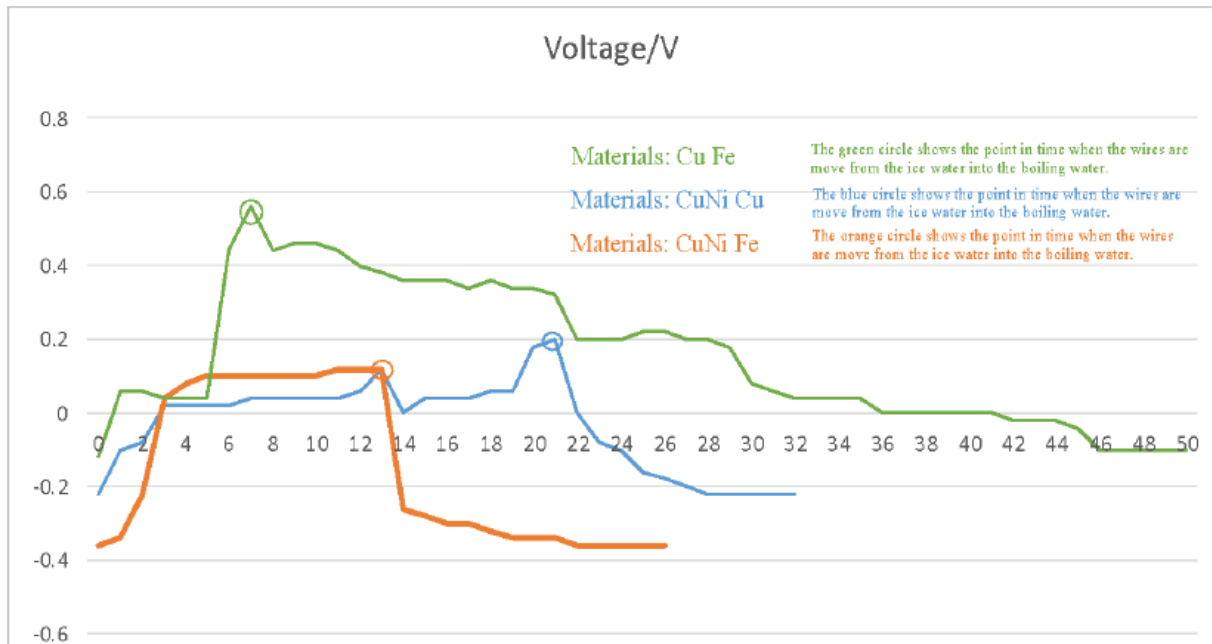
Figure 1.The voltage change over time for thermocouple made of different materials of wires (the wires were switched from the boiling water to the ice water at t=0) (n=3). The x-axis represents time in seconds, tracking the temporal progression of the experiment. The y-axis denotes voltage in volts, recording the voltage variations of the thermocouples.

Experimental Setup for Thermoelectric Investigation
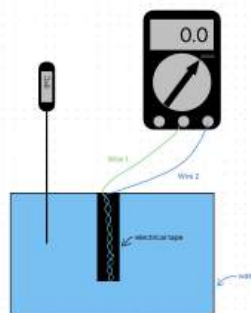
Figure2. Schematic diagram of experimental set-up. Experimental setup used in thermoelectric experiment. On the left is the thermometer. On the top right corner is the multimeter. The two wires in the water are wrapped together and taped with the electrical tape. The other end is connected to the multimeter with a measuring range of 200 mV. When the thermometer indicator reaches the specified value, observe the multimeter reading (and changes).

Tables with Captions

Wire 1	Wire 2	Room Temperature	Water temperature	Temperature Difference	Voltage
Cu	Fe	25°C	0°C	-25°C	0.04V
Cu	Fe	25°C	50°C	25°C	-0.04V
Cu	Fe	25°C	100°C	75°C	-0.12V
CuNi	Fe	25°C	0°C	-25°C	-0.12V
CuNi	Fe	25°C	50°C	25°C	0.10V
CuNi	Fe	25°C	100°C	75°C	0.34V
CuNi	Cu	25°C	0°C	-25°C	0.04V
CuNi	Cu	25°C	50°C	25°C	-0.04V
CuNi	Cu	25°C	100°C	75°C	-0.2V

Table 1. The voltage measurements obtained from pairs of copper wires, iron wires, and constantan wires, where one end of each pair was immersed in water at 0°C, 50°C, and 100°C, respectively, while the other end was connected to the multimeter.

Test Group	Thickness/mm (CuNi)	Thickness/mm (Fe)	Room Temp /°C	Water Temp /°C	Temp difference /°C	Voltage/ V
1	0.3	0.45	25	0	25	0.10
	0.4	0.45	25	0	25	0.10
	0.6	0.45	25	0	25	0.12
	0.8	0.45	25	0	25	0.12
	1	0.45	25	0	25	0.12
2	0.3	0.45	25	50	-25	-0.10
	0.4	0.45	25	50	-25	-0.10
	0.6	0.45	25	50	-25	-0.08
	0.8	0.45	25	50	-25	-0.10
	1	0.45	25	50	-25	-0.10
3	0.3	0.45	25	100	-75	-0.34

	0.4	0.45	25	100	-75	-0.34
	0.6	0.45	25	100	-75	-0.34
	0.8	0.45	25	100	-75	-0.38
	1	0.45	25	100	-75	-0.34

Table 2. The voltage measurements obtained from different combinations of constantan wires of different thickness, and iron wires. In each pairing, one end of the wires was immersed in water at temperatures of 0 degrees Celsius, 50 degrees Celsius, and 100 degrees Celsius, while the other end was measured for voltage magnitude.

Test Group	Thickness/mm (Cu)	Thickness/mm (Fe)	Room Temp /°C	Water Temp /°C	Temp difference /°C	Voltage/ V
1	0.2	0.45	25	0	25	0.04
	0.3	0.45	25	0	25	0.04
	0.4	0.45	25	0	25	0.04
	0.5	0.45	25	0	25	0.04
	0.6	0.45	25	0	25	0.04
2	0.2	0.45	25	50	-25	-0.04
	0.3	0.45	25	50	-25	-0.04
	0.4	0.45	25	50	-25	-0.04
	0.5	0.45	25	50	-25	-0.04
	0.6	0.45	25	50	-25	-0.04
3	0.2	0.45	25	100	-75	-0.12
	0.3	0.45	25	100	-75	-0.12
	0.4	0.45	25	100	-75	-0.12
	0.5	0.45	25	100	-75	-0.12
	0.6	0.45	25	100	-75	-0.12

Table 3. The voltage measurements obtained from different combinations of copper wires of different thickness, and iron wires. In each pairing, one end of the wires was immersed in water at temperatures of 0 degrees Celsius, 50 degrees Celsius, and 100 degrees Celsius, while the other end was measured for voltage magnitude.

Wire 1	Wire 2	Room Temp	Temp Difference	Voltage 100°C	Voltage 0°C	Times (s) 5 trials	Average time (s)
Cu	Fe	25°C	100°C	0.12V		6 6 5 9 7	6.6

					-0.04V		
CuNi	Fe	25°C	100°C	0.34V	-0.12V	9 8 8 11 12	9.6
CuNi	Cu	25°C	100°C	0.2V	-0.04V	5 5 8 6 4	5.6

Table 4. The time it takes the voltage to change when the temperature difference changes from 75°C（boiling water） to -25°C(ice water). Each set of measurements was conducted five times, and the average value was taken as average time.

Parameter	Copper and Iron Wires	Copper and Constantan Wires	Constantan and Iron Wires
Starting Voltage (V)	-0.12	-0.22	-0.36
Ending Voltage (V)	-0.12	-0.22	-0.36
Time to Change Voltage (s)	40 (from 6s to 46s)	7 (from 21s to 28s)	9 (from 13s to 22s)
Maximum Voltage (V)	0.56	0.2	0.12
Minimum Voltage (V)	-0.12	-0.22	-0.36
Voltage Difference (V)	0.68	0.42	0.48
Voltage Difference per Unit Time (V/s)	0.017	0.06	0.533

Table 5. Summary of data in figure1, 2, and 3.

Recent Advancements in Cell-based Therapies for Type 1 Diabetes By Mellitus
Mihir Sai Karthik Lanka

Abstract

In 2022, an estimated 8.75 million people were living with Type 1 Diabetes Mellitus (T1DM) in the world, and that number is only increasing. Latest innovations in cell-based therapies for Type 1 Diabetes Mellitus (T1DM) have made them more promising and filled with potential to replace current treatments of exogenous insulin production and whole pancreas transplants in the near future. The established methods of human and porcine islet transplants have been explored in this review, with a focus on novel methods like islet encapsulation, vitrification, and genetic modifications. These methods aim to resolve long-standing issues with islet transplants, like heavy usage of immunosuppressants and lack of storage capability. The immunomodulatory and angiogenic potentials of Mesenchymal Stem Cells are extremely useful in supporting the islets and prolonging their lifespan. Human Pluripotent Stem Cells can be differentiated into insulin-producing β-cells to replace the cells lost in T1DM. The current status, procedure, and innovations in each therapy are discussed in this review.

1. Introduction

T1DM is an autoimmune chronic disorder caused by the destruction of β-cells in the Islets of Langerhans in the endocrine region of the pancreas by T-cells, specifically CD4+ and CD8+ cells (2). β-cells are responsible for the secretion of insulin, an enzyme that regulates glucose concentrations in the body. Insulin promotes the uptake of glucose by hepatocytes, muscle, and adipose cells when glucose concentration in the blood is higher than normal fasting levels (70-100 mg/dL) and converts the glucose to glycogen which is stored in the body. Lack of insulin production leads to two conditions in T1DM patients: Hyperglycemia, which is a blood glucose concentration > 126 mg/dL, and hypoglycemia, which is a blood glucose concentration < 70 mg/dL (3).

Hypoglycemia unawareness, a condition that affects about 40% of T1DM patients, is a serious issue (4). In regular T1DM patients, hypoglycemia triggers an increase in glucagon and epinephrine production, leading to physical sensations like sweating and hunger, which help the brain detect hypoglycemia. However, if hypoglycemia is prolonged and occurs repeatedly, the body's response is dulled (Hypoglycemia-associated Autonomic Failure), reducing epinephrine release. This condition, known as Hypoglycemic Unawareness (HU), is a significant problem (4). The brain cannot recognize when the blood glucose concentration has dropped well below the standard threshold for extended periods, potentially leading to dizziness and fatigue (4). In extreme cases, this lack of glucose supply to the brain can cause cognitive impairment, underscoring the importance of new T1DM treatments that do not require constant monitoring of blood glucose concentration levels.

2. Genetic Causes of T1DM:

Although the exact cause of T1DM is still unknown, the genes discussed below have been linked to the onset of T1DM in children and are hypothesized to cause the autoimmune response against the β-cells.

On Chromosome 6, the gene coding for HLAs (Human Leukocyte Antigens) is present in almost 90% of T1DM cases in children ([5](#)). The HLA gene is highly polymorphic - it can produce a diverse array of antigens as its function is to train CD4+ and CD8+ T-cells to differentiate between self- and non-self-antigens. However, a combination of alleles, including HLA-DR3, HLA-DR4, HLA-DQ2, and HLA-DQ8, has been linked to T1DM, as they initiate the T-cells' autoimmune response to β-cells ([6](#)).

Located on Chromosome 11, the gene coding for Insulin (INS) is also hypothesized to contribute to the pathogenesis of T1DM ([7](#)). VNTRs (Variable Number of Tandem Repeats) are a repeated sequence of nucleotides in specific genes ([8](#)) ([9](#)); in INS, it regulates the expression of Insulin. VNTR-III, which displays longer tandem repeats, confers a high level of protection from T1DM as it is associated with higher expression of proinsulin in the thymus, so T-cells that are reactive against proinsulin are deleted more efficiently in the thymus itself. In contrast, an INS gene containing VNTR-I expresses significantly shorter tandem repeats, so leaves the person more susceptible to T-cells, which identify the proinsulin produced as a foreign antigen and attack the β-cells producing it. Variations in the INS gene are responsible for 10% of the genetic-related cases of T1DM ([10](#)).

Another gene that may contribute to T1DM is PTPN-22 ([11](#)). PTPN-22 is linked to the production of the protein Tyrosine Phosphatase, which hinders T-cell autoimmune response. PTPN-22, a polymorphic gene, can contain a variety of alleles, of which rs2476601 and rs1310182 ([12](#)) have been linked to T1DM.

T1DM is a genetic autoimmune disease that cannot be prevented or cured easily with current technologies. However, the therapies discussed below offer ways to prolong the lifespan of T1DM patients by releasing insulin endogenously.

3. Current cell-based Therapies:

3.1. Human Islet Cell Transplantation

Islet cell transplantation began to be considered an effective therapy for T1DM due to its numerous advantages over transplanting a whole pancreas. Firstly, individual islets are infused into the liver through the portal vein, which is much less invasive and simpler than transplanting an entire pancreas. Moreover, islet cell transplantation allows the possibility of repeated transplants if sufficient insulin independence is not achieved. The main challenges

with human islet transplants currently are the lack of availability of donors, the chronic immunosuppression required, and the issues with the storage of the islets.

3.1.1. Procedure of Human Islet Transplant

The **Edmonton Protocol** was a novel method of human islet transplantation discovered by Shapiro et al. at the University of Alberta, Edmonton, in 2000 (13). An international trial of the Edmonton Protocol showed that out of 36 hyperglycemic patients at nine different trial centers, 21 (58%) achieved insulin independence for a year (14), which served as a significant starting step for more research and trials to follow.

The Ricordi Chamber, developed in 1988, remained the primary method for automatically isolating islets from pancreases obtained from dead donors (15). The process used a combination of collagenase and 6-9 stainless steel balls in a stainless steel isolator and shaken vigorously to digest the fibrous tissue at a suitable temperature of 37ºC (16). The islets are purified and separated from the remaining tissue using Ficoll gradient centrifugation. However, the Ricordi Chamber had a few significant drawbacks, such as how the steel balls' impact on the tissue caused damage to the underlying islets, affecting their viability negatively. Furthermore, the balls are not very effective at breaking down the fibrous tissue.

The Oxford Chamber, introduced in 2004, was designed to tackle these challenges. This innovative process involves using Teflon plates connected to mesh filters situated at both ends of a glass cylinder. The cylinder is equipped with two handles that are affixed to a ring-shaped piston, allowing the piston to move in and out of the cylinder. Additionally, a central tie-rod with hooks at the end delicately separates fibrous tissue from the pancreas fragments within the cylinder**. (17).

The Oxford Chamber introduced a gentle rotation and mixing system that provides continued exposure to collagenase, reducing the need for mechanical breakdown of islets which was required in the Ricordi Chamber. The Oxford Chamber achieved a better human islet yield of 10,356 islets/g of pancreas compared to 2279 islets/g of pancreas achieved by the Ricordi Chamber. The viability of islets achieved in the Oxford Chamber was 85-95%, which is also better than the 80-90% achieved using the Ricordi Chamber. However, the former method was tested using pancreases from only five donors, so more research is required to draw a meaningful comparison. (17)

Collaborative Islet Transplant Registry (CITR) (2001):
CITR was established as a data bank for islet transplant trials conducted by 20 trial centers in North America, Europe, and Australia, which serves as a valuable resource for conducting comprehensive analyses. An analysis of the data recorded about 677 islet transplants for T1DM patients in CITR in between 3 distinct periods: early (1999-2002), middle (2003-2006), and recent (2007-2010) by Franca Barton et al. showed significant improvements in many aspects as time passed (18). The percentage of patients displaying

insulin independence increased from 27% during the early period to 44% during the recent period, and the occurrence of major hyperglycemic events also became sparser.

3.1.2. Encapsulation

A major problem with islet transplants is the chronic immunosuppressants that must be provided to sustain the islets in the body. Instant Blood-Mediated Inflammatory Reaction (IBMIR) occurs as soon as the transplanted islets come in contact with blood in the portal vein, which kills anywhere between 20-50% of the islets immediately ([19](#)). Tissue Factor on the surface of the islets triggers an aggressive response from the leukocytes, including secretion of cytokines and attack by CD4+ and CD8+ T-cells, macrophages, and NK-cells on the β-cells ([20](#)). IBMIR is currently being suppressed by the heavy intake of immunosuppressants such as tacrolimus, sirolimus, and daclizumab ([21](#)).

Islet Encapsulation is a new process that could potentially reduce the immune response by IBMIR, thus prolonging islet lifespan and viability and reducing the amount of immunosuppressants required. Encapsulation works on the principle of creating a biological barrier between the islets and the blood. This semi-permeable membrane allows nutrients and oxygen to diffuse into the islets and insulin to diffuse out but prevents T-cells and macrophages from diffusing through the membrane, thus protecting the islets from damage ([22](#)).

The material being used for encapsulation must be strong enough to protect the islets from mechanical damage while also not eliciting an immune response from the T-cells themselves. Natural materials like alginate ([23](#)), synthetic materials like polyacrylamide and polyvinyl alcohol ([24](#)) and hydrogels are currently used for cell encapsulation. Hydrogels have shown the most promise, as the cross-linking in the polymers and strong hydrogen bonds provide stability and suitable diffusion capacity to the encapsulated islets ([25](#)). The pH and temperature inside the capsule are additional factors that affect the islet viability ([22](#)).

Two major ways of encapsulation exist: microencapsulation and macroencapsulation ([26](#)). Microencapsulation pores range from 100 to 1000 µm in size and can store 1-2 islets per capsule. Hydrogels and alginate are the most common materials used in microencapsulation. Frequently, microencapsulated islets are transplanted into the peritoneal cavity due to their large islet capacity; however, the use of the omentum as a transplant site can be considered as it is significantly more vascularized ([27](#)).

Macroencapsulation uses an implantable device that measures 1mm or greater in size ([28](#)). This device is trackable and also easily removable from the body if complications arise. An example is the Flexible Bilaminar device developed by Chang et al., which used nanoporous polycaprolactone (PCL) membranes with a 20-200 nm pore size ([29](#)). This device was successful in reducing the immune response and fibrosis.

Table 1: Advantages and Disadvantages of Micro and Macro Encapsulation

	Microencapsulation	Macroencapsulation
Advantages	Faster diffusion of materials into and out of the islets due to larger surface area to volume ratio	Easily implanted and removed from the body.
	Lower islet density inside the capsule reduces hypoxia	Thicker walls provide greater protection from physical damage.
Disadvantages	They are hard to remove from the peritoneal cavity because they can stick to proteins, become surrounded by fibrous tissue, or attach to the omentum ([30]).	Greater diffusion distance and islet density lead to hypoxia, especially in the islets in the center.
	Few locations in the body where microencapsulated islets can be successfully implanted.	Delayed insulin response to increase in blood glucose concentration due to larger diffusion distance.
	Hydrogel pore sizes are variable due to chemical reactions in the body, which affects their semi-permeability ([31]).	Macrocapsule can be recognized as a foreign object, leading to fibrosis around the device, which reduces nutrient and oxygen supply to the islets ([32]).

A new macroencapsulation design known as βAir offers a unique solution to the problem of low oxygen supply to the islets as it is equipped with a refillable oxygen tank ([33]). Although the in-human study did not yield positive results, as the β-cells showed delayed insulin production and the device required overly frequent refilling, the foundation for innovative designs to remedy the current problems with encapsulation has been laid.

3.1.3. Ice-Free Vitrification of Islet Cells

Another concern with islet transplants is the short period that islets can be stored between retrieving from a dead donor till transplant (around 48 - 72h). Traditional cryopreservation methods that relied on slow cooling (<1ºC/min) resulted in the formation of extracellular ice, which caused damage to the islets.

A new method by Zhan et al. in 2022 relies on vitrification followed by rewarming (VR method). Specifically, this process uses rapid cooling into a non-crystalline, glass-like state in which the tissues are stored until they need to be thawed by rewarming ([34](#)). A specific concentration of Cryoprotective Agents (44%), such as Dimethyl Sulfoxide and Ethylene Glycol, was used to prevent ice formation while simultaneously limiting toxicity.

The new VR method has shown high survival rates (an average of 90%) for all kinds of islets, such as human, porcine, and SC (Stem cell) islets, after nine months of cryopreservation ([34](#)).

3.1.4. Alternative Sites of Implantation - Omentum

The portal vein has been the preferred implantation site for islet transplants due to its accessibility and lower morbidity. However, the portal vein also contributes to losing a majority (50-70%) of the islets. IBMIR is quite pronounced in the portal vein, which may lead to PVT (Portal Vein Thrombosis) ([35](#)). Kupffer cells and liver lymphocytes present in the liver also attack the islets. The portal vein also has a low oxygen supply, which may lead to hypoxia in the transplanted islets ([36](#)).

Among several alternate transplant sites that address the shortcomings of the portal vein, the omentum has emerged as the leading contender ([37](#)). The omentum is highly vascularized, providing an adequate supply of oxygen and nutrients to the islets, which is crucial for survival. An omental pouch can be created, which concentrates the islets into the peritoneum, from which insulin is released directly into the portal vein, mimicking the actual β-cells of the pancreas ([38](#)). A study conducted on diabetic mice showed that the mean time taken for transplanted islets in the omentum to reach euglycemia (normal blood glucose concentration), 13.9 days, was lesser than that of islets in the liver, 15.1 days ([39](#)). A combined transplant approach study, in which islets were infused both through the omentum and portal vein, showed promising results as all hyperglycemia in all four patients was controlled, and the effectiveness lasted longer than when the islets were infused only through the portal vein ([40](#)).

3.2. Porcine Islet Transplantation

Using islets derived from pigs to cure T1DM is a highly effective solution to one of the major drawbacks of human islet transplantation - the shallow donor-to-patient ratio and the fact that only islets from dead donors are being used. Porcine islets can potentially treat T1DM in humans for a few main reasons. Firstly, human and porcine islets (neonatal/adult) are quite similar in size and composition, and human and porcine insulin differ by only one amino acid at the carboxyl end of the β chain (Alanine in pigs vs Threonine in humans) ([41](#)).

A 2016 trial by Matsumoto et al. showed that upon injection of 20,000IEQ/kg porcine islets into 4 patients, all showed signs of lesser hypoglycemia unawareness and developed insulin independence for more than 600 days, showcasing the treatment's potential([42](#)).

3.2.1. Porcine Islet Sources

Neonatal Pig Islets (NPIs) are immature cells that are precursors to the islet cells. NPIs consist of 35% pancreatic endocrine cells and 57% epithelial cells, but these epithelial cells have the unique property of differentiating into β-cells. (43) Adult Pig Islets (APIs) remain the primary source of islets as a much larger number of islets can be isolated from them at a higher islet purity (44) (45).

The isolation and purification process of porcine islets is similar in many ways to human islets. The Oxford Chamber has shown promising islet yield and purity results - about 5000 islets/g pancreas can be obtained (46). A subtle difference in the process exists concerning the temperature maintained in the chamber - 35C when isolating porcine islets and 37C when isolating human islets (47). In purification, Iodixanol is preferred to Ficoll solution as it has shown better islet yield and viability (48).

3.2.2. Genetically Modified Pigs

Predictably, xenoantigens present on the surface of the porcine islets lead to an aggressive IBMIR response from the leukocytes. However, solutions to this have been discovered as genetically edited pigs.

Triple-knockout or TKO pigs have three genes removed that are linked to the production of enzymes that catalyze the synthesis of carbohydrate xenoantigens that trigger an immune response from the body (49).

Table 2: Triple-Gene Knockout Pigs in detail

Name of genetically modified pig	Enzyme associated with gene	Carbohydrate antigen
GTKO (50)	α1,3-galactosyltransferase	Gal (Galactose-α1,3-Galactose)
CMAH-KO	CMAH	Neu5Gc
β4GalNT2-KO	β-1,4N-acetylgalactosaminyl transferase	SDA

hCD46 is a human gene introduced into pigs to reduce the acute rejection faced by porcine islet cells. The hCD46 pig-sourced islets did improve islet lifespan and insulin production in the long run compared to the control pig islets, however, did not significantly improve the initial survival of the islets due to the IBMIR (51). Even still, they moderately reduced thrombosis and inflammation in response to the IBMIR (52).

CTLA4/CD152 is another human gene introduced into pigs to reduce IBMIR. T-cells usually rely on two signals before initiating an immune response - the first signal comes from recognizing the foreign antigen, and the second comes from a co-receptor pathway. The CTLA-4 protein reduces the immune response by blocking the second signal (it blocks the CD28/B7 pathway) thus, T-cells do not get activated and thus do not attack the islets (53).

3.2.3. Monoclonal antibodies

mAbs (monoclonal antibodies) function similarly to CTLA-4 - suppressing the immune response by interfering in key reactions required for T-cell activation (54). Both the Anti-CD40 and Anti-CD154 mAbs block the CD40/CD154 pathway that activates CD4+ T-cells (54).

3.2.4. PERVs (Porcine Endogenous Retroviruses)

Since the onset of research on porcine islet transplantation, the transmission of PERVs from pigs to humans has been considered a risk. However, no recorded cases of transmission of PERVs have occurred in trials. Specifically, a trial conducted by Matsumoto et al. (2014) showed that out of 14 patients who had undergone porcine islet transplantation, none tested positive for PERVs (55).

Still, it has been demonstrated that PERVs can infect human cells (PERVs infecting human cells). Recently, a method of using CRISPR-Cas9 technology to deactivate all the PERVs in pigs has been developed. The PERVs are deactivated initially within pig fibroblast cells and subsequently utilized to generate PERV-free embryos through Somatic Cell Nuclear Transfer (SCNT) (56).

3.3. Mesenchymal Stem Cells (MSCs)

Mesenchymal Stem Cells (MSCs) are multipotent stem cells that can differentiate into a range of cells: adipocytes, chondrocytes, osteoblasts, endothelial cells, and pancreatic cells (57). MSCs are helpful in the treatment of T1DM, not only due to their ability to differentiate into β-cells (58) but also their immunomodulatory effects, which are very important for preventing auto-immune rejection of the new β-cells introduced into the body. MSCs can be derived from multiple sources, including bone marrow, adipose tissue, umbilical cord, placenta, and skeletal muscles. MSCs also lack the ability to form teratomas, as their differential potential is limited to mesodermal lineages (59).

The International Society for Cellular Therapy (ISCT) has established three main criteria for using MSCs in T1DM cell therapy (60).
1. "MSCs must be plastic-adherent under standard culture conditions.

2. The cells display certain surface markers/antigens like CD105, CD73 and CD90 and do not display surface markers such as CD45, CD34, CD14, or CD11b; CD79 alpha or CD19; HLA-DR

3. MSCs must be able to differentiate to any 2 of adipocytes, chondroblasts, and osteoblasts under standard in vitro culture conditions."

3.3.1. Angiogenic potential of MSCs

The surrounding vascular tissue is removed or damaged heavily during the isolation and purification of islets before transplantation. This is problematic as islets usually have around 10 times the capillary density compared to the surrounding exocrine tissues (61). The revascularization of islets requires, firstly, the breaking down of existing vascular walls and, secondly, the induction of Endothelial Cells (ECs) to multiply and differentiate into vascular tissues (known as Sprouting of ECs).

MSCs secrete protease enzymes that help break down the extracellular matrix surrounding the ECs, which consists of collagen and other fibrous proteins, to facilitate their migration. MSCs also increase the production of Angiopoietin and vascular endothelial growth factor (VEGF), which helps increase the sprouting of the ECs (62)(63)(61)(64). The results of in-vitro trials were promising. MSCs improved the adherence of the ECs to the islets by approximately 3 times and the total sprouting of the ECs by 2 times.(61)

3.3.2. Immunomodulatory/Anti-Inflammatory Effects of MSCs

MSCs have inherent properties that significantly reduce the chances of autoimmune rejection, which reduces the patient's dependence on immunosuppressants and increases the duration of insulin independence. Co-transplantation of MSCs with islets is an effective treatment solution that has shown positive results in trials.

Firstly, MSCs express very little to no HLAs and do not produce T-cell co-stimulatory molecules like CD80 and CD86, so are quite unlikely to attract an immune response due to IBMIR (65). MSCs suppress T-cell multiplication (66) and effectiveness by secretion of soluble factors like TGF-β1 (67) and HGF, as well as suppression of CD3/CD28 antibodies (68) that activate CD4+ and CD8+ T-cells. MSCs also increase T-regs' potency by increasing their proliferation rate and the secretion of Il-10, an anti-inflammatory cytokine. (69) MSCs, through direct contact with the cells or through the aforementioned soluble factors, reduce the proliferation of NKT (70) and B-Cells, which are very important to the strength of the immune response to the islets. B-cells are arrested by the MSCs in the G0 phase of their cell cycle (71). MSCs promote the transformation of macrophages from a pro-inflammatory M1 to an anti-inflammatory M2 phenotype, aiding in inflammation resolution and tissue repair (72).

Table 3: Comparison of three main sources of MSCs

Characteristic	Bone Marrow (BM-MSCs)	Adipose Tissue (AD-MSCs)	Umbilical Cord (UC-MSCs)
Source	Bone marrow	White Adipose Tissue (PLAs)	Umbilical Cord, Wharton's Jelly
Ease of obtaining	Invasive	Minimally invasive	Non-invasive
Immunomodulatory effect	Effective	Effective	Effective
Cell Yield	Medium	High	Medium
Proliferation	Medium	High	High
Revascularization ability	Medium	High	High
Culture (Time till senescence)	Low	Medium	High
Migration ability	High	Low	Low
Existing research and clinical trials	High	Moderate	Low

3.3.3. Cell Fusion of BM-MSCs with β-cells

An extremely novel approach to using BM-MSCs in the T1DM treatment is fusing it with the β-cells to effectively produce a fused cell that displays the advantages of both cells. Cell fusion can be triggered in three different ways: electric pulses, polyethylene glycol (PEG), and inactivated viruses (73). The cell behaves like a polyploid synkaryon; its nucleus contains genetic and epigenetic information for both cells combined (74). A study by Yanai et al. using fused β-MSCs in rats and mice showed that the fused cells had marginally better insulin production rates than co-cultured MSCs and β-cells (75). In vitro, the fused cells had longer viability than the co-cultured cells (75).

3.4. Use of T-regs in T1DM Treatment

T-regs have the potential to function similarly to MSCs when they are co-transplanted with islets. They have similar immunosuppressive capabilities, like not triggering an immune response themselves and secreting anti-inflammatory factors that could reduce the strength of the IBMIR and hence prolong islet lifespan.

3.4.1. Migration capabilities

T-regs have poor migration capabilities, preventing them from exhibiting their maximum immunosuppressive function when induced along with the islets at the portal vein (76). This can be resolved by using external chemical factors such as CCL-22 to induce T-reg movement to the target site (77). Bio-engineered polymers that continuously secrete CCL-22 have been tested and shown to induce T-reg migration in vivo in mice (78).

3.4.2. Insulin inhibits IL-10

Insulin secreted by the β-cells has been shown to inhibit the release of IL-10 by T-regs (79). IL-10 is an extremely important anti-inflammatory cytokine, without which the T-regs' ability to reduce the IMBIR and provide long-run immunosuppressive functions is severely diminished (80). The provision of external insulin (not produced by the transplanted islets) for a short duration after transplant can be used to reduce the production of endogenous insulin so the T-regs' initial function of lowering the IBMIR is less suppressed.

3.4.3. Cryopreservation

T-regs' effectiveness post-cryopreservation is extremely diminished: T-regs show lesser IL-10 (81) and CCR5 production (82). Thus, T-regs cannot be stored realistically for a long time before a scheduled islet transplant.

3.5. Human Pluripotent Stem Cells

hPSCs (Human Pluripotent Stem Cells) can also be used to treat T1DM by inducing their differentiation into β-cells. hPSCs are obtained in two major ways: from the inner cell mass of a human embryo (hESCs or Human Embryonic Stem cells) or the dedifferentiation of an adult human somatic cell like fibroblasts (hiPSCs or Human Induced Pluripotent Stem Cells). hPSCs are pluripotent, so they have almost unlimited differential potential. They can be differentiated in vitro or in vivo into any human cell if suitable conditions are present.

Table 4: A Comparison between Human Embryonic Stem Cells (hESCs) and Human Induced Pluripotent Stem Cells (hiPSCs)
(84)

Property	hESCs	hiPSCs
Source	The inner cell mass of blastocyst-stage embryos (usually created using IVF).	Reprogramming adult somatic cells (usually fibroblasts) using Yamanaka Factors: Oct4, Sox2, Klf4, and c-Myc (83).
Differential Potential	Pluripotent - can differentiate into any human cell from the three germ	Similar pluripotency; however, differentiation efficiency is not as high due

	layers.	to residual genetic memory
Epigenetic Memory	None	May retain epigenetic memory of the tissue they were derived from.
Ability to form teratomas	Possible, and teratomas formed are less damaging.	More likely than hESCs, and teratomas formed are highly aggressive.

While hESCs seem like the logical choice out of the two Pluripotent Stem Cells, hESCs have many ethical concerns regarding their use, not limited to the destruction of human embryos specifically created for laboratory use, which some people view as destruction of potential human life ([85](#)). Hence, the use of iPSCs, free of ethical concerns while providing very similar pluripotent and self-renewal abilities, has been garnering a lot of excitement.

Rezania et al. described a 7-stage process for differentiating hESCs into insulin-producing β-cells, which can also be applied to hiPSCs ([86](#)). For successful differentiation, transcription factors such as MAFA, PDX1, NKX6.1, and NEUROD1 are required ([86](#)). PDX1 can induce differentiation of hPSCs into any pancreatic cell ([87](#)), but with the addition of NKX6.1 ([88](#)), only endocrine cells can be produced. NEUROD1 is essential for the production of immature β-cells and the subsequent maturation into insulin-producing β-cells ([89](#)). MAFA is needed for regulating insulin production in the mature β-cells ([90](#)).

Early studies by D'amour et al. ([91](#)) using hESCs and Tateishi et al. ([92](#)) showed proof of concept in successfully differentiating stem cells into β-cells. However, insulin production was low, and many cells produced were polyhormonal. The injection of external pancreatic factors such as Retinoic Acid (RA), Epidermal Growth Factor (EGF), and KGF (Keratinocyte Growth Factor) by Russ et al. in 2015 was effective in increasing the differentiation efficiency (from 7.3% in D'amour et al.'s study to almost 60% ([93](#))([91](#)). A decrease in the percentage of polyhormonal cells was also observed. Polyhormonal cells are considered an issue as they do not express a few important β-cell transcription factors and cannot produce insulin under hyperglycaemic conditions in vitro ([94](#)).

The first-ever human clinical trial studying the feasibility and effectiveness of Pluripotent stem cells is currently being conducted by Shapiro et al. The preliminary results are promising, with 63% of the patients showing insulin production within a year and 35.3% showing positive C-peptide levels, which indicates that excess insulin is being produced in the body. However, adverse effects stemming from heavy immunosuppression (33.7%) and post-surgical complications(27.9%) were not uncommon among the patients ([95](#)).

hPSCs are the most recent treatment discussed in this review but have shown immense potential and promising results so far.

4. Conclusion

Type 1 diabetes mellitus (T1DM) is a persistent condition that can cause numerous serious complications over the patient's lifetime. Therefore, it requires efficient and enduring treatment. The treatments examined in this review encompass a combination of established and emerging options, although they are not yet fully developed. The review focuses on recent innovations, both major and minor, that aim to solve the major issues with cell-based therapies currently so that they can become available to the broader public soon.

To overcome the high amount of immunosuppressants needed in islet transplants, the use of encapsulation or co-transplantation with MSCs or T-regs has been discovered, as well as the application of VR method to improve the duration that islets can be stored. The use of genetically edited pigs to reduce the body's immune response to porcine islets is also gaining traction. The injection of external pancreatic growth factors to improve the differentiation efficiency of hPSCs into β-cells shows that innovation is occurring even in the newest treatment so far.

Follow-up studies on the new research being conducted and new methods being developed may soon result in there being many viable methods for T1DM patients to treat their condition.

Abbreviations:
T1DM - Type 1 Diabetes Mellitus
HU - Hypoglycemia Unawareness
HLA - Human Leukocyte Antigen
VNTR - Variable Number of Tandem Repeats
PTPN22 - Protein tyrosine phosphatase non-receptor type 22
CITR - Collaborative Islet Transplant Registry
IBMIR - Instant Blood Mediated Inflammatory Reaction
VR - Vitrification and Rewarming
PVT - Portal Vein Thrombosis
GTKO - Galactosyltransferase Gene Knockout
CMAH-KO - cytidine monophosphate-N-acetylneuraminic acid hydroxylase knockout
β4GalNT2-KO- β-1,4N-acetylgalactosaminyltransferase-2 Knockout
PERV - Porcine Endogenous Retrovirus
MSC - Mesenchymal Stem Cells
IL-10 - Interleukin 10
CCR5 - C-C chemokine receptor type 5
HPSC - Human Pluripotent Stem Cell
HESC - Human Embryonic Stem Cell
hiPSC - Human induced Pluripotent Stem Cell
PDX1 - pancreatic and duodenal homeobox 1
RA - Retinoic Acid
EGF - Epidermal Growth Factor

KGF - Keratinocyte Growth Factor

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The Role of Diet and Lifestyle Patterns in the Development and Management of Hyperlipidemia and Hypercholesterolemia

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Abstract

Besides the connection of hyperlipidemia to genetics, diet, and lifestyle patterns have been found to serve as a substantial contributing factor to its development. Many individuals in the world are influenced by their diet and lifestyle, which dictates their chance of developing hyperlipidemia. Statin is a vastly common medication prescribed to people with hyperlipidemia and hypercholesterolemia. Although many consider statins to be revolutionary in lowering cholesterol levels, the medication does not work for everyone and can cause many side effects. It is widely believed that statins can reduce the risk of having atherosclerosis by lowering cholesterol levels. Research, however, has shown that statins do not have such a positive effect and may, conversely, have a negative impact on heart health. Due to the potential risks and side effects of statin use, attention has increasingly shifted towards dietary approaches and lifestyle patterns that can facilitate the management of hyperlipidemia. Diet, especially, is pivotal in managing hyperlipidemia because cholesterol is embedded in consumed foods. In managing hyperlipidemia through dietary measures, controlling lipid intake and permitting only specific types of lipids is essential. Effective dietary management requires regulating lipid intake and selecting specific types of lipids. Diets high in trans and saturated fats should be substituted with healthier unsaturated fats, such as those in tree nuts and soybeans. Additionally, RYRE (Red Yeast Rice Extract), soluble fibers, and omega-3 fatty acids are excellent replacements for a diet high in trans and saturated fats. This literature review provides an analysis of how diets and lifestyle patterns affect hyperlipidemia and hypercholesterolemia. In addition, it addresses a gap in the literature regarding the most effective dietary options for managing hyperlipidemia. This gap relates to the uncertainty over whether to replace saturated fats with carbohydrates or other types of fats, such as monounsaturated or polyunsaturated fats. A broader understanding of diet and lifestyle patterns is essential for finding alternative approaches to managing hyperlipidemia and hypercholesterolemia beyond medication.

Introduction

Hyperlipidemia is a condition for having high levels of lipids (fats) in one's blood. It's a condition that broadly represents an increase in one or more types of lipids: LDL, HDL, triglyceride. LDL (low density lipoprotein) is composed of lipids and proteins which serve as carriers of fats through one's bloodstream and to many cells in the body. LDL is commonly referred to as the "bad cholesterol" because an increased level of LDL is linked with risks of getting various heart diseases. HDL (high density lipoprotein) is a combination of lipids and proteins as well, but their job is to carry excess cholesterol from the bloodstream to the liver. HDL is commonly known as the "good cholesterol" because it removes the extra amount of cholesterol in the body by transporting cholesterol to the liver, in which the liver breaks it down and excretes it through the feces. Triglycerides are another type of lipid that the body converts excess calories into and stores as fat. Whereas hyperlipidemia is a condition that represents abnormalities in multiple types of lipids, hypercholesterolemia is characterized by high levels of LDL cholesterol and total cholesterol (a sum of HDL, LDL, and 20% of triglycerides) (Yao et al., 2020). The normal LDL cholesterol level ranges from 100 to 129 mg/dL, while high LDL-C is 160 to 189 mg/dL. An HDL level of 40 mg/dL or less is classified as low, and 60 mg/dL or above is considered high. For fasting individuals, normal triglyceride levels are under 150 mg/dL, with 500 to 886 mg/dL considered high (Lee et al., 2023).

Genetic Factors that Contribute to Familial Hypercholesterolemia (Type of Hyperlipidemia)

Familial Hypercholesterolemia (FH) is a genetic disease marked by an increased level of LDL within the blood of an individual. It escalates the chances of developing atherosclerosis and tendon xanthomas. The primary causes of familial hypercholesterolemia are the pathogenic variants within the genes that code for PCSK9 (Proprotein Convertase Subtilisin/Kexin Type 9), LDLR (LDL Receptor), or the ligand of LDLR known as APOB (apolipoprotein B). Less common factors include pathogenic variants within the genes encoding STAP1 (signal-transducing adaptor family member 1) and APOE (apolipoprotein E) (Di Taranto et al., 2020).

Patients with FH show significant variation in their genotypes.. Some patients with only one copy of the FH gene (heterozygous FH) had cholesterol levels similar to those with two

copies of the gene (homozygous FH). Additionally, some patients with heterozygous FH were found to have normal cholesterol levels. To accurately diagnose FH, it is important to recognize the variant responsible for the condition (Di Taranto et al., 2020).

Drugs for Dyslipidemia

The three metabolic pathways that significantly impact serum cholesterol levels are dietary cholesterol intake, synthesis, and cholesterol degradation. As applied in many cholesterol medications, a crucial approach to lowering serum cholesterol levels is an inhibition of the molecules within the three metabolic pathways. In the case of statins, LDL has been found to be reduced through the inhibition of HMG-CoA reductase (3-hydroxy-3-methylglutaryl coenzyme A reductase). The combination of statin with other cholesterol drugs, such as Ezetimibe and Evolocumab, is a prevalent method to control the three metabolic pathways. Ezetimibe works by blocking the molecule NPC1L1 (Niemann-Pick C1-like 1 protein), thus inhibiting the absorption of cholesterol in the intestines. PCSK9 (proprotein convertase subtilisin/kexin type 9) accelerates the degradation of LDLR (LDL Receptor), which disrupts the ability of the liver to remove LDL from the bloodstream, contributing to hypercholesterolemia. Evolocumab, a monoclonal antibody targeting PCSK9 (proprotein convertase subtilisin/kexin type 9), also contributes to lowering LDL levels. Statins are widely recognized as the most common cholesterol-lowering medications; however, their status as the safest option with no side effects is not assured. Research indicates that approximately 15% of individuals experience negative side effects when they have taken high doses of statin (Xu et al., 2020).

It is a widely accepted idea that statins reduce the chance of an individual developing atherosclerosis. However, research has found that statin can negatively impact heart health and is even associated with atherosclerosis. Statins can contribute to coronary artery calcification, leading to damaged muscles in the heart and blood vessels. It also interferes with the formation of vitamin K2, which is essential for preventing arterial calcification. Additionally, statins can hinder the production of proteins that contain selenium, like glutathione peroxidase, and therefore can interfere with relieving oxidative stress. A lack of selenium-containing proteins can increase the risk of congestive heart failure. Rather than enhancing heart health, statins carry several risk factors that may potentially lead to the development of atherosclerosis (Okuyama et al., 2015).

These negative side effects highlight the need to develop alternative approaches to managing hyperlipidemia. Diet is now recognized as one of the safest and most effective approaches, and it will be discussed in the next section.

Diets That Improve Hyperlipidemia and Hypercholesterolemia

For individuals diagnosed with hyperlipidemia, the ultimate health goal is to lower the levels of LDL, triglycerides, and total cholesterol while increasing the levels of HDL. The shared goal for those who genetically have hypercholesterolemia is to reduce LDL cholesterol and total cholesterol levels. The key to achieving these health goals is to be selective regarding the type of fat consumed and control fat intake. Effectively combating hyperlipidemia and hypercholesterolemia requires following proper dietary recommendations and making nutritional changes (Kelly, 2010).

Many diet guidelines recommend that individuals reduce their intake of saturated and trans fats and replace them with unsaturated fats (e.g., polyunsaturated and monounsaturated). Studies have shown that limiting cholesterol intake to 220 mg per day can reduce LDL levels by 9% to 12% (Van Horn et al., 2008).

Tree nuts are an example of food low in saturated fats but high in unsaturated fats. Consuming 1 to 3 oz of tree nuts daily is an effective replacement for diets high in saturated fats. Research has found that tree nuts can effectively decrease LDL, ranging from 2 to 19%, when consumed weekly or at least 5 days (Mukuddem-Ptersen et al., 2005). In addition to tree nuts, soybeans are another good option. Although soybeans do not drastically lower LDL and total cholesterol levels, they are beneficial for raising HDL levels. Therefore, a daily intake of 1 to 1.5 oz of soybeans daily is recommended (Reynolds, 2006).

Cultural foods like the RYRE (Red Yeast Rice Extract), a traditional seasoning made from Monascus purpureus, contain compounds such as lovastatin that effectively improve hyperlipidemia and hypercholesterolemia. Providing similar effects to statin medications, it is one of the most effective diet options for lowering total cholesterol, LDL, and triglyceride levels. The only concern is that during the process of preparing Red Yeast Rice Extract, it is not always possible to exclude harmful byproducts of fermentation. Considering this, Red Yeast Rice Extract may not be the best option for individuals concerned about harmful byproducts of fermentation or those who do not experience side effects of statin medications. However, it is a

good alternative diet option for those who experience side effects of statin medications like muscle pain (Becker et al., 2009).

Soluble fiber is an effective diet option for improving hyperlipidemia and hypercholesterolemia. Dietary fiber, including both soluble and insoluble, cannot be digested (i.e not broken down by the digestive enzymes in the small intestine) and originates from the carbohydrate parts of plants. Many misconceptions exist regarding the true health effects of different types of fiber. Soluble fibers, which have high viscosity (a measure of the resistance to flow), provide the most significant health benefits when it comes to lowering cholesterol levels. However, nonviscous and insoluble fibers do not yield health benefits similar to those of soluble fibers. Examples of soluble fibers include β-glucan (found in certain mushrooms, oats, and barley), psyllium (from Plantago ovata), and raw guar gum (from guar beans). Nonviscous fibers include low-molecular-weight β-glucan (found in oats and barley), methylcellulose (chemically transformed cellulose), inulin (present in various plants including onions and garlic), and wheat dextrin (derived from wheat starch). Wheat bran (found in wheat grains) and cellulose(within the cell walls of vegetables, fruits, legumes, grains) are examples of insoluble fibers (McRorie & McKown, 2017).

Omega-3 fatty acids are considered to be highly beneficial in managing triglyceride and LDL levels, which directly relates to the management of hyperlipidemia and hypercholesterolemia. For individuals who are on medications like statins or fibrates for lowering their lipid levels, omega 3 fatty acids are safe to consume because they have very little drug-to-drug interactions with other drugs. Additionally, omega 3 fatty acids do not affect the liver function, which is even better for those who are on multiple lipid-modifying medications and are worried about drug-induced liver injury. Omega-3 fatty acids can also enhance health benefits when combined with statins (Backes et al., 2016).

Low-Fat and Low-Carbohydrate (Ketogenic) Diet in Regards to Obesity, Insulin Resistance, and Insulin Sensitivity

Researchers have shown that there is a major difference in the effects of low-fat and low-carbohydrate diets on the lipid levels. Low-fat diet was found to have the most beneficial impact on LDL and total cholesterol levels, while a low-carbohydrate diet showed the most positive effect on HDL and triglyceride levels (Nordmann et al., 2006). A clinical research was

conducted, with 120 people who are overweight and have hyperlipidemia, to compare the effects of a low-fat diet to that of the low-carbohydrate (ketogenic) diet. Low-carbohydrate diet resulted in greater weight loss and higher participant retention. Additionally, at the peak of the weight loss phase, the low-carbohydrate diet led to a more significant decrease in triglyceride levels and a greater increase in HDL than the low-fat diet (Yancy et al., 2004).

Hyperlipidemia and hypercholesterolemia are directly related to the potential development of CVD(cardiovascular disease) by an individual. In response to this health risk, many diet guidelines have emphasized a drastically lower consumption of saturated fats to prevent its development. Replacing saturated fats with polyunsaturated fats has been associated with a reduction in CVD risk, though the effect is not substantial. It has been proven that replacing a saturated fat diet with monounsaturated or polyunsaturated fat lowers LDL levels. In a different study where saturated fat was replaced with large intakes of carbohydrates, it was found that triglycerides and LDL levels increased, while HDL decreased. Consuming carbohydrates, particularly refined ones with added sugars and processed grains, is closely linked to obesity and insulin resistance and can exacerbate atherogenic lipid abnormalities (Siri-Tarino et. al., 2010).

Research has demonstrated that the consumption of saturated fats can reduce insulin sensitivity, while omega-3 fatty acids can enhance it. Insulin sensitivity reflects how efficiently the body responds to insulin, and higher insulin sensitivity is crucial, as it plays a key role in preventing diabetes and obesity. In fact, saturated fats can weaken insulin sensitivity by decreasing the secretion of adiponectin and disrupting the insulin signaling pathways. These pathways are crucial for glucose uptake in white adipose tissue but can be impaired by saturated fats, thereby lowering insulin sensitivity (Siri-Tarino et. al., 2010).

Lifestyle Patterns

Exercise plays a very important role in managing hyperlipidemia and hypercholesterolemia. Aerobic exercise, in particular, has been found to positively impact individuals' HDL levels. In fact, research has shown that aerobic exercises can amplify HDL cholesterol levels by 1.9 to 2.5 mg/dL. Additionally, a decline in the levels of triglyceride,

LDL, and total cholesterol was observed, with an average of 3.9 and 7.1 mg/dL (Halbert et al., 1999). To effectively increase HDL levels, it is recommended that individuals engage in 2 hours of aerobic exercise per week, aiming to burn 900 kilocalories (Kodama et al., 2007).

Aerobic exercise had a notable impact on cholesterol levels in individuals with CVD (cardiovascular disease). HDL cholesterol levels increased by approximately 9%, while triglyceride levels reduced by about 11%. Thus, aerobic exercise is an efficient option for individuals who already have CVD and those at a high risk of developing it (Kelley et al., 2006).

Conclusion

In order to lower the levels of LDL, triglyceride, and total cholesterol, an individual should be strictly selective about the type of lipids in their diet. A diet that is high in trans and saturated fats are recommended to be avoided the most and should be replaced with the following: unsaturated fats found in tree nuts and soybeans and other healthy replacements, including RYRE (Red Yeast Rice Extract), soluble fibers, and omega-3 fatty acids. Additionally, regarding the uncertainty over whether to replace saturated fats with carbohydrates or with other types of fats(monounsaturated and polyunsaturated), carbohydrates are not recommended because they increase the risk of insulin resistance and obesity. As for amplifying the levels of HDL, it is highly recommended that individuals who are at the risk of developing hyperlipidemia and who have CVD practice aerobic exercises on a weekly basis. The significance of diets and lifestyle patterns in the development and management of hyperlipidemia and hypercholesterolemia has been clearly presented. However, if dietary and lifestyle recommendations are not followed consistently, success in managing hyperlipidemia may vary significantly.. In order for individuals to reach their goal in managing their cholesterol levels, their diet options and lifestyle patterns should be personalized and customized.

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Bridging Minds: How AI Can Help Unravel the Differences Between Bonobos and Chimpanzees by <u>Alegre Maurer, Sofia,</u>[1] Ross, Miriam,[2] Gil Dolz, Jose[3]

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Research Question

"How do chimpanzees and bonobos compare in their behavior, culture, and communication and can artificial intelligence tools from other species be applied to better understand these differences?"

Abstract

This paper explores the comparative behavior, societal structures, and communication patterns of chimpanzees (Pan troglodytes) and bonobos (Pan paniscus), including their xenophobic or xenophilic tendencies. The study synthesizes existing research contrasting the social dynamics of these closely related species. Chimpanzees often display xenophobic behaviors marked by aggression and intergroup conflict, while bonobos exhibit more xenophilic tendencies, emphasizing tolerance and affiliative interactions even with unfamiliar individuals. By analyzing these behaviors, the paper explores the communication of primates including gestures, vocalizations and actions and the nuances of their social interactions. This paper proposes that because of this complexity, advancements in artificial intelligence (AI) hold significant potential for deeper insights while interpreting primate communication. Enhanced AI will provide more precise decoding of vocalizations, gestures, and other communicative signals, offering a more granular understanding of primate social behavior and interspecies relations. In better understanding the chimpanzee and bonobo differences we may also gain insight into human nature and evolution. This paper explores advances in AI across other species and evaluates their applicability to the open questions around bonobo behavior.

Introduction

Investigating the differing social behaviors of chimpanzees and bonobos is important for understanding the evolution of sociality in all primates, including humans. These two species are very similar genetically but have markedly different social structures, offering a unique opportunity to explore the underlying mechanisms driving these behaviors (Wrangham and Pilbeam). Chimpanzees are sometimes aggressive with xenophobia towards outsiders, including humans (Mitani and Watts). In contrast, bonobos are known for their more peaceful and cooperative social interactions (Abbink). They display xenophilic behaviors even towards strangers (Hare and Yamamoto). Analyzing behavioral differences and similarities like these can provide insights into the evolutionary pressures and environmental factors that shape social strategies and intergroup relations. Investigating these differences is important for the following reasons:

1. Biology and Evolution: Understanding the distinct social behaviors of chimpanzees and bonobos may help understand how evolution led to human behaviors and society (Wrangham and Pilbeam).

2. Cognitive Science: This research contributes to the broader fields of cognitive science and ethology by providing ideas to study the problem-solving abilities and methods of various species that might apply to bonobos (Tomasello and Call).

3. Artificial Intelligence: With the recent advances of artificial intelligence, its application in primate communication analysis holds promise for figuring out the intricate vocalizations, gestures, and other communication used by these species (Petkov and Jarvis). While this paper does not conduct AI analysis, it highlights the potential of AI to enhance our understanding of primate communication and evaluates which tools and techniques used in other species might hold the most promise.

4. Conservation Efforts: Insights into how these species interact with humans can inform conservation strategies in the wild and mental health insights for captive primates (Hockings).

Perhaps the key to human aggression is hidden in these bonobo and chimpanzee differences and AI could help decipher it. As an example, if broadly speaking chimps tend to be more xenophobic and bonobos xenophilic, why has that distinction not extended to behavioral phenomena like the reaction each have to other primates, such as visitors to a zoo? Or, if chimps are male dominated and bonobos female dominated, might we expect to see more difference in the reaction of each sex to possible threats? We believe it is possible that there are different reactions in both cases but it is hard to capture them given the limitations of observational ethology and AI might better yield these distinctions and insights.

By combining current research in AI, with open questions around bonobos, this paper aims to advance our comprehension of primate behavior and improve our methods for studying them.

Literature Review and Background Research

Overview of chimpanzees

Chimpanzees live in large groups of 20 to 120 families, but sometimes breaking into smaller groups and coming back together. The family ties are strong, with mothers and sons particularly sharing lifelong bonds. Females move to new groups when they mature, while males stay in their birth group. Female chimps have babies every 5 years, nurturing them closely until they are about 5 years old. If a mother dies, others in the group, like siblings or adult females, often take over care, although this can be challenging. For example, Jane Goodall observed a young male named Sniff adopting his baby sister after their mother died.

Chimps also have a rich culture, using vocal calls to communicate about food and danger. They learn behaviours like making nests and using tools through imitation. Grooming is a big part of their social life, fostering trust and bonding. They have complex emotions and behaviours similar to humans, from nurturing and play to aggression and reconciliation. Chimps forage and hunt together, respecting a social hierarchy led by a dominant male, with politics influenced by alliances and coalitions(*Chimpanzee Society | Chimpanzees | Project R&R*).

Biological review of chimpanzees and bonobos

Common chimpanzees (Pan troglodytes) are described by their size, weight, and coloration. Behaviorally, they are adept brachiators, omnivorous with a preference for fruit and vegetation but also engaging in hunting, and exhibiting advanced cognitive abilities including tool use and medicinal plant consumption.

Chimpanzees live in fluid groups with fission-fusion pattern, where individuals form alliances and hierarchies centered around alpha males. Reproduction is polygynandrous, with females mating with multiple males and males competing for access to females during estrus periods.

Biologically the four ways bonobos can be visually distinguished from chimps are body size and shape, the way they walk, facial features and the sounds they make (*Biological Overview of Chimpanzees | Animal Legal & Historical Center*).
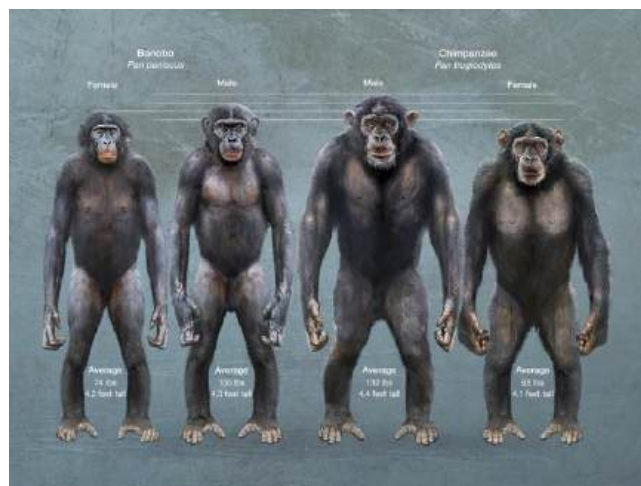

Figure 1: (Image by National Geographic)

Bonobos and chimpanzees are similar in their appearance which isn't surprising as they share 99.6% of their DNA. And the parts they don't share with humans are different for each. Bonobos are smaller, more likely to walk on their hind legs, bonobos are black face with pink pigmentation, and they have higher pitched voices that use less grunting and hooting. The bonobos are slightly smaller and have higher voices (Grawunder et al.).

One other biological difference "is that bonobos and humans, but not chimps, have a version of a protein found in urine that may have similar function in apes as it does in mice, which detect differences in scent to pick up social cues" (Gibbons). However, other than small differences like this, the genetics and biology are surprisingly similar as the Figure 1 shows.
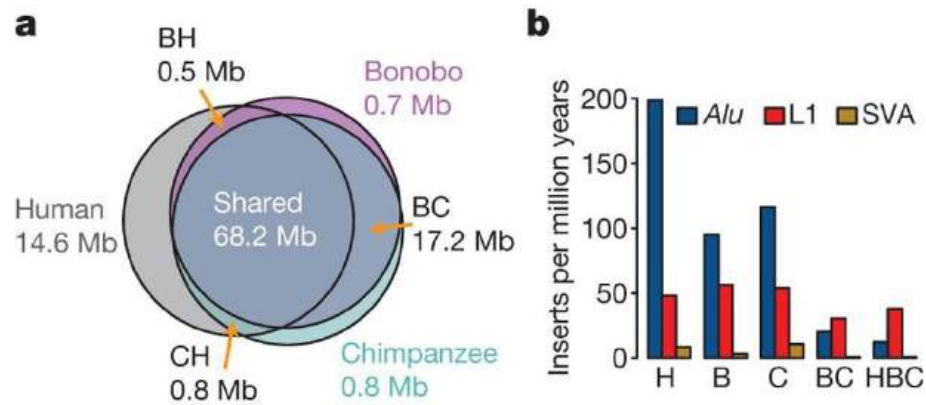
Figure 2: **a**, Venn diagram showing segmental duplications in the human (H), chimpanzee (C) and bonobo (B) genomes. Each number of megabases refers to the total amount of sequence that occurs in segmental duplications (section 4). **b**, Accumulation of different retrotransposon classes on each lineage (Prüfer et al.).

Additionally, a comparison of bonobo and chimpanzee brain microstructure revealed differences in the socio-emotional connections (Issa et al.)   "The story that the bonobo can be safely ignored or marginalized from debates about human origins is now off the table," says de Waal (Gibbons).

A brief review of other articles shows there are not many other genetic or morphological differences between chimps and bonobos, making their social and behavioral differences all the more interesting.

Open questions around bonobos

When it comes to behaviors, the differences between bonobos and chimps are more pronounced especially across gender roles, fear of strangers, aggression, and sex. We will consider those, as well as the animal well-being and conservation in these six sections.

1. Social dynamics and hierarchy
2. Communication
3. Cognitive abilities and problem solving
4. Emotional intelligence, aggression and empathy
5. Visitor effect and mental health
6. Conservation

We will then select relevant AI progress from other species for each.

1.   Social dynamics and hierarchy

Roles: Bonobos Live in Female Dominated Societies

Both bonobos and chimpanzees live in groups that practice male philopatry, which means the males generally spend their whole lives with their birth group, while females tend to leave and join another group around adolescence (Bonobos). Second, like chimps, bonobo females are smaller than bonobo males so bonobo females don't take the upper hand by just strength. And third, because bonobo females leave their natal groups to migrate to new places, they do not have friends or family to turn to for help navigating the social relations of their new groups.

Sex in bonobo society is non-discriminant. Females have sex with males, males with males, females with females, young with old, old with old, and even little ones with each other. Most of it has nothing to do with making babies. This is the unique way bonobos have evolved. They use sexual contact as a tool to build close group relationships, to calm each other down, and to resolve social conflicts. The secret to the female domination comes from two bonobo behaviors: xenophilia and strong female friendships.

Chimp vs bonobo differences in parenting style:

A baby bonobo named Rubin was smacked by an adult bonobo, Olive, right in front of his mom, Rose, in the Congo rainforest. You'd expect Rose to step in, but she didn't, which surprised the observing primatologist, Rachna Reddy. Reddy's study revealed that bonobo moms rarely intervene when their kids are bullied, unlike chimpanzee moms who act like helicopter moms most of the time. This was unexpected because bonobos are generally more peaceful than chimps. The study found that bonobo moms only become involved in 8% of the time when their offspring are in trouble, compared to 50% for chimp moms. Even bonobo bystanders are less likely to help than chimp bystanders (Reddy et al.).

Reddy's team thought bonobo moms might hold back to keep good relations with other females, but they found this wasn't true. Instead, it seems chimps' more violent society makes them more protective and it is theorized that in chimpanzee society, the risks of conflict escalating is far higher/more dangerous than for bonobos. The study challenged the current assumptions about bonobos and suggests that different species of primates can have different ways of parenting.

On the other hand, a study in *Current Biology* shows that bonobo mothers greatly boost their sons' chances of fathering offspring, tripling their paternity success when present. They help by protecting sons from rivals and giving access to fertile females. This doesn't happen in chimpanzees, highlighting the key role bonobo mothers play in their sons' mating, unlike in chimpanzee societies where male dominance limits this influence. Essentially a male bonobo with a mother living in the group had more success finding a mate (Surbeck et al.).

2.   Communication

Bonobos have different communicative behaviors compared to chimpanzees, particularly interactions and vocalizations.

Bonobos and chimpanzees share many gestures, with 88% to 96% looking the same (Fröhlich). However, the meanings of these gestures sometimes differ. Bonobos often respond before a gesture is "fully made", using them in a more anticipatory way. In contrast, chimpanzees take more time, using longer pauses and more gestures in their interactions (Graham).

Bonobos are known for making "peeping" sounds, which researchers believe might be similar to how human babies babble. These sounds can have different meanings based on the situation. Unlike chimpanzees, whose vocalizations are more fixed and tied to specific emotions or events, bonobos' vocal habits suggest they may be evolving toward more advanced ways of communicating (Clay et al., "Functional Flexibility in Wild Bonobo Vocal Behaviour")

The differences in how bonobos and chimpanzees communicate might come from their social structures and environments. Bonobos are usually more cooperative and social, which could lead to more varied and flexible ways of communicating. They also stay closer to each other during interactions, making it easier for them to communicate effectively (Fröhlich).

Both species have advanced communication skills, but bonobos seem to interact more quickly and flexibly than chimpanzees, especially in social situations. This suggests bonobos might be more "talkative" in their adaptable communication. Overall, both share core communication traits from their shared evolution and social behaviors.

3.   Cognitive abilities and problem solving

Chimpanzees and bonobos are genetically similar but show different cognitive abilities and problem-solving approaches, which may help understand human cognitive evolution (Herrmann et al.). Bonobos do better in social cognition, particularly in tasks related to understanding others' mental states, known as "theory of mind" (Grueneisen et al.). They are also more socially tolerant and cooperative, which may boost their cognitive skills in social settings. Brain differences suggest bonobos might have greater empathic sensitivity than chimpanzees (Rilling et al.).

Chimpanzees, on the other hand, are better at physical cognition, excelling in tasks like tool use and understanding physical causality (Herrmann). This may stem from their reliance on extractive foraging in the wild. Chimpanzees also have enhanced visual processing abilities, indicated by the expansion in their visual cortical regions and higher fractional anisotropy values along visual system white matter pathways (Rilling).

Both species use different communication and problem-solving strategies. Bonobos respond better to combinatorial signaling (two signals are used together to achieve an effect that is different to the sum of the effects of the parts) and use a wider range of gestures (Fröhlich). They engage in cooperative turn-taking similar to human conversations and often communicate in close proximity to their partners. When solving problems, both species can adjust their actions based on whether they are cooperating or competing, but bonobos generally perform better in cooperative situations, while chimpanzees excel in competitive ones (Krupenye).

These cognitive differences provide valuable insights into human evolution. Bonobos' social skills may be a precursor to shared intentionality, which is a key for language development in humans. Meanwhile, chimpanzees' physical cognition might reflect early stages of human technological progress. Bonobos' empathic tendencies could also suggest an evolutionary path toward human emotional intelligence (Herrmann; Riling et al). Understanding these differences may even provide insights into evolution of human cognition.

4.   Emotional intelligence, aggression and empathy

While chimpanzees are xenophobic, meaning they are wary of strangers, bonobos are the opposite. Chimpanzees refuse to share food with unknown individuals and often even refuse to share with friends. They are also known to patrol their territory in the wild, often acting aggressively towards strangers or even launching full blown attacks on neighboring troops. But bonobos, despite being so genetically similar, are xenophiles: they adore strangers. Scientists found that a captive bonobo population preferred to share food with a stranger than with a group member (Tan and Hare).

A recent study has challenged these previous assumptions about bonobos and chimpanzees. It found that both species shared food at similar rates, indicating comparable tolerance levels. However, when food could be monopolized, bonobos showed greater cooperation than chimpanzees, consistent with earlier findings. These results question the idea that bonobos are inherently more cooperative due to higher tolerance levels, highlighting the complexity of primate social behavior (Nolte et al.).

Overall though bonobo's, humans closest living relative, are highly tolerant and, even in the wild, are capable of having affiliative interactions with strangers. Bonobos will forego their own food for the benefit of interacting with a stranger and will even help strangers acquire out-of-reach food when no desirable social interaction is possible. This prosocial behavior does have limits, as bonobos won't share food they possess if there's no opportunity for social interaction (Tan and Hare).. These findings suggest that concern for others, even strangers, is not exclusive to humans. Language, social norms, warfare, and cooperative breeding aren't required for the evolution of stranger-directed sharing. Instead, prosocial behavior toward strangers likely evolves through selection for social tolerance, enabling individuals to expand their social networks. Human social norms and language may have later amplified this and extended it to other situations (Tan and Hare).

For instance, when two groups of bonobos meet in the jungle, it often results in uncontained excitement, even varying forms of sex between multiple members. In other words, when bonobos meet other bonobos, they generally say hello by conducting a quick sex interview - AKA "the bonobo handshake." What this means for immigrating females is that they are welcomed when they arrive in a new group. Unlike new chimpanzee females, who sometimes suffer beatings and intense aggression.

They integrate any new female into the strong network of female friendships that allow bonobo females - through strength in numbers - to keep the power and the peace even though they are not as

physically strong as bonobo males. While chimpanzee males are known engage in violent fights over rank, kill infants, rape and beat females, and even murder other chimpanzees, bonobo societies run on the operative, "make love, not war." Bonobos females stick together to keep aggressive behaviors in check and ensure that males stay in line. They resolve conflicts with affection - such as hugging, kissing, playing, and having sex with each other.
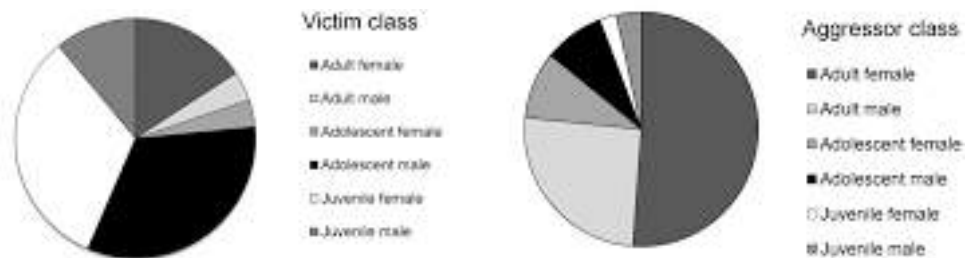

Figure 3: Pie charts show the percentage of total agonistic conflicts (N=356) encountered by different victim (a) and aggressor classes (b) in the bonobo population at the Lola ya Bonobo Sanctuary (Clay and De Waal).

A recent report (Mouginot et al.) did call into question bonobo's peace loving reputation, but it actually shows that while they fight more often, the intensity is lower, and in fact the bickering was more one-on-one than groups against one like the chimpanzees. Chimpanzee aggression was also more likely to involve "coalitions" of males (13.2% vs. 1% of bonobo aggressions). It does show that aggressive males had more success sexually in both species. (Mouginot et al.)

At Lola ya Bonobo, bonobos demonstrate a unique form of kindness by willingly sharing food and avoiding aggression, promoting peace through cooperation and social bonding. This compassionate behavior has drawn scientists from around the world to study them, as it offers insights into the evolutionary roots of human kindness and cooperation (Hamilton). In one study, captive bonobos would release another bonobo from a locked room in order to share food rather than eat alone; in another experiment with sanctuary animals, bonobos were found to actually prefer sharing with strangers than with family or friends, presumably so as to broaden their social group. (Hare and Kwetuenda)

"One day, Camillo, the alpha male from the western community, killed a small antelope, called a duiker, for a meal. Over the next half-hour, females from both communities patiently and demurely asked for a helping by peering at him and stretching out their hands; all the females from his own community, plus a female named Agbaya from the other community, got some of the food. Later, Agbaya took the kill's head and shared the meat with females from both sides of the river. "They grabbed the duiker and shared it. That's really extraordinary," says Fruth."(Fruth and Hohmann)

5.   Visitor effect and mental health

Bonobos, arguably our closest primate relatives, are sometimes kept in zoos and sanctuaries where they may encounter human visitors. The impact of these visitors on bonobo behavior, known as the "visitor effect", has been a subject of keeper and scientific interest.

Research suggests that the presence of visitors can influence bonobo behavior in various ways. A study by Laméris in 2021 found that zoo-housed bonobos exhibited different levels of abnormal behaviors depending on factors such as their rearing history and personality traits (Daan W. Laméris et al.). While this study didn't directly focus on visitor effects, it highlights the importance of considering individual differences when assessing bonobo behavior in captive settings.

Another study examined social tolerance in bonobos and chimpanzees, including their behavior during feeding times (Daan W Laméris et al.) Although it also didn't directly evaluate visitor effects it emphasized the significance of group-specific behaviors in apes. This suggests that the impact of visitors on bonobos may vary between different groups or communities. In fact, each group of bonobos may respond differently. The sanctuary or zoo's visitor protocols, the bonobos' personalities, and their group dynamics all might have some affect in how they react to human visitors. More focused research on bonobo-specific visitor effects would be valuable for improving their welfare captivity.

6.   Conservation
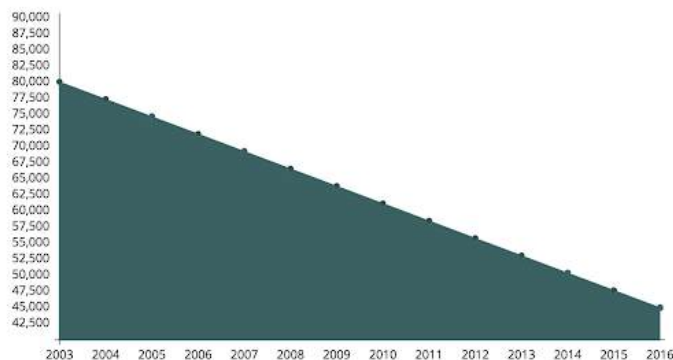
Figure 4: Bonobos (Pan paniscus) are endangered great apes and they are found in the wild in the Democratic Republic of Congo (DRC). Their population has declined significantly, with most current estimates from The IUCN Red List of Threatened Species suggesting around 15,000-20,000 individuals remaining in the wild.

The main threats to bonobos include hunting for bushmeat, habitat loss due to deforestation, civil unrest in the DRC (Democratic Republic of the Congo).

Figure 5: Sources: Global Forest Watch; IUCN

Conservation efforts are being made but face substantial challenges. Anti-poaching measures and community engagement are key strategies being employed by organizations like the Bonobo Conservation Initiative. Recent research has used geospatial modeling to identify priority areas for conservation. A range-wide habitat suitability model found that only about 28% of the bonobo's range contains suitable habitat, with just 27.5% of that located in protected areas.

Conservation groups are working to establish and expand protected areas, train anti-poaching teams, engage local communities in conservation and rescue and rehabilitate orphaned bonobos.

Despite these efforts, bonobos remain highly threatened. Their low reproductive rate makes population recovery difficult. Experts say continued research, funding, and cooperation between local and international partners are crucial for the long-term survival of this unique great ape species.

Summary

In conclusion, there are several interesting open questions or issues around bonobos, that could be explored using AI tools that have been successfully applied to other species:

1. Social dynamics and hierarchy
2. Communication
3. Cognitive abilities and problem solving
4. Emotional intelligence, aggression and empathy
5. Visitor effect and mental health
6. Conservation

Next we explored interesting recent results of AI across all species and found which might be most applicable to these open bonobo questions.

Results

Evaluating the open questions in relation to the progress made in other species results in this table, suggesting the primary (dark green) and secondary (light green) uses of the most promising tools or techniques. The discussion section will then explore this in greater detail.

	Dogs	Whales	Elephants	Dolphins	Polar bears	Crows
Social dynamics and hierarchy		light green	light green	dark green		
Communication		dark green	light green			
Cognitive abilities and problem solving	light green					dark green
Emotional intelligence, aggression and empathy	dark green			light green		light green
Visitor effect and mental health		light green	light green		dark green	
Conservation		light green	dark green			

Figure 6: Author rendering

Discussion

To clarify, this section is not a review of all AI tools available or data sets, as that has been done by https://arxiv.org/html/2405.14002v1 and others. Nor is it how to use AI to analyze animals, here are two resources for that:
https://www.thetransmitter.org/spectrum/six-steps-to-using-machine-learning-for-animal-behavior-research/ or https://www.opencv.ai/blog/animal-behavior-recognition-using-machine-learning.

Additionally, there are many other tools available:

1. **FACS** Facial Coding System is a detailed tool that identifies muscle movements using the so-called facial action units. These units identify and classify emotional states as neutral, fear, anger, and pleasure based on the position and movement of the muscles.

2. **SuperAnimal**: This tool is a deep learning model developed by researchers at the École Polytechnique Fédérale de Lausanne. It is designed to detect animal motion across various species and environments without human annotations. SuperAnimal can automatically identify keypoints (which are usually animal joints) in over 45 animal species, making it highly efficient for tracking animal movements and analyzing behaviors such as foraging, mating, and social interactions. It is particularly useful in fields like veterinary medicine, conservation, and agriculture.

3. **Bioacoustic AI**: Led by AI researcher Dan Stowell from the Naturalis Biodiversity Center, this project focuses on analyzing animal sounds to understand their

communication. Bioacoustic AI is part of a bigger effort to monitor wildlife by uncovering details of animal populations and behaviors through their songs and calls. The project involves a group of universities and businesses across Europe, aiming to revolutionize the understanding of animal sounds using machine learning techniques.

4. **SUBTLE**: Developed by a research team led by Director C. Justin Lee and Cha Meeyoung, SUBTLE is an AI tool that classifies and analyzes animal behavior based on 3D movement data. It uses a novel metric called the Temporal Proximity Index (TPI) to evaluate behavioral data clusters, providing insights into standardized behavior patterns. SUBTLE is particularly advantageous in industries requiring behavior pattern recognition, such as robotics, and aims to minimize human intervention in behavioral analysis.

Rather than evaluate or catalog these tools and uses, we list them for reference and then us the discussion section as a selection of interesting and relevant advances in using these and other AI in species that we believe are applicable to bonobos.

1. Social Dynamics and Hierarchy

Open Question: How do the social dynamics and hierarchies in bonobo groups differ from those in chimpanzee groups, and what does this tell us about human social evolution?

AI Tool and Species: AI-based social network analysis tools, which have been successfully applied to study the social dynamics of dolphins, could be used here. Researchers used machine learning to analyze the social networks in dolphin pods, and they found an intriguing network and many hidden patterns in their social interactions. This approach could be applied to bonobos, especially given the similarities in their social structures compared to chimpanzees. particularly through the study of their vocalizations and behaviors (Herzing)

Recent advancements in machine learning technologies are enabling researchers to decode dolphin communication by analyzing their unique vocalizations. These vocalizations, which include clicks and whistles, are believed to form a complex language. By applying AI algorithms to extensive datasets collected over decades, researchers aim to uncover patterns that might reveal insights into dolphin social structures and interactions.

The Wild Dolphin Project, with Denise Herzing leading, has studied underwater video and sound data for more than 25 years. This vast collection helps researchers understand how dolphins behave in their social settings, improving insights into their communication and social structures. AI technology is used to identify individual dolphins and track their interactions, which is vital for exploring family relationships and social hierarchies (Herzing).

Studies have employed social network analysis to assess personality differences and social affiliations among bottlenose dolphins. For instance, research indicated that personality traits influence social behaviors, where bold dolphins tend to have stronger social ties compared to shyer

individuals. This analysis not only sheds light on individual roles within dolphin communities but also on the broader social structures that govern their interactions (Díaz López).

The application of AI in studying dolphin communication could extend beyond this species, potentially offering insights into the social structures of other intelligent animals. The ongoing research emphasizes the importance of understanding animal communication as a means to explore the cognitive abilities and social complexities of non-human species.

Link to Species: Dolphins - AI has been used to map out social relationships and hierarchies within dolphin groups, providing insights into their social behavior.

2. Communication and Language-Like Behavior

Open Question: How does the communication system of bonobos compare to that of chimpanzees or even humans in terms of complexity?

AI Tool and Species: Natural Language Processing (NLP) tools, like the ones used by CETI to decode whale songs, could be applied to bonobo communication. AI has been employed to identify patterns in the vocalizations of whales, suggesting complex structures that could resemble the precursors of language. This technique could be used to analyze the vocalizations and gestures of bonobos to see if they exhibit more comprehensive, developed or different communicative behaviors compared to chimpanzees.

Researchers used it to decode the complex communication of sperm whales, revealing that their vocalizations are more complex than previously understood at MIT's Computer Science and Artificial Intelligence Lab analyzed over 8,700 recordings of sperm whale codas (Sharma).

The researchers identified a structured communication system akin to human language, uncovering a "phonetic alphabet" of distinct click patterns that suggest these codas convey nuanced meanings depending on context. This work, part of Project CETI, emphasizes the potential for AI to unravel the intricacies of animal communication and provides a foundation for future studies aimed at understanding interspecies interactions(Sommer).

The findings indicate that sperm whales utilize rhythmic sequences of clicks that can be combined and varied to create a rich tapestry of communication. The researchers noted that the whales' vocalizations are not random but exhibit patterns reflecting social dynamics and environmental contexts. This research challenges previous assumptions about whale communication and opens new avenues for exploring the cognitive abilities of marine mammals (Gero 2024).

The other challenge is the limited amount of data available. Even with 20 years' worth of recordings of elephants or sperm whales, it's still far too little to train a large language model (LLM). Additionally, how the data is collected is problematic—recording whales only when they surface near a boat offers a very limited view of their lives. This has been likened to studying human culture by only recording conversations at a dentist's office; you'd end up thinking terms like "root canal"

and "cavity" are essential to English-speaking culture. (Rhiannon)

Gero explains that understanding sperm whale communication reveals their social priorities. Even without AI, researchers have discovered that sperm whales use dialects. For example, one group near Dominica uses a "1+1+3" click pattern, while another clan near Martinique and St. Lucia uses a "5R" pattern of five clicks. This highlights how their social lives influence their communication. This shows that their social structure influences their communication. According to Gero, "who you are, where you come from, and with whom you belong" plays a crucial role in what these animals communicate (Rhiannon).

Sperm whale calves, like humans, take about two years to learn their communication, starting with babbling. Similarly, Project Ceti's AI model will go through a learning phase, producing random sounds until it can generate clear, distinct patterns.

There is also relevant research from ESP (Earth Species Project) from bats and elephants could also benefit bonobos, as the high pitched sounds bonobos make are harder for humans to process but well within the range of AI who has made progress with infrasonic and ultrasonic communication in multiple species.(Corbyn)

Figure 7:   Frequency of communication (Corbyn)

AI is also better than us at sorting out the "cocktail party problem" which is what researchers call the issue of overlapping conversations.
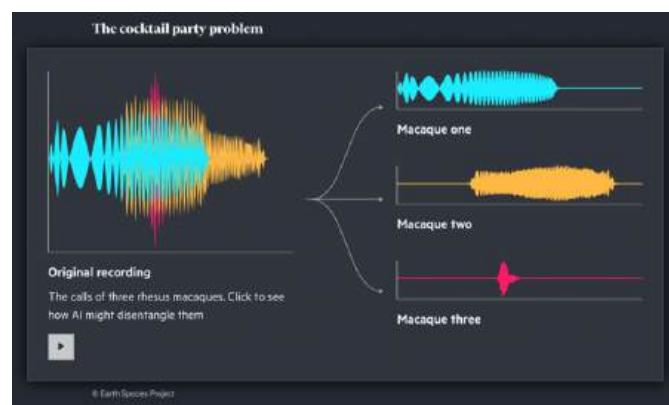

Figure 8: Cocktail party problem of overlapping rhesus monkeys

So the work from CETI and Earth Species Project could both be useful building blocks for better understanding bonobo vocalizations, which seem to be tantalizingly closer to human speech than other primates.

Link to Species: Whales - AI has been used to analyze the structure and meaning of whale songs, revealing insights into their communication systems.

3. Cognitive Abilities and Problem Solving

Open Question: Do bonobos demonstrate different ways of thinking or approaches to solving problems compared to chimpanzees, and how do these relate to human cognition?

AI Tool and Species: AI-driven video analysis has been utilized in studying the problem-solving behavior of crows, which have demonstrated advanced cognitive abilities. Machine learning models analyzed thousands of hours of footage to identify patterns in the crows' tool use and problem-solving techniques.

Observing New Caledonian crows in their use of tools has demonstrated that these crows can combine tools to solve complex tasks, showcasing advanced cognitive skills. For instance, a study revealed that crows could insert one stick into another to create a longer tool, allowing them to retrieve food from a puzzle box. This behavior indicates that they can predict the function of a tool before creating it, reflecting a form of mental simulation (Bayern et al.).

Additionally, AI techniques have been employed to assess how experience influences their problem-solving strategies. Crows were found to adapt their tool use based on prior encounters with similar tasks, suggesting a level of learning and innovation not previously attributed to non-human animals (Boeckle et al.). These findings underscore the cognitive parallels between crows and primates, highlighting the potential for AI to further explore animal intelligence and inform robotic problem-solving capabilities (Bayern et al.).

The study by Gruber et al. investigated New Caledonian crows' ability to solve "metatool" problems using mental mind maps. Researchers showed crows with a series of out-of-sight tools and obstacles, requiring them to plan a sequence of actions to get the food. The crows successfully solved these problems, demonstrating their capacity to mentally represent the sub-goals and final goals of complex tasks. They kept track of the locations and identities of unseen tools, showing flexibility in their problem-solving approach. This research provides evidence that these birds can use mental representations to plan ahead and solve multi-step problems, a cognitive ability previously associated mainly with great apes (Boeckle et al.).

If this isn't convincing enough - at Puy du Fou, a French amusement park, six trained rooks (a type of crow) collect litter, including cigarette butts, in exchange for food. This raises awareness about littering while showing the birds' intelligence - though it won't replace the cleaning staff (Domonoske).

Applying a similar AI tool to study bonobos might help identify unique thinking traits and compare them to those observed in chimpanzees and humans. Particularly as chimpanzees show more diverse and frequent tool use in the wild, especially for foraging and extractive tasks. Bonobos show less tool use in nature but display comparable problem-solving skills in captivity, often employing tools for social and play purposes and do better on cooperative problem solving(Gruber et al.).

Link to Species: Crows - AI has been used to study the problem-solving abilities of crows, revealing complex reasoning similar to that of primates.

4. Emotional Intelligence and Empathy

Open Question: How does the emotional intelligence and empathetic actions of bonobos compare to chimpanzees and even to humans, and can we learn about the evolution of empathy in humans?

AI Tool and Species: Facial recognition and emotion detection AI tools, FACS, similar to those used to study the emotional states of dogs, could be applied to bonobos. These tools have been used to detect and analyze the emotional expressions of dogs in different social contexts.

Algorithms have been used to analyze the emotional states of dogs through facial recognition and emotion detection tools. One significant study employed deep learning techniques to automate the recognition of canine emotions, focusing on diverse facial expressions. Using the Dog Facial Action Coding System (DogFACS), researchers classified emotions such as frustration and anticipation in Labrador Retrievers, achieving over 89% accuracy with deep learning models (Franzoni et al.). The study highlighted the complexity of canine facial morphology, which presents unique challenges compared to human emotion recognition, such as variability among breeds and the absence of micro-expressions in dogs (Boneh-Shitrit et al.).

Another innovative application is the development of the "Happy Pets" app, which analyzes pet facial expressions to determine emotions like happiness, sadness, and anger. This app utilizes convolutional neural networks to isolate and interpret facial features, demonstrating that dogs are generally easier to read than cats due to their more expressive faces ("Wondering If Your Pet Is Happy or Sad, Angry or Scared?"). The advancements in AI emotion detection not only enhances our understanding of canine emotional states but also might improve empathy between humans and their pets, potentially aiding animal welfare and human-animal interactions (Franzoni et al.).

Applying this AI to bonobos could help in understanding the nuances of their emotional expressions and compare them with those of chimpanzees, shedding light on the evolutionary roots of empathy.

Link to Species: Dogs - AI has been used to analyze emotional expressions in dogs, providing insights into their emotional states and social bonds.

5. Visitor Effect on Behavior and Well-being

Open Question: How does the presence of human visitors affect the behavior and well-being of bonobos in captivity?

AI Tool and Species:

If measuring the pain in cats' faces is possible, then it seems likely that type of technology could be applied to bonobos, who have expressions and faces much more similar to humans where most of the facial recognition has been done (Feighelstein et al.).
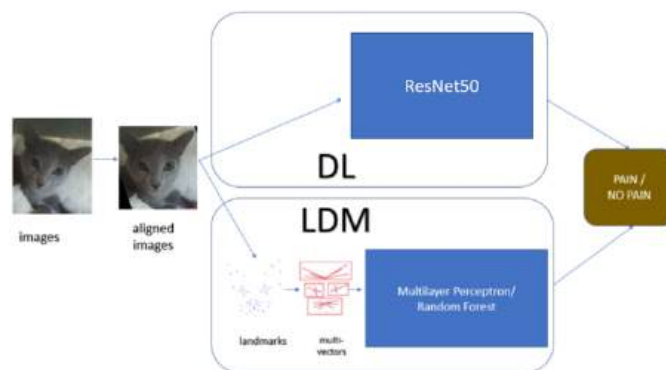

Figure 9: Cat pain machine learning model Image: (Feighelstein et al.)

But perhaps a more relevant option is a study by Zuerl et al. (2022), who developed an automated video-based analysis framework using deep learning to monitor the behavior of polar bears at the Nuremberg Zoo. This system allows for continuous observation, providing insights into the animals' physical and psychological health by analyzing their behavior patterns and activity levels. The framework improves upon traditional manual observation methods by offering a more efficient and accurate means of monitoring animal welfare. This innovative approach helps zookeepers and researchers better understand and manage the well-being of captive polar bears.

Researchers developed an AI-powered video analysis system to monitor polar bear behavior in zoos. The framework detects and tracks individual bears, analyzing their locations, movement patterns, and activity levels. It achieved an 86.4% F1 score for bear identification and localization, outperforming manual methods. The system provides insights into bear behavior and welfare through a graphical interface (Zuerl et al.).

Perhaps for this subject there isn't one single other species as the best source of a tool or technique. Introductory work to measure stress across all types of animals seems to be progressing and might be the ideal tool to better monitor bonobo stress in captivity to improve their well-being. Researchers developed an AI system to automatically detect stereotypical behaviors in captive wild animals using surveillance videos from zoos and animal reserves (Yin et al.).

Link to Species: Polar bears - AI has been used to track psychological health of polar bears in zoos, but the conclusion on this topic is that it is likely a mix of tools that cross species that will best

fit the need.

6. Conservation Strategies and Habitat Use

Open Question: How can we optimize conservation strategies for bonobos by understanding their habitat use patterns and responses to environmental changes, particularly in comparison to chimpanzees?

AI Tool and Species: AI-based habitat modeling, similar to the tools used in tracking and conserving elephant populations, could be employed here. For elephants, AI models have been developed to predict migration patterns and identify critical habitats by analyzing GPS tracking data alongside environmental factors.

AI is increasingly being used to monitor elephants and enhance conservation efforts through innovative technologies. One significant application is the WildEyes AI system, which employs cameras equipped with computer vision to detect elephants in real-time. When triggered, these cameras send alerts to local guardians, enabling them to prevent potential human-elephant conflicts before they escalate ("WildEyes AI").

Additionally, AI techniques analyze vast datasets collected from various sensors, including audio and seismic data, to improve understanding of elephant behavior and movement patterns. This capability allows for more accurate monitoring and management of elephant populations in their natural habitats (Brickson et al., "Elephants and Algorithms")(*Improving Elephant Monitoring with the Help of AI | Royal Society*).

Collaborative efforts between AI specialists and conservationists are crucial for tailoring these technologies to address specific challenges faced in the field, such as poaching and habitat destruction. By integrating AI into conservation strategies, researchers aim to foster coexistence between elephants and human communities, ultimately supporting the long-term survival of these majestic animals (Brickson et al., "Elephants and Algorithms").

Applying a similar type of tool and analysis could help identify the most crucial areas for the bonobos' survival and understand how they are affected by deforestation and other detrimental human activities. By comparing those patterns to those of chimpanzees it could lead to more targeted and effective conservation strategy.

Link to Species: Elephants - AI has been used to model habitat use and predict migration patterns, informing conservation efforts by identifying critical habitats and human-wildlife conflict zones, for bonobos whose main threat is human activity this could easily translate.

Current AI in primates

While these provide six useful examples from other species for application to bonobos, AI is also becoming a crucial tool in primate research. Recent advancements have focused on using AI for automated analysis of primate behavior and communication. One tool is BORIS, but in 2023, researchers developed a more complex deep learning-based system called "DeepPrimateID" used for identifying and tracking individual primates in complicated environments (Marks et al.). It achieved high accuracy in identifying multiple primate species, including bonobos, chimpanzees, and gorillas. It has great potential for long-term behavioral studies and conservation efforts.

The Toronto Zoo is using artificial intelligence software to discreetly monitor orangutan locations, estimate their positions, and analyze their behavior. This technology enables large-scale data collection, allowing zookeepers and researchers to closely observe the well-being, behaviors, and other important factors for each orangutan. (Congdon et al.)

Scientists have discovered (using AI) that chimpanzees use specific sounds, similar to human words, and even combine them into simple structures, forming a unique language. Through experiments involving snakes, researchers observed chimps using "alarm-huus" and "waa-barks" to communicate danger and call for help. This suggests that the cognitive foundation for language may have existed in the common ancestor of humans and chimps, challenging the belief that complex language is unique to humans. This study could potentially offer insights into how human language evolved from early forms of communication among related animals (Heenan)

AI has also been applied to decoding primate noises and vocalizations. A study on bonobo communication used machine learning algorithms to analyze and classify different call types, providing new insights into their social dynamics and cognitive abilities(Clay et al., "Functional Flexibility in Wild Bonobo Vocal Behaviour") Furthermore, AI-powered camera traps have revolutionized field studies by automatically identifying and tracking primates in their natural habitats, aiding in population monitoring and conservation planning (Crunchant et al.).

Researchers developed a deep learning model to identify individual lemurs from facial images with 99.5% accuracy. The system was programmed based on 3,000 images of 129 red-bellied lemurs and it outperformed human experts. This non-invasive method enables long-term monitoring of wild lemur populations, aiding in conservation efforts and behavioral studies (Crouse et al.).

Finally, when chimpanzee ethology examines animal behavior large datasets are difficult to process manually. Researchers have created a deep learning system to automate behavior recognition in wild chimpanzees. By analyzing both audio and video, the system tracks individuals and identifies specific behaviors like nut cracking and drumming, overcoming challenges like poor lighting (Bain et al.).
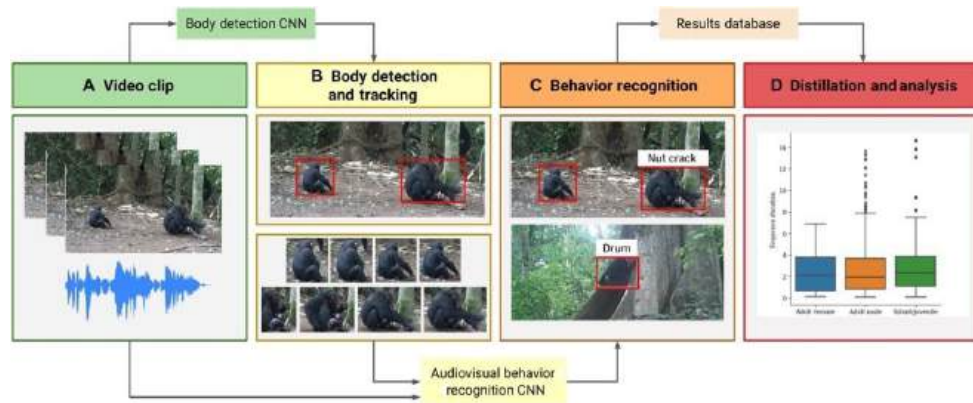
Figure 10: Fully unified pipeline for wild chimpanzee behavior recognition and analysis from raw video footage (Bain et al.)

The pipeline consists of the following stages: **(A)** Frames and audio are extracted from raw video. **(B)** Body detection is performed over the video frames using a deep CNN single-shot detector (SSD) model, and the detections are tracked using a Siamese tracker. **(C)** The body tracks are classified (e.g., is this individual cracking nuts?) using the audio data and spatiotemporal visual information for the track by a deep CNN audiovisual behavior model. The system only requires the raw video as input and produces labeled body tracks and metadata as temporal and spatial information. This automated system can be used to perform large-scale analysis **(D)** of behavior. (Bain et al.) Photo credit: Kyoto University, Primate Research Institute.

Conclusion

This paper has identified open questions in the study of bonobo behavior, communication, and conservation, and has reviewed how AI tools from other species can be applied to these challenges. For instance, using AI-driven behavioral tracking techniques from dolphins, we can gain a deeper understanding of bonobo social dynamics and conflict resolution strategies, shedding light on their unique matriarchal structures. AI algorithms used in communication studies of animals such as whales, elephants or even dogs can decode the complexities of bonobo vocalizations and gestures, unlocking the meanings behind their interactions. Additionally, AI models that analyze tool use in other animals such as crows can be adapted to study bonobo problem-solving behaviors, allowing comparisons with other primates. Lastly, tools evaluating the visitor effect on penguins and tracking the habitat of elephants present ideas for improving the well-being of captive bonobo populations and protecting their wild habitats from emerging threats.

Using AI in bonobo research and conservation fills current gaps in knowledge and opens new ways for helping the survival of this species. The future of bonobo studies lies at the intersection of AI and traditional field research, where technology and conservation can work together to protect these primates

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Introduction to The Hidden Connection: How Gum Health Impacts Your Heart By Minju Jung

Abstract

Gum disease is a common disease that begins with mild symptoms such as bleeding gums, sensitive teeth, or breath odor. If not treated in time, it can lead to teeth loss. However, many people don't realize that gum disease can affect not only oral health but also overall health, particularly heart health. Recent research reveals an unexpected link between gum health and heart problems such as heart attack, stroke, and high blood pressure. This study explores the significant connection between oral health, particularly gum health, and overall health, with a focus on heart health. Gum disease can have serious effects on the heart as bacteria from infected gums may enter the bloodstream, causing inflammation and potentially worse symptoms like heart attacks and strokes. The important thing is that maintaining good oral hygiene through regular brushing, flossing, and visiting the dentist is essential not only for keeping teeth and gums healthy but also for protecting heart health. The study suggests that recognizing this link could impact public health strategies, emphasizing oral care to prevent heart disease. A collaborative approach between dentists and physicians could enhance preventive and treatment measures, improving overall public health. The study emphasizes that simple steps in oral care can have a substantial positive impact on long-term well-being. If more people understood that caring for their gums could help protect their hearts, there could be a stronger focus on preventing both gum disease and heart disease, leading to significant improvement in public health.

Introduction

Gum disease, or periodontal disease, is a common disorder affecting the gums and tissues that support your teeth. It may begin with minor symptoms such as bleeding gums or foul breath, but if not treated, it can progress to significant issues such as tooth loss. Many individuals are unaware that gum disease does not only affect the mouth; it can also influence your whole health, particularly the heart. Recent research has revealed an unexpected association between gum health and cardiac problems such as heart attacks, strokes, and high blood pressure (Shmerling). This discovery has prompted additional research into how dental health affects overall health.

Heart disease is a leading cause of death around the world (CDC, 2024a). Historically, high blood pressure, smoking, and eating unhealthy diets were thought to be the leading causes of heart disease. Scientists are now learning that gum infections and inflammation may possibly contribute to the development of heart disease. The link between gum disease and heart health is "bi-directional." This means that not only does poor gum health increase the risk of heart disease, but heart disease can also exacerbate gum problems. This demonstrates the importance of viewing the body as a connected system, where what happens in one portion can also impact other sections.

This new study can potentially transform our understanding of dental and cardiovascular health. Most people believe that visiting to the dentist is only about keeping your teeth white or preventing cavities. Still, this link implies that proper oral hygiene is also vital for protecting your heart. If more people realize the link between gum disease and heart disease, they can improve their dental and cardiovascular health. This understanding may lead to increased collaboration among healthcare providers, such as dentists and doctors, to keep patients healthy overall. For example, if a dentist notices evidence of gum disease that could harm the heart, he or she may refer the patient to another doctor.

This discovery has significant consequences for public health. If more individuals understood that caring for their gums may help protect their hearts, there might be a greater emphasis on preventing both gum and heart disease. This could imply improved dental care, increased education about the importance of oral hygiene, and specialized programs for persons who are at high risk for both gum disease and heart disease. Learning about the connection between our gums and our hearts can help us improve our general health and save lives.

Finally, this study will investigate the link between gum disease and heart disease and how dental health affects general health. Understanding this link explains why it's crucial to care for our gums—not just for good teeth but also for a healthy heart. This article will explain how gum disease affects the heart, provide scientific proof for this connection, and offer advice on safeguarding your oral and cardiovascular health.

Chapter One: Understanding Periodontal Disease

Definition and Types of Periodontal Disease

Periodontal disease, often known as gum disease, affects the tissues surrounding and supporting the teeth. There are two types of periodontal disease: gingivitis and periodontitis (see Figure 1). Gingivitis is the mildest and earliest stage of gum disease. If you have gingivitis, your gums may turn red, inflamed, and bleed when you brush or floss. Although unpleasant gingivitis is usually treatable with proper oral care, such as regular brushing, flossing, and dental cleanings (ClevelandClinic, 2023a).

Figure 1 – Progression of Gum Disease, MedlinePlus (2022)

However, if gingivitis is not treated, it can progress to the more severe illness known as periodontitis. Periodontitis develops when inflammation extends deeper, affecting the gums, bone, and tissue that keep your teeth in place. Over time, your gums may recede, resulting in gaps or "pockets" between your teeth and gums. Bacteria can collect in these areas, causing illnesses. Periodontitis can weaken the gums and bone if left untreated, eventually leading to tooth loss. Periodontitis is not readily treated and may necessitate more significant procedures, including deep cleaning treatments, drugs, or even surgery to prevent tooth loss (ClevelandClinic, 2023a).

Causes of Periodontal Disease

The most common cause of periodontal disease is inadequate oral hygiene. If you don't brush and floss properly, plaque—a sticky film made up of bacteria—will form on your teeth. If the plaque is not removed, it will harden into tartar (also known as calculus), which may only be removed by a dentist or dental hygienist. Plaque and tartar buildup irritates your gums, causing inflammation and ultimately leading to gingivitis. If tartar accumulates, the inflammation can extend deeper into your gums and lead to periodontitis (MedlinePlus, 2024).

While poor dental hygiene is the primary cause, several additional variables might increase the likelihood of getting periodontal disease. Smoking is one of the major contributors. Smoking lowers your immune system, making it difficult to battle diseases such as gum disease. Smokers are much more likely to acquire gum disease, and their cases are more severe than nonsmokers (Beklen et al.). Genetics also play a part in gum disease, as some people are predisposed to getting it, even if they practice good oral hygiene. In some circumstances, a person's family history increases their risk of developing severe periodontal disease.

Hormonal changes might also make the gums more sensitive to gum disease. For example, during pregnancy, menstruation, or menopause, the body's hormone levels fluctuate,

making the gums more prone to inflammation and infection. Pregnant women are at a higher risk of developing pregnancy gingivitis, which, if left untreated, can progress to periodontitis.

Diabetes is also a key influence. People with diabetes are more likely to acquire gum disease because high blood sugar levels impair their body's capacity to fight infections. Gum disease and diabetes have a two-way relationship: patients with gum disease may have difficulty controlling their blood sugar levels, and uncontrolled blood sugar makes gum disease more likely to develop (Preshaw et al.).

Symptoms and Diagnoses

Recognizing periodontal disease signs early on is critical for preventing the disease from progressing. One of the first indicators of gum disease is when your gums bleed during brushing or flossing. Healthy gums rarely bleed, so if you notice some, pay heed. Another typical symptom is persistent foul breath, which is caused by germs and plaque in the mouth. People with periodontal disease frequently have gum recession, a condition where the gums peel away from the teeth, making them appear longer than usual. This can expose the teeth's roots, increasing sensitivity, particularly when eating or drinking hot, cold, or sugary foods (ClevelandClinic, 2022a).

As periodontal disease advances, the symptoms worsen. The gums may become swollen and painful, making chewing or talking difficult. In severe stages, the gums may begin to split from the teeth, creating deep pockets for bacteria to flourish. These pockets can cause infections, destroying the bone and tissue that support your teeth. When this happens, your teeth may loosen or shift, producing bite issues. Tooth loss may ensue if the illness is not treated (ClevelandClinic, 2023b).

A dental examination is required to diagnose periodontal disease. During the exam, your dentist will look for symptoms of gum inflammation and measure the pockets between your teeth and gums with specific equipment. Periodontal probing is a method that determines how far the disease has gone. Healthy gums often have pockets that are 1 to 3 millimeters in depth. Pockets that are deeper than 4 millimeters may suggest gum disease. Sometimes, your dentist may use X-rays to detect bone loss around the teeth. The deeper the pockets and the more bone loss, the more severe the periodontal disease (MayoClinic, 2023).

Risk Factors and Prevention

Periodontal disease can affect anyone, but certain factors raise your risk. Smoking and tobacco use are major risk factors. Smokers are more prone to develop severe gum disease, which is more difficult to cure because smoking impairs the body's capacity to heal and fight infections. Smoking is regarded as the most preventable risk factor for gum disease (CDC, 2023).

Your age may also raise your risk. Older folks are more likely to develop gum disease because years of plaque buildup can harm your gums and teeth. Furthermore, stress might make it difficult for your body to fight infections like gum disease. High-stress levels may cause you to

clench or grind your teeth, exacerbating gum disease by putting additional strain on your tooth's supporting structures (WebMD, 2023).

Gum disease can be prevented by practicing good dental hygiene. The most crucial steps are to brush your teeth twice a day with fluoride toothpaste and to floss every day. Regular dental cleanings are also necessary since a dentist can remove tartar that you cannot get rid of on your own. Using antimicrobial mouthwash can also assist in reducing bacteria in the mouth. Quitting smoking is one of the most effective strategies to lower the risk of getting periodontal disease. Managing underlying health issues such as diabetes is also important for preventing gum disease because regulating blood sugar can help protect your gums (ClevelandClinic, 2019).

Why Early Detection Matters

Early detection and treatment of periodontal disease can significantly improve management outcomes. Gum disease, known as gingivitis, can typically be reversed if identified in its early stages. If it proceeds to periodontitis, therapy becomes more complex, and the damage to the gums, tissue, and bone may be irreversible. Regular dental check-ups are crucial for detecting gum disease early. Your dentist can help you control the illness and keep it from worsening.

To summarize, periodontal disease is a dangerous but avoidable disorder that affects a large population. Understanding gum disease's origins, symptoms, and treatments allows you to take preventative measures to protect your gums and teeth. Regular brushing, flossing, and dental check-ups can help prevent gum disease, and identifying it early can save you from the more catastrophic implications of untreated periodontitis.

By doubling the length, this part provides a more extensive description of periodontal disease while remaining understandable to a high school reader.

Impact on Quality of Life

Periodontal disease can have a significant influence on one's quality of life. Physically, it can cause discomfort, trouble eating, and, in severe cases, tooth loss, impairing a person's ability to talk and chew properly. Periodontal disease can also have a major psychological impact. Bad breath and apparent indicators of gum disease, such as swollen gums or loose teeth, can lower self-esteem and make it difficult to smile or communicate with others. Individuals who are afraid of being judged or embarrassed by the appearance of their teeth may withdraw from social situations, thus harming their mental health and overall well-being (Broomhead et al.). To summarize, periodontal disease is a serious condition that demands attention and care. Understanding the reasons, detecting the symptoms, and seeking early treatment can help to avoid disease progression and maintain both oral and overall health.

Periodontal disease can significantly affect your general health in addition to being a gum disease. Studies have revealed a high correlation between periodontal disease and many severe chronic illnesses, such as Alzheimer's disease, diabetes, heart disease, respiratory problems, and

cancer (AAP, 2024). These long-term illnesses have the potential to significantly lower your quality of life and eventually cause more serious health issues.

It is imperative to closely monitor periodontal health as a result. It's critical to treat the illness as soon as possible, especially if symptoms are still moderate. Good oral hygiene habits and routine dental exams can help stop periodontal disease from getting worse and lower your chance of getting certain related chronic conditions. You may greatly enhance your general well-being and long-term health by implementing these actions.

Chapter Two: Cardiovascular Disease Definition and Overview of Cardiovascular Disease

Cardiovascular diseases (CVDs) are a collection of illnesses affecting the heart and blood arteries. These include heart attacks, strokes, heart failure, and abnormal heartbeats. A heart attack occurs when blood flow to a region of the heart is obstructed, usually by a blood clot, causing damage to the heart muscle. A stroke happens when blood flow to the brain is disrupted, causing significant damage to brain cells and altering how the body functions. The cardiovascular system, which includes the heart and blood vessels, is essential because it transports oxygen and nutrients throughout the body while also eliminating waste (NHS, 2022).

Causes and Risk Factors for Cardiovascular Disease

Numerous factors can contribute to cardiovascular disease. High blood pressure and cholesterol are key factors because they can produce fatty deposits in the arteries, which is known as atherosclerosis. This buildup can obstruct blood flow, resulting in heart attacks or strokes (see Figure 2). Obesity and a bad diet—particularly one high in harmful fats and sugars—can exacerbate these issues. Not getting adequate exercise also raises the risk because physical activity helps keep the heart and blood arteries healthy (CDC, 2024b).
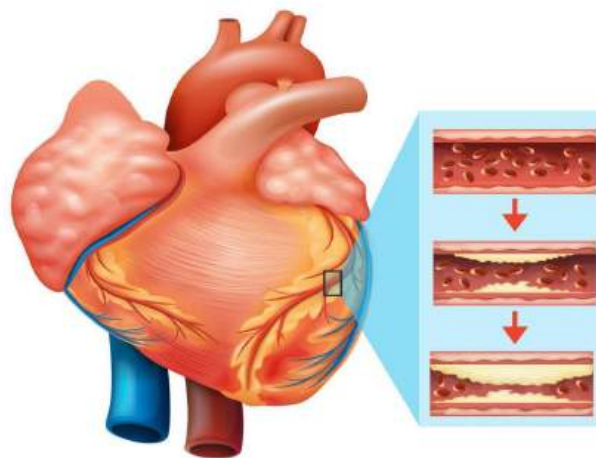

Figure 2 - Plaque builds up, causing heart disease, Harvard Health Publishing (2021)

Other risk factors include smoking and excessive alcohol consumption, which can harm the heart and blood vessels. Smoking makes the arteries sticky, allowing more fatty deposits to

attach to them. Stress can also contribute to heart disease since it frequently leads to harmful behaviors such as overeating and inactivity (Hardesty).

Symptoms and Diagnosis for Cardiovascular Disease

Cardiovascular illness can manifest in numerous ways. Common symptoms include chest pain or discomfort, which might feel like squeezing or pressure. This pain may move to the arms, neck, or jaw. Shortness of breath, dizziness, and feeling lightheaded are all warning signals. If someone is having a stroke, they may have numbness or weakness in their face, arm, or leg, usually on one side of the body. They may also get disoriented and have difficulty speaking or walking (AHA, 2024a).

Doctors utilize a variety of methods to diagnose cardiovascular illness. An electrocardiogram (ECG) examines the heart's electrical activity to detect any abnormalities. Blood testing can detect cholesterol levels and other factors suggesting cardiovascular disease. A stress test examines how the heart functions when the body is busy, which can identify underlying issues. Angiography is an imaging examination that examines blood arteries in the heart to determine whether they are blocked or constricted (MayoClinic, 2024a).

The role of inflammation in cardiovascular disease

Inflammation plays an essential function in heart disease. When persistently inflamed, the body can damage the arteries, allowing fatty deposits to form more easily. These deposits can cause atherosclerosis, which is when the arteries thin or become blocked. If a fatty deposit ruptures, it can form a blood clot, potentially leading to a heart attack or stroke. Understanding how inflammation contributes to heart disease highlights the importance of managing inflammation through a healthy lifestyle (HarvardHealth, 2023).

Chapter Three: The Bidirectional Relationship

How Periodontal Disease Can Cause Cardiovascular Disease

Periodontal disease, often known as gum disease, is not limited to the mouth; it can damage the entire body, including the heart. When your gums become infected, bacteria can enter your bloodstream. This occurs because the gums are filled with small blood vessels. When the gums become inflamed and infected, bacteria can enter these blood arteries and move through your bloodstream to other body regions, including your heart (Shmerling).

Once these germs reach the heart, they can also cause inflammation. Inflammation is the body's natural response to illness, but it can be hazardous when it occurs in the arteries surrounding the heart. The inflammation can constrict the arteries, making it difficult for blood to flow through them. This can result in a heart attack or stroke when blood flow to the heart or brain is disrupted (Lee).

On the other hand, cardiovascular disease can have a major effect on how severe and quickly periodontitis advances. Blood flow to the oral tissues is compromised by conditions like

high blood pressure and atherosclerosis, which is important for preserving healthy periodontal tissues. Decreased blood flow weakens the gums' immunological response and hinders the healing process (Bassani et al.).

Atherosclerosis, for example, is a disorder in which plaque accumulation causes arteries to stiffen and constrict, which might result in less blood and oxygen reaching the tiny blood vessels in the periodontal tissues. This decrease in circulation may worsen periodontal disease by making it more difficult for the body to fight off dangerous germs (Jung). Therefore, compared to people with robust cardiovascular systems, those with cardiovascular issues may see a faster decline in their periodontal health.

Treatments for cardiovascular conditions may also inadvertently affect oral health. Gingival overgrowth has been linked to some drugs, including calcium channel blockers, which are used to treat high blood pressure and other cardiac issues. This side effect results in an abnormal growth of gum tissue, which can lead to functional problems such as chewing pain and feeding difficulty, as well as cosmetic concerns (Tungare et al.).

The intricate connection between periodontal disease and cardiovascular health is highlighted by these interactions. It is imperative to manage both illnesses effectively since treating one can affect how the other develops. The detrimental impacts of these interconnected health conditions must be prevented and managed with regular dental checkups and thorough monitoring of cardiovascular health.

Scientific Studies and Evidence

Scientists have conducted numerous investigations to determine the link between gum disease and heart disease. They discovered that patients with gum disease are more likely to develop heart problems than those with healthy gums. One study found that persons with severe gum disease were twice as likely to suffer a heart attack as those without gum disease (HarvardHealth, 2022).

The biological cause of this relationship is the body's response to germs. When germs from the gums reach the bloodstream, they cause inflammation. This inflammation causes the arteries around the heart to thicken and narrow, resulting in atherosclerosis, a leading cause of heart attack and stroke (HarvardHealth, 2023). Understanding this process enables doctors and dentists to collaborate on preventing these major health risks.

Real-world Implications

Knowing that gum disease might harm heart health has altered the way doctors and dentists approach therapy. Dentists today play an important role in not just caring for teeth and gums, but also in preventing cardiovascular disease. They educate patients about the need of proper oral hygiene in protecting not only their mouths but also their hearts (AHA, 2024b). Doctors are also more aware of the link and may inquire about your dental health when determining your risk for heart disease. This understanding enables them to prescribe

preventative steps such as improved oral care or early cardiac screenings to minimize the risk of developing heart disease (AHA, 2024c).

Chapter Four: Preventive Measures and Health Strategy

Dental Hygiene Practices

Taking care of your teeth and gums is the first step toward avoiding gum disease and heart disease. Regular brushing and flossing are crucial. Brushing twice a day helps remove plaque that can accumulate on your teeth and gums. Flossing once a day cleans the gaps between your teeth that a toothbrush cannot reach (ClevelandClinic, 2022b).

Mouthwash can also help reduce bacteria in your mouth, but it should not replace brushing and flossing. Regular dental checkups for professional cleanings are also necessary. During these appointments, your dentist can remove tartar (hardened plaque) and detect early signs of gum disease, which can be treated before it worsens (ClevelandClinic, 2022b).

Diet & Lifestyle

What you consume influences your gum and heart health. A diet strong in sweets and bad fats can increase your chances of developing gum disease and heart disease. Avoid sugary snacks, processed foods, and anything high in saturated and trans fats. These can cause plaque buildup not only on your teeth but also in your arteries (HarvardHealth, 2022).

Instead, aim for a heart-healthy diet high in fruits, vegetables, whole grains, and lean proteins. These meals help to keep your gums healthy and your arteries clear. Drinking enough of water and minimizing alcohol consumption help to improve oral and cardiovascular health (MayoClinic, 2024b).

Regular Medical Check-Ups

Regular check-ups with your dentist and doctor are critical for early detection of potential issues. Dental visits should be scheduled at least twice a year so that your dentist can detect and treat gum disease before it progresses to more significant complications. Cardiovascular examinations, such as measuring blood pressure and cholesterol levels, can also help detect heart disease early (ClevelandClinic, 2023b).

Early identification of gum and heart problems can help prevent issues in the future. For example, early treatment of gum disease can prevent bacteria from entering the bloodstream and causing heart problems. Similarly, treating excessive blood pressure or cholesterol early on can help prevent a heart attack or stroke (PennMedicine, 2022).

Public Health Campaigns

Public health campaigns have significantly raised awareness about the link between dental and cardiovascular health. For example, the American Heart Association launched The American Heart Association's Healthy Smiles, Healthy Hearts™ initiative to focus on oral health

clinicians in prevention and early detection of heart disease. The initiative aims to engage oral health professionals to establish a new standard of care for heart health screenings at dental offices, emphasizing blood pressure checks and referrals to primary care, while also educating healthcare providers and patients about the connection between cardiovascular health and oral health (AHA, 2024c).

Education in schools and communities has also proven important. Programs that educate pupils on the value of dental hygiene and a healthy lifestyle will help them form habits that will safeguard their gums and hearts for the rest of their lives. These initiatives have demonstrated that taking care of your mouth is a critical step toward caring for your heart (Saccomanno).

Chapter Five: Conclusion

Summary of Findings

In this study, we investigated the substantial relationship between oral health, specifically gum health, and overall health, particularly heart health. We've seen that periodontal disease, often known as gum disease, can have major effects on your heart. Bacteria from infected gums can enter the circulation, causing inflammation and potentially worsening cardiovascular disorders such as heart attacks and strokes. The primary point is that excellent oral hygiene—regular brushing, flossing, and dental visits—is critical not only for preserving healthy teeth and gums but also for safeguarding your heart and overall well-being (MayoClinic, 2024c).

Implications for Future

The outcomes of this study could have significant ramifications for public health strategies. Recognizing the link between gum disease and heart disease allows health officials to promote better oral hygiene to prevent major cardiac diseases. This could lead to more comprehensive health campaigns emphasizing the value of oral care as part of overall health. Furthermore, these findings underscore the need for a more interdisciplinary approach to healthcare, in which dentists and physicians collaborate to evaluate and enhance both dental and cardiovascular health. Such partnership could result in more effective preventative and treatment efforts, boosting public health in general (AHA, 2024c).

Final Thoughts

As we've discovered, caring for your mouth is about more than just having a lovely smile; it's also crucial to maintaining your long-term health. Brushing and flossing regularly, eating a well-balanced diet, and going to the dentist for regular check-ups can all help to lower your risk of gum and heart disease. It's critical to act in your own life to keep these healthy behaviors. Remember that your health is interconnected, and even simple measures to enhance your oral hygiene can have a major impact on your overall health. Make it a point to care for your teeth and gums, and you'll be looking after your heart and future.

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