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Blue Zones: The Key to Neurodegenerative Disease Prevention

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ABSTRACT

Due to increased life expectancies and aging populations around the world, there has been a significant increase in the rate of neurodegenerative disease diagnoses in recent years. Although cases of neurodegenerative diseases have generally increased globally, there are still significant disparities, and some regions suffer substantially more from neurodegenerative diseases than others. Blue Zones, areas of the world with significantly low rates of neurodegenerative diseases, have been specifically researched to determine how people in these regions are able to circumvent deterioration to their cognitive health. After intensive research into the impacts of common lifestyle habits on neurological health, a general blueprint for neurodegenerative disease prevention was created, outlining the activities and practices that individuals should take into consideration in their decision-making. This paper concluded that easily alterable factors such as healthy nutrition, consistent sleep, and reduced alcohol consumption can play a vital role in the prevention of neurodegenerative diseases. Additionally, the RS NeuroDiet, a nutritional plan that is both advantageous for cognitive health and affordable, was created to allow people with varying financial resources to pursue a diet that will reduce brain inflammation and prevent neurodegeneration. This research could allow areas with high rates of neurodegeneration to reduce deaths caused by cognitive deterioration by spreading knowledge of prevention methods. Overtime, this research could allow for a decrease in disparities in neurodegeneration around the world and potentially bring various populations closer to the cognitive prosperity that exists in Blue Zones.

Introduction

Blue Zones are areas of the world in which people live the longest lives, with many people consistently reaching 100 years old. Blue zones include cities in regions such as Italy, Greece, Japan, and Costa Rica. One factor behind the increased life expectancy in these areas is their low rates of neurodegenerative diseases, with over 75% fewer cases of dementia than in the U.S. each year (National Library of Medicine, 2021). Research on the impacts of lifestyle on the development of neurodegenerative diseases of people in Blue Zones would allow people in non-Blue Zone areas such as the state of Texas to prevent the development of these diseases. Questions have been raised about why people in non-Blue Zone areas are affected so much more by neurodegenerative diseases. The sleep schedule, dietary habits, physical activity, and overall lifestyle practices of people in Blue Zones should be assessed to determine how these populations manage to circumvent neurodegenerative diseases. There is currently a gap in research concerning what lifestyle changes people can make to prevent a future diagnosis of neurodegenerative diseases, and observing Blue Zones would be an effective way to do just that.

Around the world, rates of neurodegenerative diseases greatly vary. For example, Japan, a Blue Zone holder, has the lowest prevalence of both dementia and Alzheimer's disease in the world. In contrast, China has one of the highest rates of neurodegenerative diseases, with the greatest population of Parkinson's disease worldwide (Rizzi et al., 2014). One potential reason for this difference could be the high rates of smoking in

China, as they are the world's largest producer and consumer of tobacco. Smoking is an example of a risk factor that can play a vital role in the development of neurodegenerative diseases and can affect neurodegenerative disease rates around the world.. Analyzing the international landscape of neurodegenerative diseases will help to pinpoint what combination of actions and habits to follow and what to avoid.

In the United States, Alzheimer's and dementia are the 4th leading cause of death. This could be due to a number of reasons, including genetics, poor lifestyle habits such as alcoholism and smoking, and vascular conditions. Alcohol abuse is very common in the U.S., with over 3 million new cases per year (Chadwick, 2023). Alcohol use is associated with a number of neurodegenerative diseases, including Wernicke-Korsakoff syndrome, a chronic memory disorder. The intensive use of alcohol in the United States is one lifestyle habit that leads to neurodegenerative disease diagnosis in the nation.

Texas experiences many cases of neurodegenerative diseases each year, which can be traced back to specific lifestyle choices, including eating habits. In Texas, vascular conditions - which are often incited by unhealthy eating habits - are the third leading cause of death. Research suggests that vascular conditions can compromise blood flow to the brain, which has the potential for the development of neurodegenerative diseases. This means that unhealthy eating habits in Texas can indirectly lead to the development of neurodegenerative diseases. Texas has an obesity rate of 35.8%, resulting in a high number of people with vascular diseases, which could lead to a significant number of cases of neurodegenerative diseases in the state (Texas Department of State Health Services, 2020). Making similar discoveries on why regions are affected the way they are by neurodegenerative diseases can allow for the implementation of prevention methods that tailor to that population's needs.

This research is significant because it has the potential to provide insight on how individuals can alter their lifestyles to prevent neurodegeneration to the greatest extent possible. Many instances of neurodegeneration occur due to or partially due to a deliberate or unintentional choice that a patient made in their lifetime. Assessing lifestyle decisions that result in lower rates of neurodegenerative disease, especially in Blue Zones, could provide insight for regions or communities that experience high rates of neurodegeneration diagnoses. Overall, collecting information on the ideal actions for neurodegenerative disease prevention could provide populations with a blueprint to maintaining or reaching optimal cognitive health. A monumental achievement such as this could result in increased life expectancies in many regions of the world as well as an overall rise in quality of life. There would be a significant reduction in the number of people living with Alzheimer's disease, Parkinson's disease, and Huntington's disease among others, and there would be an increase in the average age of diagnosis for these diseases.

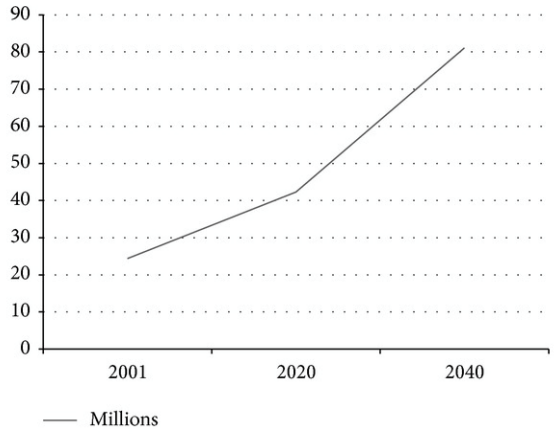

Figure 1. Estimate of people living with dementia worldwide. Source: Rizzi et al., 2014. Description: The statistic shown in the diagram suggesting that rates of dementia are greatly increasing over time emphasizes the need for intervention to prevent the current trend from continuing in the future.

Methodology

The central goal of this research was to observe habits and lifestyle choices associated with neurodegenerative disease diagnosis in order to better understand what individuals can do to prevent neurodegeneration at a global scale. This study utilized a literature review, using several informational and diverse primary sources. Qualitative data was an essential factor to this study because it allowed for the investigation of several factors' effects on cognitive health and their prevalence in Blue Zone regions. To pursue this qualitative data analysis, several primary studies were analyzed to explore the different facets of neurodegenerative disease diagnosis and prevention. Firstly, the anthropogenic causes of neurodegenerative diseases were examined to determine potential actions that individuals can partake in that could result in detrimental consequences to their neurological health. Second, the environmental origins of neurodegeneration were explored to deeply understand how people can unknowingly be affected by harmful agents in the atmosphere. Next, neurodegenerative diseases in Blue Zones were viewed as a whole to better understand what communities in these regions do to achieve lower rates of diagnosis. Further, sources regarding general neurodegenerative disease prevention were used to conclude the actions and lifestyle activities that all individuals should take part in with the goal of preventing neurodegenerative disease. This research only utilized online sources, and no physical tools or materials were used. This study effectively diminished research biases by analyzing various sources with differing research objectives, time periods, locations, and authors to guarantee that many diverse perspectives were taken into consideration.

Anthropogenic Causes of Neurodegenerative Diseases

Though the causes for many known neurodegenerative diseases derive from genetics, the consequences of human actions also play a role in the origin and development of several neurodegenerative diseases. Human actions can impinge the brain in numerous ways. Lifestyle habits such as dietary practices, smoking, and sleep cycles can impact an individual's neurological health. Pinpointing the sources of human-caused neurodegenerative diseases could be a significant asset in reducing the prevalence of these diseases around the world.

A lot of research indicates that certain aspects of nutritional diet can play an important role in the degeneration of neurons. Data shows that malnutrition and low BMI is associated with higher rates of dementia and mortality (Bianchi, 2019, p. 810). This emphasizes the impact that the amount of food a person intakes can have on their brain health. There is also evidence that the nature of the food that an individual consumes can be significant to the development of neurodegenerative diseases. Some researchers have been able to observe the intestinal microbiota of an individual as an indicator of that person's cognitive health. One journal written with this knowledge concluded that ultra-processed foods or diets high in fat and simple carbohydrates can lead to neuroinflammation and a reduction in cognitive function (Leo & Campos, 2020). These findings suggest that specific eating habits can have worse effects on cognitive health than others. This also surfaces the concern that countries such as the United States, in which ultra-processed foods are becoming increasingly popular, might suffer more from neuroinflammation and reduction in cognitive function than other countries around the world.

Similar to nutrition, sleep schedules and conditions such as insomnia can play principal roles in neurodegenerative disease diagnoses. Abbot & Videnovic (2016) study the correlations between chronic sleep disturbance and neurodegenerative disease. Their findings revealed that there is emerging evidence that disturbed sleep may contribute to the development of several neurodegenerative disorders. There are specific sleep phenotypes associated with different diseases, and research on these sleep phenotypes is being studied to target

particular neurodegenerative diseases such as Alzheimer's, Parkinson's, and Huntington's diseases. The study suggests that sleep disturbances such as circadian disruption, insomnia, and rapid eye movement disorder can impact the likelihood of developing neurodegenerative diseases (p. 55). This brings up the notion that countries with bigger cities and louder neighborhoods may have higher rates of neurodegenerative diseases due to more sleep disturbances.

Moreover, the intake of alcohol into the human body at large amounts can increase the potential for neurodegeneration. One study on alcohol's effect on the brain mentions that alcohol is a neurotoxin, and alcoholic dementia is the second most common cause of adult dementia in the United States. Long term consumption of alcohol can have severe effects on cognitive function over time. There are even some diseases that are directly caused by alcohol abuse, such as Korsakoff's syndrome, which is caused by a deficiency in thiamine due to great alcohol intake (Crews, 1999, p. 379). This research indicates that countries with higher quotas of alcoholism may also have greater rates of neurodegenerative disease diagnoses.

To put these research papers into perspective, neurodegenerative diseases can be directly caused or furthered by an individual's lifestyle habits. These can include dietary habits and nutritional values, sleep disturbances, and alcohol abuse. Although one individual's choices may not seem to impact the rates of neurodegenerative disease in an entire country, sometimes there are underlying reasons for their habits. For example, more urbanized countries would likely have more restaurants with ultra-processed food and more sleep disturbances, which could stimulate neurodegeneration. For this reason, studying the overall lifestyle habits in countries may aid in finding the key to reducing rates of neurodegenerative disease globally.

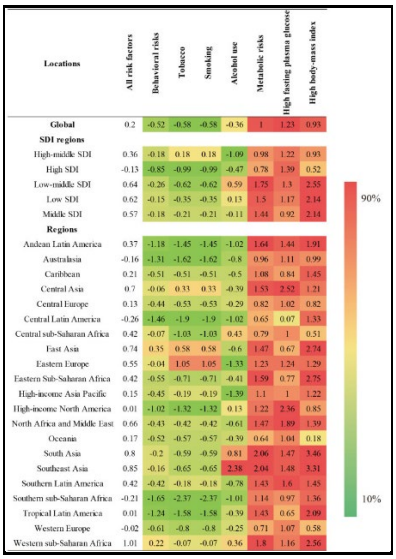

Figure 2. Prevalence of neurodegeneration risk factors around the world and their estimated annual percentage change (EAPC). Source: Getzzg, 2023. Description: The chart demonstrates the inequalities in neurodegeneration risk in various regions around the world, providing examples of why certain regions may have more rates of neurodegenerative diseases than others.

Environmental Causes of Neurodegenerative Diseases

An individual's interaction with the environment can also impact their neurodegeneration, and oftentimes, those environmental hazards are directly caused by human activity. As studies are conducted on the effects of environmental hazards on cognitive health, researchers may be able to interpret a country's likelihood of having high rates of neurodegeneration based on the presence of environmental issues in that region.

A study done by Bondy (2016) on how anthropogenic pollutants may incentivize neurodegenerative disease concluded that it is likely that some unknown factors promoting neurodegenerative diseases may involve the incidence of toxic materials in the environment. The study suggests that almost all neurodegenerative disorders have a relatively small genetic element and a much larger unknown component, which in many cases could be these toxins in the environment. (p. 41). This study elicits the notion that countries with higher levels of toxins in the atmosphere, especially countries with large industries or mining sites, may also have higher levels of neurodegenerative disease. If this is found to be true, one method to counteract the development of neurodegeneration caused by toxins would be to make sure that people who could potentially come in contact with these toxins are given proper protection to prevent them from intaking dangerous substances.

Similarly, another study evaluated the blood levels of some of the most researched metals (Cu, Se, Zn, Pb, and Hg) in patients most affected by chronic neurodegenerative diseases such as Alzheimer's disease and multiple sclerosis. The study established that Alzheimer's disease, more than others, had a strong correlation to the people with higher levels of heavy metals in their blood. The tested people with higher traces of heavy metals in their blood were individuals living in an area exposed to dust and volcano fumes, making them subject to a potentially contaminated environment (Giacoppo et al., 2014, p. 151). These findings assert that countries with more air-borne dust particles and landforms such as volcanoes may also be subject to higher rates of neurodegenerative diseases, such as Alzheimer's Disease.

Another study specifically observes the potential pathogenic role of lead and mercury in the development of neurodegenerative diseases. According to this research, lead and mercury interfere with many intracellular targets, contributing to processes common to neurodegenerative disorders such as mitochondrial dysfunction, deregulation of protein turnover, oxidative stress, and inflammation of the brain. These heavy metals cause harm through acute neurotoxicity or accumulation over a prolonged period of an individual's life. Exposure to heavy metals in early stages of life can be a precondition for later development of a neurodegenerative disease such as Alzheimer's and Parkinson's (Monnet-Tschudi, 2005, p. 105).

To summarize the results of these studies, human exposure to harmful substances in the environment, such as heavy metals can be a precursor to the development of neurodegenerative disorders. Some substances, such as lead and mercury have been more definitively connected to the development of these diseases. Similarly, some diseases are more linked to environmental toxins than others, with Alzheimer's having one of the greatest connections. This information suggests that areas with volcanic activity, large amounts of particulate matter, and industrial facilities would have more exposure to heavy metals and higher rates of neurodegenerative diseases, especially Alzheimer's.

Neurodegenerative Diseases in Blue Zones

In Blue Zones, people have an average higher lifespan than other countries of the world, with a large population reaching over 100 years old. A lowered rate of neurodegenerative disease is partially accountable for this statistic. Individuals in Blue Zones experience higher lifespans and fewer neurodegenerative disorder diagnoses due to a number of factors in their lifestyles.

Figure 3. Locations of Blue Zones around the world. Source: Hassanzadeh, 2023. Description: The map provides specific locations of Blue Zones, regions around the world with the longest lifespans and low rates of neurodegenerative disease.

Firstly, a long-term vegetarian diet contributes to the maintenance of people's cognitive health. A study hypothesized that a long-term vegetarian diet could affect circulating mRNA expression to moderate health. The study compared the miRNAs between vegetarians and non-vegetarians in Loma Linda, California, one of the five Blue Zones in the world. They concluded that a vegetarian diet impacts aging-associated miRNAs, which may be beneficial to an individual's health span and reduce the likelihood of neurodegenerative diseases (Liu et al., 2020, p. 245). This research suggests that a vegetarian diet could be a key asset in bringing non-Blue Zone areas to the health span of Blue Zones.

A study conducted by California State University on Alzheimer's in Blue Zone communities revealed that several factors contribute to people in Blue Zones avoiding the development of dementia and Alzheimer's. One factor that largely contributes to the circumvention of neurodegenerative diseases is consistent exercise, which improves cognitive health and functionality of the brain (Daisy, 2021). This study revealed exercise to be a contributing factor to Blue Zones' low levels of dementia and Alzheimer's, which could be used to educate non-Blue Zone communities on how to prevent development of these diseases.

Parker (2023) wrote a paper discussing a UC Davis collaboration with the Blue Zones Activate Initiative which aims to make Sacramento county more dementia-friendly, as Blue Zones are today. The task force is working toward preparing the area for an aging population and preventing further Alzheimer's diagnosis. To do this, the project is promoting a life of continuous learning and brain stimulation as well as exercise, taking up hobbies, and being socially active. These practices were chosen because they were to credit for Blue Zones' low rates of Alzheimer's. This project was an example of using Blue Zones as a model for helping aging populations all over the world.

Neurodegenerative Disease Prevention

Many studies have been conducted on preventative measures that can be taken to prevent complex disorders such as Alzheimer's disease. One article outlines prevention and reserve against dementia and other neurodegenerative diseases. It identifies that human and financial resources as well as lifestyles and neurobiological parameters should be observed to develop a higher resilience against the symptoms of neurodegeneration. This study recognizes the need for further coordinated research to properly transfer fundamental research findings to tangible public health interventions (Perneczky, 2022, p. 53). It is important to consider that people with fewer financial resources can still make efforts toward neurodegenerative disease prevention. For example,

money is not necessary to ensure a consistent and healthy sleep cycle, which can effectively reduce brain inflammation and the risk of obtaining neurodegenerative diseases. Similarly, a vegetarian diet, which is considered to be beneficial for cognitive health, is often more affordable than a non-vegetarian diet because produce generally costs less money to produce than meat does. It is important to consider what resources are available to the common individual that don't cost too much money.

Banerjee et al. (2021) stressed the importance of a healthy diet in lowering the risk of several neurodegenerative disorders. The study informs that an intake of sufficient antioxidants, polyunsaturated fatty acids, and polyphenols in a habitual diet can delay the onset of chronic neurodegeneration. Diet directly affects gene expression, apoptosis, cell signaling models, and the inflammatory pathway correlated with neurodegenerative disorders. Therefore, a nutritious diet can lower the risk of dementia, provide symptomatic relief, and prevent the death of motor neurons in patients (p. 1). This study illustrates the necessity of a healthy habitual diet for the prevention of chronic neurodegeneration.

More specifically, studies have been done on specific diets around the world and their impact on cognitive impairment. One research study asserts that most epidemiologic studies report that an adherence to a Mediterranean diet (MD) is associated with protection from neurodegeneration. Recent clinical data also support the hypothesis. Some evidence suggests that a Mediterranean diet can protect individuals from the risk of Parkinson's disease. This can be explained by the plant polyphenols in MD which activate similar molecular pathways as calorie-restrictive diets (Gardener & Caunca, 2018, p. 10). Using MD as a model, individuals can determine what the best diet would be for them to prevent neurodegeneration. The foundation of MD is built around vegetables, fruit, herbs, nuts, beans, and whole grains. Red meat is eaten only occasionally. This information could be utilized to create a blueprint of healthy nutrition for cognitive health.

Marques-Aleixo et al. (2021) focus on the role of physical exercise on cognitive function. According to the study, physical exercise has been considered to be able to modulate brain structure and function because it is a nonpharmacological alternative to neurodegenerative pharmacological therapies. The study categorizes physical exercise as a stimulant of a healthier and "fitness" neurological phenotype. This study proves the beneficial effects of exercise on neurodegenerative disease prevention.

Another study focuses on the dangers of metal-based neurodegenerative diseases, and possible therapeutic strategies that could be used to diminish the neurodegenerative process. The study states that currently, therapeutic strategies treat and prevent the pathology of neurodegeneration rather than its etiology. Apart from drugs which can regulate and change neurotransmitter levels, therapeutic strategies are currently being researched in depth. Although there is currently not much definitive research on metal-targeted therapies, there is potential for its use in the future as more concrete conclusions are made (Crichton et al., 2008, p. 1189).

Results

The purpose of this study was to synthesize an ideal lifestyle that would make neurodegenerative disease diagnosis as unlikely as possible. After considering several aspects of humans' behavior and surroundings as well as effective measures used in Blue Zones, a basic blueprint can be created.

Firstly, concerning nutrition, individuals should consume a healthy quantity of food, as malnutrition and a low BMI are correlated with neurodegeneration. Individuals should avoid ultra-processed food and red meat as much as possible. They should also engage in a Mediterranean diet and ingest vegetables, fruit, herbs, nuts, beans, and whole grains on a daily basis. Individuals should get a consistent eight hours of sleep everyday to avoid sleep insomnia. Additionally, individuals should aim for at least half an hour of exercise everyday. Alcohol should be avoided as a whole, as alcohol is considered to be a neurotoxin. They should avoid areas known to have significant levels of heavy metals in the atmosphere. As a whole, communities should take action to avoid activities that discharge heavy metals into the environment, such as manufacturing paints, pipes, and batteries that use these neurotoxins.

Although abiding by these practices constantly may prove to be a challenge, knowledge of this blueprint could allow individuals to compare their current lifestyles to this one. By doing so, they may be able to observe any high-risk behaviors they may be participating in and begin to avoid them to some extent.

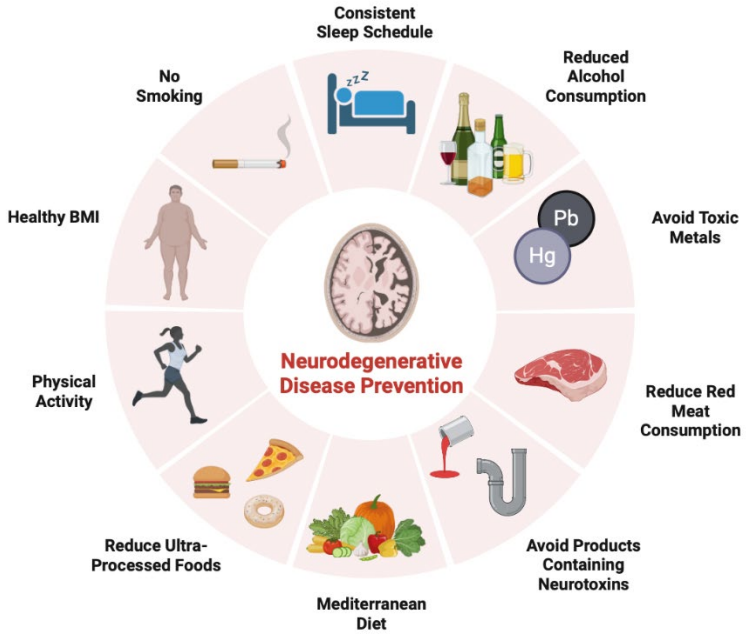

Figure 4. Activities and habits individuals can partake in to reduce their risks of neurodegeneration. Source: Sajan, 2024. Description: The figure provides a compilation of several factors that affect neurodegeneration risk, outlining actions that should be maintained or avoided to affirm cognitive health.

As previously mentioned, it is important to consider the impact that an individual's financial resources and socioeconomic status can have on their ability to follow the created blueprint. In order to consider this obstacle, a new diet called the RS NeuroDiet has been created to provide an effective nutritional plan for neurodegenerative disease prevention that is both affordable and accessible. Foods to avoid in the RS NeuroDiet include red meat, ultra-processed foods, sugary foods (soda drinks, candies, foods with excessive added sugars, etc.), baked beans, fried foods, and alcohol. Foods to prioritize include nuts and seeds (almonds, walnuts, flax seeds, chia seeds, etc.), whole grains (oats, barley, quinoa, etc.), green leafy vegetables (kale, spinach, lettuce, etc.), coffee (in moderation), avocados, eggs, and oily fish (salmon, trout, sardines). These foods reduce brain inflammation and promote overall cognitive health, which can in turn prevent neurodegenerative diseases. A comparison was created between an RS NeuroDiet meal and a standard McDonald's fast food meal to prove the affordability of the RS NeuroDiet. The prices for the RS NeuroDiet ingredients were taken from the cheapest options at a Super Target in Texas. The prices below have been calculated for one serving of food.

McDonald's Standard Meal:
Quarter pounder with cheese - $3.69
Medium soft drink - $2.49
Medium fries - $1.99
Total - $8.17

RS NeuroDiet Meal:

RS Sandwich (whole grain oat bread, canned salmon, spinach, ranch) - $3.97
Chips and Guacamole (avocado, onion, whole grain chips) - $4.15
Small cup of coffee - $0.27
Total: $8.39

This RS NeuroDiet meal costs roughly the same amount of money as a standard McDonald's meal, but the benefits of the RS NeuroDiet meal on the human brain are monumental, especially in comparison with the McDonald's meal. Over a long period of time, adherence to the RS NeuroDiet could greatly decrease people's chances of getting diagnosed with a neurodegenerative disease by reducing brain inflammation substantially. The RS NeuroDiet could be implemented in areas of the world with higher rates of poverty to ensure that people can acquire meals for neurodegenerative disease prevention at a cost affordable to them. Rather than resorting to the cheap appeal of fast food restaurants and their ultra-processed foods, people would be given an alternative healthier option for the same price using the new RS NeuroDiet. Additionally, by purchasing ingredients for the RS NeuroDiet in bulk, individuals can save money over time by avoiding buying a new meal everyday as they would in a fast food restaurant. In summary, the newly created RS NeuroDiet has the promise of reducing disparities in neurodegeneration by creating a dietary plan for people in need of affordable meals, while still incorporating the ingredients necessary for optimal cognitive health.

Conclusion

Currently, there are huge disparities in rates of neurodegenerative disease diagnosis around the world. While some regions experience high mortality rates as a result of neurodegeneration, others encounter relatively high life expectancies, partially due to low neurodegeneration rates. Blue zones are a significant example of the latter, and objective information on the reasons these regions have such low rates of neurodegenerative diseases could effectively provide other areas of the world vital direction to improving the cognitive health of their populations. The research in this study aims to do just that, and its results could be used as a basis for improving cognitive health across the globe. The complex compilation of advantageous and disadvantageous lifestyles provided in this study could aid in the development of communication mediums to inform people in regions with high levels of neurodegenerative disease rates on measures to prevent their own potential future diagnoses.

Although this study went into considerable detail on several different factors of an individual's life, more detail could be researched on each individual topic in the future. For example, this study discussed the effects of sleep insomnia on cognitive health, but further research could be done on the number of hours needed to prevent neurodegenerative diseases, and how this number may vary between different age groups and sexes. Additionally, further research could be done on specific areas of the world to compare how some of these prevention methods could be effectively used depending on the region and population. Although the ingredients mentioned in the RS NeuroDiet may not be found in all regions of the world, it would still be a valuable tool globally because many ingredients could be substituted for similar foods. More research could be done into how the RS NeuroDiet could be implemented in various regions of the world to make it truly accessible to everyone. In the future, more versatile blueprints similar to the RS NeuroDiet could be synthesized to create a detailed prevention plan that dives into all aspects of prevention mentioned in this research.

Limitations

This study sought to explore and discuss qualitative data considering the aspects of human life that could have potential consequences to neurological health. As a secondary literature review, this research paper observes several primary sources to make comparisons and connections utilizing their data. The researcher made efforts

to consider many varying perspectives from different sources around the world, especially considering that the topic of this study considers neurodegenerative diseases from a global perspective. This research also took care to involve examples from a variety of backgrounds and perspectives to prohibit as much bias as possible. However, the scope of this study was still somewhat limited. Firstly, some topics discussed may apply more to certain regions of the world than others, meaning they may not be relevant to the whole globe as discussed. For example, the regions of the world facing the highest levels of neurodegenerative diseases may not necessarily be the same regions facing the highest rates of alcoholism. Secondly, although a relatively large sample size was taken into consideration, the research of more primary sources would have refined this research to a greater extent. Thirdly, there were not a great amount of existing sources considering the scant existence of neurodegenerative diseases in Blue Zone regions, making it difficult to research primary sources of such a specific topic. Although relevant sources were found and applied to this research, there could have been a deeper focus on Blue Zones if there had been more previous research done on the topic. In summary, this research made great efforts to have an unbiased and global perspective, but there were still some limitations on the scope and content of the study.

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