A Brief Discourse in Preventing and Predicting Alzheimer's Disease

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Introduction

I remember the day my grandmother misremembered me as someone else. She looked at me with an angry expression, letting loose a string of angry words, and I knew something was wrong. It wasn't until a bit later that I realized she was confusing me with her first husband (whom I'm told I looked a lot alike at the time). The doctors weren't 100% sure if she had Alzheimer's, and she died shortly thereafter from lung-related issues. But it seemed like she was mentally traveling back in time, slowly and permanently rewinding all her memories, as many who have dementia often do. Understanding probable causes for the disease, acknowledging the false leads that have been manufactured, to predicting symptoms at an early age, and developing effective treatments at later stages—there is still much work to be done in the field. And it will take many more scientists working together to make a difference in the lives of those affected by Alzheimer's and other age-related conditions—and hopefully, end the pain and torture inflicted upon everyone by this disease.

Alzheimer's can be defined as a neurodegenerative disease that occurs in mid to late adulthood and is characterized by a progressive and irreversible damage to memory and other cognitive abilities (Editors of Encyclopedia Britannica, 2023). In terms of gerontology—the study of aging—it is directly linked with and of high importance as Alzheimer's is responsible for nearly one-third of all deaths past 60 years old (Alzheimer's Association, 2023). This paper intends to briefly discuss three key areas of the disease through the review of recent studies. These areas are prevention, prediction, and a deeper sleep connection—pun intended. Furthermore, I predict that glucose and insulin resistance in the brain will prove to be the key players in predicting, preventing, and defeating Alzheimer's disease in the future.

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Prevention

The first study examined the importance of amyloid-beta (Aβ) in Alzheimer's disease (AD). They used a cross-sectional study, which can strongly establish correlations (and are great baselines) but not causation. They wanted to see if they could find any relationship between sleep self-reported and cortical amyloid in participants without dementia. They had 143 participants at the age of 70 or greater (median: 73 years [70–85]; 87 females) who said they had memory issues but no dementia. They collected data via PET scan and took sleep interviews for overnights and validated questionnaires for daytime sleep durations. They computed cortical standard uptake value ratios (SUVr) for six regions and analyzed additional parameters with logistic regression models. They found (overall for each of these) that 40% were positive for amyloid, 40% were apnea risks, 13% had restless leg syndrome, 35% had insomnia issues, 22% had daytime sleepiness, and 18% took drugs. However, no significance was found between amyloid and sleep duration. Further regression showed no associations between SUVr and sleep. They concluded that the situation is much more complex than described (Gabelle et al., 2019).

The next study reviewed the existing research on Ginkgo biloba and its potential effects on AD—highlighting the plant's anti-inflammatory, antioxidant, and neuroprotective properties. The study's findings suggest that Ginkgo biloba may be a promising natural remedy for AD, but more investigation is required to fully comprehend its effects and potential interactions with other drugs. These results may underline the potential advantages of using natural compounds as neuroprotective agents and have significant implications for developing novel AD therapies.

The last study of this category used a 14-year longitudinal design (with a case-control study) (Cavaillès et al., 2022). While not all experiments within this category will reveal a cause

and effect (specifically, cross-sectional and autocorrelations do not), cross-lag correlations can establish temporal precedence.[1] The longitudinal study had 1,749 participants; for the study, they had 719 control and 182 incident dementia cases. They would assess for dementia at each visit (using Cox models for risk assessment) and take self-reported sleep patterns. They did this at 2, 8, 10, 12, and 14 years. They found that dementia participants with longer nighttime baselines and sleep periods longer than nine hours (up to 24 hours) may have caused a change in dementia incidence (Cavaillès et al., 2022). The promotion of sound sleep practices may be a key tactic for lowering the risk of cognitive decline and dementia in older adults, according to these findings, which have significant implications for preventing and managing dementia. The study also emphasizes the need for additional study to fully comprehend the intricate connection between sleep and brain health as people age.

Strengths and Limitations

This section does have some noticeable strengths. The first study increased the reliability of its findings by using a large sample size and gathering data using PET scans and validated questionnaires. The second study employed a longitudinal design that, as previously mentioned, made it possible to evaluate the temporal order in which sleep and dementia are related. The second study also had a sizable sample size, which could improve the generalizability of the results.

Some limitations point to how the second study was executed. The study was based on participants' self-reported sleep patterns, which could be biased and not accurately represent how they actually sleep. Additionally, it did not account for any potential confounding factors, such

[1] A quick review: causation has three criteria: covariance, temporal precedence, and internal validity.

as lifestyle choices or underlying illnesses, which might impact the association between sleep and dementia.

Prediction

In terms of prediction, the next design was a hybrid. After collecting the needed data, they analyzed their longitudinal data sets with the cross-sectional design to attain correlational information. They also utilized MRI data from over 100 participants, each of whom was scanned at least once. During their data gathering, they classified 72 of the 150 as non-demented and 64 as demented. Next, they began machine learning (ML) applications. This means they used artificial intelligence and computers programmed in the same way that our brains are connected.[2]

Applying this technology to AD symptom prediction is obvious in hindsight but genius in realization. They used several data learning methods like decision trees, random forest, and support vector machines (Kavitha et al., 2022). Computers are quick and accurate at this kind of analysis, so it is no surprise that their results suggest many possibilities with symptom prediction via machine learning. These findings have significant ramifications for improving early intervention and treatment and developing more precise and effective diagnostic tools for AD. More research is required to validate and improve these models in larger and more diverse populations and find additional biomarkers and risk factors for AD.

Next, the study on glucose and sleep regulation used a repeated measures approach to their study and analysis. They can be similar to longitudinal studies with data collected over a

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[2] Programmatically, there are two main approaches, learning and knowing. The first model would be similar to a young child who has to learn all the rules of the physical world, like walking, talking, etc. The other method is to supply the program with all this information and let it make informed decisions. Neither method is 'better' than the other. On the contrary, both methods, when working together, find an ideal machine-learning situation. And because computers lack desire or any other requirements (aside from electrical energy), they can rapidly simulate and resolve many scientific questions in multiple iterations.

long period if the variables are measured under the same circumstance or matched subjects are utilized. The study was about sleep deprivation, blood sugar, and hunger. It may not appear to have anything to do with dementia on the surface. However, there is a connection between the diabetic brain (those incapable of controlling blood sugar) and the AD-ravaged brain—as seen by the KEGG pathway diagram[3] (Kanehisa Laboratories, 2021). There isn't enough data to imply temporal precedence, but there is a link and a relationship of some kind. Ultimately, they wanted to know how sleep deprivation changed hunger states and blood sugar control. They used data from a PREDICT trial where participants had meals and sleep cycles controlled for. They are measured via actigraphy, which is a motor sensor worn as a watch on the wrist. They're known to have moderate levels of accuracy. The participants' food and sleep were controlled for two weeks. They found that modifying sleep schedules had a noticeable effect on hunger and sugar control within the body. The results demonstrated that sleep deprivation increased postprandial glucose concentrations and decreased insulin concentrations, indicating impaired glucose control (Tsereteli et al., 2021). Overall, this study emphasizes the value of getting enough sleep for maintaining healthy blood glucose regulation and hypothesizes that sleep deprivation may increase the risk of developing diabetes—all of which may or may not be a key factor in dementia prevention.

Strengths and Limitations

Both studies used longitudinal and cross-sectional designs. The first study may have allowed for a more comprehensive analysis of data. The use of ML in the first study enabled the researchers to quickly and accurately analyze large amounts of data and identify potential

[3] For this correlation, please see https://www.genome.jp/kegg-bin/show_pathway?hsa05010 Where both conditions, with enough severity, will eventually lead to cell death.

biomarkers for AD. The repeated measures approach in the second study allowed the researchers to collect data under controlled circumstances and accurately measure the effects of sleep deprivation on glucose control.

These studies did have their limits, however. The first study included a small sample size of participants (n=136) and may not represent the larger population. The second study may not be generalizable to long-term effects due to measuring the effects of sleep deprivation on glucose control over two weeks. Neither study seemed to account for all possible confounding variables—which could limit the validity of the findings.

The Sleep Connection

The idea that sleep—and the lack thereof—can play a pivotal role in our lives is further reviewed in the next study, which is about pain regulation and sleep. According to the study, sleep deprivation increases activity in brain regions linked to pain processing while decreasing activity in regions linked to pain modulation, which suggests that sleep deprivation may increase pain intensity and make it harder to deal with (Krause et al., 2019). These findings have major possibilities regarding the interaction between sleep and pain. They emphasize the value of encouraging sound sleep practices to ease pain and raise the general quality of life. Furthermore, the results may provide a window or application of prediction and prevention regarding AD.

Finally, the last study looked at circadian dysfunction concerning AD. AD frequently causes sleep problems and circadian rhythm disruptions, but it is unclear how these problems are caused and how they relate to the disease (Rigat et al., 2023). This study investigates how this may affect the development and course of the disease. The Aβ protein, a supposed defining feature of AD, was found to be associated with changes in circadian rhythms and sleep quality (Rigat et al., 2023). This study implies the possibility of delaying the onset and progression of

AD through early interventions to regulate circadian rhythms and enhance sleep quality. While these implied findings are possible, no studies I have found thus far have suggested a thoroughly tested line of logic that Aβ expresses anything more than a mere biproduct of some other cause concerning AD and its progression.

Public Policy Statement

AD is a worldwide issue that affects everyone and their families. It is a progressive neurological disorder that directly affects older citizens and is defined by cognitive and functional decline, which leads to disability and usually death. In regards to Sustainable Development Goal Three (SDG 3) of UNESCO—which aims to ensure healthy lives and promote well-being for all ages—overcoming and defeating AD is essential for achieving this goal and a multi-dimensional approach that focuses on prevention, early detection, and effective management of the disease are required.

AD prevention involves healthy lifestyles engaging in physical exercise, healthy diet, and brain-stimulating activities—all of which can help reduce the risk of developing AD. Early detection of AD is vital. Early diagnosis and intervention can improve the quality of life for individuals living with the disease. Thus, UNESCO encourages the development of screening and diagnostic tools to help identify individuals at risk of AD at an early stage. Effective management of AD means sufferers have access to appropriate healthcare services—including medical treatment, support for caregivers, and community-based services. UNESCO encourages research and innovation in the field of AD to develop new and effective treatments and improve the quality of care for individuals living with the disease.

Conclusions

AD is a true monster and neurodegenerative condition that causes progressive and irreversible damage to memory and other cognitive functions. It is a leading cause of death in people over 60 years of age. This paper mentioned recent research on prevention, prediction, and the relationship between sleep and health. The first study challenged earlier findings about the significance of Aβ and AD. In the second study, we examined whether Ginkgo biloba could be used to treat and prevent AD. The third study focused on the complex relationship between sleep and brain health and emphasized the need for more investigation. The results of the fourth study, which used machine learning to predict the likelihood of dementia and cognitive decline based on MRI scans, were encouraging. Future research may reveal the importance of glucose and insulin resistance in the brain in terms of diagnosing, treating, and preventing AD.

Future Research

Additional research into the connection between sleep and neurodegenerative conditions like AD may yield crucial information about prevention and treatment options. Studies that examine how sleep duration, quality, and sleep patterns affect older adults' brain health will likely be useful. The potential advantages and risks of using natural ingredients, like Ginkgo biloba, in preventing or treating AD—while hopeful—seem rather inconclusive and require further study. Brain insulin and glucose resistance need to be looked into further as possible causes and risk factors of AD. Studies that examine these factors' contributions to the disease's development and their potential to predict via biomarkers may be helpful. Machine learning and AI will likely become indispensable in predicting, preventing, and possibly curing AD.[4] All in

[4] Machine learning is a path I am personally considering putting great effort into pursuing.

all—the extremely tired trope that—continued research in these areas is required. Nonetheless, persistence will ultimately lead to more effective prevention and treatment strategies—and, one day, to a cure.

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