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The Intersection of Lifestyle, Health, and Cognitive Decline in Alzheimer's Disease

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ABSTRACT

Alzheimer's Disease (AD) is a cognitive neurodegenerative disease that is coupled with the prevalence of dementia and cognitive decline. There is currently no known cure for AD, so the best way to combat it, along with dementia and cognitive decline, is to target modifiable lifestyle factors. This paper's aim is to assess the current known risk factors and discuss the relationship that each factor has with the development of AD, dementia, and cognitive decline to provide suggestions for people's future behaviors and address gaps in knowledge and areas needing further research.

Introduction

Alzheimer's Disease (AD) is a cognitive neurodegenerative disease that causes a decline in one's memory, thinking, and reasoning ability (i.e. cognitive decline). Coupled with the fact that AD is the 7th leading cause of death in the US, it is often associated with dementia, and AD is represented as the leading cause of dementia in the United States. In many cases, especially late-stage, a sick individual will need a primary caretaker to help care for them for the remainder of their life. (NIH, 2023). 90% of all AD cases that require a caretaker have the caretaker be a family member of the ill. People with AD, along with their caretakers, are faced with far greater burdens than just the AD. There is an economic burden – over $271.6 billion was unattainable due to over 16 billion hours in unpaid caretaking; There is long-term psychological demand placed on both the diseased and the caretaker since most report an average caretaking period of approximately 5 years (JHU, 2023). Thus, not only do individuals who have AD live a more difficult life, but the lives of those around them, and in the greater community, are also affected drastically as well.

Currently, around 55 million people worldwide suffer from dementia, and this number is expected to increase by 10 million yearly. (WHO, 2023). By 2050, this number is expected to be over 130 million. While age is most commonly the largest factor - especially if one is 65 years of age or older - in determining the likelihood of one having AD, and thus dementia, it's not the sole factor. Physical activity, obesity, diet, tobacco use, alcohol use, mid-life hypertension, genetics, diabetes, educational level, cognitive stimulation, depression, sleep, and social engagement, are other modifiable (and some unmodifiable) lifestyle factors that affect the risk of cognitive decline, and thus dementia and AD (WHO, 2015). While there are medications that people can take such as Cholinesterase inhibitors, NMDA receptor antagonists, and medications for select risk factors, there exists no known cure for AD at this point in time; therefore, those who acquire AD are likely to face neurodegeneration until their eventual death which embodies the urgency in many researchers in discovering more regarding this rapidly progressing disease (Alzheimer's Association, 2024). As of now, the best method of fighting against Alzheimer's and dementia is understanding and targeting the modifiable risk factors to lower the likelihood of acquiring them, and the intensity of one's cognitive decline (CDC, 2024).

Cardiovascular Disease

Under the title of cardiovascular disease, four items have been listed: diabetes, weight, mid-life hypertension (high blood pressure in middle age), and hyperlipidemia (elevated cholesterol). Overall, studies suggest that those with various vascular issues, especially chronic throughout one's life, have not only a heightened risk of cognitive decline but an accelerated one as well.

Looking closer, the prevalence of diabetes has seen a positive correlation with cognitive impairment that leads to dementia in both longitudinal and cross-sectional studies. In addition, there have been numerous studies performed looking at the relationship between diabetes and the risk of cognitive impairment that have all come to the similar conclusion of a positive relationship, suggesting that there is strong evidence for this relationship to be evident. Adding on, studies testing the relationship between weight, specifically mid-life obesity, and cognitive impairment show that there is strong evidence suggesting that an increase in weight is correlated with an increase in cognitive impairment; however, it is important to note that other researchers have pointed out there is a likelihood that the specifics of this relationship can be influenced by age since they found some evidence supporting the idea that if one is overweight, or at times obese, later in life, there is a decreased risk of dementia; however, a large portion of data does still support the idea that being overweight or obese in mid-life is associated with an increased risk of cognitive impairment. Similarly, the prevalence of hypertension in late life has been associated with a decreased risk of cognitive decline in a randomized control study; however, unlike the relationship with weight, a longitudinal study done to find the relationship between late-life hypertension and cognitive impairment concluded the opposite, suggesting that further research needs to be done on the subject. However, studies have consistently shown that mid-life hypertension is associated with an increased risk of cognitive decline and dementia. Lastly, research regarding the relationship between hyperlipidemia and the prevalence of dementia in middle or late life has produced mixed results; thus, the relationship between the two is ambiguous and requires further testing going forward. While there is unclear evidence regarding hyperlipidemia and the prevalence of dementia, there is some, not conclusive, but present, evidence that suggests that some medications that lower cholesterol decrease the risk of dementia, but again, there is only a little evidence to support this claim; therefore, these conclusions should, likewise, be treated as unclear pending future research (Baumgarta, 2015).

Lifestyle Risk Factors

The relationship of the following risk factors that will be looked at will vary based on every individual due to the decisions they make that determine whether they will partake in the following activities or to what degree they will partake in the following activities.

Diet

Given the strong and varying aspects that can be prevalent in a diet, there is no clear-cut relationship between one's diet and the risk of cognitive decline and dementia because of the difficulty associated with finding patterns from other studies using a varying amount of food choices; however, a whole diet that consists of an adequate amount of all food groups is suggested.

Researchers attempted to study the effect that select diets had. For instance, several cohort studies were performed to find a relationship between a Mediterranean and Mediterranean-DASH (a Mediterranean diet with an additional focus on reducing hypertension). The relationship discovered suggests that there is moderate evidence that these diets are associated with a decreased risk for dementia. Therefore, these findings also hint that one's diet plays a role in their risk of cognitive decline and dementia (

Other research groups did cross-sectional studies on caffeine specifically – viewing it as a psychoactive drug that accelerates the central nervous system improving memory, and cognitive function, among other things. The researchers found that only 4 out of 7 (~57.1%) cross-sectional studies found the hypothesized thought that caffeine heightened memory, and thus cognitive function, to be accurate. Also, only 3 out of 11 (~27.3%) cohort studies saw the same relationship and 5 out of the other 8 (~45.6%) cohort studies saw this relationship only in women or under specific conditions. Therefore, while there is some evidence that suggests a negative relationship between cognitive decline and caffeine intake, particularly coffee and tea, the conflicting data suggests that more research needs to be done in this area to form an accurate conclusion (Beydoun, 2014).

Alcohol and Smoking

Alcohol and smoking are two common activities that people, at large, decide to take part in. Therefore, it is vital that people recognize the risks involved in these activities. In general, there are many negatives associated with both activities in terms of one's health; hence, it is likely that some of the following effects may be influenced by other, separate factors that come into play along with one's risk of cognitive decline, dementia, and AD.

Researchers theorized that there is potential for alcohol intake to be associated with a lower risk of cognitive decline because of the potential reduction of cardiovascular risks and an enhanced release of acetylcholine in the hippocampus (improving learning and memory). When performed, the Rotterdam study found that a U-shaped or J-shaped graph was an accurate representation of the results where the number of drinks was on the x-axis and the rate of cognitive decline was on the y-axis. Finding that 1-4 drinks seemed to be an optimal amount. In total, 8 out of 18 cohort studies found these solutions, and 9 out of 12 cross-sectional studies found similar results. The rest of the results suggested the opposite or mixed results. Therefore, while there is a slight edge that indicates that alcohol consumption may reduce the rate of cognitive decline, researchers say that, due to the mixed results of the studies, further research needs to be done on the topic (Beydoun, 2014). However, researchers, for the same reason, also do not suggest beginning to drink to reduce one's rate of cognitive decline because of the fact that the results are mixed and require further research (Baumgarta, 2015).

Smoking, on the other hand, is associated with an increased risk of countless cardiovascular diseases, so, as mentioned prior, there is already an indirect increase in the rate of cognitive decline through the rise in cardiovascular issues. It is also believed to play a key role in Alzheimer's neurodegeneration which results in the death of neurons further hindering one's cognitive abilities. Generally, there is strong evidence from numerous cohort studies that link the idea that the rate of cognitive decline, along with the prevalence of AD, and thus dementia, is associated with smoking and tobacco use. 20 out of 29 cohort studies found some positive relationship between smoking and an increased rate of cognitive decline, but only 4 out of 7 cross-sectional studies found the same relationship. Also, this factor is, at times, difficult to research because of other factors at play such as age of smoking, and heavy smoking, among others. Hence, the result of this factor is mixed, slightly leaning toward the idea that smoking is associated with an increased rate of cognitive decline, but further research is still needed to come to a concrete solution (Beydoun, 2014).

Physical Activity

Physical activity has been effective against many known cognitive diseases. However, many researchers point out that many studies are out there that come to the same conclusion, they would still like to perform more research on this factor because there are still many unknowns associated with it such as what age is physical activity most important, or how much and what type of physical activity is most important? (

that increases a neuron's life span, and more. 21 out of 24 cohort studies found an inverse relationship between physical activity and the rate of cognitive decline. Two of the other studies found the same relationship in a specific case (when the ApoE4 allele, a genetic factor believed to influence cognitive impairment, was present, and when the ApoE4 was not present). The Rush Memory and Aging Project checked in with 716 dementia-free older adults four years apart and found that, after controlling for other variables, those with a daily active lifestyle found that they had a lower risk of having incident AD. Another cross-sectional study with over 9000 participants over the age of 65 years saw the same results that showed those who had more physical activity throughout their lives exhibited a lower risk of cognitive impairment. In short, there is quite a strong association that an increase in physical activity will lead to a decrease in the rate of one's cognitive decline; however, researchers are still working on the specifics of how much physical one needs, and at what point in one's life physical activity is more important, among other questions (Beydoun, 2014).

Education and Occupational Complexity

One of the biggest and most studied factors is education. According to the 'Use it or Lose it Hypothesis,' education is a great method to keep the brain stimulated as one keeps learning more since it creates positive neurochemical and structural alterations along with improving one's cognitive function or cognitive abilities. This consistent stimulation helps prompt new neural synapses and strengthens existing ones which helps in keeping memory active and strong. As for the structural changes, the neurotransmitter levels will increase which assists in the increasing of white matter content which helps process information between regions of the brain. Overall, studies show there is an inverse relationship between the level of education one has achieved and their rate of cognitive decline. The relationship is the same when one's level of education is replaced with intellectual occupational complexity (Beydoun, 2014).

Researchers found that there was a relationship that suggested that those with a greater level of educational attainment faced an overall better cognitive outcome – i.e. one's cognitive abilities were heightened higher in comparison to those who had attained a lower level of education. 18 out of 27 (~66.7%) cohort studies reported this exact relationship, one Netherland's study (out of the remaining 9) found this same relationship, but viewed IQ as a better predictor, and 2 other studies found this relationship in a specific case as they tested for this relationship in women and with the prevalence of the ApoE4 allele (Beydoun, 2014). Another longitudinal study was conducted with 10,195 participants from 6 countries spanning 4 continents (Asia, Australia, Europe, and North America) where the researchers harmonized the educational levels of all participants according to the ISCED 1997 (International Standard Classification of Education) as listed by the UNESCO (United Nations Educational, Scientific, and Cultural Organization). The researchers created 5 categories that people could fit into based on their educational attainment level: incomplete elementary school, completed elementary school, completed middle school, completed high school, completed post-secondary. The researchers checked in on the participants over time, and, after controlling for all other factors, they found that those who had at least a 'high school completion' level of education developed a greater dementia-free survival time compared with those who had only attained a 'completed middle school' or below level of education. Specifically, those who had completed high school had a 26% increase in their dementia-free survival time after controlling for age and gender as influential factors; when adding a control factor for occupational complexity – touched on later – a 20% increase in dementia-free survival time was found. In addition, attaining above a 'high school completion' level of education lended itself to a 27% increase in dementia-free survival time in comparison to those who only attained a 'completed middle school' or below level (Hyun, 2022). These studies suggest that there is an overwhelming inverse relationship between educational attainment and the prevalence of dementia, furthering the thought that keeping the brain active and stimulated is a vital aspect in reducing the time spent without dementia. This correlation highlights the importance of further education in keeping the brain healthy and deterring the risk of developing early cognitive decline, dementia, and AD.

Often going together with one's educational achievements is one's occupation, and, by extension, the complexity of one's occupation. The aforementioned researchers also performed a simultaneous study on the same 10,195 participants and tested what influence occupational complexity had on one's dementia-free survival time. When dividing occupations into categories, the researchers used the ISCO-08 (International Standard Classification of Occupations) classifications and the substantive complexity of work scores from the US Dictionary of Occupational Titles (DOT). First, they evaluated the skill level of the occupation on a scale of 1 to 4 (with 4 being the most complex) based on the complexity of problem-solving, decision-making, and creativity, which required a high level of literacy and numeracy; in other words, they evaluated the mental processing needed for the occupation. Levels 3 & 4 were declared high skill level, 2 was an intermediate skill level, and 1 was a low skill level. For instance, managers and professionals would have a high level of skill, office workers would have an intermediate level of skill, and laborers would have a low level of skill. The DOT provides detailed descriptions of over 12,000 occupations which helped the researchers evaluate and organize occupational complexity more effectively into a high, intermediate, or low level. This, along with data from over 60,000 workers from the April 1971 Current Population Survey and the 1970 Census occupational codes, provided the opportunity for the researchers to effectively evaluate the complexity associated with more than 12,000 occupations in the DOT. When determining whether participants had the prevalence of dementia or not, the researchers used the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria where a score of 1, 2, or 3 represents mild, moderate, or severe dementia respectively. Once any rate of dementia was found in participants, the researchers documented this time as the participant's dementia-free time. Data regarding age, sex, race, and cardiovascular conditions (with intensity being scored at a rate of 0 to 4), were used at baseline (the beginning of the study) to help ensure that the effect of occupational complexity was being analyzed to its fullest potential. The researchers found that those who had high occupational complexity compared with low occupational complexity had a 23% increase in dementia-free survival time. Those who had an intermediate occupational complexity had a 12% increase in dementia-free survival time compared with those who had a low level of occupational complexity. Suggesting that occupational complexity plays a large role in determining the likelihood and the expected time frame of one acquiring dementia in their late life (Hyun, 2022).

Another study (from 1998) evaluated the occupational type and evaluated its relation to cognitive decline and dementia in late life. All participants from this study were men from Australia at least 70 years of age or older (women were excluded from this study since they were mainly kept to household duties in the past and the youngest person in this study would have been born in 1928). The researchers used 6 categories, controlling for educational and socio-economic background, to align one's occupation: realistic (skilled trades, service, etc.), investigative (scientific and technical), artistic (artists, musicians, and literary.), enterprising (managerial, sales, etc.), and conventional (office and clerical). The participants were interviewed and asked which category their main job in life fit into and the years of formal education they received. The researchers used multivariable linear regression (a method of statistics that looks at how much effect each independent variable has on the dependent variable) by introducing one variable at a time. The goal of the study's longitudinal analysis was to analyze the rate when dementia set in for each occupational group over two waves (wave 1 was the initial and wave 2 was when the researchers checked back in on the participants). To study the rate at which dementia was prevalent between the two waves, the researchers performed a method called the difference score approach, which involved calculating changes in cognitive test scores between the two waves for each participant. Through the use of statistical analysis, the researchers attempted to discover if any of the occupational groups had an accelerated or delayed onset of dementia. The results of this study found that those who had the lowest scores belonged to the realistic group, but they also had the lowest years of formal education (suggesting the influence of the aforementioned educational relationship). However, when looking longitudinally (3.5 years after the initial starting point), the rate of cognitive decline didn't change much between occupations. Thus, the study concluded that while there may not be a difference in the rate of cognitive decline in individuals of differing occupations, the baseline differences (differences at the start of the study or during an individual in their

70s outside of this study) in the group varied wildly. For instance, the enterprising group had a dementia prevalence of 8.6% while the realistic group had a far larger dementia prevalence of 17.7%. In short, occupation may not worsen the decline, but it will affect how bad the situation is when it starts (Jorm, 1998).

However, it's important to note that this study was conducted in the late 90s, so a new study was also done in South Korea that tried to study the same relationship in 2023. This study includes unpaid work such as housework and caregiving because they are underrepresented in other similar studies. The participants were obtained from the 2006 KLoSA (Korean Longitudinal Study of Aging) Survey and were interviewed on labor/employment, sociodemographic, lifestyle, and heat-related characteristics. Those who refused to participate, had intellectual disabilities, or refused to report their Korean Mini-Mental State Examination (K-MMSE) were excluded. In the end, the study had over 5,865 participants and an average of 3.82 observations (the number of times participants were examined and updated over the longitudinal time period). Each wave was when a survey was done, but not everyone was surveyed every wave. Once all participants took the K-MMSE, they were put into two groups based on their score: no cognitive impairment (score < 24) and cognitive impairment (score > 24). There were 12 occupational groupings (the first three are unpaid, and the rest are paid): (1) homemakers; (2) unemployed; and (3) retired (4) managers; (5) professionals and related workers; (6) clerks; (7) service workers; (8) sales workers; (9) skilled agricultural, forestry, and fishery workers; (10) craft and related trades workers; (11) plant and machine operators and assemblers; and (12) elementary workers and armed forces. There were 6 lifestyle covariates (factors that could influence the result): smoking, alcohol, routine physical exercise, obesity, chronic disease, and depressive symptoms. And there were 8 demographic covariates: gender, age, marital status, religion, residential area, educational level, household income adjusted for household size, and housing tenure. The study used 3 models to examine the effects of occupation. Model 1: cross-sectional Analysis analyzed at baseline. Model 2: longitudinal study without evaluating the effect of covariates. Model 3: longitudinal study while evaluating the effect of covariates. In total, 7 analyses were done (model 1 had one wave - since it was cross-sectional - while models 2 and 3 had 3 waves - since they were longitudinal). The results of the study found that men had a greater cognitive function compared to women at baseline (wave 1), but they were also associated with an education level of at least college level, and only worked paid jobs. This suggests that those who worked unpaid jobs faced an increased risk of cognitive decline. The study also found that the prevalence of cognitive impairment differed greatly between occupations (women were nearly double the rate that men had in select categories). Men saw the highest rates in the retired (14.5%) and homemaker (9.2%) categories while the lowest were in clerks (2.3%) and managers (2.9%). Women, on the other hand, saw the highest rates in the skilled agriculture and forestry and fishery (22.3%) and homemaker (14.1%) categories while the lowest were in managers and professionals categories (0%). Model 2 concluded that women had a greater risk of cognitive impairments and that the risk of cognitive impairment between occupations wasn't relatively consistent with gender. However, using model 3, the researchers found that there was a significant difference between each occupation and cognitive decline in both genders (not just women), hinting that the covariates were playing a role in influencing the results. The differences in the odds ratios (suggests the likelihood of the results being repeated) of cognitive impairment across occupation categories were more pronounced in women compared to men. This suggests that the data from future studies is more likely to repeat data for women as found in this study. In summary, the study found that there was a risk of cognitive impairment that is influenced by both gender and occupation and that these studies will likely have differing results depending on the developmental position of the country due to its effect on the education prevalent and the occupational roles associated with genders (Chung, 2023).

Factors to Consider

Now that a general layout has been made, it's important to recognize how these factors may influence one another. For instance, many of the lifestyle choices overlap. The prevalence of diabetes, being overweight or

obese, and certain cardiovascular conditions, are related to one's diet, so decisions in one factor begin to have a bleeding effect into other factors that can influence one's risk unknowingly. In addition, studies have shown that there is an inverse relationship between smoking and education attainment (Cao, 2023). This means that, once again, by making certain decisions regarding one modifiable factor, one opens oneself up to other possible negative side-effects. So, it is vital to consider how actions and decisions pertaining to one modifiable risk factor will affect others.

Going Forward

While there has been extensive study on the risk factors associated with cognitive decline, dementia, and AD, there is still room to grow and further study because, as seen above, many studies were mixed suggesting that while the current thought and relationship believed to be present now is accurate, there is a possibility that experts do not recognize certain aspects of a factor that may drastically effect how people should approach their behaviors and decisions. Also, there are still gaps in the knowledge of the specifics of certain factors. For instance, how much physical activity one needs, how many alcoholic drinks one can have, what kinds of physical activity should be performed, and more. Finally, the rate at which new jobs are coming and going is drastically changing, and since there is not a lot of long-term longitudinal data regarding these new jobs and the activities that are associated with them, there are still a lot of unanswered questions about the effect they have on one's cognitive abilities as they age.

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