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The Relation Between Concentration of Vitamin D and Cognition in Young Adulthood into Elderhood: A Correlational Study

Ashley Woodin
Mount Saint Mary College, Newburgh, New York

Alzheimer's disease is a very serious condition affecting more and more people every day. The disease eventually attacks the nervous system and can destroy memory and cognitive ability (National Institute of Neurological Disorders and Stroke, 2014). There is no cure but research has found that vitamin D has helped with improving cognitive function in those with dementia such as Alzheimer's disease (Chandra, 2001; Koven, Cadden, Murali, & Ross, 2013; Llewellyn, Lang, Langa, & Melzer, 2011; Llewellyn, Lang, Langa, Muniz-Terrera, Phillips, Cherubini, Ferrucci, & Melzer, 2010; Peterson, Murchison, Zabetian, Leverenz, Watson, Montine, Carney, Bowman, Edwards, & Quinn, 2013; Wilkins, Sheline, Roe, Birge, & Morris, 2006). There is little research to determine if Vitamin D is important to the maintenance of memory throughout the life span. This proposed longitudinal study would involve women between the ages of 23 and 25 with a history of Alzheimer's disease who will be assessed cognitively using the Mini-Mental State Exam. They will also have blood drawn every six months to determine levels of serum 25-hydroxyvitamin D (Vitamin D in the blood). These women will be part of this study for 50 years. The purpose of this correlational study is to determine if higher levels of Vitamin D are associated with better cognitive function over a long period of time and if it pushes back the onset of cognitive issues of Alzheimer's disease.

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Dementia is a type of cognitive impairment that typically results in loss of memory, trouble reasoning, decreased ability to think, and behavioral problems (National Institute of Neurological Disorders and Stroke, 2014). There are many different types of dementia with the most prevalent form being Alzheimer's disease. Alzheimer's disease affects about five million Americans over the age of 65 (National Institute of Neurological Disorders and Stroke, 2014) and the number of people suffering is expected to nearly triple in the next 35 years (Middleton & Yaffe, 2009). Around16 percent of women and 11 percent of men aged 71 years or older have dementia (Alzheimer's Association, 2014). Old age is the most severe risk factor (National Institute of Neurological Disorders and Stroke, 2014). Cognitive decline is more common in the elderly (Llewellyn, et al., 2010) and people aged 75 years or more make up 70% of the population suffering from dementia (Mangialasche, Kivipelto, Solomon, & Fratiglioni, 2012). Brain scans, cognitive and neuropsychological tests, laboratory tests, presymptomatic tests, and psychiatric evaluations are used in the diagnosis process (National Institute of Neurological Disorders and Stroke, 2014). There are limited drugs available that treat symptoms, but no cures have been discovered.

Drugs such as cholinesterase inhibitors are used to stabilize memory temporarily (National Institute of Neurological Disorders and Stroke, 2014). In 1997, Simpkins, Green, Gridley, Singh, De Fiebre, and Rajakumar tested the effects of estrogen therapy on women with Alzheimer's disease. Previous research suggests that estrogen is necessary for healthy neural

Ashley Woodin (*awooo077@my.msmc.edu)* is a student at Mount Saint Mary College majoring in psychology and is planning to pursue a Master's Degree in Social Work.

development and function and those women who have estrogen deficiencies are more likely to develop dementias, including Alzheimer's disease. Simpkins et al. (1997) discovered that when women were being tested for memory and learning, estrogen hormones were active showing that estrogen is necessary in the learning process of cognition. Researchers also examined the effects of intranasal insulin on Alzheimer's disease and discovered a link between decreased levels of intranasal insulin in patients with Alzheimer's disease (Freiherr, Hallschmid, Frey, Brunner, Chapman, Holscher, Craft, De Felice, & Benedict, 2013). Intranasal insulin intervention seemed to have improved memory in healthy patients and was also linked to an improvement in cognition of the mildly impaired (Freiherr et al., 2013). Vitamin supplementation is another more recently researched phenomenon that may have a link to decreased risk of dementia. Brain function is highly dependent on proper nutrients and specific vitamins are vital for particular central nervous system maintenance and function (Selhub, Bagley, Miller & Rosenberg, 2000). One specific vitamin that has been and is still being studied is Vitamin D.

Vitamin D is a dietary nutrient that is most well known for its help in maintaining healthy bones (NIH, 2011). Vitamin D is produced by a person's skin when exposed to sunlight and then carried through the body (Wilkins et al., 2006) or through ingestion of certain foods such as milk, fatty fish, or oral supplementation (NIH, 2011). In comparison to the younger generation, the elderly are not as frequently exposed to sunlight and their skin does not convert sunlight into Vitamin D as well (Lips, Graafmans, Ooms, Bezemer, & Bouter, 1996). In the United States and Europe, over 40% of the elderly suffer from deficiencies with Vitamin D (Llewellyn et al., 2010). Vitamin D receptors exist on many cells in the body including neural and glial cells in the human brain (Annweiler, Schott, Allali, Bridenbaugh, Kressig, Allain, Herrmann, & Beauchet, 2010). There is new evidence that Vitamin D receptor develops early in rodent brain development (Lu'o'ng & Nguyen, 2013) which shows that those receptors are important in the brain from the early stages of life. Patients with Alzheimer's disease have been shown to have less expression in Vitamin D receptors in the hippocampus, which is an area of the brain that is crucial for memory (Annweiler et al., 2010). Elderly women with Alzheimer's disease are more likely to have Vitamin D deficiency than elderly women who do not have Alzheimer's disease. (Lu'o'ng & Nguyen, 2013).

Many researchers are examining the concentration of 25-hydroxyvitamin D or serum 25(OH)D to determine the effects of concentration on cognition. Chandra (2001) performed a one-year, double blind, placebo-controlled study involving 96 healthy men and women between the ages of 66 and 88. Some participants were given a placebo while others were given a Vitamin D supplement and their cognitive qualities were assessed. The results of the study showed statistically significant increases in scores on cognitive function tests in the patients receiving multivitamin supplementation over a 12-month period (Chandra, 2001).

Wilkins et al. (2006) performed a cross sectional study where 40 of the participants had Alzheimer's and another 40 did not. Researchers determined the clinical dementia rating (CDR) of each participant using assessments such as the Mini-Mental State Examination and the Short Blessed Test (SBT). Using blood tests, researchers determined the concentration of Vitamin D in each participant's blood. Researchers discovered that participants with Alzheimer's who were Vitamin D deficient scored lower on the SBT and showed more signs of dementia on the CDR than those who were not Vitamin D deficient (Wilkins et al, 2006).

In a cohort study performed by Llewellyn et al. (2010) it was discovered that elderly who were Vitamin D deficient had lower cognitive tests scores than those who were not. The Mini-Mental State Examination and Trail Making Tests were used to determine levels of cognitive functioning in each participant. Previous to cognitive testing, researchers took blood samples to test for levels of serum 25(OH)D for each participant. Those with levels less than 25nmol/L were considered to be Vitamin D deficient. More recently, Llewellyn, Lang, Langa, and Melzer (2011) studied larger elderly populations in the United States and examined the effects of Vitamin D deficiency on cognition. Following blood tests, neuropsychological tests were performed on each participant to measure their levels of orientation, memory, and attention. The results showed an increased risk of cognitive impairment in elderly participants lacking Vitamin D (Llewellyn et al., 2011).

Gschwind, Bischoff-Ferrari, Bridenbaugh, Hardi, and Kressig (2014) assessed if Vitamin D supplementation could influence cognition in patients 65 years or older over a three year period. They drew blood from each patient to determine levels of 25(OH)D and they assessed cognition using the MMSE. They discovered that those who had lower levels of 25(OH)D also scored lower on the MMSE giving just cause to do more research involving Vitamin D and cognition as variables (Gschwind et al., 2014).

In an additional study, performed by Koven, Cadden, Murali, and Ross (2013), a small sample size of 35 individuals with Multiple Sclerosis (MS) was assessed. MS is a disease where individuals suffer impaired attention and long-term memory. Researchers determined where each participant ranked cognitively using a battery of different neuropsychological tests. Each individual's blood was tested to find out levels of Vitamin D in each person before testing. The results showed that those with MS who had higher Vitamin D levels had better nonverbal long-term memory capability (Koven et al., 2013). Where MS can cause dementia like symptoms, Vitamin D has been shown to decrease those effects.

In a study from the past year, Peterson et al. (2013) performed a longitudinal add-on study involving participants with Parkinson's disease to determine how Vitamin D affects their memory and mood. Cognitive states were measured using the Mini-Mental Status Exam,

Montreal Cognitive Assessment, Mattis Dementia Scale, Hopkins Verbal Learning Tests, Benton Line Orientation, Trails Making Test and Digit Symbol Substitution. Blood samples were taken to determine levels of 25(OH)D in the blood of each participant. The research results indicated significantly higher scores on verbal fluency and verbal memory in participants with higher levels of Vitamin D that were not suffering from dementia (Peterson et al., 2013). These results could mean Vitamin D helps cognition but more research must still be done.

Contrary to all the significant results found in previous research, there are still some studies that show no effects of supplementing Vitamin D on cognition. Dean, Bellgrove, Hall, Phan, Eyles, Kvaskoff, and McGrath (2011) researched the effects of supplementing Vitamin D in young adults on their cognition and emotions. In a randomized controlled six-week long experiment, 128 young adults, aged at least 18 years, were randomly placed into groups either receiving Vitamin D supplements or a placebo. Blood samples were taken to determine levels of 25(OH)D and cognition and emotional states were assessed using nine different qualitative assessments. Dean et al. (2011) discovered no significant effects of Vitamin D supplementation on cognition in young adults.

Alzheimer's disease is a very debilitation condition that affects more people every year, especially women over 65 years old (Alzheimer's Association, 2014). There is no known cure for Alzheimer's disease but some research suggests that increased levels of Vitamin D might aid with cognition and memory (Chandra, 2001; Koven et al., 2013; Llewellyn et al., 2010; Llewellyn et al., 2011; Peterson et al., 2013; Wilkins et al., 2006). More research is needed to better establish the role Vitamin D plays in cognition and memory. This longitudinal study is proposed to examine the relationship between levels of Vitamin D and cognition from early adulthood to elderhood. It is hypothesized that in women with a family history of Alzheimer's disease, those who have a higher volume of Vitamin D will experience less dementia-like symptoms of memory loss from early adulthood to elderhood.

PROPOSED METHOD

Participants

This study will consist of a sampling of 2000 young adult women in the United States between the ages of 23 and 25. Participants must have a family history of Alzheimer's disease but otherwise be healthy. Participants cannot have any other disorders or pre-existing conditions that may affect their memory or cognitive function. Participants must also disclose all medications or therapies they are taking throughout the study in order to account for any potential confounds or side effects of said medications or therapies.

Measures

Blood concentration of Serum 25(OH)D will be measured by taking blood samples and doing a serum 25(OH)D plasma test in a doctor's office (Dugdale, 2013). A concentration of 25(OH)D less than 10 ng/mL will constitute as being Vitamin D deficient (Kennel, Drake & Hurley, 2010).

Cognitive abilities will also be measured using The Mini-Mental State Exam (MMSE) (Folstein, Folstein, & McHugh, 1975). The MMSE is a 30-item task exam where the subject will be asked to perform different tasks. Tasks will test the ability to pay attention and calculate, short and long-term memory, language skills, and orientation.

Procedure

Participants will be recruited through their doctors' offices. Doctors from around the United States will call patients who have a history of Alzheimer's disease and ask if they would like to take part in the study. All who choose to participate will provide informed consent before taking part in the study. Participation will be for a 50-year longitudinal study and participants will be compensated for their participation with $150 each year. Participants will be randomly placed into two groups of 1,000. Half of the participants will be given a lifetime supply of gummy vitamins containing Vitamin D while the other half will be given similar gummy vitamins without Vitamin D. The vitamins will add some variation in concentrations of Vitamin D in participants throughout the study. It is expected that some participants may already be on a multivitamin and some may simply choose to not take the provided gummies. All participants will be required to fast for 12 hours and go to a local clinic or medical office to provide blood samples once every month and take an MMSE and short-term memory tests every six months in their own homes. At every sixth month period, average blood concentration for 25(OH)D will be calculated and recorded for each participant along with her scores for each of the memory tests. Participants are free to exit the study at any time but may also forfeit any compensation once they have left.

CONCLUDING REMARKS

Limitations

There are many limitations to this study. Being that this experiment is longitudinal, there is a much greater risk of participants dropping out, moving, being injured or not being able to travel to testing sites, becoming ill or even dying. It may be difficult to acquire 2000 participants in such a limited age range who all have a history of Alzheimer's disease. Participants are also taken from a convenience sample of people rather than being randomly selected, which would make results more generalizable. It is important to remember that correlation is not equal to causation and the results of this study would not justify a cause and effect relationship between Vitamin

D and cognition. Also, without regulating what people are eating, medications they are taking, or what vitamin supplements they may be taking, results of blood concentration tests could end up being skewed in one direction. For example, all participants could end up having high levels of Vitamin D and or other vitamins and those could, in turn, also be affecting their cognitive abilities. It would also be hard to generalize any conclusions to all women in the world since the sample is a small portion of women from the United States, regardless of their backgrounds. All results are only related to women and none can be used for men without first doing trials with men as well.

Significance

Alzheimer's disease affects many of the elderly today and the number is increasing at a dramatic rate. With no cure currently available, finding ways to delay or prevent the onset of the condition is still a major goal for researchers today. Strides are being made with exploring Vitamin D as an aid to improving the cognitive impairments associated with Alzheimer's disease. Wilkins et al. (2006) discovered a link between low levels of Vitamin D in elderly patients suffering from Alzheimer's disease and low scores on cognitive tests. Other researchers, more recently, discovered that participants of their study who had higher levels of Vitamin D and no dementia scored higher on memory tests than those with lower levels of Vitamin D (Peterson et al., 2013). The results from the current research provide evidence that Vitamin D could be useful in improving or preserving memory and cognitive ability.

This study aims to add to the existing research by providing insight into Vitamin D's effects on the cognition of young adult women as they age into elderhood. This research could help increase the knowledge of the potential Vitamin D has in helping cognitive function of those who are or could eventually be suffering from Alzheimer's Disease. Vitamin D supplementation would be an extremely cost effective way to help treat Alzheimer's Disease or other related dementias.

REFERENCES

Alzheimer's Association (2014). Alzheimer's disease facts and figures. *Alzheimer's & Dementia, 10(2)*, 1-75. Retrieved from http://www.alz.org/downloads/facts_figures_2014.pdf

Annweiler, C., Schott, A. M., Allali, G., Bridenbaugh, S. A., Kressig, R. W., Allain, P., Herrmann, F. R., & Beauchet, O. (2010). Association of vitamin D deficiency with cognitive impairment in older women. *Neurology, 74*, 27-32. doi: 10.1212/WNL.0b013e3181beecd3

Chandra, R. K. (2001). Effect of vitamin and trace-element supplementation on cognitive function in elderly subjects. *Nutrition, 17*, 709-712. doi: 10.1016/S0899-9007(01)00610-4

Dean, A. J., Bellgrove, M. A., Hall, T., Phan, W. M. J., Eyles, D. W., Kvaskoff, D., & McGrath, J. J. (2011). Effects of vitamin D supplementation on cognitive and emotional functioning in young adults- A randomized controlled trial. *PLoS ONE, 6*, 1-7. doi: 10.1371/journal.pone.0025966

Folstein, M. F., Folstein, S. F., & McHugh, P. R. (1975). Mini-Mental State: A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*, 189-198. doi: 10.1016/0022-3956(75)90026-6

Freiherr, J., Hallschmid, M., Frey, W. H., Brunner, Y. F., Chapman, C. D., Holscher, C., Craft, S., De Felice, F. G., & Benedict, C. (2013). Intranasal insulin as a treatment for Alzheimer's disease: A review of basic research and clinical evidence. *CNS Drugs, 27*, 505-514. doi: 10.1007/s40263-013-0076-8

Gschwind, Y. J., Bischoff-Ferrari, H. A., Bridenbaugh, S. A., Hardi, I., Kressig, R. W. (2014). Association between serum vitamin D status and functional mobility in memory clinic patients aged 65 years and older. *Gerontology, 60*, 123-129. doi: 10.1159/000355667

Dugdale, D. C. (2013). Venipuncture. *Medline Plus*. Retrieved from http://www.nlm.nih.gov/medlineplus/ency/article/003423.htm

Kennel, K. A., Drake, M. T., & Hurley, D. L. (2010). Vitamin D deficiency in adults: When to test and how to treat. *Mayo Clinic Proceedings, 85*, 752-758. doi: 10.4056/mcp.2010.0138

Koven, N. S., Cadden, M. H., Murali, S., Ross, M. K. (2013) Vitamin D and long-term memory in multiple sclerosis. *Cognitive & Behavioral Neurology, 26*, 155-160. doi: 10.1097/WNN.0000000000000009

Lips, P., Graafmans, W. C., Ooms, M. E., Bezemer, P. D., & Bouter, L. M. (1996). Vitamin D supplementation and fracture incidence in elderly persons: A randomized, placebo-controlled clinical trial. *Annals of Internal Medicine, 124*, 400-406. doi: 10.7326/0003-4819-124-4-199602150-00003

Llewellyn, D., Lang, I. A., Langa, K. M., & Melzer, D. (2011). Vitamin d and cognitive impairment in the elderly U. S. population. *Journal of Gerontology, 66A*, 59-65. doi: 10.1093/Gerona/glq185

Llewellyn, D. J., Lang, I. A., Langa, K. M., Muniz-Terrera, G., Phillips, C. L., Cherubini, A., Ferrucci, L., & Melzer, D. (2010). Vitamin D and risk of cognitive decline in elderly persons. *Arch Intern Med, 170*, 1135-1141. doi: 10.1001/archinternmed.2010.173

Lu'o'ng, K. V. Q. & Nguyen, L. T. H. (2013). The role of vitamin D in Alzheimer's disease: Possible genetic and cell signaling mechanisms. *American Journal of Alzheimer's Disease and Other Dementias, 28*, 126-136. doi: 10.1177/1533317512473196

Mangialasche, F., Kivipelto, M., Solomon, A., & Fratiglioni, L. (2012). Dementia Prevention: Current epidemiological evidence and future perspective. *Alzheimer's Research & Therapy, 4*, 1-8. doi: doi: 10.1186/alzrt104

Middleton, L. E. & Yaffe, K. (2009). Promising strategies for the prevention of dementia. *Archives of Neurology, 66*, 1210-1215. doi: 10.1001/archneurol.2009.201

National Institute of Neurological Disorders and Stroke (2014). Dementia: Hope through research. *NIH*. Retrieved from http://www.ninds.nih.gov/disorders/dementias/detail_dementia.htm

NIH (2011). Vitamin D. *U.S. Department of Health & Human Services*. Retrieved from http://ods.od.nih.gov/factsheets/VitaminD-Consumer/

Peterson, A. L., Murchison, C., Zabetian, C., Leverenz, J. B., Watson, G. S., Montine, T., Carney, N., Bowman, G. L., Edwards, K., & Quinn, J. F. (2013). Memory, mood, and vitamin d in persons with Parkinson's disease. *Journal of Parkinson's Disease, 3*, 547-555. doi: 10.3233/JPD-130206

Selhub, J., Bagley, L. C., Miller, J., & Rosenberg, I. H. (2000). B vitamins, homocysteine, and neurocognitive function in the elderly. *The American Journal of Clinical Nutrition, 71*, 614-620. Retrieved from http://ajcn.nutrition.org/content/71/2/614s.full

Simpkins, J. W., Green, P. S., Gridley, K. E., Singh, M., de Fiebre, N. C., & Rajakumar, G. (1997). Role of estrogen replacement therapy in memory enhancement and the prevention of neuronal loss associated with Alzheimer's disease. *The American Journal of Medicine, 103*, 19-25. doi: 10.1016/S0002-9343(97)00260-X

Wilkins, C. H., Sheline, Y. I., Roe, C. M., Birge, S. J., & Morris, J. C. (2006). Vitamin D deficiency is associated with low mood and worse cognitive function in older adults. *The American Journal*

of Geriatric Psychiatry, 14i, 1032-1040. doi: 10.1097/01.JGP.0000240986.74642.7c

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