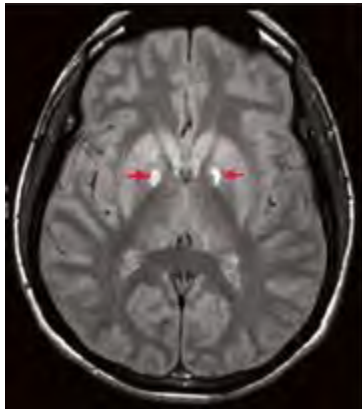


Duke University researchers connect vitamin D with brain lesions

Author: Amy Proal

24 Oct 2007

Is biomedical researcher Trevor Marshall PhD the only person implicating vitamin D in disease? No. A recent study by researchers at Duke University found that elderly men and women who consumed higher levels of calcium and, in particular, vitamin D are significantly more likely to have greater volumes of brain lesions, indicating regions of damage that can increase risk of cognitive impairment, dementia, depression and death. The team found that vitamin D intake, (mean 341 IU and maximum intake 1014 IU), was the only variable that retained a significant correlation with the brain lesions when analyzed by a multivariate analysis.^[1]



Payne found that subjects who consumed vitamin D were markedly more likely to have a higher total volume of brain lesions.

The research team was led by Dr. Martha E. Payne, an assistant professor in the department of psychiatry and behavioral sciences with the Neuropsychiatric Imaging Research Laboratory at Duke. Payne reported her findings at the 2007 Experimental Biology Conference in Washington D.C. Her presentation, which took place on May 1, is part of the scientific program of the American Society for Nutrition.

“This is one of the first studies to examine the relationship between diet and brain lesions,” said Payne. “Our finding of a relationship between brain lesions and consumption of both calcium and vitamin D raises the question about a possible downside to high intakes of these nutrients.”^[2]

The team examined magnetic resonance imaging (MRI) scans from 232 men and women (79 men, 153 women) between the ages of 60 and 86 (average age 71). All the subjects had at least some brain lesions of varying sizes, including the extremely miniscule ones often seen in even healthy older persons, but those who reported consuming more calcium and vitamin D were markedly more likely to have a higher total volume of brain lesions as measured by MRI scans.^[3]

Even after controlling for other factors known to be related to brain lesions such as age, hypertension, and other medical conditions, the strong relationship between total lesion volume and high intake of calcium and vitamin D remained. Since the calcium/vitamin D research was part of a longitudinal study of late-life depression, almost half the subjects had been diagnosed

with depression. However, the presence or absence of depression also did not appear to influence the relationship between vitamin D and brain lesions.^[4]

In earlier studies, Payne and team had found that individuals who consumed more high-fat dairy products had more brain lesions than those who did not follow such a diet but determined that fat intake in general was not a significant factor. However vitamin D is found in high fat dairy products, and a large number of dairy products are fortified with extra vitamin D. Hence the team's idea to investigate the effect of vitamin D on brain lesions.

Unaware of the latest research on the immunosuppressive properties of high levels of vitamin D, the researchers hypothesized that the calcium rather than the vitamin D was the main culprit in causing the lesions. They speculated that in patients given extra calcium, the calcium might be deposited inside the blood vessels of the brain rather than the bone. According to their theory, vitamin D would accelerate the process because it is involved in regulating calcium absorption and metabolism.

In what is emerging as a new understanding of chronic disease, a much more likely explanation is that the lesions result when L-form bacteria in the brain cause the release of cytokines that damage the tissues. Sometimes the resulting inflammation damages blood vessels and promotes calcification, but it is the L-form bacteria, not the calcium that is the true culprit.

The connection between bacteria and calcification in heart disease has already been noted. Researchers at the Hospital Das Clinicas in Brazil found significantly higher concentrations of *Chlamydia pneumoniae* and *Mycoplasma pneumoniae* in calcified nodes of blood vessels throughout the body, including the heart and the aorta - causing them to suggest that "these bacteria may be associated with the development of calcification and inflammation."^{[5][6]}

Nearly everyone acquires L-form bacteria as they age. Rolf Zinkernagel at the Institute of Experimental Immunology in Switzerland demonstrated that viruses are able to persist for decades in the brain, so why not other pathogens? It's not surprising then, that Dr. Alan Macdonald at St. Catherine of Sienna Medical Center found evidence of L-form bacteria in the brain of patients with Alzheimer's disease.^[7]



Elderly patients are particularly susceptible to the immunosuppressive effects of 25-D.

Researchers at the University of British Columbia in Canada have also implicated bacteria in Alzheimer's Disease.^[8] The data obtained from patients on the Marshall Protocol study site also confirms that L-form bacteria are able to infect the tissues of the central nervous system, since patients with a wide variety of mental illnesses and types of cognitive impairment are responding to antibiotic therapy. Studies like these support the view that the elderly patients in Payne's study had acquired substantial levels of L-form bacteria during their lifetimes.

Why would ingesting vitamin D affect the proliferation of L-form bacteria in the brain? New molecular modeling research by biomedical researcher Trevor Marshall of Autoimmunity Research Foundation has revealed that the precursor form of vitamin D – the steroid 25-D - binds and inactivates the Vitamin D Receptor (VDR), a fundamental receptor of the body that controls the activity of the innate immune system. As people consume products fortified with vitamin D or take supplements containing vitamin D, the level of 25-D rises, often to the level at which it becomes immunosuppressive. It appears that the elderly patients in Payne's study were consuming levels of vitamin D that were sufficient to block the VDR. As their immune function decreased, the L-form bacteria in their brains were able to spread, proliferate and consequently stimulate the release of an increasing number of cytokines that damaged the tissues of the central nervous system and caused brain lesions.^[9]

Furthermore, elderly patients are particularly susceptible to the immunosuppressive effects of 25-D. Bacteria have been identified that can bind and block the VDR in a manner similar to 25-D.^[10] Since elderly patients generally have had more time to accumulate bacteria, they would tend to have a greater level of bacterial substances already blocking the VDR. Consequently, 25-D will be likely to exacerbate immunosuppression from VDR blockage already taking place. This means that even relatively low levels of vitamin D supplementation can negatively affect the activity of the immune system in elderly patients.

Certainly, then, it comes as no surprise that the researchers found that only the vitamin D, and not calcium, remained significantly positively associated with brain lesion volume. Since it was an observational study, the researchers used surveys to track how much vitamin D and calcium the subjects obtained from food and supplements. Many supplements and dairy products contain both calcium and vitamin D so a multivariate analysis was used to statistically separate the two variables.

If the calcium had been the primary problem, then the calcium should have had an independent association with the lesions in the multivariate analysis, apart from the vitamin D, and it did not. Only vitamin D had a significant correlation when the effect of calcium was removed. And this occurred even though patients were not ingesting particularly high levels of vitamin D. No patient was consuming more than 1015 IU of vitamin D and only a handful were getting more than 800 IU of vitamin D from foods and supplements combined.

Interestingly, most of the articles written by journalists about the research fail to mention this incredibly important detail, and make it sound as if the calcium was a greater culprit than the vitamin D in causing the brain lesions. Only a few articles mention that calcium was not actually associated with the brain lesions when the researchers analyzed it in the multivariate analysis.

Why is there a bias with regard to vitamin D? There are multiple explanations, among them the fact that researchers seem unable to fathom the idea that any negative effects might be caused by the cherished "sunshine vitamin." (More info available [here](#).)



MRI testing is used to detect brain lesions.

Not surprisingly, brain lesions are connected to a variety of diseases that are likely to be caused by L-form bacteria. A study by researchers at National Cheng Kung University in Taiwan found that brain lesions shown by MRI were associated with late life depression.^[11] Researchers at the University of California at Davis correlated brain lesions with a number of neuropsychiatric disorders, including vascular dementia and Alzheimer's disease.^[12] A team at McLean Brain Imaging Center and Harvard Medical School found an association between brain lesions and bipolar disorder.^[13] Another study conducted by researchers at the University of Michigan followed a group of community dwelling older adults for 11 years. They found that the group with the greatest volume of brain lesions experienced an approximately two-fold increased mortality rate.^[14] Brain lesions have also been correlated with major depressive disorder with anger attacks^[15], conduct disorder/attention deficit disorder^[16] and suicidal tendencies.^[17]

Additionally, researchers at the University of New South Wales in Australia found that brain lesion volume as shown by MRI correlated with several measures of brain atrophy.^[18] Another recent study of 51 healthy volunteers (average age 71) by the same Australian team confirmed that these lesions are typically progressive, although 8 subjects had a slight decrease in lesion volume over 3 years, indicating the potential for lesion reversal.^[19]

Consequently, there is great hope that people who develop brain lesions can reverse damage to the brain by using the Marshall Protocol – a treatment that effectively kills L-form bacteria over the course of several years. While on the treatment, patients greatly lower their intake of vitamin D.

“We have seen no sign that the brain doesn't heal,” says Marshall, who created the protocol. “The adults recover all their lost faculties as they heal on the MP, and the several children on the MP, who have had a variety of difficulties, also are recovering fully. So our data (at this point) shows that the body heals as bacteria are killed and immune function is restored. All of the body. Including the brain.”

Of course, many doctors justify telling the elderly to supplement with vitamin D because they think it will help increase their bone mass. However, the largest meta-analysis of calcium and vitamin D trials in people over 50 found that the “addition of vitamin D supplementation was not shown to offer additional risk reduction over and above the use of calcium alone.”^[20] Similarly, a study by researchers at the Indiana University School of Medicine found that calcium supplementation (about 1300 mg) improved bone density over a four-year period, whereas vitamin D supplementation (600 IU) had no effect. In fact, the effect of calcium on bone loss was blunted in subjects with the highest levels of vitamin D, causing the team to point out the danger of over-supplementation of the elderly with vitamin D if they are on an adequate calcium intake.^[21]

One can hope then, that Payne's study on the connection between vitamin D and brain lesions is just the beginning of more research in this area. "A longitudinal study," Payne concludes, "is urgently needed in order to determine if calcium and vitamin D lead to vascular calcification and brain lesions in the long term." The urgency is certainly justified considering the increasing tendency of certain researchers and supplement manufacturers to promote a greater intake of vitamin D, particularly among the elderly.

This [article](#) by Joyce Waterhouse, Ph.D. discusses additional information on brain lesions, vascular calcification, osteoporosis, vitamin D and calcium.

REFERENCES

1. Payne, M. E., Anderson, J., & Steffens, D. C. (2007). [Calcium and vitamin D intakes are positively associated with brain lesions in depressed and non-depressed elders](#). *The FASEB Journal*. [[↵](#)]
2. [Calcium, Vitamin D Intake May Harm Aging Brain](#). (2007). Forbes.com. [[↵](#)]
3. Payne, M. E., Fetzer, D. L., MacFall, J. R., Provenzale, J. M., Byrum, C. E., Krishnan, K. R. R., et al. (2002). [Development of a semi-automated method for quantification of MRI gray and white matter lesions in geriatric subjects](#). *Psychiatry research*, 115(1-2), 63-77. [[↵](#)]
4. [Brain Lesions In Seniors Associated With Higher Calcium And Vitamin D Intakes](#). (2007). Medicalnewstoday.com. [[↵](#)]
5. Higuchi-Dos-Santos, M. H., Pierri, H., Higuchi, M. D. L., Nussbacher, A., Palomino, S., Sambiasi, N. V., et al. (2005). [Chlamydia pneumoniae and Mycoplasma pneumoniae in calcified nodes of stenosed aortic valves](#). *Arquivos brasileiros de cardiologia*, 84(6), 443-8. [[↵](#)]
6. Góis, J., Higuchi, M., Reis, M., Diament, J., Sousa, J., Ramires, J., et al. (2006). [Infectious agents, inflammation, and growth factors: how do they interact in the progression or stabilization of mild human atherosclerotic lesions?](#) *Annals of vascular surgery*, 20(5), 638-45. [[↵](#)]
7. MacDonald, A. B. (2007). [Alzheimer's disease Braak Stage progressions: reexamined and redefined as Borrelia infection transmission through neural circuits](#). *Medical hypotheses*, 68(5), 1059-64. [[↵](#)]
8. Miklossy, J., Kis, A., Radenovic, A., Miller, L., Forro, L., Martins, R., et al. (2006). [Beta-amyloid deposition and Alzheimer's type changes induced by Borrelia spirochetes](#). *Neurobiology of aging*, 27(2), 228-36. [[↵](#)]
9. Marshall, T. G. (2006). [Molecular mechanisms driving the current epidemic of chronic disease](#). [[↵](#)]
10. Marshall, T. G. (2007). [Bacterial Caprine Blocks Transcription of Human Antimicrobial Peptides](#). *Nature Precedings*. [[↵](#)]
11. Chen, P. S., McQuoid, D. R., Payne, M. E., & Steffens, D. C. (2006). [White matter and subcortical gray matter lesion volume changes and late-life depression outcome: a 4-year magnetic resonance imaging study](#). *International psychogeriatrics / IPA*, 18(3), 445-56. [[↵](#)]

12. Yoshita, M., Fletcher, E., Harvey, D., Ortega, M., Martinez, O., Mungas, D. M., et al. (2006). [Extent and distribution of white matter hyperintensities in normal aging, MCI, and AD](#). *Neurology*, 67(12), 2192-8. [[↵](#)]
13. Ahn, K. H., Lyoo, I. K., Lee, H. K., Song, I. C., Oh, J. S., Hwang, J., et al. (2004). [White matter hyperintensities in subjects with bipolar disorder](#). *Psychiatry and clinical neurosciences*, 58(5), 516-21. [[↵](#)]
14. Kerber, K. A., Whitman, G. T., Brown, D. L., & Baloh, R. W. (2006). [Increased risk of death in community-dwelling older people with white matter hyperintensities on MRI](#). *Journal of the neurological sciences*, 250(1-2), 33-8. [[↵](#)]
15. Iosifescu, D. V., Renshaw, P. F., Dougherty, D. D., Lyoo, I. K., Lee, H. K., Fraguas, R., et al. (2007) [Major depressive disorder with anger attacks and subcortical MRI white matter hyperintensities](#). *The Journal of nervous and mental disease*, 195(2), 175-8. [[↵](#)]
16. Lyoo, I. K., Lee, H. K., Jung, J. H., Noam, G. G., & Renshaw, P. F. [White matter hyperintensities on magnetic resonance imaging of the brain in children with psychiatric disorders](#). *Comprehensive psychiatry*, 43(5), 361-8. [[↵](#)]
17. Ehrlich, S., Breeze, J. L., Hesdorffer, D. C., Noam, G. G., Hong, X., Alban, R. L., et al. (2005). [White matter hyperintensities and their association with suicidality in depressed young adults](#). *Journal of affective disorders*, 86(2-3), 281-7. [[↵](#)]
18. Wen, W., Sachdev, P. S., Chen, X., & Anstey, K. (2006). [Gray matter reduction is correlated with white matter hyperintensity volume: a voxel-based morphometric study in a large epidemiological sample](#). *NeuroImage*, 29(4), 1031-9. [[↵](#)]
19. Sachdev, P., Wen, W., Chen, X., & Brodaty, H. (2007). [Progression of white matter hyperintensities in elderly individuals over 3 years](#). *Neurology*, 68(3), 214-22. [[↵](#)]
20. Tang, B. M. P., Eslick, G. D., Nowson, C., Smith, C., & Bensoussan, A. (2007). [Use of calcium or calcium in combination with vitamin D supplementation to prevent fractures and bone loss in people aged 50 years and older: a meta-analysis](#). *Lancet*, 370(9588), 657-66. [[↵](#)]
21. Peacock, M., Liu, G., Carey, M., McClintock, R., Ambrosius, W., Hui, S., et al. (2000). [Effect of calcium or 25OH vitamin D3 dietary supplementation on bone loss at the hip in men and women over the age of 60](#). *The Journal of clinical endocrinology and metabolism*, 85(9), 3011-9. [[↵](#)]