

# How Dietary Habits Can Affect Abnormal Protein Buildup in the Brain

Sevil Yasar, MD, PhD

*Neurology*<sup>®</sup> 2023;100:e2321-e2323. doi:10.1212/WNL.0000000000207413



## Related Article

Association of Mediterranean-DASH Intervention for Neurodegenerative Delay and Mediterranean Diets With Alzheimer Disease Pathology

<http://dx.doi.org/10.1212/WNL.0000000000207176>

Alzheimer disease is a brain disease that mainly affects older people. The number of people living with Alzheimer disease has increased steadily over time,<sup>1</sup> resulting in greater interest in strategies for preventing it. A major effort has been made in medication development. However, over the past decade, many studies have also evaluated nonmedication interventions, such as diet changes, for disease prevention. Multiple studies have shown that Mediterranean and DASH (Dietary Approaches to Stop Hypertension) diets reduce the risk for Alzheimer disease. The Mediterranean diet is based on vegetables, legumes, nuts, fruits, herbs, and spices. Olive oil is the main source of fat in this diet, and it also includes fish and poultry. The DASH diet was developed to help treat high blood pressure. It is rich in vegetables, fruits, and whole grains and includes low-fat dairy products, fish, poultry, beans, and nuts.<sup>2</sup> However, although these diets have been shown to offer many health benefits, little is known about how these diets may improve brain health.

## What Did the Authors Study?

In their study, Dr. Agarwal and colleagues<sup>3</sup> looked at the connection between diet and brain abnormalities seen in Alzheimer disease. Specifically, they studied the relationship between the Mediterranean diet and the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet, specific food components, and beta-amyloid and tau protein accumulation (a condition typically seen in Alzheimer disease), using brains from deceased people.

## How Was the Study Done?

The authors used information collected from 581 participants in a memory and aging study. This study had collected the participants' diet information and, eventually, their brain autopsy

data. The researchers were able to use this collection of data from this study to examine the relationship between diet and brain changes.

Diet information was collected using questionnaires that the participants were asked to take each year. Using the data from these questionnaires, the authors developed a MIND score and Mediterranean diet score for each participant. The authors also separated food groups into 14 distinct groups (leafy vegetables, fish and seafood, whole grains, wine, butter and margarine, pastries, sweets, fried and fast food, etc.) to determine how each type of food affected the participants' risk for Alzheimer disease. The participants were followed until their deaths. At that time, participants donated their brains for autopsy study. Their brains were then examined under a microscope and tested for buildup of beta-amyloid and phosphorylated tau proteins, the hallmarks of Alzheimer disease. Their brains were also examined for neuritic amyloid plaques (the accumulation of beta-amyloid proteins outside the neurons) and neurofibrillary tangles (the accumulation of twisted tau protein strands within the neurons).

### What Did the Study Show?

This study showed much lower levels of neuritic amyloid plaques and neurofibrillary tangles in participants who closely followed a Mediterranean or MIND diet. Lower levels of these abnormalities were seen even in participants without any memory impairment at the time of death. Similarly, lower levels of beta-amyloid protein were found in the brains of these participants. Increased consumption of green, leafy vegetables was associated with lower levels of neuritic amyloid plaques and neurofibrillary tangles. However, participants who consumed more fried and fast food had increased levels of phosphorylated tau proteins. Participants who drank 2 glasses of wine per day also had much lower levels of neuritic amyloid plaques and neurofibrillary tangles.

This study also considered the effect of genes and sex. One genetic marker for higher risk of Alzheimer disease is called *APOE-ε4*. The authors found that participants who did not have this gene and who also drank between 1 glass of wine a month and 6 glasses of wine a week had greater reduction of beta-amyloid load, while those who ate more beans and leafy greens had fewer neurofibrillary tangles. By contrast, study participants from the group without the *APOE-ε4*

marker who ate more fried and fast food had increased neurofibrillary tangles.

This study also showed differences in the participants' results that seemed to be related to their sex. Female participants who consumed 1 glass of wine once a week had lower amyloid plaques than participants who did not do so. Furthermore, female participants who ate more red and processed meat had more amyloid plaques. Male participants who drank between 1 glass of wine a month and 6 glasses of wine a week and who had higher fish intake than other male participants had lower amyloid plaques. However, male participants with the same wine consumption as and higher nut intake than other male participants had more neurofibrillary tangles.

### What Did the Researchers Find?

The researchers who conducted this study found that the Mediterranean and MIND diets, as well as general increased intake of green and leafy vegetables, seemed to lead to lower buildup of abnormal proteins (especially beta-amyloid protein) seen in Alzheimer disease. They found that this was the case even in study participants who were not yet showing symptoms of the disease.

### Why Does This Study Matter?

This study tried to help explain how diet may affect the brain. This study is different from other Alzheimer disease studies in that it considers detailed lifestyle and brain autopsy data from participants together. This allowed the researchers to make important connections between about the possible relationship between diet and brain changes.

### What Remains Unknown?

It is known that there are other changes in the brain beyond abnormal protein buildup that occur during the course of Alzheimer disease. These include inflammation, oxidative stress (an imbalance between free radicals and antioxidants in the body), and structural changes in blood vessels. These can be affected by diet and should also be studied. Although race is not listed in this study, the study population was primarily White. A similar study should be undertaken with a more diverse population to investigate how diet changes may affect various populations.

# About Alzheimer Disease

## What Is Dementia? What Is Alzheimer Disease?

Dementia is a group of symptoms—typically, problems with memory, language, thinking, and/or organization skills—that are severe enough to affect a person’s ability to perform the activities of daily independent living.

There are many causes for dementia. Alzheimer disease is the most common one, with 60%–80% of dementia cases being caused by Alzheimer disease.<sup>1</sup> Approximately 10 percent of people in the United States who are older than 65 years have Alzheimer disease, and more than 66% of those affected by the disease are women.

## What Causes Alzheimer Disease?

There is no clearly identified cause for Alzheimer disease. However, research has determined that there are many risk factors, including older age, family history of Alzheimer disease in a close relative, and carrying genes that can cause or increase the risk of Alzheimer disease.<sup>1</sup> Although we do not know the exact cause, we do know that brain changes take place early during the development of Alzheimer disease, even before symptoms arise. One of these changes is the buildup of abnormal proteins in the brain. Beta-amyloid proteins organize into clumps (called amyloid plaques) outside neurons, and tau proteins organize into clumps (called neurofibrillary tangles) inside the neurons. Other changes, such as inflammation and oxidative stress, have also been found in Alzheimer disease. These changes eventually result in the death of neurons.<sup>1</sup>

## What Are the Symptoms of Alzheimer Disease?

The most common symptom of Alzheimer disease is memory loss. A person with the disease may forget conversations, names, or appointments or may frequently misplace items. Other symptoms may include difficulty finding words when speaking, difficulty making decisions, or difficulty understanding abstract ideas such as numbers (for example, a person with Alzheimer disease may have trouble managing their finances). Confusion about time or place may also be seen. A person with Alzheimer disease may also experience impaired judgment or may have personality and behavioral changes.<sup>1</sup>

## How Is Alzheimer Disease Treated?

For a long time, there was no medication available for Alzheimer disease that would change the course of the disease. However, in 2022 and 2023, the FDA approved 2 beta-amyloid-lowering drugs, called aducanumab and lecanemab. These drugs are for mild Alzheimer disease and mild cognitive impairment, respectively. The Centers for Medicare and Medicaid Services (CMS), however, decided that it would only pay for the drugs if they were part of a clinical trial that showed not only a reduction of beta-amyloid but also improvement in symptoms in a diverse population.<sup>1</sup>

Other currently available medications are only helpful for treating Alzheimer disease symptoms and do not affect

disease progression. These drugs include tacrine, donepezil, rivastigmine, and galantamine. They increase the levels of a chemical called acetylcholine in the brain. A fifth drug, memantine, reduces a brain chemical called glutamate that is damaging to neurons. Donepezil, rivastigmine, and galantamine are often given in combination with memantine.<sup>1</sup>

## Can Alzheimer Disease Be Prevented?

Owing to the staggering number of people affected by Alzheimer disease, there is a major interest in prevention. A recent study that was published in the journal *Lancet* showed that 40% of dementia types can be delayed or prevented throughout a person’s lifetime.<sup>4</sup> Prevention starts with obtaining an education at an early age. Other important factors include treating hearing loss and elevated blood pressure, reducing obesity, avoiding head trauma, avoiding drinking more than 21 alcoholic drinks per week (which could be translated into consuming more than 2 bottles of wine per week) in midlife, engaging in regular physical activity, avoiding social isolation, quitting smoking, treating depression and diabetes, and avoiding air pollution exposure if possible (especially in late life).<sup>4</sup> More studies like this can help us better understand the role of diet in dementia prevention.

### For More Information

#### **Brain & Life**

[brainandlife.org](http://brainandlife.org)

#### **Alzheimer’s Association**

[alz.org](http://alz.org)

#### **Alzheimer’s Foundation of America**

[alzfdn.org](http://alzfdn.org)

#### **Alzheimer’s Drug Discovery Foundation**

[alzdiscovery.org](http://alzdiscovery.org)

### References

1. Alzheimer’s Association. [alz.org](http://alz.org). Accessed March 2023.
2. Devranis P, Vassilopoulou E, Tsironis V, et al. Mediterranean diet, ketogenic diet or MIND diet for aging populations with cognitive decline: a systematic review. *Life*. 2023;13(1):173.
3. Agarwal P, Leurgans SE, Agrawal S, et al. Association of Mediterranean-DASH Intervention for Neurodegenerative Delay and Mediterranean diets with Alzheimer disease pathology. *Neurology*. 2023;100(22):e2259-e2268.
4. Livingston G, Huntley J, Sommerlad A, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *Lancet*. 2020;396(10248):413-446.

# Neurology®

## How Dietary Habits Can Affect Abnormal Protein Buildup in the Brain

Sevil Yasar

*Neurology* 2023;100:e2321-e2323

DOI 10.1212/WNL.0000000000207413

**This information is current as of May 29, 2023**

<b>Updated Information &amp; Services</b>	including high resolution figures, can be found at: <a href="http://n.neurology.org/content/100/22/e2321.full">http://n.neurology.org/content/100/22/e2321.full</a>
<b>References</b>	This article cites 2 articles, 0 of which you can access for free at: <a href="http://n.neurology.org/content/100/22/e2321.full#ref-list-1">http://n.neurology.org/content/100/22/e2321.full#ref-list-1</a>
<b>Permissions &amp; Licensing</b>	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: <a href="http://www.neurology.org/about/about_the_journal#permissions">http://www.neurology.org/about/about_the_journal#permissions</a>
<b>Reprints</b>	Information about ordering reprints can be found online: <a href="http://n.neurology.org/subscribers/advertise">http://n.neurology.org/subscribers/advertise</a>

*Neurology*® is the official journal of the American Academy of Neurology. Published continuously since 1951, it is now a weekly with 48 issues per year. Copyright © 2023 American Academy of Neurology. All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.

