

Can the foods you eat enhance brain health, or even help manage a neurologic condition? We spoke to the experts about popular diets and reviewed the evidence to find the answers.

BY MARISA COHEN

e eat for energy, for sustenance, and for pleasure. But what we put in our mouths—carbohydrates or fats, whole foods or processed snacks—may also have a significant effect on our brains.

For at least the last century, doctors and researchers have seen a correlation between diet and the management of neurologic conditions such as epilepsy, dementia, and stroke. And while no single ingredient can magically cure neurologic diseases—no matter what you may read on the internet—several well-studied diet plans have been associated with a positive effect on the brain.

"Growing and compelling evidence from large longitudinal studies and randomized trials suggests that diet matters for brain health," says Alberto Ascherio, MD, DrPh, professor of nutrition and epidemiology at the Harvard T.H. Chan School of Public Health and professor of medicine at Harvard Medical School. "But a lot remains to be discovered," he adds. "We need studies that also take into account existing diseases, neurologic and otherwise, as well as lifestyle, environment, physiological characteristics such as age, sex, and body mass, and genes. Because Alzheimer's, Parkinson's, and other neurodegenerative diseases develop over decades, maximal benefits will require early and prolonged dietary changes."

In general, more studies need to be conducted to see how diet may affect the underlying processes of neurologic conditions such as Alzheimer's disease, says Jennifer Rose Molano, MD, FAAN, associate professor of neurology at Cincinnati Academic Health Center.

We review the evidence for three diets for specific conditions. Before starting any new eating plan, discuss it with your neurologist, including whether to add wine if you are a nondrinker, and a dietitian who works with people with neurologic conditions.

Mediterranean Diet

SAMPLE MENU

Breakfast: Greek yogurt with sliced fruit and chopped walnuts **Lunch:** Whole wheat pasta with olives, tomatoes, red bell peppers

Dinner: Grilled salmon, wild rice, sautéed broccoli, glass of red wine

What it may protect against: Alzheimer's disease, Parkinson's disease, vascular dementia, stroke.

What to eat: Whole grains, nuts, legumes, fruits and vegetables, fish, monounsaturated fats (mainly olive oil), plus red wine in moderation. Saturated fats from animal products, such as red meat and butter, are limited. A typical meal might include chicken grilled in extra-virgin olive oil, couscous, steamed vegetables, and a glass of Merlot. A snack might be a handful of almonds or hummus on whole wheat pita bread.

How it works: The combination of monounsaturated fats, lean proteins, fruit, vegetables, and whole grains is linked to a lower level of low-density lipoprotein (LDL) cholesterol, which builds up deposits in the walls of the arteries. Less LDL cholesterol means a clearer pathway for blood to travel from the heart to the brain, which reduces the risk of stroke and vascular dementia. The diet may also reduce both inflammation and blood pressure, which in turn lowers the risk of stroke and dementia.



Scientists don't know exactly what is happening in the brain to produce these changes, says Nikolaos Scarmeas, MD, MS, a neurologist at Columbia University Medical Center who has done extensive research on dementia and diet. "In addition to the vascular benefits, the diet may have anti-inflammatory and antioxidant effects, or may directly affect neurodegeneration pathological changes that lead to Alzheimer's," he explains.

The secret may be in how the diet affects brain volume. A Scottish study published this year in *Neurology* showed that older people with the lowest adherence to a Mediterranean-style diet experienced a far greater rate of brain atrophy, one of the hallmarks of neurodegenerative illnesses such as Alzheimer's.

Importantly, it seems likely that the benefit is not just from one ingredient, but in the overall diet, says Dr. Scarmeas. In studies of individual aspects of the diet, researchers may miss an effect against Alzheimer's disease, he says, but when they look at combinations of foods such as in the Mediterranean diet, or other dietary patterns, they may be able to identify the protective effect.

Evidence for stroke: In the 1960s, researchers noticed that the rates of cancer and coronary artery disease were lower in countries along the Mediterranean, such as Italy and Greece, where meals are centered on whole grains, fish, and olive oil. Since then, multiple long-term studies have confirmed the cardiovascular benefits of a Mediterranean-style diet, including a 2015 review in *Circulation* of more than 100,000 women, in which researchers at Columbia University Medical Center found that those who adhered to the diet most closely had an 18 percent reduction in the rate of ischemic stroke.

The diet is very important for people at high risk for cardiovascular disease. An analysis of the large European PREDIMED



study, which looked specifically at the Mediterranean diet's effect on cardiovascular disease, published in the *New England Journal of Medicine* in 2013, found that people at higher risk of cardiovascular events, including stroke, who stuck to the diet reduced their overall risk by up to 30 percent—especially when supplementing it with extra-virgin olive oil and/or nuts.

Evidence for Alzheimer's disease: A follow-up paper based on the PREDIMED study published in the *Journal of Neurology, Neurosurgery, and Psychiatry* in 2015 found that after six and a half years, adults who followed the Mediterranean diet performed better on tests of cognition than those on a controlled low-fat diet. One major study from Columbia University Medical Center published in *Annals of Neurology* in 2006 showed that adults who followed the diet most closely had as much as a 40 percent lower risk of Alzheimer's disease than those who did not adhere closely. A follow-up study in 2009 showed that when exercise was added, the risk for Alzheimer's disease dropped more. Among those who did develop the disease, those with a healthier diet lived an average of four years longer.

Evidence for Parkinson's disease: A 2012 study in *Movement Disorders* showed the diet may both lower the risk for Parkinson's or push back the age of onset.

What the experts say: With decades of solid research behind it as well as a clear connection between its cardiovascular benefits and brain health, the Mediterranean diet is recommended by groups such as the Alzheimer's Association and the Parkinson's Foundation. "Diets designed to reduce vascular risk factors appear to offer protection against neurodegenerative disease, as well as other conditions," says James E. Galvin, MD, MPH, director of the Comprehensive Center for Brain Health at the Charles E. Schmidt College of Medicine at Florida Atlantic University. "Combined with mental and cognitive activity, social engagement, physical activity, and management of comorbid diseases, the diet may offer ways to improve brain health and stave off, or at the very least delay, the development of dementia."

"A lot of this Parkinson's research is new, so it's very exciting and interesting," says Carrolee Barlow, MD, PhD, chief executive

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-MARTHA CLARE MORRIS, SCD

officer of the Parkinson's Institute and Clinical Center, a Parkinson's Foundation Center of Excellence in Sunnyvale, CA. "We've known for a long time that a Mediterranean diet decreases the risk of vascular problems related to the brain, but we don't think of Parkinson's disease as being related to vascular risk factors," she says. The research suggests that there may be other ways in which the diet is good for the brain. "We're still trying to identify whether the benefits are causal or associative, but it clearly looks like the Mediterranean diet can help on multiple fronts," she says.

MIND Diet

(Mediterranean-DASH Intervention for Neurodegenerative Delay)

SAMPLE MENU

Breakfast: Oatmeal topped with blueberries, strawberries, and almonds

Lunch: Turkey breast with a slice of avocado on whole wheat toast with mustard

Dinner: Roasted chicken on a bed of couscous and lentils, kale salad with vinaigrette dressing, glass of red wine

What it may protect against: Cognitive decline, dementia, Alzheimer's disease.

What to eat: The MIND diet focuses on 10 brain-healthy food groups: chicken, fish, green leafy vegetables, other vegetables, berries, nuts, olive oil, wine, beans, and whole grains. Foods to avoid include red meat, butter and stick margarine, cheese, pastries and sweets, and fried or fast food.

How it works: In 2015, Martha Clare Morris, ScD, a nutritional epidemiologist at Rush University Medical School in Chicago, and colleagues created the MIND diet, a mix of the Mediterranean diet and the DASH (Dietary Approaches to Stop Hypertension) diet, which she tweaked specifically to stave off cognitive decline.

"We took those two diets as the basis, in the context that they provide a well-rounded diet for the prevention of the chronic diseases of aging, and then we modified them to reflect the best scientific evidence for nutrition and the brain," she explains. For example, whereas the Mediterranean diet recommends eating three to four servings of any type of vegetable per day, the MIND diet specifically recommends one serving of green leafy vegetables and one serving of any other kind of vegetable per day. "In epidemiological studies, green leafy vegetables show the strongest effects in slowing cognitive decline and lowering the risk of dementia, and the benefit level was at two servings per week," Dr. Morris explains.

Parsing the research also revealed that the benefit of eating fish leveled out at one serving per week, far less than the six recommended in most versions of the Mediterranean diet. Also, the only fruits specifically recommended in the MIND diet are blueberries and strawberries. "Fruit itself is not associated with slower cognitive decline," Dr. Morris explains. "But separate studies looking specifically at blueberries and strawberries, which are rich in polyphenols [compounds found in plants that can protect against cellular damage], show they are associated with slower cognitive decline."

Blueberries in particular are high in the polyphenol anthocyanin, which has antioxidant effects. In animal studies, mice who consumed more anthocyanin had higher levels of the chemical in the brain, and those with the highest levels performed best on memory tests and had a larger hippocampus, a primary memory center, says Dr. Morris.

"We have a long way to go to understand the biomechanics of the diet, but I know from 20 years of being immersed in all the literature that these nutrients and foods are important for brain health," she says.

Evidence for cognitive decline and Alzheimer's disease:

Though the MIND diet is new, the research is promising. In a 2015 study led by Dr. Morris and published in *Alzheimer's & Dementia*, adults who adhered to the MIND diet most rigorously had a 53 percent reduction in the rate of Alzheimer's disease compared with those who followed it the least. Even those who adhered moderately had a 35 percent reduction—a difference more dramatic than observed in those with the highest and lowest rates of adherence to the Mediterranean and DASH diets. Interestingly, those results were independent of other lifestyle changes and risk for cardiovascular disease, suggesting that the diet has benefits for the brain that go beyond the auxiliary ones of decreasing dementia risk factors such as heart disease, diabetes, obesity, and hypertension.

What the experts say: As with the Mediterranean diet, the MIND diet gets high scores from neurologists, who are impressed with the solid research behind it. "Higher scores on the MIND diet are associated with significantly less global cognitive decline and less pathology in individuals followed longitudinally to autopsy," says Dr. Galvin, who points out that studies on individual nutrients in the diet do not show as strong a protective effect as the diet as a whole. "This suggests that the combination of nutrients—rather than simply taking multiple supplements—may provide a number of neuroprotective benefits," he says.

CONTINUED ON PAGE 33



CONTINUED FROM PAGE 25

Ketogenic Diet

SAMPLE MENU

Breakfast: Cheese omelet cooked with heavy cream

Lunch: Chicken nuggets made with coconut flour and cream

Dinner: Crab cakes made with mayonnaise, almond flour, and eggs; salad with creamy dressing

What it may protect against: Seizures in children and adults with epilepsy. In some cases, the diet may also be helpful for people with migraines and other neurologic conditions.

What to eat: Unlike the Mediterranean and MIND diets, which are safe and healthy for anyone, the ketogenic diet is considered a medical therapy, only to be attempted for a specific condition under a doctor's guidance. The diet is extremely high in fat, very low in carbohydrates, and includes modest amounts of protein—typically three to four grams of fat for every one gram of carbohydrate and protein. The fats primarily come from butter, heavy whipping cream, mayonnaise, and oils such as canola and olive oil. The strictest form of the diet completely eliminates sweets such as candy, cookies, and desserts and other carbohydraterich foods such as bread, potatoes, rice, and pasta. Groups such as the Charlie Foundation (charliefoundation.org), Matthew's Friends (matthewsfriends.org), and the Epilepsy Foundation (epilepsy.com) provide kid-friendly recipes. **How it works:** The ketogenic diet dates back about 100 years, when doctors first noted that patients with epilepsy experienced fewer seizures when they fasted. Over time, this developed into the high-fat, low-carbohydrate ketogenic diet, which has been shown to reduce seizures by about 50 percent in up to half of children with treatment-resistant epilepsy, and eliminate them altogether in about 10 percent, according to the Epilepsy Foundation.

On a normal diet, the body converts carbohydrates into glucose, which it then uses as fuel for all functions. However, when the body is starved of carbohydrates and can't convert enough to keep it working, a backup system kicks in: The liver converts fats from food into fatty acids to use as fuel. A byproduct of this process is the creation of ketone bodies, acidic chemicals that can cross the blood-brain barrier.

While ketones may be important for controlling the electrical impulses in the brain that cause seizures, experts are still debating the exact mechanisms of the therapy, says Eric H. Kossoff, MD, a child neurologist and medical director of the Ketogenic Diet Project Program at Johns Hopkins Hospital in Baltimore. "One theory is that high-fat foods are directly beneficial to neural activity and neurotransmitters; another theory is that keeping your carbohydrates low and keeping your blood glucose stable is what helps control seizures."

Evidence for pediatric epilepsy: A 2016 Cochrane review found that study results vary wildly, but most confirmed the level of benefit. Traditionally, the diet has been recommended for children with daily seizures who have not responded to at least two medications, but some doctors may recommend a trial even sooner, says Dr. Kossoff. "For the last 10 years or so, the opinion from ketogenic diet centers has been that if the diet works, why wait until multiple medications have failed? For specific conditions, such as infantile spasms and gluten-1 (Glut-1) deficiency, we may try it as a first-line treatment or after just one medication has failed."

Evidence for adult epilepsy: A 2014 review published in *Neurology* by researchers at the Mid-Atlantic Epilepsy and Sleep Center in Bethesda, MD, found that the ketogenic diet could reduce seizures by more than 50 percent in 32 percent of adults with medication-resistant epilepsy, while the similar but less restrictive modified Atkins diet had a 29 percent success rate. About 9 percent of adults experienced a more than 90 percent reduction, compared with 5 percent in those on the modified Atkins diet.

Evidence for migraine: A small Italian study published in the *Journal* of *Headache and Pain* in 2016 found that after one month on the ketogenic diet, migraine patients experienced a reduction in both the frequency and duration of headaches. This may be because ketones provide an energy boost in the brains of people with migraine, in addition to their anti-inflammatory effects, the author suggested.

Evidence for other conditions: "Investigational studies are in progress to see whether the diet is helpful for trauma, dementia, multiple sclerosis, cancer, and autism," says Dr. Kossoff.

Caveats: This diet must always be followed under the supervision of a neurologist and dietitian, cautions Dr. Kossoff. Side effects can include gastrointestinal problems such as constipation, nausea, and acid reflux. Higher cholesterol, kidney stones, and growth problems are risks in children. But the biggest concern is that the diet is extremely difficult to follow over the long term. In fact, the 2014 review in *Neurology* found that about half of the adult patients gave up the diet before completion of the study. "To some degree, all patients have trouble sticking to the diet," says Dr. Kossoff. "It's a bigger concern for adults, but it is still an issue in children. When we talk to families, we make sure they realize that this is not something you're going to do for a month, but potentially for many years."

What the experts say: "The diet can be extremely effective, especially for some seizure types like Doose syndrome, seizures associated with Glut-1 deficiency, and Dravet syndrome," says Jacqueline A. French, MD, FAAN, co-director of research and clinical trials at NYU's Comprehensive Epilepsy Center. "It's somewhat less effective in focal epilepsy, and for adults. Some children who become seizure free on the diet may be able to eventually come off the diet and maintain seizure control."

For Real or Fads?

iets fall in and out of favor all the time as new evidence refutes or confirms their benefits or as nutritional trends change. We assessed two diets—one that has been around for decades and another that has been touted recently—to determine whether the evidence supports their claims. Here's what we found.

FEINGOLD DIET

THE DIET: No foods with artificial colors (especially red and orange), artificial flavors, sweeteners, preservatives, or salicylates, a chemical found in medicines and naturally in almonds, berries, tomatoes, and other foods. This means ditching almost all fast food, packaged food, candy, and sweets—plus any toothpastes or medicines with artificial ingredients—and sticking to all-natural foods, other than those with salicylates. Permitted foods include pineapple, bananas, plain bread, meat, some cereals, milk, and eggs.

THE CLAIM: Calms children with attention deficit hyperactivity disorder (ADHD).

THE EVIDENCE: Developed by pediatric allergist Ben Feingold, MD, in the 1960s, the diet was originally designed to alleviate asthma and eczema. When Dr. Feingold noticed that it calmed children, he began to recommend it for hyperactive kids.

Dr. Feingold theorized that artificial ingredients could irritate the brain and cause symptoms of ADHD, but little evidence has supported that over the years. Early enthusiasts claimed the diet reduced hyperactivity in more than 50 percent of children who tried it, but no controlled study has been able to duplicate those results, says Michelle Yee, a pediatric nurse practitioner in the neurology department at the Ann & Robert H. Lurie Children's Hospital of Chicago, who co-authored a 2012 review of ADHD diets in *Pediatrics*. Some research suggests the benefit may have come from the extra attention paid to the child by the family while on the diet.

More recently, a large European meta-analysis published in 2013 in *The American Journal of Psychiatry* concluded that restricting foods with artificial coloring had a modest impact on ADHD symptoms, but likely only in children who already had a sensitivity to the chemicals. The only other dietary intervention found to be helpful for ADHD was supplementation with fatty acids, including omega-3 fatty acid and omega-6 fatty acid, or both. But the effects were small, says Bruce H. Cohen, MD, FAAN, director of the NeuroDevelopmental Science Center at Akron Children's Hospital. And because different molecules were used in different studies, the exact mechanism of action is unclear.

In a recent *Pediatrics* study of the Mediterranean diet and ADHD, the authors specifically linked a higher consumption of sugar and candy, cola beverages, and non-cola soft drinks which contain artificial colors, sweeteners, and flavors—with increased rates of ADHD. The authors acknowledged the study's limitations, including the possible effect of socioeconomic disadvantages on ADHD symptoms, but the suggestion that diet may play a role in ADHD "is fascinating, and makes one wonder if a healthier diet may reverse some symptoms of ADHD," says Dr. Cohen, adding that the mechanism of the benefit, if it exists, may be due to one not yet known.

111

A downside, though, is the diet's restrictiveness, which makes it hard to stick with or enforce, says Yee. "I always tell parents that they can control what's in the house, but they can't control what their kids eat at school, whether from a vending machine or in the school cafeteria."

THE UPSHOT: While a healthy diet limiting foods containing additives has many benefits, it is not clear that improving ADHD symptoms is one of them, says Dr. Cohen. "The initial studies have not panned out," he says. "Eliminating GMO foods, artificial preservatives, contact with plastic, diets high in saturated fats, and so forth seem like reasonable ideas, but the claim that this prevents all the conditions touted is not proven."

THE INTERMITTENT-FASTING DIET

THE DIET: Several fasting strategies exist. On the 5:2 plan, adherents eat whatever they want five days a week; on the two other days, they eat no more than 500 calories per day. (One day's intake might include a cup of nonfat yogurt, a small salad with sliced egg, a bowl of quinoa with vegetables, and a small piece of fruit.) Another is the 16-hour fast, in which you eat all your meals between 10 AM and 6 PM, and fast the rest of the time.

THE CLAIMS: Delays cognitive decline, may ease symptoms of Parkinson's disease.

THE EVIDENCE: Most studies of intermittent fasting have been done in mice. One study from the University of Southern California published in *Cell Metabolism* in 2015 showed that in older mice, periodic fasting led to a period of hippocampal neurogenesis and improved cognition when regular feeding was resumed. In a 2016 review published in *Ageing Research Reviews*, investigators

at the National Institute on Aging looked at the effects of intermittent or periodic fasting in mice, and found a link between restricted eating and improved neural connections in the hippocampus. This may stem from the same process that occurs in the ketogenic diet: When your body is put into stress mode due to a lack of carbohydrates to convert into glucose, the body's emergency systems kick in, creating ketones, which may have a positive effect on the structure of the synapses involved in memory and learning. The stress on the brain is akin to a strength-building exercise, according to the researchers.

For Parkinson's disease in particular, fasting may offer an added benefit since the Parkinson's medication levodopa should not be taken with meals, as protein can interfere with its absorption.

THE UPSHOT: Despite the intriguing research, organizations such as the Alzheimer's Association do not recommend fasting since it can be dangerous for vulnerable older people who already may be dealing with loss of appetite and difficulty getting proper nutrition. "It is still unclear if intermittent fasting can prevent cognitive decline or dementia," says Maria Carrillo, PhD, chief science officer of the Alzheimer's Association.

It can be equally risky for people with Parkinson's disease, who may be dealing with low blood pressure, dehydration, and poor balance, says Carrolee Barlow, MD, PhD, chief executive officer of the Parkinson's Institute and Clinical Center, a Parkinson's Center of Excellence in Sunnyvale, CA. Restricting food intake may lower glucose levels, which could exacerbate those problems. "Parkinson's disease is a complex disorder, and a diet like that might be really difficult for some people. You don't want to add more complexity without a clear benefit," she says.