IN SEARCH OF THE OPTIMAL BRAIN DIET

The field of nutritional psychiatry is taking off as scientists home in on the ingredients for good mental health and cognitive staying power

BY BRET STETKA
Carolyn feels great these days. She exercises. She’s socially active. She spends as much time with her four grandchildren as possible. But it wasn’t always that way. A retired radiology film librarian from Pittsburgh, she began feeling apathetic and isolated seven years ago. “I’d just lost my mother, and my two sons had moved away,” recalls Carolyn, now 75. She also struggled with excess weight, diabetes and chronic lung disease. She was grieving, eating a worrisome amount of junk food and slipping into what looked a lot like depression.

A few years later a friend told Carolyn about a depression-prevention study at the University of Pittsburgh. She signed up immediately. All 247 participants were, like her, older adults with mild depressive symptoms—people who without treatment face a 20 to 25 percent chance of succumbing to major depression. Half received about five hours of problem-solving therapy, a cognitive-behavioral approach designed to help patients cope with stressful life experiences. The rest, including Carolyn, received dietary counseling. Guided by a social worker, she discovered that she liked salmon, tuna and a number of other “brain-healthy” foods—which quickly replaced all the chips, cake and candy she was eating.

When the trial concluded in 2014, the results came as a surprise—to the researchers at least. The dietary counseling was not meant to have any substantial effect; Carolyn’s group was the experiment’s control. And yet psychiatrist Charles Reynolds and his colleagues discovered that both interventions had significantly reduced the risk of depression—by approximately the same amount. When they reviewed the data, all the patients scored on average 40 to 50 percent lower on the Beck Depression Inventory test, a common measure of depressive symptoms, 15 months after their sessions ended. What is more, only about 8 percent, regardless of the therapy they received, had fallen into major depression.

It cannot be ruled out that a placebo effect contributed to the improvements seen in both groups. Meeting with a health care professional and being proactive about getting better in and of itself may have helped participants feel more upbeat. In Carolyn’s view, however, she had reversed her downward spiral largely by changing how she ate.

She is not alone in making that connection. Among scientists and clinicians there is a growing appreciation of the critical interplay between diet and brain health. The evidence is preliminary, and it is hard to tease out cause and effect. Perhaps people who eat well are also apt to have other healthy brain habits, such as regular exercise and good sleep routines. Or maybe depressed people tend to self-medicate with Oreos. But the data continue to accumulate. Every year the list of correlations between certain foods and mental well-being grows: fish and other sources of omega-3 fatty acids might help fend off psychosis and depression; fermented foods such as yogurt, pickles and sauerkraut seem to ease anxiety; green tea and an-

FAST FACTS
PRESCRIPTION HAPPY MEALS

1. Research indicates that traditional diets from the Mediterranean, Scandinavia and Japan help to preserve our psychological and cognitive well-being.
2. These diets all feature fish, one of the best sources of omega-3 fatty acids—nutrients that play a vital role in promoting neuronal health and that may have helped drive the evolution of the human brain.
3. Studies indicate that diet changes may alleviate a range of psychiatric symptoms, and mental health practitioners may start to complement therapy and pharmaceutical treatments with recommended eating plans in the near future.
tioxidant-rich fruits may help keep dementia at bay. And so on.

There is probably no single ingredient, no happy seed from the jungles of beyond, that is sure to secure a better mood or mental acuity into old age. But there do appear to be specific dietary patterns—calibrated by millions of years of human evolution—that boost our cognitive and psychological fitness. Within the nascent field of nutritional psychiatry, consensus is building about just what types of diets are best. And perhaps most exciting is the prospect that dietary intervention could serve as a valuable adjunct to medication and other therapies for mental disorders—just as it does in so many other areas of medicine.

**Good Diet, Bad Diet**

When it comes to promoting brain health, the diet supported by the strongest data draws on traditional eating patterns from Italy, Greece and Spain. The so-called Mediterranean diet consists primarily of fruits, vegetables, nuts, whole grains, fish, lean meats in moderation, olive oil and maybe a little red wine. In 2011 public health expert Almudena Sánchez-Villegas of the University of Las Palmas de Gran Canaria and her colleagues assessed the relation between this diet and depression in more than 12,000 healthy Spaniards over the course of a median of six years each. They found that compared with people who did not eat a Mediterranean diet, those who did were significantly less likely to succumb to depression. For the subjects who followed the diet most closely, the risk dropped by a substantial 30 percent. Sánchez-Villegas later confirmed the association in another large trial. The PREDIMED (Prevention with Mediterranean Diet) study—a multicenter research project evaluating nearly 7,500 men and women across Spain—initially looked at whether a Mediterranean diet, supplemented with extra nuts, protects against cardiovascular disease. It does. But in 2013 Sánchez-Villegas and other investigators also analyzed depression data among PREDIMED’s participants. Again, compared with subjects who ate a generic low-fat diet, those who adhered to the nut-enriched Mediterranean diet had a lower risk for depression. This was especially true among people with diabetes, who saw a 40 percent drop in risk. Perhaps these patients, who cannot adequately process glucose, benefited the most because the Mediterranean diet minimized their sugar intake.

Indeed, a central feature of the diet is that it is low in sugar, as well as processed foods and fatty meats, which are commonplace on most Western menus. Leading nutritional psychiatry researcher Felice N. Jacka of Deakin University and the University of Melbourne in Australia was one of the first to demonstrate an association between stereotypical Western diets and depression and anxiety. Most recently, she has drawn another link between poor diet and, quite literally, a shrinking brain. In

**Traditional Diets for Healthy Brains**

**MEDITERRANEAN**

Research consistently finds the dietary patterns of cultures hugging the Mediterranean Sea to be among the healthiest in the world. Ingredients common to Greek, Italian, Spanish and Middle Eastern cuisine (below) are linked with improved cardiovascular, mental and neurological function.

- Olive oil
- Omega-3-rich fish (sardines, tuna, salmon)
- Antioxidant-rich fruits and vegetables (tomatoes, peppers, eggplant)
- Whole grains
- Legumes
- Moderate amounts of lean meat and red wine
- Limited sugar and processed food

**OKINAWAN**

According to the World Health Organization, the Japanese have the highest life expectancy in the world—in part thanks to the population of Okinawa. Staples of the island group’s traditional diet (below) include the nutrient-rich purple sweet potato, often eaten in place of rice. Indeed, Okinawans tend to eat less fish, meat, rice and sugar—and fewer calories overall—than do those in other parts of the country.

- Antioxidant-rich vegetables (Okinawan purple sweet potatoes)
- Seaweed
- Some fish
- Some meat
- Limited sugar and white rice intake

**SCANDINAVIAN**

Swedish meatballs aside, Scandinavians cook, collect and cultivate a host of foods that together constitute the new Nordic diet, one of the world’s healthiest. It is associated with reduced inflammation and decreased risk for cardiovascular disease and diabetes, both of which can influence brain health. Of particular note, Scandinavians tend to cook with canola oil, also called rapeseed oil, which contains far more omega-3 fatty acids than olive oil.

- Fruits (lingonberries)
- Vegetables (potatoes)
- Nuts/whole grains (rye breads very common)
- Seafood
- Moderate amounts of meat and dairy
- Canola (rapeseed) oil
September 2015 she and her colleagues discovered that older adults who consumed a Western diet for four years not only suffered higher rates of mood disorders but also had a significantly smaller left hippocampus on MRI scans. The hippocampus, composed of two seahorse-shaped arcs of brain tissue deep underneath our temples, is critical to memory formation. Jacka focused on the hippocampus because animal studies have also noted diet-related changes there.

Scientists have proposed a number of possible mechanisms to explain this damage. Jacka’s findings parallel other research revealing that high-sugar diets can prompt runaway inflammation and trigger a cascade of other metabolic changes that ultimately impair brain function. Ordinarily inflammation is part of our immune system’s arsenal to fight infection and encourage healing, but when it is misdirected or overly aggressive, it can destroy healthy tissues as well. According to numerous studies, inflammation plays a role in a range of brain disorders—from depression and bipolar disorder to possibly autism, schizophrenia and Alzheimer’s disease.

Two meta-analyses from 2010 and 2012 collectively reviewed data from 53 studies and reported significantly elevated levels of several blood markers of inflammation in depressed patients. And numerous studies have reported increased or altered activity of immune cells called microglia—which play a key role in the brain’s inflammatory response—in patients with psychiatric disorders, including depression and schizophrenia. It is not clear whether inflammation causes mental illness in some cases, or vice versa. But the evidence suggests that many if not most known risk factors for psychiatric disorders, especially depression, promote inflammation; these include abuse, stress, grief and certain genetic predilections.

Jacka’s work repeatedly points to traditional diets such as Mediterranean, Japanese and Scandinavian ones—all of which tend to be noninflammatory—as being best for our neurological and mental health. “There is no doubt that stress and uncomfortable emotions can cause us to reach for the biscuit tin—they don’t call them comfort foods for nothing!” she admits. “But consistently the data show that the main constituents of a healthy brain diet include fruits, vegetables, legumes, nuts, fish, lean meats and healthy fats such as olive oil.”

**Brain-Building Fatty Acids**

Increasingly, researchers are finding that the power of these more traditional diets extends beyond just supplanting bad food with good. Last summer neuroscientists Amandine Pelletier, Christine Barul, Catherine Féart and their colleagues at the University of Bordeaux in France discovered that a Mediterranean diet may actually help physically preserve neuronal connections in the brain. They used a highly sensitive neuroimaging analysis technique called voxel-based morphometry to identify subtle changes in brain anatomy over time. And last September nutritional epidemiologist Martha C. Morris of Rush University and her co-workers reported that the MIND diet—a hybrid of the Mediterranean and the high-nutrient, low-salt DASH diet—may help slow cognitive decline and possibly even help prevent Alzheimer’s. When they tested cognitive ability in 960 older adults, those who had followed the MIND diet for roughly five years achieved scores matching those of people 7.5 years younger.

Our evolutionary backstory could explain these neuroprotective effects. Sometime between 195,000 and 125,000 years ago, humans may have nearly gone extinct. A glacial period had set in that probably left much of the earth icy and barren for 70,000 years. The population of our hominin ancestors plummeted to possibly only a few hundred in number, and most experts agree that everyone alive today is descended from this group. Exactly how they—or early modern humans, for that matter—managed to stay alive during recurring glacial periods is less clear. But as terrestrial resources dried up, foraging for marine life in reliable shellfish beds surrounding Africa most likely became essential for survival. Graduate student Jan De Vynck of Nelson Mandela Metropolitan University in South Africa has shown that one person working those shellfish beds can harvest a staggering 4,500 calories an hour.
The archaeological record corroborates the idea and indicates that our ancestors depended on a diet heavy in shellfish and cold-water fish—both rich sources of omega-3 fatty acids. These fats may have driven the evolution of our uniquely complex brains, which are 60 percent fat in composition. One omega-3 in particular, docosahexaenoic acid, or DHA, is arguably the single nutrient most strongly associated with brain health.

In 1972 psychiatrist Michael A. Crawford, now at Imperial College London, co-published a paper concluding that the brain is dependent on DHA and that DHA sourced from the sea was critical to mammalian brain evolution, especially human brain evolution. For more than 40 years he has argued that the rising rates of brain disorders are a result of post–World War II dietary changes—especially a move toward land-sourced food and, subsequently, the embrace of low-fat diets. He feels that omega-3s from seafood were critical to the human species’ rapid neural march toward higher cognition [see box above].

Many studies have confirmed DHA’s importance to the de-
Cold-water fish, such as salmon, tuna and sardines (above), are rich sources of DHA, a fatty acid that contributes to the growth, structure and function of nerve cells.

Fatty acids aside, there is another important link between our ancestors’ diets, inflammation and mental health. As we evolved, the 100 trillion bacteria, fungi and other microorganisms that colonize our bodies and constitute 90 percent of our cells came along for the ride. This so-called microbiota—and its collective genes, the microbiome—makes a critical contribution to the formation and function of our digestion and immune system. A growing number of findings now suggest that disrupting it through poor eating habits comes at a cost to the brain.

A Blow to the Gut

In one striking (if slightly nauseating) experiment in 2014, then 23-year-old student Tom Spector wiped out about a third of the bacterial species in his gut by limiting his diet to McDonald’s fast food. It took only 10 days. Spector played the guinea pig for two reasons: as a project to complete his genetics degree and to provide data for his father, Tim, a genetic epidemiology professor at King’s College London, who studies how processed diets affect gastrointestinal bacteria. The Spector family’s research did not assess specific health consequences—they were measuring only the drop in floral diversity in Tom’s gut—but Tom did report feeling lethargic and down after days of burgers, fries and sugary soda. The decline in species was so drastic that Tim sent the results to three laboratories for confirmation.

Diet-induced shifts in the microbiota of the kind Spector brought on himself can rapidly ratchet up inflammation in the gut. On top of the ill effects just described, gastrointestinal inflammation can deplete our supply of serotonin, a neurotransmitter long tied to depression and other psychiatric disorders. About 90 percent of our serotonin is produced in the gut when certain microbes interact with cells lining the gastrointestinal tract (some microbes even produce a portion of our serotonin themselves). But by-products of inflammation convert serotonin’s metabolic precursor, tryptophan, to a compound that generates neurotoxic metabolites linked with depression, schizophrenia and Alzheimer’s.

The good news is that dietary changes can not only wreck our microbial diversity, they can boost it, reducing gastrointestinal inflammation in the process. In 2015 a group at the University of Pittsburgh conducted a study in which 20 African-Americans from Pennsylvania swapped diets with 20 rural black South Africans. In place of their usual low-animal-fat, high-fiber diet, the Africans consumed burgers, fries, hash browns, and the like. The Americans eschewed their normal fatty foods and refined carbohydrates for beans, vegetables and fish. After just two weeks the Americans’ colons were less inflamed, and fecal samples showed a 250 percent spike in butyrate-producing bacterial species. Butyrate is thought to reduce the risk of cancer. The South Africans, on the other hand, underwent microbial changes associated with increased cancer risk.

“Dietary changes are the easiest way to alter your microbiome and help to control inflammation,” says psychiatrist Emily Deans of Harvard Medical School. She believes diet is every bit as important as pills and psychotherapy in managing mental illness—a view informed by her own clinical practice. “I discuss nutrition with just about all of my patients,” she adds, “and
I think it can really help in managing conditions like depression, at least in some people.” Deans also feels that timing of meals can influence mood, and research suggests that eating on a regular schedule can improve mental health.

Deans acknowledges that science has a long way to go before we fully understand the brain-diet relation. She is also wary of the massive probiotic industry that has, like the supplement industry in general, barreled ahead of the minimal but growing scientific evidence suggesting that probiotics might be effective in preventing or treating mental illness. “You can do studies with, for example, certain vitamins, and some might turn out positive and others negative,” she explains. “But the truth is vitamins exist in all sorts of different chemical states in food and in just one state in supplements.” This difference in form between nutrients in food versus pills explains why the data tend to favor nutrition state in supplements. “I think we can safely say that certain dietary patterns seem to promote a healthy microbiome,” Deans speculates, “like the Mediterranean diet and diets that include lots of fiber, fermented foods and fish.” And a healthy microbiome may be essential for a healthy brain.

Food for Thought

For seven years now Carolyn has been eating better—focusing on seafood and cutting back on sugar. She has lost weight, and her diabetes is under control. “It’s part of a whole new way of life,” she glows, “knowing that what I eat can affect how I feel.” That awareness is building momentum among patients and practitioners alike. In March 2015 a large team of clinicians and researchers published a report in the Lancet Psychiatry on behalf of the International Society for Nutritional Psychiatry Research—an organization Jacka co-founded in 2013. Citing modest therapeutic gains yielded by many psychiatric drugs, the authors called for the integration of nutrition-based approaches into mental health care. “The emerging and compelling evidence for nutrition as a crucial factor in the high prevalence and incidence of mental disorders,” they wrote, “suggests that diet is as important to psychiatry as it is to cardiology, endocrinology, and gastroenterology.”

Thanks to our evolutionary lineage (and plenty of fish), attention to our diets may prove critical to reversing the rising rates of mental illness around the world; lowering the proportion of people struggling with various forms of dementia; and staving off milder psychiatric symptoms and disorders. There is little doubt that eating right can help shuttle us through tough times—just as it may have done 160,000 years ago for a small group of humans huddled in coastal African caves.

One of the leading proponents of leveraging diet to better brain health, Jacka is encouraged that interventional studies—in which patients are actually “prescribed” a particular diet and tracked over time—are finally getting under way. Such research will be able to offer more definitive proof of the connection between diet and mental and cognitive well-being. Jacka’s own group is now conducting a randomized controlled investigation to assess the effectiveness of dietary changes in adults with major depression. “Our current trial is the first to attempt to directly address the question: ‘If I improve my diet, will my depression improve?’ ” she says, adding, “The preliminary results look very exciting.” Her team hopes to have answers later this year.

In the meantime, many doctors and patients are beginning to see dietary interventions as a beacon of hope after several decades of disappointing psychiatric drug development. Too many patients suffering from mental illness or dementia do not respond adequately to existing medications, if at all. For example, selective serotonin reuptake inhibitors such as Prozac—one of the most commonly prescribed drug classes for treating depression—appear effective only in severe cases; they are often no better than placebo for moderate disease. As scientists learn more about the pathologies behind mental and cognitive disorders, new and promising therapeutic targets will surely emerge. But it is clear that nutrition-based treatment plans—free from side effects and low in cost—will also figure prominently in the future of dementia and psychiatric care.
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