Rethinking Dietary Approaches for Brain Health

David Perlmutter, MD, FACN, ABIHM

In his new book Grain Brain,[1] *David Perlmutter, MD, FACN, ABIHM, describes gluten and carbohydrates as being potential root causes of major degenerative diseases, such as Alzheimer's disease and other forms of dementia, depression, attention-deficit hyperactivity disorder (ADHD), and other conditions. In this interview, Dr. Perlmutter explains the basis of these ideas and outlines, specifically, how dietary choices may affect neurologic health.*

Q: Please share your main idea regarding the effects of carbohydrates and glucose on the brain.

David Perlmutter: The major thesis of *Grain Brain* is that both carbohydrates and glucose are detrimental to brain health. Well-respected and peer-reviewed journals have published reports that higher levels of blood glucose are specifically damaging and detrimental to the brain in general, and more specifically, to the hippocampus, which mediates memory function.

A recent article in *Neurology* reported that elevations of blood glucose and glycated hemoglobin [HbA1c] translate into two things: memory compromise and shrinkage of the hippocampus.[2] Another recent article in *The New England Journal of Medicine* demonstrated that even mild elevations of blood sugar translate dramatically into an increased risk for developing dementia.[3] It is a profound correlation to recognize that even subtle elevations of blood glucose—well below levels to be considered diabetic—may already be damaging the brain. If we understand that elevated blood glucose and glycation of proteins relate to an increased risk for cognitive dysfunction, as well as brain shrinkage, what should a dietary evaluation look like?

A study in the *Journal of Alzheimer's Disease*, demonstrated that individuals who consumed higher amounts of carbohydrates in their diets had about an 89% increased risk for developing dementia, in contrast to people whose diets were highest in fat and whose risk was reduced by 44%.[4]

We live with this notion that a calorie is a calorie, but, at least in terms of brain health—and I believe for the rest of the body as well—there are very big differences between our sources of calories in terms of the impact on our health. Carbohydrate calories, which elevate blood glucose, are dramatically more detrimental to human physiology—and specifically to human health—than are calories derived from healthful sources of fat.

The diet that I recommend—high in fat and low in carbohydrates—has simply been what we have eaten for a million years, so it has a bit of a track record. The notion that this is a revolutionary new diet has to be put into context. In reality, the diet that people are now consuming, which is dreadfully high in carbohydrates and low in fat, as our governmental institutions are recommending, is the biggest challenge to human physiology that we have ever experienced, and this is very, very worrisome.

In terms of gluten consumption, we have come a long way from our understanding that celiac disease exists, and we now recognize that, according to top researchers, non-celiac gluten sensitivity also exists, which may affect 30% of humanity. Marios Hadjivassiliou [MD, department of neurology, Royal Hallamshire Hospital, Sheffield, United Kingdom] has said, so poetically, that gluten sensitivity may at times be a pure neurologic disease that is basically extraintestinal, and that we do not need to have intestinal issues to define gluten sensitivity. In fact, we are now seeing literature that points the finger clearly at gluten sensitivity as a culprit in a variety of neurologic problems, including depression, cognitive dysfunction, seizures, and even headaches.

According to the work of Alessio Fasano [MD, chief of pediatric gastroenterology and nutrition at MassGeneral Hospital for Children, Boston, Massachusetts], gluten stimulates the production of zonulin, and zonulin makes the bowel hyperpermeable, which allows proteins access to the bloodstream, where they might normally have been excluded.[5] More importantly, what Dr. Fasano's research has revealed is that the same mechanism is involved—gluten-stimulating zonulin—in increasing the permeability of the blood–brain barrier. While clinicians may be concerned about patients having leaky bowels, I can promise that having a leaky brain is certainly of much more concern. What is so compelling about Dr. Fasano's work is that, according to

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his research, this gluten–zonulin signaling cascade is present to some degree in 100% of humans.

In the clinical arena, when we see children with ADHD, or elderly individuals with depression or dementia, we may see improvement in these clinical presentations simply by removing gluten, reducing carbohydrates, and adding healthy fats back into the diet. We understand the benefits of doing this from both the literature and clinical observation.

Foods that contain gluten tend to be high in carbohydrates. Breads, pasta, cookies, crackers, and other common gluten-containing foods are foods with extremely high glycemic indices and should be avoided. That said, people who are gluten-sensitive may suddenly become attracted to the gluten-free aisle in the grocery store and gravitate toward gluten-free pastas, breads, and crackers. These people are not doing themselves a favor because they are still dramatically pounding their bodies with high levels of carbohydrates.

I want to address another important point. Typically, clinicians assess average blood glucose control by ordering an HbA1c test. However, I want to point out that the HbA1c, as a marker of average blood glucose, tells us not only about what that person's glucose has been for the prior 3–4 months but also serves as a marker of *protein glycation*. HbA1c is glycation of the protein hemoglobin and, as such, serves as a marker of protein glycation.

When HbA1c begins to elevate, it is an indication that not only is hemoglobin being glycated but all the proteins in the body are being glycated. This is significant because glycation of proteins does two things: first, it dramatically increases the body's production of inflammatory chemicals such as cytokines; and second, it also dramatically upregulates the production of free radicals. Oxidative stress may be increased up to fiftyfold when proteins become glycated. In fact, research suggests that the most valuable metric for monitoring risk for Alzheimer's disease is the HbA1c. The take-home message is that HbA1c is a powerful marker for the risk of annual brain shrinkage.[6] The empowering part of this story is that we have control over this—people control their HbA1c based on the foods they choose to eat.

We are living during a time when 5.4 million Americans have been diagnosed with Alzheimer's disease, for which there is no treatment, and yet, there is clear evidence of ways of keeping it from happening. Research by Deborah Barnes [PhD, an associate professor in the department of psychiatry at the University of California–San Francisco] indicates in an article in *The Lancet Neurology* that more than half of Alzheimer's cases could have been prevented with simple lifestyle changes, including diet and avoiding obesity.[7]

Q: Does your advice relate only to highly refined and processed carbohydrates or to carbohydrates from whole-food sources as well?

Dr. Perlmutter: The glycemic index of foods is a very powerful metric in terms of not only how high a person's blood glucose goes but for how long it remains elevated after consuming the food item. Thus, this has significant implications in terms of protein glycation. In fact, many people would be surprised to learn that whole-grain bread is ranked higher than white bread in terms of glycemic index and actually ranks significantly higher than a chocolate candy bar. So the idea that whole grains are somehow healthful for us is actually inappropriate, because the glycemic index may be very high, and one may actually increase available blood glucose and enhance glycation.

The reality is that, for 99.5% of our time on this planet, we did not eat much in the way of grains. We were eating a gluten-free and low-carbohydrate/high fat diet, and that is the environment in which our genome perfected itself. We are still interacting with that same genome that wants to express perfect health but cannot do so because we are challenging our genome with bizarre epigenetic signals of a high-carbohydrate/low-fat diet, and a diet that contains potentially threatening proteins, such as gluten and wheat-germ agglutinin, for example.

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Q: What has your clinical experience been in terms of providing dietary advice to help patients maintain optimal physical and mental health?

Dr. Perlmutter: There are many, many case examples of how people's lives were turned around and their health improved by following these dietary recommendations. I have seen dramatic results in people who have had intractable headaches, movement disorders, cognitive impairment, and even hemifacial spasms, not to mention nonneurologic issues, including arthritis, inflammatory bowel disease, and skin disorders. I have seen people who were told that they needed aggressive medical interventions or even surgery, who, when they made these recommended dietary changes, experienced significant improvements. Every day, I am surprised that yet another problem with a patient who I am dealing with has been resolved by going on a gluten-free program. These are people with depression, low-energy, cognitive issues, seizures, and many other conditions.

Q: What is your advice to clinicians regarding your suggested dietary approaches?

Dr. Perlmutter: Louis Pasteur said that chance favors the prepared mind, and the mission here is for me not to own this information. I want the message to be that this approach is one that anyone can follow. I recommend that clinicians learn

about this approach and recognize that this simply follows what current science is supporting. Gluten sensitivity is very real and pervasive, and the information we now have about this can be so helpful for addressing many disease processes that are founded on information that we did not have before.

There is no downside of cutting gluten out of a patient's dietary program. Clinicians can recommend stopping consumption of gluten-containing foods and monitor what happens with patients. Any issue in human pathophysiology that relates to inflammation might well have its origin in gluten sensitivity.

That being said, certainly gluten sensitivity and adopting a high-fat/low-carbohydrate diet is not going to be the answer to every problem. I want to be clear that I am not offering this up as playing a causal role in every disease that we see, but it is certainly much more significant than we have ever thought about in the past. ■

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