



“Ultraprocessed” foods seem to trigger neural signals that make us want more and more calories, unlike other foods in the Western diet

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*Photography by Jamie Chung*



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UTRITION RESEARCHER KEVIN HALL STRIVES TO PROJECT A ZEN-LIKE STATE OF equanimity. In his often contentious field, he says he is more bemused than frustrated by the tendency of other scientists to “cling to pet theories despite overwhelming evidence that they are mistaken.” Some of these experts, he tells me with a sly smile, “have a fascinating ability to rationalize away studies that don’t support their views.”

Among those views is the idea that particular nutrients such as fats, carbs or sugars are to blame for our alarming obesity pandemic. (Globally the prevalence of obesity nearly tripled between 1975 and 2016, according to the World Health Organization. The rise accompanies related health threats that include heart disease and diabetes.) But Hall, who works at the National Institute of Diabetes and Digestive and Kidney Diseases, where he runs the Integrative Physiology section, has run experiments that point fingers at a different culprit. His studies suggest that a dramatic shift in how we make the food we eat—pulling ingredients apart and then reconstituting them into things like frosted snack cakes and ready-to-eat meals from the supermarket freezer—bears the brunt of the blame. This “ultraprocessed” food, he and a growing number of other scientists think, disrupts gut-brain signals that normally tell us that we have had enough, and this failed signaling leads to overeating.

Hall has done two small but rigorous studies that contradict common wisdom that faults carbohydrates or fats by themselves. In both experiments, he kept participants in a hospital for several weeks, scrupulously controlling what they ate. His idea was to avoid the biases of typical diet studies that rely on people’s self-reports, which rarely match what they truly eat. The investigator, who has a physics doctorate, has that discipline’s penchant for precise measurements. His first study found that, contrary to many predictions, a diet that reduced carb consumption actually seemed to slow the rate of body fat loss. The second study, published this year, identified a new reason for weight gain. It found that people ate hundreds more calories of ultraprocessed than unprocessed foods when they were encouraged to eat as much or as little of each type as they desired. Participants chowing down on the ultraprocessed foods gained two pounds in just two weeks.

“Hall’s study is seminal—really as good a clinical trial as you can get,” says Barry M. Popkin, a professor of

nutrition at the University of North Carolina at Chapel Hill, who focuses on diet and obesity. “His was the first to prove that ultraprocessed foods are not only highly seductive but that people tend to eat more of them.” The work has been well received, although it is possible that the carefully controlled experiment does not apply to the messy way people mix food types in the real world.

The man who designed the research says he is not on a messianic mission to improve America’s eating habits. Hall admits that his four-year-old son’s penchant for chicken nuggets and pizza remains unshakable and that his own diet could and probably should be improved. Still, he believes his study offers potent evidence that it is not any particular nutrient type but the way in which food is manipulated by manufacturers that plays the largest role in the world’s growing girth. He insists he has no dog in any diet wars fight but is simply following the evidence. “Once you’ve stepped into one camp and surrounded yourself by the selective biases of that camp, it becomes difficult to step out,” he says. Because his laboratory and research are paid for by the national institute whatever he finds, Hall notes that “I have the freedom to change my mind. Basically, I have the privilege to be persuaded by data.”

### THE CARB TEST

HALL ONCE HAD GREAT SYMPATHY for the theory that specific nutrients—in particular carbs—were at fault for our collective losing battle with body weight. “I knew that consumption of carbohydrates increases insulin levels in the blood and that insulin levels affect fat storage and fat cells,” he says. “So it was certainly plausible that consumption of carbohydrates versus other macronutrients could have a deleterious effect on body weight. But while plausible, it wasn’t certain, so I decided to test it.”

In Hall’s carb study, 10 men and nine women, all obese, were sequestered in a hospital ward at the National Institutes of Health and fed a high-carbohydrate/low-

#### IN BRIEF

Many nutrition scientists blame overeating fats or carbohydrates for the world’s obesity pandemic. But new research points to “ultraprocessed” foods such as chicken nuggets and instant soup mixes that dominate modern diets. These foods seem to distort signals between the gut and brain that normally tell us we are full, so instead people overeat.



ULTRAPRO-CESSSED foods and drinks are designed to be ready-to-consume, with numerous additives that can include oils, fats, color enhancers, flavor enhancers, non-sugar sweeteners, and bulking and firming agents. (No specific brand has been linked to obesity.)

SOURCE FOR PHOTOGRAPHS ON PAGES 41, 43 AND 44: "NOVA," THE STARSHINES BRIGHT," BY CARLOS A. MONTEIRO AT ALI, IN WORLD NUTRITION, VOL. 7, NO. 1, JANUARY-MARCH 2016

fat diet for two weeks. Then they left for a short time and returned to repeat another two-week stint. For the first five days of each stay, the balance was kept at 50 percent carbohydrate, 35 percent fat and 15 percent protein, with calorie intakes matched to their energy expenditure—measured in a specially constructed metabolic chamber—to ensure they neither gained nor lost weight. Over the next six days of each stay, they ate a diet with 30 percent fewer calories from the carb category.

“We were not surprised to find that when you manipulate the level of carbohydrates versus fats, you do see very different insulin levels,” Hall says. He had expected the low-carb diet would reduce insulin activity. “But what did surprise us was that we did not see a significant effect of the sharply lower insulin levels on the rate of

calories burned over time or on body fat.” Typically lowered insulin affects the way fat cells burn calories. Yet, Halls says, “we found that the reduced-carbohydrate diet slightly slowed body fat loss.” It also slightly increased the loss of lean body mass. A year later Hall and his colleagues did a similar experiment over a longer, eight-week period. This time they cut carbohydrates to very low levels. In the end, they found no meaningful difference in body fat loss or calorie expenditure between the very low-carb diet and a baseline high-carb/high-sugar diet. The scientists published the first results in 2015 in the journal *Cell Metabolism* and the second set in 2016 in the *American Journal of Clinical Nutrition*.

If it's not carbohydrates, what is to blame for our global obesity problem? Sure, meal portions today are

larger, food more abundant, and many of us are eating more calories than people did decades ago. But with temptations so plentiful, almost all Americans could be overeating—yet a good number do not. That, Hall thinks, is the real nutrition mystery: What factors, for some people, might be acting to override the body's inborn satiety mechanisms that otherwise keep our eating in check?

### PROCESSED CALORIES

HALL LIKES TO COMPARE humans to automobiles, pointing out that both can operate on any number of energy sources. In the case of cars, it might be diesel, high-octane gasoline or electricity, depending on the make and model. Similarly, humans can and do thrive on any number of diets, depending on cultural norms and what is readily available. For example, a traditional high-fat/low-carb diet works well for the Inuit people of the Arctic, whereas a traditional low-fat/high-carb diet works well for the Japanese. But while humans have evolved to adapt to a wide variety of natural food environments, in recent decades the food supply has changed in ways to which our genes—and our brains—have had very little time to adapt. And it should come as no surprise that each of us reacts differently to that challenge.

At the end of the 19th century, most Americans lived in rural areas, and nearly half made their living on farms, where fresh or only lightly processed food was the norm. Today most Americans live in cities and buy rather than grow their food, increasingly in ready-to-eat form. An estimated 58 percent of the calories we consume and nearly 90 percent of all added sugars come from industrial food formulations made up mostly or entirely of ingredients—whether nutrients, fiber or chemical additives—that are not found in a similar form and combination in nature. These are the ultra-processed foods, and they range from junk food such as chips, sugary breakfast cereals, candy, soda and mass-manufactured pastries to what might seem like benign or even healthful products such as commercial breads, processed meats, flavored yogurts and energy bars.

Ultra-processed foods, which tend to be quite high in sugar, fat and salt, have contributed to an increase of more than 600 available calories per day for every American since 1970. Still, although the rise of these foods correlates with rising body weights, this correlation does not necessarily imply causation. There are plenty of delicious less processed foods—cheese, fatty meats, vegetable oil, cream—that could play an equal or even larger role. So Hall wanted to know whether it was something about ultra-processing that led to weight gain. “Basically, we wondered whether people eat more calories when those calories come from ultra-processed sources,” he says.

Tackling that question is not simple. The typical nutritional study, as noted earlier, relies on self-reports of individuals who keep food diaries or fill out questionnaires from memory. But Hall knew that in the case of ultra-processed foods, that approach would fail

to provide convincing evidence either way. For one thing, nutrition study participants are notorious for cheating on dietary surveys—claiming more broccoli and fewer Double Stuf Oreos than they actually eat or “forgetting” drinking that third beer with friends. For another, with such a large percentage of the American diet coming from ultra-processed foods, it would be hard to find a group of people with a markedly different diet for comparison.

To avoid these and related problems, in 2018 Hall turned once again to the metabolic ward, where he randomly assigned 20 adult volunteers to receive either ultra-processed or unprocessed diets for two weeks. Then people switched: if they had been on one diet, they went on the alternative one for two more weeks. (Clearly, 20 is not a large enough sample size from which to draw conclusions that apply to the public as a whole, but this pilot study was meant as a “proof of concept” on which to build future, larger studies. Subjecting more people to the strict study regimen at this preliminary stage, Hall says, “would be unethical.”) Dietitians scrupulously matched the ultra-processed and processed meals for calories, energy density, fat, carbohydrate, protein, sugars, sodium and fiber. They also made sure that the research subjects had no taste preference for one category of food over the other. On both diets, participants were instructed to eat as much or as little of the meals and snacks as they liked.

This past spring, in his office, Hall showed me color photographs of each of the meals and snacks. The ultra-processed meals included food such as canned ravioli, hot dogs, burgers topped with processed cheese, white bread, margarine and packaged cookies. Breakfast in this category had foods such as turkey bacon, sugared cereals, egg substitutes, Tater Tots, fruit-flavored drinks (most sweetened with artificial sweetener) and Spam. The unprocessed meals had dinners with roast beef, rice pilaf, couscous and pasta and breakfasts with nuts, vegetable omelets fried in oil, hash browns cooked with butter, and full-fat yogurt.

Roast beef, pasta and fried eggs are very appealing to many of us, and it would not have been shocking if people ate more of these than they ate, say, ultra-processed Spam. But that's not what happened. Hall's results, published earlier this year in *Cell Metabolism*, showed that on the ultra-processed diet people ate about 500 extra calories every day than they did when eating the unprocessed diet, an increase that caused them to gain about two pounds in two weeks. “What was amazing about Hall's findings was how many extra calories people eat when they are faced with ultra-processed foods,” says Carlos Augusto Monteiro, a physician and professor of nutrition and public health at the School of Public Health at the University of São Paulo in Brazil.

### A GUT-BRAIN DISCONNECT

WHY ARE MORE of us tempted to overindulge in egg substitutes and turkey bacon than in real eggs and hash brown potatoes fried in real butter? Dana Small, a



PROCESSED FOODS add a few substances such as sugar, fat, and salt to natural food products, with the goal of improving preservation or sharpening taste. The category includes canned vegetables and fish, cured and salted meats, cheeses, and fermented drinks such as wine and beer.

neuroscientist and professor of psychiatry at Yale University, believes she has found some clues. Small studies the impact of the modern food environment on brain circuitry. Nerve cells in the gut send signals to our brains via a large conduit called the vagus nerve, she says. Those signals include information about the amount of energy (calories) coming into the stomach and intestines. If information is scrambled, the mixed signal can result in overeating. If “the brain does not get the proper metabolic signal from the gut,” Small says, “the brain doesn’t really know that the food is even there.”

Neuroimaging studies of the human brain, done by Small and others, indicate that sensory cues—smells and colors and texture—that accompany foods with

high-calorie density activate the striatum, a part of the brain involved in decision-making. Those decisions include choices about food consumption.

And that is where ultraprocessed foods become a problem, Small says. The energy used by the body after consuming these foods does not match the perceived energy ingested. As a result, the brain gets confused in a manner that encourages overeating. For example, natural sweeteners—such as honey, maple syrup and table sugar—provide a certain number of calories, and the anticipation of sweet taste prompted by these foods signals the body to expect and prepare for that calorie load. But artificial sweeteners such as saccharin offer the anticipation and experience of sweet taste without the energy boost. The brain, which had antici-

**UNPROCESSED FOODS** are the edible parts of plants (such as seeds or roots or leaves) and animals (such as meat and eggs). The main processing of this food type is freezing, drying or pasteurizing to extend storage life. Salts, sugars, oils and fats are not added.



pated the calories and now senses something is missing, encourages us to keep eating.

To further complicate matters, ultraprocessed foods often contain a combination of nutritive and nonnutritive sweeteners that, Small says, produces surprising metabolic effects that result in a particularly potent reinforcement effect. That is, eating them causes us to want more of these foods. “What is clear is that the energetic value of food and beverages that contain both nutritive and nonnutritive sweeteners is not being accurately communicated to the brain,” Small notes. “What is also clear is that Hall has found evidence that people eat more when they are given highly processed foods. My take on this is that when we eat ultraprocessed foods we are not getting the metabolic

signal we would get from less processed foods and that the brain simply doesn’t register the total calorie load and therefore keeps demanding more.”

Small says that animal studies bear out the theory that ultraprocessed foods disrupt the gut-brain signals that influence food reinforcement and intake overall. “We’ve gone in with this cavalier attitude, that a calorie is a calorie, but a lot of foods have unintended consequences,” she says. “For example, in the natural world, carbohydrates almost always come packaged with fiber, whereas in ultraprocessed foods, fiber is either not there at all or included in a form not found in nature. And it is rare to find carbohydrates and fat in the same food in nature, but ultraprocessed foods tend to have both in one package. We’ve created all these

hyperpalatable foods filled with fat, sugar, salt and additives, and we clearly prefer these foods. But these foods don't necessarily provoke satiety. What they seem to provoke is cravings."

Small and other scientists speculate that ultra-processed foods in some sense resemble addictive drugs, in that consuming them leads not to satisfaction but to a yearning for more. Neuroscientist Ann Graybiel of the Massachusetts Institute of Technology, a recognized expert on habit formation, says that external cues—like the mere sight of a candy bar—can provoke a reflexive response that causes the brain to encourage a behavior almost automatically. "Part of what's happening when habits form is 'chunking,'" she says. "You learn the behavior pattern, and your brain packages the whole sequence, including the beginning and the end markers, so you don't have to think about it further." (Certain neurons in the striatum are responsible for grouping behaviors into a single, habitual routine.)

Eating large amounts of ultraprocessed foods may actually change brain circuitry in ways that increase sensitivity to food cues, adds Kent Berridge, a professor of psychology and neuroscience at the University of Michigan. He has shown this effect in rodents. "When you give rats junk-food diets, some gain weight, but others do not. In those that became obese, their dopamine systems changed, and they became hypersensitive to food cues—they became superfocused on that one reward. They showed no more pleasure, but they did show more wanting, and that wanting led to more actions—that is, more food-seeking behavior."

But this is not a uniform reaction, Berridge emphasizes, and he does not think it will turn out to be the only cause of overeating. "It's very plausible that altering foods (through ultraprocessing) could trigger this response in some of us, but my guess is that we aren't going to find that it affects all of us in the same way. My guess is that in the case of obesity, we are going to find subgroups—that is, that there are different avenues to becoming obese depending on one's genes."

## FOOD FIGHT

NOT ALL RESEARCHERS agree that Hall's avenue—the ultraprocessed one—is the major road leading to obesity. Rick Mattes, a professor of nutrition science at Purdue University and the incoming head of the American Society of Nutrition, says that he is concerned that Hall is damning a whole food category without sufficient cause. "He's saying that ultraprocessed foods result in overeating, but there is no [large] body of evidence to support that claim. My view is that how items are manipulated may not be the primary driver of our response to them but that it is the nutrient composition that is the more relevant factor."

Hall points out that he did match the nutritional composition of the diets, but Mattes has several other objections. Perhaps the most serious is that the participants were offered only ultraprocessed or unprocessed

foods in each leg of the study. "In the real world, people would mix" different food types, he wrote in an e-mail. "This is not a fault with the study, but it is a serious issue when attempting to extrapolate the findings to free-living people."

Another possible factor driving overconsumption of ultraprocessed foods is that they are eaten quickly, so people could devour a lot before any satiation mechanisms kick in to slow them down. Ultraprocessed foods tend to be energy-dense and pack a relatively large number of calories into a relatively small package. This, too, might encourage rapid consumption that bypasses satiety mechanisms. Still, fast eating does not explain why people continued to eat more ultraprocessed food at their next meal, when, at least in theory, they should have been less hungry.

If ultraprocessed foods are indeed a big problem, the question is what, if anything, we can and should do about them. When I asked Hall, he was reluctant to call for stringent measures such as a tax on these foods. "I worry that because almost 60 percent of our calories come from ultraprocessed foods, taxing those foods might add to some people's food insecurity," he says. "We've found an association of ultraprocessed foods and overeating, and there are many hypotheses about the causal mechanism. But until you fully understand the mechanism, it's too early to intervene. It could be that the additives and artificial flavoring are having an impact or that ultraprocessed foods have micronutrient deficiencies that the body senses and responds to by overeating. There are likely other factors as well. We just don't know—yet."

At the same time, he does think the available evidence on ultraprocessed foods is a reason to worry about them: "We can change our diet to minimize the damage. And for now I think that's where we need to set our sights." The food industry can help, perhaps by designing more foods with less processing, but people have to show they want such food by buying more of it. "I'm no evangelist," Hall asserts, "but I do think that the public demand on the food system is more powerful than any government regulation." His job in all this, he says, is to get the science right. ■

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## MORE TO EXPLORE

- Calorie for Calorie, Dietary Fat Restriction Results in More Body Fat Loss Than Carbohydrate Restriction in People with Obesity.** Kevin D. Hall et al. in *Cell Metabolism*, Vol. 22, No. 3, pages 427–436; September 1, 2015.
- Energy Expenditure and Body Composition Changes after an Isocaloric Ketogenic Diet in Overweight and Obese Men.** Kevin D. Hall et al. in *American Journal of Clinical Nutrition*, Vol. 104, No. 2, pages 324–333; August 2016.
- Processed Foods and Food Reward.** Dana M. Small and Alexandra G. Difeliceantonio in *Science*, Vol. 363, pages 346–347; January 25, 2019.
- Ultra-Processed Diets Cause Excess Calorie Intake and Weight Gain: An Inpatient Randomized Controlled Trial of Ad Libitum Food Intake.** Kevin D. Hall et al. in *Cell Metabolism*, Vol. 30, No. 1, pages 67–77 and e1–e3; July 2, 2019.

## FROM OUR ARCHIVES

**The Food Addiction.** Paul J. Kenny; September 2013.

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