

NEWS RELEASE 3-MAR-2020

Artificial sweeteners combined with carbs may be more harmful than those sweeteners alone

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The influence of artificial sweeteners on the brain and ultimately metabolism has been hotly debated in recent years. Some studies have found adverse effects on blood sugar and insulin levels, while others have not. In a study publishing March 3 in the journal *Cell Metabolism*, researchers say the discrepancies in these studies may be due to how the sweeteners are consumed--or, more specifically, what they are consumed with.

Investigators report that the artificial sweetener sucralose seems to have no negative impact on its own, but when it is consumed with a carbohydrate, it induces deleterious changes in insulin sensitivity and decreases the brain's response to sweet taste as measured by fMRI.

"When we set out to do this study, the question that was driving us was whether or not repeated consumption of an artificial sweetener would lead to a degrading of the predictive ability of sweet taste," says senior author Dana Small, a neuroscientist who is a professor of psychiatry and the director of the Modern Diet and Physiology Research Center at Yale University. "This would be important because sweet-taste perception might lose the ability to regulate metabolic responses that prepare the body for metabolizing glucose or carbohydrates in general."

The trial enrolled 45 volunteers between the ages of 20 and 45 who didn't normally consume low-calorie sweeteners. All of them were of healthy weight and had no metabolic dysfunction. Other than consuming seven beverages in the lab over a two-week period, they didn't make any changes to their diet or other habits. The investigators conducted studies on the volunteers before, during, and after the testing

period, including performing fMRI scans to look at changes in the brain in response to sweet tastes, as well as other tastes like salty and sour. They also measured taste perception and did an oral glucose tolerance test to look at insulin sensitivity.

The sweeteners were consumed as fruit-flavored beverages with added sucralose, or with table sugar for comparison. In what was intended to be a control group: some of the volunteers had the carbohydrate maltodextrin added to their sucralose drinks. The researchers chose maltodextrin, a non-sweet carbohydrate, to control for the calories of sugar without adding more sweet taste to the beverage. Surprisingly, it was this control group that showed changes in the brain's response to sweet taste and the body's insulin sensitivity and glucose metabolism. Given the surprising result, the researchers added a second control group, in which the participants drank beverages with maltodextrin alone. They found no evidence that consuming maltodextrin-containing beverages over the seven-day period alters insulin sensitivity and glucose metabolism.

"Perhaps the effect resulted from the gut generating inaccurate messages to send to the brain about the number of calories present," Small says. "The gut would be sensitive to the sucralose and the maltodextrin and signal that twice as many calories are available than are actually present. Over time, these incorrect messages could produce negative effects by altering the way the brain and body respond to sweet taste."

She notes that a subset of the previous studies of artificial sweeteners have involved mixing the sweeteners with plain yogurt, adding carbohydrates from the yogurt and leading to the same effects seen here as with the maltodextrin. This could explain why previous findings about artificial sweeteners have been in conflict with each other.

Small says that her team began doing similar studies in adolescents, but they ended the trial early when they saw that two of the kids who were getting the sucralose-carbohydrate combination had their fasting insulin skyrocket.

"Previous studies in rats have shown that changes in the ability to use sweet taste to guide behavior can lead to metabolic dysfunction and weight gain over time. We think this is due to the consumption of artificial sweeteners with energy," she notes.

Future studies will look at whether other artificial sweeteners, as well as more natural sweeteners like stevia, have the same effects as sucralose. Small expects that many of them will. "It's hard to say, because we still don't fully understand the mechanism," she concludes. "That's also something we hope to study further, especially in mice."

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This work was supported by the National Institutes of Health.

Cell Metabolism, Dalenberg et al.: "Short-term consumption of sucralose with, but not without, carbohydrate impairs neural and metabolic sensitivity to sugar"

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