

Low-calorie sugar substitute consumption during adolescence appears to impair memory later in life

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A high-sugar diet early in life has been shown to harm brain function, but what about low-calorie sugar substitutes? A new study reveals they

may take a heavy toll on the developing brain and gut.

In a study published Sept. 13 online in the journal *JCI Insight*, scientists at the USC Dornsife College of Letters, Arts and Sciences show that adolescent rats that consumed the [low-calorie sweeteners](#) saccharin, ACE-K and stevia exhibited long-term impairments in memory.

- The findings align with those from earlier studies in which the researchers show that adolescent rats that consume sugar suffer lingering memory impairment.
- Consuming low-calorie sweeteners also affected metabolic signaling in the body, which can lead to diabetes and other metabolism-related diseases.
- Rats that consumed low-calorie sweeteners as adolescents were less willing to work for sugar as adults, but they consumed more sugar if it was freely available, another factor that might affect the likelihood of developing metabolic disease.

Advice on what to eat and when to eat it varies widely. Findings from studies like this can help consumers and clinicians make healthier choices throughout the lifespan, say the researchers.

"While our findings do not necessarily indicate that someone should not consume low-calorie sweeteners in general, they do highlight that habitual low-calorie sweetener consumption during [early life](#) may have unintended, long-lasting impacts," said Scott Kanoski, associate professor of biological sciences at USC Dornsife.

While most studies of low-calorie sweeteners focus on one substance and use amounts far exceeding the norm, the researchers made sure the study was in line with real-life conditions for people.

- Sweeteners tested include saccharin, acesulfame potassium (ACE-

- K) and stevia—which are commonly used in sweetened foods.
- The amount of sweetener consumed fell within FDA-approved guidelines for humans.

"Research using rodent models and low-calorie sweeteners has typically involved [consumption levels](#) that far exceed the FDA 'acceptable daily intake' (ADI) levels and used only a single sweetener. To design our research to be more applicable to humans, we kept consumption levels within the ADI and used multiple low-calorie sweeteners to determine if effects were specific to a given sweetener or general across sweeteners," says Lindsey Schier, Gabilan assistant professor of biological sciences at USC Dornsife.

To determine the effect of low-calorie sweetener consumption on memory, the researchers used methods that test [object recognition](#) and spatial recognition.

- Rats were provided water sweetened with either stevia, ACE-K or saccharin or plain water, along with their normal food.
- After a month, the rats' memory was tested using two different methods—one tests if they remember an object they've seen before and the other is a maze.

In the end, rats consuming sweetener were less likely to remember an object or the path through the maze than those that drank only plain water.

The scientists also found other effects among the rats after they consumed sweeteners.

- They had fewer receptors on their tongues that detect sweet taste.
- The biological mechanism in their intestines that transports glucose into the blood was altered.

- Their brains had changed, specifically in regions associated with memory control and reward-motivated behavior.

Kanoski and Schier say the findings reveal more questions worth exploring, including:

- How do sweetener substitutes cause a reduction in sweet taste receptors and how does that affect later dietary behavior?
- What does the change in the nutrient transport in the gut mean for health?
- What biological mechanisms link sweetener consumption with the changes to the brain?

The researchers say they intend to explore ways to reverse the long-lasting effects of adolescent low-calorie [sweetener](#) consumption and to study how it influences food choices and preferences later in life.

More information: Linda Tsan et al, Early life low-calorie sweetener consumption disrupts glucose regulation, sugar-motivated behavior, and memory function in rats, *JCI Insight* (2022). [DOI: 10.1172/jci.insight.157714](#)

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