



Invited Commentary | Nutrition, Obesity, and Exercise

Nonnutritive Sweeteners and Neural Reward Response in Women and Individuals With Obesity

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Nonnutritive sweeteners (NNSs) are present in a variety of foods and beverages as a way to provide sweet taste with few or no calories. Sucralose is the most commonly used NNS. Although there is clear evidence that sugar-sweetened foods and drinks contribute to obesity and its related comorbidities as type 2 diabetes, there is a lack of consensus in the scientific community on whether NNSs are beneficial or harmful for health.¹⁻³ Given the growing use of NNSs,⁴ it is of great relevance to resolve the ongoing controversy on the consumption of NNSs. In particular, human studies have been largely limited to male cohorts of normal weight, lacking the effects of individual biological factors on the neurobehavioral and metabolic consequences of NNS ingestion.

The study by Page and colleagues⁵ shows that adiposity and sex are significantly associated with the neurobehavioral outcome of acute sucralose ingestion. Page et al⁵ investigated brain activity, metabolic responses, and eating behaviors after consumption of sucralose (NNS) compared with sucrose (nutritive sugar) among 74 healthy young adults with a wide body mass index (weight in kilograms divided by height in meters squared) range of 19.18 to 40.27. Neural reactivity was examined in response to different visual food cues during a functional magnetic resonance imaging measurement. Blood was sampled at different time points before and after the ingestion of the 300-mL drinks containing either sucrose, sucralose, or water as a control. Ad libitum meals were presented at the end of each measurement day. As expected, endocrine responses were greater after sucrose than sucralose ingestion, but there were no significant differences based on sex and adiposity. The most prominent and novel findings were observed on a neurobehavioral level. Individuals with obesity, but not overweight or healthy weight, exhibited greater neural responses to food images in prefrontal reward-related areas after ingesting sucralose vs sucrose. Moreover, female participants, but not male participants, responded with increased neural food-cue reactivity and consumed more calories during the buffet meal after sucralose compared with sucrose ingestion. This was especially the case for female participants with obesity, who exhibited greater neural responsivity to high-caloric food cues, particularly in the medial and orbital prefrontal cortices. These frontal regions have been shown in previous studies⁶ to represent the reward value and subjective pleasantness of the smell, sight, taste, and texture of food, with stronger activations with increased liking for food. Moreover, the ventromedial prefrontal cortex is implicated in decision-making about the reward value of food, making this region a key player in successful body weight management.⁶

The study by Page and colleagues⁵ is of great importance as it provides novel insights into how adiposity and sex are associated with neural and behavioral outcomes of NNS ingestion. They show for the first time that female individuals with obesity are particularly vulnerable to greater neural responsivity elicited by acute sucralose consumption, particularly in prefrontal reward-associated brain regions. This raises the possibility that adding NNSs to our diet to increase sweetness could impair the brains' responsivity to food, with negative consequences for eating behavior and metabolism, particularly in women. Concomitantly, a recent study¹ suggests that short-term daily consumption of sucralose can alter neural and metabolic sensitivity to sugar when consumed in the presence of carbohydrates. Hence, in addition to the individual biological factors discussed by Page et al,⁵ neurobehavioral and metabolic consequences of NNS ingestion may also depend on how they are consumed.¹ Because freely living humans commonly consume NNSs in combination with a meal, further research is needed to evaluate whether the observed obesity-related and sex-related

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associations in response to sucralose are still observed in combination with specific macronutrients. Furthermore, before recommending or discouraging the use of NNSs as part of a healthful diet, further studies of the effects of NNSs on a variety of neurobehavioral and metabolic outcomes are warranted. The study by Page et al⁵ clearly points out the importance of considering sex and adiposity in future research to give individual tailored dietary recommendations for body weight management.

ARTICLE INFORMATION

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