Obesity impairs the brain's response to nutrients, suggests study

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Brain responses to specific nutrients are diminished in individuals with obesity and are not improved after weight loss, according to a study led by Amsterdam UMC and Yale University, published today in *Nature*

Metabolism.

"Our findings suggest that long-lasting brain adaptations occur in individuals with obesity, which could affect eating behavior. We found that those with obesity released less dopamine in an area of the brain important for the motivational aspect of food intake compared to people with a healthy bodyweight. Dopamine is involved in the rewarding feelings of food intake," says Mireille Serlie, lead researcher and Professor of Endocrinology at Amsterdam UMC.

"The subjects with obesity also showed reduced responsivity in brain activity upon infusion of nutrients into the stomach. Overall, these findings suggest that sensing of nutrients in the stomach and gut and/or of nutritional signals is reduced in obesity and this might have profound consequences for food intake."

Food intake is dependent on the integration of complex metabolic and neuronal signals between the brain and several organs, including the gut and nutritional signals in the blood. This network triggers sensations of hunger and satiation, regulates food intake as well as the motivation to look for food. While these processes are increasingly better understood in animals, including in the context of metabolic diseases such as obesity, much less is known about what happens in humans. Partly due to the difficulty in designing experimental setups in the clinic that could shed light on to these mechanisms.

In order to address this lack of knowledge, Serlie, who is also a professor at Yale, and colleagues from both institutions designed a controlled trial. This trial consisted of infusing specific nutrients directly into the stomach of 30 participants with a healthy bodyweight and 30 individuals with obesity, while simultaneously measuring their brain activity through the use of MRI and dopamine release using SPECT scans.

While the participants with a healthy bodyweight displayed specific patterns of brain activity and dopamine release after nutrient infusion, these responses were severely blunted in participants with obesity. Moreover, 10% body weight loss (following a 12-week diet) was not sufficient to restore these brain responses in individuals with obesity, suggesting long-lasting brain adaptations occur in the context of obesity and remain even after weight loss is achieved.

"The fact that these responses in the brain are not restored after weight loss, may explain why most people regain weight after initially successful weight loss," concludes Serlie.

More information: Mireille Serlie, Brain responses to nutrients are severely impaired and not reversed by weight loss in humans with obesity: a randomized crossover study, *Nature Metabolism* (2023). DOI: 10.1038/s42255-023-00816-9. www.nature.com/articles/s42255-023-00816-9

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