Brain's 'appetite control center' found to be different in people who are overweight or living with obesity

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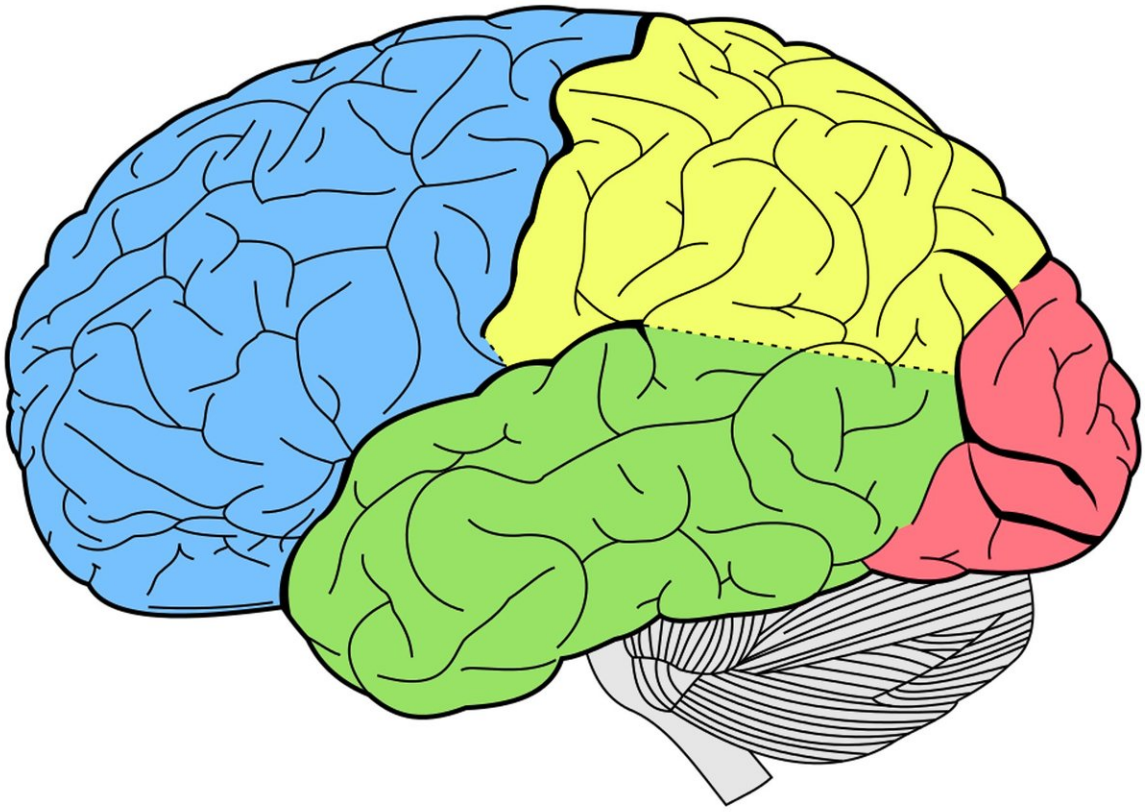

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Cambridge scientists have shown that the hypothalamus, a key region of

the brain involved in controlling appetite, is different in the brains of people who are overweight and people with obesity when compared to people who are a healthy weight.

The researchers say their findings add further evidence to the relevance of brain structure to weight and food consumption.

Current estimations suggest that over 1.9 billion people worldwide are either overweight or obese. In the UK, according to the Office for Health Improvement & Disparities, almost two-thirds of adults are overweight or living with obesity. This increases an individual's risk of developing a number of health problems, including type 2 diabetes, heart disease and stroke, cancer and poorer mental health.

A large number of factors influence how much we eat and the types of food we eat, including our genetics, hormone regulation, and the environment in which we live. What happens in our brains to tell us that we are hungry or full is not entirely clear, though studies have shown that the hypothalamus, a small region of the brain about the size of an almond, plays an important role.

Dr. Stephanie Brown from the Department of Psychiatry and Lucy Cavendish College, University of Cambridge, said, "Although we know the hypothalamus is important for determining how much we eat, we actually have very little direct information about this brain region in living humans. That's because it is very small and hard to make out on traditional MRI brain scans."

The majority of evidence for the role of the hypothalamus in appetite regulation comes from animal studies. These show that there are complex interacting pathways within the hypothalamus, with different cell populations acting together to tell us when we are hungry or full.

To get around this, Dr. Brown and colleagues used an algorithm developed using machine learning to analyze MRI brain scans taken from 1,351 young adults across a range of BMI scores, looking for differences in the hypothalamus when comparing individuals who are underweight, healthy weight, overweight and living with obesity.

In a study published in *Neuroimage: Clinical*, the team found that the overall volume of the hypothalamus was significantly larger in the overweight and obese groups of young adults. In fact, the team found a significant relationship between volume of the hypothalamus and body-mass index (BMI).

These volume differences were most apparent in those sub-regions of the hypothalamus that control appetite through the release of hormones to balance hunger and fullness.

While the precise significance of the finding is unclear—including whether the structural changes are a cause or a consequence of the changes in body weight—one possibility is that the change relates to inflammation. Previous animal studies have shown that a high fat diet can cause inflammation of the hypothalamus, which in turn prompts insulin resistance and obesity.

In mice, just three days of a fat-rich diet is enough to cause this inflammation. Other studies have shown that this inflammation can raise the threshold at which animals are full—in other words, they have to eat more food than usual to feel full.

Dr. Brown, the study's first author, added, "If what we see in mice is the case in people, then eating a high-fat diet could trigger inflammation of our appetite control center. Over time, this would change our ability to tell when we've eaten enough and to how our body processes blood sugar, leading us to put on weight."

Inflammation may explain why the hypothalamus is larger in these individuals, the team say. One suggestion is that the body reacts to inflammation by increasing the size of the brain's specialist immune cells, known as glia.

Professor Paul Fletcher, the study's senior author, from the Department of Psychiatry and Clare College, Cambridge, said, "The last two decades have given us important insights about appetite control and how it may be altered in obesity. Metabolic researchers at Cambridge have played a leading role in this."

"Our hope is that by taking this new approach to analyzing brain scans in large datasets, we can further extend this work into humans, ultimately relating these subtle structural brain findings to changes in appetite and eating and generating a more comprehensive understanding of obesity."

The team say more research is needed to confirm whether increased volume in the hypothalamus is a result of being overweight or whether people with larger hypothalami are predisposed to eat more in the first place. It is also possible that these two factors interact with each other causing a feedback loop.

More information: Stephanie S.G. Brown Conceptualisation et al, Hypothalamic volume is associated with body mass index, *NeuroImage: Clinical* (2023). DOI: 10.1016/j.nicl.2023.103478

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