Medical Xpress

Large genetic analysis identifies numerous gene variants linked with differences in food intake

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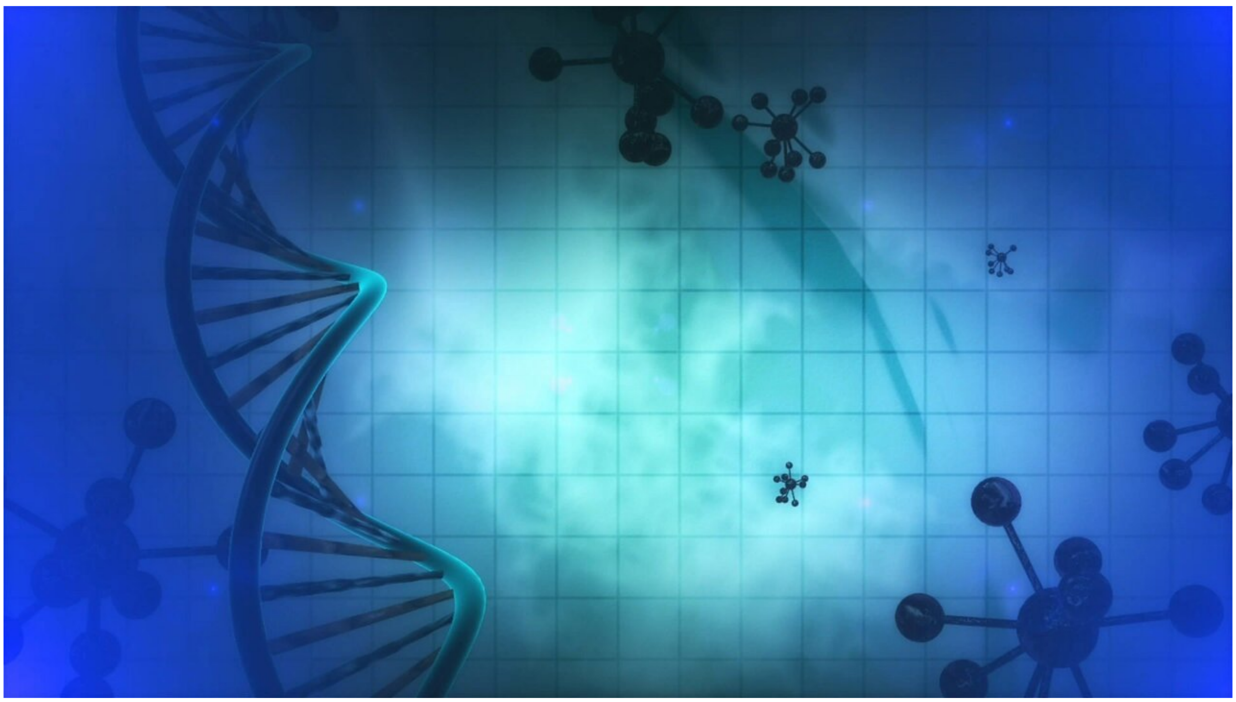

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A team of researchers at Massachusetts General Hospital (MGH), Boston University School of Public Health (BUSPH), and other institutions have identified more than two dozen genetic regions that may affect individuals' food intake. The investigators hope that the discovery, which is described in *Nature Human Behaviour*, will point to new treatment strategies to curb the obesity epidemic.

The brain is influenced by various signals to affect people's eating behaviors and regulate their bodies' energy balance, for example by changing appetite and energy expenditure in response to blood levels of key metabolic hormones and nutrients. Therefore, genetic variation in these signals can lead to extreme hunger and obesity.

"People with obesity and diabetes are often stigmatized for making unhealthy food choices. While food intake is shaped by many factors including social, demographic, religious, or political forces, previous studies have shown that inherited individual differences contribute to what, when, why, or how much we eat," says co–lead author Jordi Merino, Ph.D., a research associate at the Diabetes Unit and Center for Genomic Medicine at MGH and an instructor in medicine at Harvard Medical School. "These early studies are starting to identify brain regions and molecular processes that influence food intake, but there has been limited research in humans to identify molecular signatures underlying variable susceptibility to food choice behavior."

To provide insights, Merino and his colleagues conducted a genetic analysis and examined the food consumption of 282,271 participants of European ancestry from the UK Biobank and the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium. The study is the largest to date to examine genetic factors related to food intake.

The team identified 26 genetic regions associated with increased preference for foods containing more fat, protein, or carbohydrate, and these regions were enriched for genes expressed in the brain. "Downstream computational analyses highlighted specific subtypes of specialized neurons distributed across the central nervous system that are responsive to protein, fat, or carbohydrate, and when activated may explain why people are more likely to prefer foods or meals with higher amount of fat, protein, or carbohydrate," says Merino.

The researchers also found that two main groups of genetic variants were differently associated with obesity and coronary artery disease. "The joint analysis of fat, protein, and carbohydrate intake coupled with clustering analyses helped to define more homogeneous subsets of genetic variants characterized by specific nutritional profiles and with different metabolic signatures," says co-lead author Chloé Sarnowski, Ph.D., an instructor of biostatistics at BUSPH at the time of the study, and now a faculty associate at the University of Texas Health Science Center at Houston.

The discovery of these genetic variants can be used in future analyses—such as Mendelian randomization, a causal inference approach—to determine whether diet composition is causally related to metabolic and other diseases. "While we know that diet composition is related to diseases, the causal link is harder to prove," says co-senior author Josée Dupuis, Ph.D., chair and professor in the Department of Biostatistics at BUSPH. "These loci will allow for future Mendelian randomization analyses to determine the causal impact of diet on type 2 diabetes, obesity, and other metabolic diseases."

The findings will also likely lead to a better biological understanding of why food consumption behavior differs among individuals, and they could provide new avenues for preventing and treating obesity and other metabolic diseases. "Our findings provide a starting point for functional research that might aid in the discovery of new molecular targets and drugs," says co-lead author Hassan Dashti, Ph.D., an instructor in the Department of Anesthesia, Critical Care and Pain Medicine at MGH and instructor of Anesthesia at Harvard Medical School. "Our results could also help identify people more likely to follow specific dietary recommendations for the prevention of obesity or diabetes. For example, if someone has a higher genetic susceptibility for preferring fatty foods, this information can be used to help this individual to choose foods with higher amount of healthy fats rather than recommending other dietary approaches that might compromise adherence to these interventions."

More information: Jordi Merino et al, Genetic analysis of dietary intake identifies new loci and functional links with metabolic traits, *Nature Human Behaviour* (2021). [DOI: 10.1038/s41562-021-01182-w](https://dx.doi.org/10.1038/s41562-021-01182-w)

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