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One high-fat diet, two different outcomes: The path to obesity becomes clearer

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Why is it that two people can consume the same high fat, high-calorie Western diet and one becomes obese and prone to diabetes while the other maintains a slim frame? This question has long baffled scientists, but a study by Yale School of Medicine researchers provides a simple explanation: weight is set before birth in the developing brain.

The results are reported online the week of August 2 in the Proceedings of the National Academy of Sciences.

Led by Tamas Horvath, chair and professor of comparative medicine and professor of neurobiology and obstetrics & gynecology at Yale School of Medicine, the research team analyzed the same question in specific groups of rats. These animals have been bred so that their vulnerability to diet-induced obesity is known before they would be put on high-fat, high-calorie diet diets.

Horvath said animals that become obese already had a significant difference in the feeding center of the brain. Neurons that are supposed to signal when you've eaten enough and when to burn calories, are much more sluggish in these animals because they are inhibited by other cells. In animals resistant to obesity, these satiety signaling neurons are much more active and ready to signal to the rest of the brain and peripheral tissues when enough food has been consumed.

"It appears that this base wiring of the brain is a determinant of one's vulnerability to develop obesity," said Horvath, who is also co-director

of the Yale Program in Integrative Cell Signaling and Neurobiology of Metabolism. "These observations add to the argument that it is less about personal will that makes a difference in becoming obese, and, it is more related to the connections that emerge in our brain during development."

Horvath points to other unwanted consequences of these brain mechanisms. "Those who are vulnerable to diet-induced obesity also develop a brain inflammation, while those who are resistant, do not," he said. "This emerging inflammatory response in the brain may also explain why those who once developed obesity have a harder time losing weight."

Diet-induced obesity has become one of the most critical medical problems in the United States. In particular, the incidence of childhood obesity has reached unprecedented levels. Since genetics alone cannot explain the surge of obesity in society, investigators have been trying to determine the primary underpinnings of the vulnerability to develop obesity on a Western diet.

"What genetic, epigenetic and environmental factor determines this base wiring in the brain is a very important issue to address," said Horvath. "Specifically, the emerging view is that besides genetics, maternal impact on the developing brain is likely to be critical to imprint these feeding circuits thereby determining one's vulnerability or resistance to obesity."

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