Offspring of mice fed imbalanced diets shown to be neurologically 'programmed' for obesity

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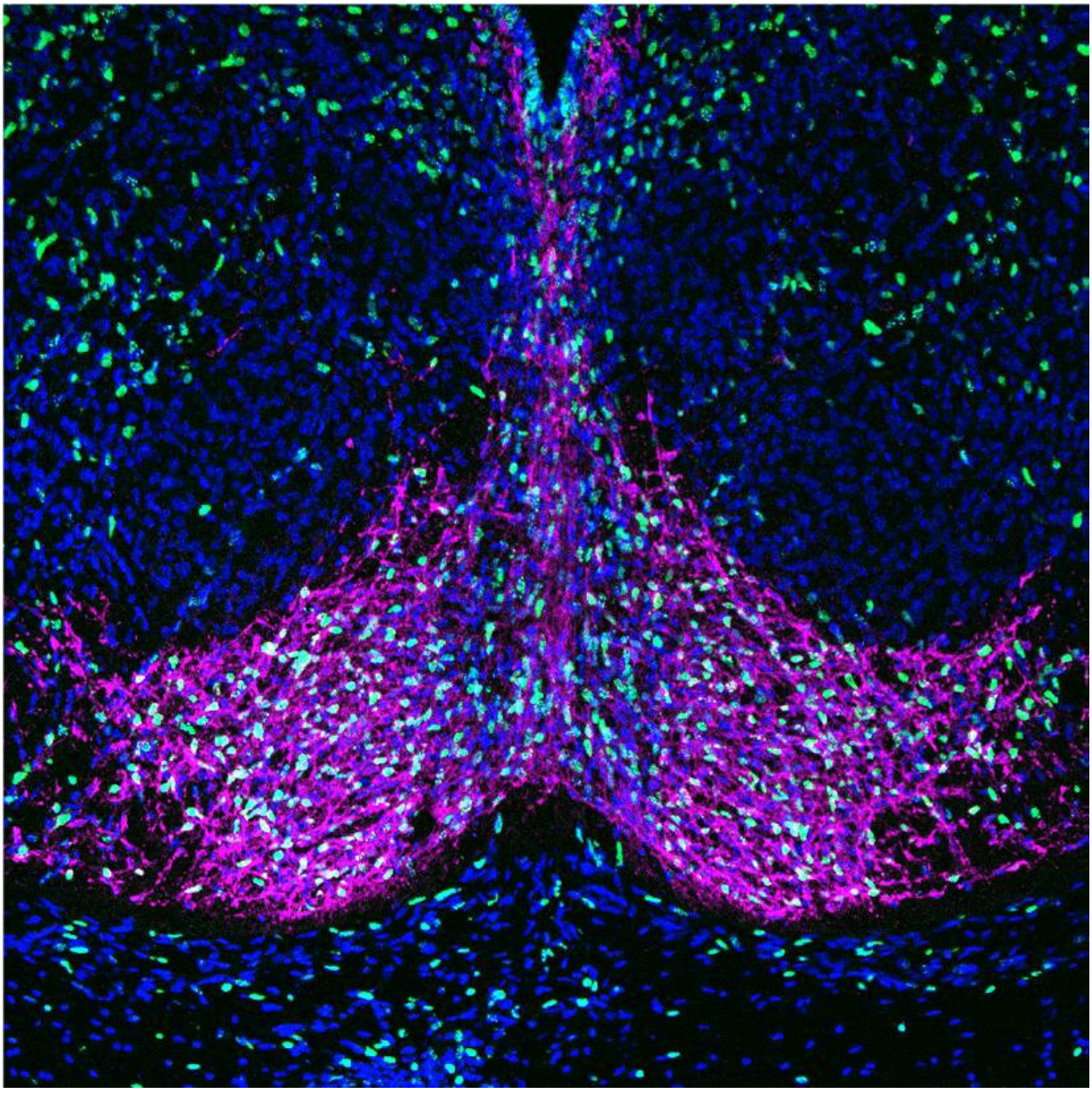

Newly generated brain cells that release dopamine, which drive hedonic eating in adulthood. Image caption: The magenta staining shows brain cells that release dopamine. The green staining shows newly generated cells. The blue staining shows all cells. Image credit: Nobuyuki Sakayori, Hiroshima University. Image usage restrictions: News organizations may use or redistribute this image, with proper attribution, as part of news coverage of this paper only. Credit: Hiroshima University

Pregnant mice fed a diet high in omega-6 fats and low in omega-3 fats produce offspring that go on to exhibit "hedonic"—pleasurable but excessive—levels of consumption of hyper-caloric diets, according to researchers at Hiroshima University.

Omega-6 fats are found in grapeseed oil, corn oil and sesame oil, and are a staple of several salad dressings in world cuisine. Omega-3 fats are found in fish, perilla oil, and linseed oil. A diet balanced with these fats is considered essential for healthy brain growth.

The researchers also found that the offspring exhibit increased in utero growth of dopamine-producing neurons in the midbrain—the neurological reward system. They believe that exposure to this high omega-6/low omega-3 diet increases growth in these neurons in the fetus's brain during a specific period during pregnancy, driving dopamine release in the offspring's brain, and thus primes the offspring for hedonic consumption of sugar- or fat-rich diets over the course of their life.

The findings were published in the peer-reviewed journal *Communications Biology*, on August 28.

Meanwhile, mice whose mothers had not consumed the imbalanced omega-6/omega-3 diet did not exhibit as much overeating behavior, even when tempted by the presence of such food.

Since the 1960s, the Western diet has experienced a significant uptick in the presence of polyunsaturated omega-6 fats, and in ratios to polyunsaturated omega-3 fats that historically humans had never experienced before.

The ratio between these two types of fats is important because biochemically they compete with each other for incorporation into cell membranes, and an omega-6/omega-3 imbalance in the membranes of red blood cells is correlated with weight gain. An earlier study on mice had found that consumption of an imbalanced omega-6/omega-3 diet by the pregnant mother replicates this imbalance in the offspring's brain and even impairs brain development.

The Hiroshima researchers also found that a dopamine-inhibiting drug eliminates the hedonic consumption of the offspring, further supporting the notion that the dopamine signaling plays a critical role in driving this behavior.

"This suggests that adult mice gorging themselves on hyper-caloric diets were in effect neurologically programmed to do so by their mother's own consumption patterns," said Nobuyuki Sakayori, paper author and assistant professor from the Graduate School of Biomedical and Health Sciences at Hiroshima University.

The scientists were keen to stress that the ratio of omega-6 to omega-3 fat in the mouse diet is much higher than that experienced by most humans, and that their work lays the foundation for further, epidemiological studies on humans to see if the pattern holds for us.

But if it does, this could provide a new strategy for preventing obesity in children by managing the type of fats that pregnant mothers consume, akin to how mothers today generally avoid consumption of alcohol.

"This could work much better than existing anti-obesity campaigns or food taxes," Sakayori continued, "because instead of fighting against the brain's reward system, such a strategy focuses right from the start on the development of that system."

More information: Nobuyuki Sakayori et al. Maternal dietary imbalance between omega-6 and omega-3 fatty acids triggers the offspring's overeating in mice, *Communications Biology* (2020). DOI: 10.1038/s42003-020-01209-4

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