

# Obesity may be wired in the brain, rat study suggests

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A predisposition for obesity might be wired into the brain from the start, suggests a new study of rats in the February issue of *Cell Metabolism*.

Rats selectively bred to be prone to obesity show abnormalities in a part of the brain critical for appetite control, the researchers found. Specifically, the researchers show that the obese rats harbor defects in neurons of the arcuate nucleus (ARH) of the hypothalamus, which leaves their brains less responsive to the hunger-suppressing hormone leptin.

“The neurodevelopmental differences in these animals can be seen as early as the first week,” said Sebastien Bouret of the University of Southern California. “The results show that obesity can be wired into the brain from early life. The three-million-dollar question now is how to get around this problem.”

It is increasingly accepted that obesity results from a combination of genetic and environmental factors, the researchers said. Rodent models of obesity can provide valuable insights into the biological processes underlying the development of obesity in humans. The “diet-induced obese” (DIO) rats used in the current study are particularly suited to the task, according to Bouret, because their tendency to become overweight shares several features with human obesity, including the contribution of many genes.

Previous studies had suggested that the brains of DIO rats are insensitive to leptin, the researchers added. Circulating leptin, produced by fat

tissue, acts as a signal to the brain about the body's energy status. Leptin is also critical for the initial development of ARH neurons.

In the new study, the researchers examined the obesity-prone rats for signs of abnormal brain development. They found that the animals' brains had fewer neural projections from the ARH, a deficiency that persisted into adulthood. Those projections are needed to relay the leptin signal received by the ARH to other parts of the hypothalamus, Bouret said.

The researchers found further evidence that those changes in brain wiring stem from a reduced responsiveness of the brain to leptin's action during development.

“It seems [in the case of these rats] that appetite and obesity are built into the brain,” Bouret said. While their condition might be ameliorated by exercising and eating right, he added, the findings suggest that the propensity to gain weight can't be reversed.

But there is hope yet. It's possible that treatments delivered during a critical early period of development might be capable of rewiring the brain, Bouret said.

Source: Cell Press

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