Hunger hormone in infancy may link to lifelong obesity risk

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Credit: Anna Langova/public domain

Our subconscious motivation to eat is powerfully and dynamically regulated by hormone signals. The gut-derived hormone ghrelin is one such key regulator, promoting appetite through its effects on neurons in a small region of the brain called the hypothalamus.

Researchers at The Saban Research Institute of Children's Hospital Los

Angeles now reveal an unexpected role for ghrelin in early brain development and show its long-term impact on appetite regulation. Their study will be published online January 20 by *The Journal of Clinical Investigation*.

"We've shown that neonatal ghrelin directly influences development in the part of the brain related to appetite and the regulation of metabolism," said principal investigator Sebastien G. Bouret, PhD, of the Developmental Neuroscience Program at CHLA and associate professor of Pediatrics at Keck School of Medicine of the University of Southern California. "This study suggests a link between maturation of the gut-brain axis and later susceptibility to obesity, diabetes and cardiovascular disease."

Body weight and energy balance are regulated by a sophisticated network of neural circuits. At its center is a collection of neurons or nerve cells in the hypothalamus of the brain called the arcuate nucleus, which contains sets of neurons that are sensitive to peripheral signals, such as metabolic hormones. For example, when the stomach is empty, ghrelin is secreted and acts on the arcuate nucleus to initiate feeding. However, until now, little was known about the importance of ghrelin on development of brain mechanisms regulating body weight and appetite.

The researchers identified the physiological and neurobiological importance of ghrelin during early life, conducting two types of experiments in mice. They blocked the hormone soon after birth, which resulted in more axonal projections in the arcuate nucleus and caused lifelong metabolic disturbances, including obesity and diabetes. They also increased ghrelin levels during this key developmental period and found that it impaired the normal growth of arcuate projections and caused metabolic dysfunction.

"Our study underlines the importance of maintaining a healthy hormonal

balance - including ghrelin - during early life, to ensure proper development of brain-feeding centers," said Bouret, adding that the correct timing and amount of both hormones is necessary for normal development of neural circuits in the hypothalamus.

Clinically, an elevated ghrelin level is a hallmark of patients suffering from Prader-Willi Syndrome. This elevation occurs prior to the development of obesity in such patients, which is caused by the insatiable hunger that is a symptom of the disorder. Patients with the syndrome also have a slowed metabolism.

"A better understanding of the relationship between ghrelin levels early in life and the development of disorders such as Prader-Willi syndrome or childhood obesity will be crucial as we seek to develop interventional studies to treat and, hopefully, reverse symptoms of metabolic diseases," Bouret concluded.

Provided by Children's Hospital Los Angeles