MedicalXpress

New method reveals roles of GABA in the control of appetite and metabolism

March 15 2016, by Dipali Pathak

In the last 40 years, obesity has more than doubled around the world. In the United States, the average American is more than 24 pounds heavier today than in 1960. Researchers at Baylor College of Medicine, Technion-Israel Institute of Technology and the University of Washington are studying the problem of obesity from the inside out.

The researchers developed a new laboratory method that allowed them to identify GABA as a key player in the complex brain processes that control appetite and metabolism. The team's results were published in the journal *Proceedings of the National Academy of Sciences*.

Dr. Qi Wu, assistant professor of pediatrics at the USDA/ARS Children's Nutrition Research Center at Baylor and Texas Children's Hospital led the team that for several years searched for new laboratory methods to better study the function of GABA in the brain.

GABA is a chemical messenger produced by brain cells. It binds to other brain cells via specific receptors and reduces the cells' activity. Research has implicated GABA in the complex neurological processes that control fear and anxiety, and also in those related to the control of appetite and metabolism. But direct proof of the role GABA plays in weight control has been elusive in part for the lack of better methodology to precisely control GABA production by brain cells.

"We developed a new experimental system based in in-frame, nonsense mutations and aminoglycosides, which allowed us to abruptly stop the

synthesis of GABA in adult animals," Wu said. "We were able to silence the genes involved in the synthesis of GABA in a particular set of cells located in the hypothalamus, the brain area that controls appetite. As a result, these cells, called AgRP neurons, stop producing GABA as quick as in four days."

Wu and colleagues then observed the changes in weight and the behavior of these mice lacking GABA in their brain area for control of appetite.

The researchers studied two groups of mice; two month old young adults, and 8 month old mice. The young adult mice without GABA stopped eating, lost tremendous amount of weight, increased their physical activity and became glucose intolerant. On the other hand, the much older mice only lost their appetite temporarily.

The findings are significant to the study of obesity as they strongly indicate that GABA is a potential candidate for targeted drug design that may lead to medications that help control appetite and metabolism.

"Our hope is that the new and better methodology we have developed will be used by other genetics labs as a tool for selectively silencing other genes," Wu said.

More information: Fantao Meng et al. New inducible genetic method reveals critical roles of GABA in the control of feeding and metabolism, *Proceedings of the National Academy of Sciences* (2016). DOI: 10.1073/pnas.1602049113

Provided by Baylor College of Medicine