Research on obesity targets the brain's use of fatty acids

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Researchers at the University of Colorado School of Medicine have created a new and exciting mouse model to study how lipid sensing and metabolism in the brain relate to the regulation of energy balance and body weight. The research team, led by Hong Wang, PhD, created mice with a deficiency of lipoprotein lipase (LPL) in neurons, and observed two important reactions. First, the mouse models ate more and second, they became sedentary. Because LPL is important to the delivery of fatty acids to the brain, these responses spotlight the importance of fatty acid delivery to the brain in the regulation of body weight.

"This work may have important impact in understanding the causes of obesity and providing new treatments for this epidemic of our time," said Robert H. Eckel, MD, corresponding and senior author of "Deficiency of Lipoprotein Lipase in Neurons Modifies the Regulation of Energy Balance and Leads to Obesity" which was published today in Cell Metabolism.

The genetically-modified mouse (NEXLPL) has a defect in the breakdown of dietary lipoprotein triglycerides into fatty acids in the brain. These mice became obese on a standard chow diet between three and six months. At that point, the mice ate less and were less active.

The research also looked at which areas of the brain have the greatest impact on regulating body weight and learned that the hypothalamus may be the key area to observe as NEXLPL mice have increases in hypothalamic AgRP/NPY gene expression before obesity. AgRP/NPY

cause increases in food intake and decreases in energy expenditure. Researchers also noted that the NEXLPL mice demonstrate deficiencies in n-3 fatty acids in the hypothalamus. Overall, this research indicates that the lipoproteins are sensed in the brain by an LPL-dependent pathway and provide lipid signals for the central regulation of body weight and energy balance.

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