Sex hormone signaling helps burn calories

February 26 2007

Heavyweight. Female mice without a receptor for an estrogen hormone in the part of their brain linked to energy balance grew to several times the weight of normal mice. Scientists say the weight gain was linked not to overeating, but to a lack of physical activity. Credit: Rockefeller University

Any dieter can tell you: Body weight is a function of how much food you eat and how much energy you use. The trick to maintaining a healthy weight lies in regulating the balance. Now new research from Rockefeller University suggests that brain cell receptors linked to sex hormones may play a role in the process by which we maintain that balance.

The findings show that metabolic syndrome, a cluster of conditions that includes obesity, insulin resistance and reduced physical activity, occurs in female mice when estrogen signaling in specific areas of the brain is shut down.

“It is well documented that mice missing the gene for estrogen receptor a become obese,” says Pfaff, head of the Laboratory of Neurobiology and Behavior. “But because every cell in these ‘knockout’ mice has been missing estrogen signaling from birth, these results are confounded by potential effects on overall brain development. Using a targeted approach, we interfered with the receptor’s synthesis only in the neurons in the ventromedial nucleus of the hypothalamus, and found that these mice also become obese.”

The ventromedial nucleus plays an essential role in the control of energy balance: When intentionally harmed, the mice become obese. Nerve cells in this area of the brain also express estrogen receptor a at very high levels.

Using a novel method of genetic manipulation developed by Sergei Musatov, a former postdoc and first author of the current paper, the scientists tested the role of estrogen receptor alpha in specific areas of the brain. The technique uses a virus to deliver strands of interfering RNA to the neurons that would halt production of the estrogen receptor a protein. The affected mice immediately started to gain weight, even though the amount of food they were initially eating didn’t change.

“We found that the increase in food was secondary, the weight gain occurred first and the mice started to eat more simply to maintain their new body weight,” says Musatov. “Estrogen signaling obviously plays an important role in the ventromedial nucleus to help maintain normal body weight.”

The mice missing estrogen receptor alpha also expended less energy – they were less active than regular mice and had a slower metabolism. They also developed several hallmark features of metabolic syndrome in humans, including glucose intolerance and resistance to insulin.

Citation: *Proceedings of the National Academy of Sciences* 104(7): 2501-2506 (February 13, 2007)

Source: Rockefeller University