Body fat hormone leptin influences runner's high
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Leptin is a fat cell-derived hormone that signals to the brain when the body has enough fuel and energy. Low leptin levels have been previously shown to be associated with exercise addiction, fast marathon times, and training status in humans and also correlate with greater running speed and duration in mice. Despite these associations, the role leptin played in the process of runner's high, the feeling of euphoria associated with endurance running, was unknown.

To address this question, Fulton and her team used genetically engineered mice that lack a leptin-sensitive protein called STAT3, which relays the leptin signal specifically in neurons that release the reward chemical dopamine. While normal mice ran 6 kilometers per day on a running wheel, the STAT3-deficient mice ran an impressive 11 kilometers per day.

Moreover, STAT3-deficient mice spent more time in the side of the chamber associated with running than did normal mice, suggesting that a drop in leptin-induced STAT3 signaling increases the rewarding effects of running. STAT3 deficiency also led to blunted dopamine signaling, which has been linked to enhanced reward seeking in humans.

The findings could also have clinical implications for anorexia. Past research has shown that leptin signaling in the brain's reward center inhibits wheel running in a rat model of anorexia-induced hyperactivity. Moreover, individuals with anorexia have low fat-adjusted leptin levels that are associated with increased restlessness and hyperactivity. "We speculate that the mechanism described in this work could potentially underlie the hyperactivity associated with anorexia," Fulton says.

In future studies, Fulton and her team will test their hypothesis of running reward being associated with food seeking. They will also examine which neural pathways downstream of dopamine neurons...
contribute to the runner's high, may have evolved to enhance stamina, and increase the probability of success while foraging and hunting.

"We do not want people to think that leptin is the only metabolic signal controlling the rewarding effects of running. Likewise, dopamine is not the only brain chemical involved," Fulton says. Now that leptin's role in runner's high is beginning to be established, "More work is needed to parcel out the precise contribution of dopamine, opioid, and endogenous cannabinoid signals and the manner by which they interact to impact physical activity and its rewarding effects."

More information: Cell Metabolism, Fernandes et al.: "Leptin Suppresses the Rewarding Effects of Running via STAT3 Signaling in Dopamine Neurons" dx.doi.org/10.1016/j.cmet.2015.08.003

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