Fat hormone influences baseline dopamine levels and our motivation to eat

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As we all know from experience, people eat not only because they are hungry, but also because the food just simply tastes too good to pass up. Now, a new study in the August 6th *Cell Metabolism,* a Cell Press publication, helps to explain how leptin, a hormone produced by fat tissue, influences that motivation to eat.

The researchers describe for the first time a new bunch of leptin-responsive (LepRb) neurons in the brain's lateral hypothalamic area (LHA). Those LHA neurons feed directly into the mesolimbic dopamine system seated in the ventral tegmental area (VTA) of the brain, which controls the rewarding properties we assign to things.

"Dopaminergic neurons in the VTA and their downstream targets represent the site of action for drugs of abuse, and also control motivation for food, sex or a fancy car," explained Martin Myers, Jr., of the University of Michigan, Ann Arbor. Put simply, "they control our wanting of stuff."

The study therefore adds to growing evidence that leptin doesn't turn the appetite on and off just by controlling satiety - for instance, whether we feel hungry or full.

"Most who have studied leptin in the brain have focused on an important circuit in the ARC," and the leptin-responsive neurons there, Myers said. ARC stands for arcuate nucleus and is an area in the brain's hypothalamus that controls energy balance by controlling satiety. "It has

been assumed that leptin action in the ARC - if not the be all and end all - was responsible for the vast majority of leptin's effect on appetite."

But in fact, neurons bearing leptin receptors exist in many other parts of the brain too. Earlier studies revealed the role of leptin action on the VTA and its influence on dopamine. The new findings show that leptin also has direct effects on the LHA, which in turn exerts greater influence on the dopamine system of the VTA.

The new study shows that leptin injected in the LHAs of rats causes the animals to eat less and lose weight. Leptin action in the LHA also raises dopamine content in the brains of otherwise leptin-deficient animals.

While in general higher dopamine release tends to be associated with wanting things - food or something else - Myers said he suspects the higher dopamine at baseline may in fact dampen the response to food temptations, making them easier to resist.

"Some people may over-eat rewarding food because of a perceived 'reward deficit,'" Myers suggested. "When leptin is turned up, it might fix that deficit and make us feel better about a lot of things."

It's not yet clear how the leptin-responsive neurons in the LHA and VTA work together to control dopamine and with it our motivations, according to the researchers.

"The unique roles played by these subpopulations of LHA LepRb neurons, as well as those played by VTA LepRb neurons, remain unclear, but could include the requirement for leptin to differentially regulate specific populations of midbrain dopamine neurons and/or to distinctly modulate the incentive for feeding relative to other behaviors. Going forward, it will be important to determine how these various populations of mesolimbic dopamine system-interacting LepRb neurons

differ in terms of their wiring and the control of different aspects of mesolimbic dopamine signaling."

The new findings do highlight the LHA neurons as a major link between leptin's anorectic action and the mesolimbic dopamine system, they conclude. "These findings reveal important mechanisms that underlie the regulation of the mesolimbic dopamine system by a crucial signal of energy stores. In the future, it will be crucial to address the potential dysregulation of these neurons in states of obesity."

Source: Cell Press (news : web)