

Food restriction increases dopamine receptor levels in obese rats

October 25 2007

A brain-imaging study of genetically obese rats conducted at the U.S. Department of Energy's Brookhaven National Laboratory provides more evidence that dopamine - a brain chemical associated with reward, pleasure, movement, and motivation - plays a role in obesity. The scientists found that genetically obese rats had lower levels of dopamine D2 receptors than lean rats. They also demonstrated that restricting food intake can increase the number of D2 receptors, partially attenuating a normal decline associated with aging.

"This research corroborates brain-imaging studies conducted at Brookhaven that found decreased levels of dopamine D2 receptors in obese people compared with normal-weight people," said Brookhaven neuroscientist Panayotis (Peter) Thanos, lead author of the current study, which will be published in the journal *Synapse*.

It's not clear whether reduced receptor levels are a cause or consequence of obesity: Overeating may chronically reduce receptor levels, which, over the long term, could eventually contribute to obesity. But having genetically low receptor levels may also lead to obesity by predisposing the individual to overeating in an attempt to stimulate a "blunted" reward system. Either way, revving up receptor levels by restricting food intake could enhance the impact of this common strategy for combating obesity.

"Consuming fewer calories is obviously important for people trying to lose weight, plus improving the brain's ability to respond to rewards



other than food may help prevent overeating," Thanos said. Because food intake can have such a dramatic effect on dopamine receptor levels, "this study also provides further evidence for the interplay of genetic factors with the environment in the development of obesity in our society," he said.

The finding that food restriction can attenuate the effects of aging on the brain's ability to respond to dopamine may also help explain why food restriction slows down other changes associated with aging, such as declines in locomotor activity and sensitivity to reward.

Study methods and main findings

The researchers measured dopamine D2 receptor levels in adolescent and young adult genetically obese Zucker rats and lean rats. Between measures, half of the rats in each group were given free access to food while the other half were given 70 percent of the daily average amount of food eaten by the unrestricted group.

The scientists measured D2 receptor levels using two different techniques: micro-positron emission tomography (microPET) in living animals, which uses a radioactively tagged molecule that competes with the brain's natural dopamine for D2 receptor binding sites, and autoradiography, which uses a tracer that binds more strongly than natural dopamine but can only be used in tissue samples rather than in living animals. Together these two methods indicate the absolute number of D2 receptors found in the brain and how many are available or free during day-to-day function, which might be relevant to further elucidating the role of dopamine in obesity.

One main finding was that the overall number of D2 receptors was lower in obese than in lean rats. Also D2 receptor levels decreased with age, but this decline was significantly blunted in food-restricted rats



compared with those given free access to food. This attenuation was most apparent in the obese rats.

Another main finding was that D2 receptor availability - that is, the number of receptors available for binding dopamine - was greater at adulthood in the obese rats compared to the lean rats. This suggests that perhaps the release of dopamine had significantly decreased with age in the obese unrestricted animals more than in the restricted ones or the lean rats. The possibility of lower release of dopamine in obese subjects is presently being examined, the researchers say.

Source: Brookhaven National Laboratory

Citation: Food restriction increases dopamine receptor levels in obese rats (2007, October 25) retrieved 10 April 2024 from

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