

Blunted Activation of Brain Reward Circuitry Increases Risk for Future Weight Gain

In the October 17, 2008 issue of *Science*, Oregon Research Institute (ORI) senior scientist Eric Stice, Ph.D., and colleagues provide evidence that blunted activation of brain regions when eating is related to current and future weight gain in young females. Results from two studies – the first prospective brain imaging studies on the development of obesity as it relates to decreased dopamine output -- suggest that individuals who experience weaker activation of reward circuitry when eating are more likely to be obese and are more likely to gain weight over time. This effect is even more pronounced for people with a gene that is associated with compromised dopamine signaling in this brain reward circuitry.

These studies are the result of a unique collaborative effort between clinical psychologists from Oregon Research Institute and the University of Texas and sensory neuroscientists from the John B. Pierce Laboratory and the Yale University School of Medicine. The research was funded by a grant (R1MH64560A) from the National Institutes of Health Roadmap for Medical Research.

“Although recent findings suggested that obese individuals may experience less pleasure when eating, and therefore eat more to compensate, this is the first prospective evidence for this relationship,” notes Stice. “The evidence of temporal precedence suggests it is a true vulnerability factor that predates obesity onset. In addition, the evidence that this relation is even stronger for individuals at genetic risk for compromised signaling in these brain regions points to an important biological factor that appears to increase risk for obesity onset.”

Dopamine is the primary neurotransmitter involved in the reward pathways in the brain. Food intake is associated with dopamine release and the degree of pleasure from eating correlates with the amount of dopamine release. Evidence shows that obese relative to lean humans have fewer dopamine (D2) receptors in the brain and it is thought that obese individuals overeat to compensate for this reward deficit. People with fewer of the dopamine receptors need to take in more of a rewarding substance -- such as food or drugs -- to get an effect that other people get with less.

Using Functional Magnetic Resonance Imaging (fMRI), Stice’s team measured the extent to which a certain area of the brain (the dorsal striatum) was activated in response to the individual’s receipt of a taste of chocolate milkshake (versus a tasteless solution). Participants in the studies were also tested for the presence of a genetic variation linked to a lower number of dopamine D2 receptors, the Taq1A1 allele. Researchers tracked

participants' changes in body mass index (BMI) over a 1-year follow up. Results showed that those participants with decreased striatal activation in response to milkshake receipt and those with the A1 allele were more likely to gain weight over time.

“These results suggest that individuals with hypofunctioning reward circuitry are at increased risk for unhealthy weight gain,” said Stice. “Thus, it is possible that behavioral or pharmacological interventions that correct this reward deficit may help prevent and treat obesity – an avenue we are currently pursuing in our research.”

Funded by the National Institutes of Health (NIH), Stice has been studying eating disorders and obesity for 18 years. He has conducted this line of research at Stanford University and the University of Texas, and now continues at the Oregon Research Institute in Eugene, Oregon. This research program has produced several prevention programs that reliably reduce risk for onset of eating disorders and obesity.

Oregon Research Institute is a non-profit, independent behavioral research center with headquarters in Eugene. Founded in 1960, it also has offices in Portland, Oregon and Albuquerque, New Mexico.

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