Obesity predisposition traced to the brain's reward system

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The tendency toward obesity is directly related to the brain system that is involved in food reward and addictive behaviors, according to a new study. Researchers at Tufts University School of Medicine (TUSM) and colleagues have demonstrated a link between a predisposition to obesity and defective dopamine signaling in the mesolimbic system in rats. Their report appears in the August 2008 issue of *The FASEB Journal*.

The mesolimbic system is a system of neurons in the brain that secretes dopamine, a neurotransmitter or chemical messenger, which mediates emotion and pleasure. The release of the neurotransmitter dopamine in the mesolimbic system is traditionally associated with euphoria and considered to be the major neurochemical signature of drug addiction.

"Baseline dopamine levels were 50 percent lower and stimulated dopamine release was significantly attenuated in the brain reward systems of obesity-prone rats, compared with obesity-resistant rats. Defects in brain dopamine synthesis and release were evident in rats immediately after birth," said Emmanuel Pothos, PhD, assistant professor in the department of pharmacology and experimental therapeutics at TUSM and member of the neuroscience program faculty of the Sackler School of Graduate Biomedical Sciences.

"Previous research has demonstrated that food intake leads to an increase in the release of dopamine, in the circuits that mediate the pleasurable aspects of eating," Pothos explains. "Also, chronic food deprivation resulting in decreased body weight leads to decreased

dopamine levels. Therefore, increased food intake may represent a compensatory attempt to restore baseline dopamine levels."

Pothos says, "These findings have important implications in our understanding of the obesity epidemic. The notion that decreased dopamine signaling leads to increased feeding is compatible with the finding from human studies that obese individuals have reduced central dopamine receptors." He speculates that an attenuated dopamine signal may interfere with satiation, leading to overeating.

Pothos and colleagues conducted their research using obesity-prone and obesity-resistant rats. Adult obesity-prone rats consumed more food and were 20% heavier than obesity-resistant rats.

The researchers measured electrically-evoked dopamine release from nerve terminals. "We also measured regulators of dopamine synthesis and release in midbrain dopamine pathways," explains Brenda Geiger, first author and graduate student in the pharmacology and experimental therapeutics department at TUSM. "Our molecular analysis suggests that the central dopamine deficits are most likely caused by reduced expression of the genes encoding two proteins, one that is involved in dopamine synthesis, and another that is a transporter responsible for packaging dopamine into vesicles from which it is later released upon stimulation."

"Obesity has so far been approached mostly as a metabolic rather than as an addictive disorder; and obesity research has primarily focused on brain systems that regulate body weight through the maintenance of energy balance. The current study challenges this approach by focusing on brain pathways implicated in pleasure and reward. These pathways could override energy balance and induce hyperphagia and obesity by altering the reward value of food, particularly palatable high-energy food, very early in life," says Pothos, who is the study's corresponding

and senior author.

According to Gerald Weissmann, MD, editor-in-chief of *The FASEB Journal*, "Now we know why so many people stay addicted to food: it fuels the mid-brain pleasure machinery. We eat not only for nourishment, but also for pleasure. This study provides the molecular link between eating and mental health." *The FASEB Journal* (http://www.fasebj.org) is published by the Federation of American Societies for Experimental Biology (FASEB).

Source: Tufts University