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Study Offers New Clues to Brain-Stomach Interaction in Overeating

Findings implicate brain circuits involved in drug craving and emotional response to food

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UPTON, NY - Researchers at the U.S. Department of Energy's Brookhaven National Laboratory have found new clues to how the brain and the stomach interact with emotions to cause overeating and obesity. By looking at how the human brain responds to "fullness" messages sent to the brain by an implanted device that stimulates the stomach, the scientists have identified brain circuits that motivate the desire to overeat in the obese - the same circuits that cause addicted individuals to crave drugs. The scientists have also verified that these circuits play a critical role in eating behaviors linked to soothing negative emotions. The study appears in the October 17, 2006 issue of the Proceedings of the National Academy of Sciences, published online in PNAS Early Edition the week of October 2.

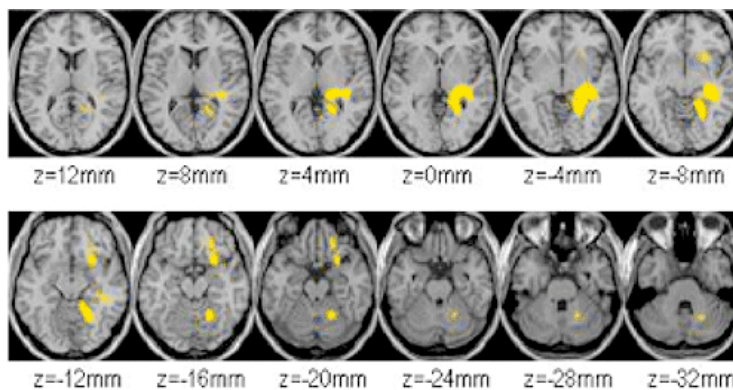
"This study opens new territory in understanding how the body and brain connect to each other, and how this connection is tied to obesity," said lead author Gene-Jack Wang of Brookhaven Lab's [Center for Translational Neuroimaging](#). "We were able to simulate the process that takes place when the stomach is full, and for the first time we could see the pathway from the stomach to the brain that turns 'off' the brain's desire to continue eating."

Wang and colleagues studied the brain metabolism of seven obese individuals who had gastric stimulators implanted for one to two years. The stimulator, an investigational device much like a pacemaker, provides low levels of electrical stimulation to the vagus nerve, causing the stomach to expand and produce peptides that send messages of "fullness" to the brain. The device has been shown to reduce the desire to eat. This study provides the first direct evidence of which brain regions are involved in this response and gives new clues to how satiety signals sent by the stomach affect eating behavior.

Participants in the study received two separate positron emission tomography (PET) brain scans two weeks apart: one with the gastric stimulator on, the other with the stimulator off. Participants were not told whether their stimulator was on or off. Prior to the scans, subjects were injected with a radioactively labeled form of glucose, which the scanner could track to monitor brain metabolism.



[Gene-Jack Wang](#) (click image to download hi-res version)



These brain images highlight the regions that had higher metabolic activity during gastric stimulation (the "on" condition) compared with when the stimulator was off. These were the right hippocampus, the right cerebellum, the right orbitofrontal cortex, and the right striatum.

"We found that implantable gastric stimulators induced significant changes in metabolism in brain regions associated with controlling emotions, effectively shutting down these obese subjects' desire to eat," said Wang.

The changes were particularly pronounced in the hippocampus, where metabolism was 18 percent higher during gastric stimulation. The hippocampus is linked with emotional behaviors, learning and memory, and processing of sensory and motor impulses. The hippocampus also plays a role in the retention of memories related to prior drug experiences in addicted individuals, implying that memories of satiety in the obese might also be stimulated by hippocampal activation.

The stimulators also sent messages of satiety to brain circuits in the orbitofrontal cortex and striatum, which have been linked to craving and desire for drugs in drug-addicted patients.



At each brain scanning session, participants were also asked to answer a questionnaire, which measured three aspects of eating behavior: cognitive restraint, uncontrolled eating, and emotional eating. The questionnaire determined correlations between eating behaviors and areas of the brain activated by the stimulator. During gastric stimulation, scores on a measure of self-described "emotional eating" were 21 percent lower than when the stimulator was off.

[Click here](#) to view a video of Gene-Jack Wang explaining the implications of this research (Real player required.)

"This provides further evidence of the connection between the hippocampus, the emotions, and the desire to eat, and gives us new insight into the mechanisms by which obese people use food to soothe their emotions," said Wang. "This new pathway should be explored in further studies to determine if there are any implications for treating or preventing obesity."

The study was funded by the Office of Biological and Environmental Research of the U.S. Department of Energy's Office of Science, the National Institute on Drug Abuse (NIDA), the Intramural Research Program of the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and the General Clinical Research Center at University Hospital Stony Brook. Study coauthors include Nora Volkow, Director of NIDA; Julia Yang, Frank Telang, Yeming Ma, Christopher Wong, Dardo Tomasi, Peter Thanos, and Joanna Fowler at Brookhaven Lab (with Telang, Ma, and Thanos working under the auspices of NIDA and NIAAA's Intramural Research Program; Fowler has a dual appointment at the Mount Sinai School of Medicine); and Wei Zhu, Stony Brook University. Yang was an employee of implantable gastric stimulator manufacturer Transneuronix, Inc. (now part of Medtronic) at the time of the study; the company provided no funding. DOE has a long-standing interest in research on brain chemistry gained through brain-imaging studies. Brain-imaging techniques such as MRI and PET are a direct outgrowth of DOE's support of basic physics and chemistry research.

Note to local editors: Gene-Jack Wang lives in Port Jefferson, New York.

NOTE: The current study is part of a major focus of research at Brookhaven Lab on the neurobiology of eating disorders and obesity and their treatment. Earlier studies at the Lab have shown that levels of dopamine receptors, which receive chemical messages of well being and reward in the brain, are decreased in the brains of obese individuals (<http://www.bnl.gov/bnlweb/pubaf/pr/2001/bnlpr020101.htm>); that parts of the brain responsible for sensation in the tongue, mouth, and lips are more active in the obese (<http://www.bnl.gov/bnlweb/pubaf/pr/2002/bnlpr062002.htm>); and that the mere sight and smell of favorite foods spikes levels of dopamine in the brains of food-deprived people - just as it spikes this pleasure chemical in the brains of those with drug addictions in response to their drug of choice (<http://www.bnl.gov/bnlweb/pubaf/pr/2002/bnlpr052002.htm>).

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