Compulsive eating shares addictive biochemical mechanism with cocaine, heroin abuse: study

March 28 2010

In a newly published study, scientists from The Scripps Research Institute have shown for the first time that the same molecular mechanisms that drive people into drug addiction are behind the compulsion to overeat, pushing people into obesity.

The new study, conducted by Scripps Research Associate Professor Paul J. Kenny and graduate student Paul M. Johnson, was published March 28, 2010 in an advance online edition of the journal Nature Neuroscience.

The study's startling findings received widespread publicity after a preliminary abstract was presented at a Society for Neuroscience meeting in Chicago last October. Articles heralding the new discovery appeared in news publications around the world, focusing on the point obese patients have been making for years - that, like addiction to other substances, junk food binging is extremely difficult to stop.

The study goes significantly further than the abstract, however, demonstrating clearly that in rat models the development of obesity coincides with a progressively deteriorating chemical balance in reward brain circuitries. As these pleasure centers in the brain become less and less responsive, rats quickly develop compulsive overeating habits, consuming larger quantities of high-calorie, high-fat foods until they become obese. The very same changes occur in the brains of rats that

overconsume cocaine or heroin, and are thought to play an important role in the development of compulsive drug use.

Kenny, a scientist at Scripps Research's Florida campus, said that the study, which took nearly three years to complete, confirms the "addictive" properties of junk food.

"The new study, unlike our preliminary abstract, explains what happens in the brain of these animals when they have easy access to high-calorie, high-fat food," said Kenny. "It presents the most thorough and compelling evidence that drug addiction and obesity are based on the same underlying neurobiological mechanisms. In the study, the animals completely lost control over their eating behavior, the primary hallmark of addiction. They continued to overeat even when they anticipated receiving electric shocks, highlighting just how motivated they were to consume the palatable food."

The scientists fed the rats a diet modeled after the type that contributes to human obesity—easy-to-obtain high-calorie, high-fat foods like sausage, bacon, and cheesecake. Soon after the experiments began, the animals began to bulk up dramatically.

"They always went for the worst types of food," Kenny said, "and as a result, they took in twice the calories as the control rats. When we removed the junk food and tried to put them on a nutritious diet - what we called the 'salad bar option' - they simply refused to eat. The change in their diet preference was so great that they basically starved themselves for two weeks after they were cut off from junk food. It was the animals that showed the "crash" in brain reward circuitries that had the most profound shift in food preference to the palatable, unhealthy diet. These same rats were also those that kept on eating even when they anticipated being shocked."

Lethally Simple

What happens in addiction is lethally simple, Kenny explained. The reward pathways in the brain have been so overstimulated that the system basically turns on itself, adapting to the new reality of addiction, whether its cocaine or cupcakes.

"The body adapts remarkably well to change—and that's the problem," said Kenny. "When the animal overstimulates its brain pleasure centers with highly palatable food, the systems adapt by decreasing their activity. However, now the animal requires constant stimulation from palatable food to avoid entering a persistent state of negative reward".

After showing that obese rats had clear addiction-like food seeking behaviors, Johnson and Kenny next investigated the underlying molecular mechanisms that may explain these changes. They focused on a particular receptor in the brain known to play an important role in vulnerability to drug addiction and obesity - the dopamine D2 receptor. The D2 receptor responds to dopamine, a neurotransmitter that is released in the brain by pleasurable experiences like food or sex or drugs like cocaine. In cocaine abuse, for example, the drug alter the flow of dopamine by blocking its retrieval, flooding the brain and overstimulating the receptors, something that eventually leads to physical changes in the way the brain responds to the drug.

The new study shows that the same thing happens in junk food addiction.

"These findings confirm what we and many others have suspected," Kenny said, "that overconsumption of highly pleasurable food triggers addiction-like neuroadaptive responses in brain reward circuitries, driving the development of compulsive eating. Common mechanisms may therefore underlie obesity and drug addiction."

Consistent with common mechanisms explaining addiction and obesity, levels of the D2 dopamine receptors were significantly reduced in the brains of the obese animals, similar to previous reports of what happens in human drug addicts, Kenny noted. Remarkably, when the scientists knocked down the receptor using a specialized virus, the development of addiction-like eating was dramatically accelerated.

"This addiction-like behavior happened almost from the moment we knocked down the dopamine receptors," Kenny noted. "The very next day after we provided access to the palatable food, their brains changed into a state that was consistent with an animal that had been overeating for several weeks. The animals also became compulsive in their eating behaviors almost immediately. These data are, as far as we know, the strongest support for the idea that overeating of palatable food can become habitual in the same manner and through the same mechanisms as consumption of drugs of abuse."

More information: "Addiction-Like Reward Dysfunction and Compulsive Eating in Obese Rats: Role for Dopamine D2 Receptors," *Nature Neuroscience,* March 28 2010.

Provided by The Scripps Research Institute