Addicted to FOOD?

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What drives people, against their better judgment, to eat more food than they need? Scientists look to the brain for answers

By Oliver Grimm

It's been a long day, and you are still at the office. With your blood sugar plummeting, your brain starts to obsess: Where can I get some food? You gather your money and dash across the street to the fast-food place. But as you bite into the greasy burger, your conscience suddenly kicks in: What am I doing?

It is a common scenario for many of us. Hunger is a potent, if only temporary, condition that can overpower our very best nutritional intentions. In its absence, the brain's cerebrum—governing conscious behavior—helps us make healthy, informed decisions about what we eat. But when our stomachs begin to growl, too often they drown out any good advice coming from our brains. Unfortunately, the short-sighted decisions we make with our stomachs are having an increasingly negative effect on our health.

Research into overeating and obesity has accelerated in recent years, and with good reason: excess weight is the most important risk factor for cardiovascular disease and diabetes. According to a study by researchers at the Centers for Disease Control and Prevention and the National Cancer Institute, obesity was associated with about 112,000 deaths in 2000 in the U.S. In addition, a 2002 study in the journal *Health Affairs* estimated annual medical spending on overweight and obese patients to be as much as $92.6

billion—or 9.1 percent of the country's health expenditures. Physicians define obesity as having a body mass index, or BMI, higher than 30. Anyone with a BMI above 25 is overweight. (You can calculate your own BMI at www.nhlbisupport.com/bmi) By these measures, about one third of American adults are overweight, and nearly another third are obese, according to the National Health and Nutrition Examination Survey, conducted between 2003 and 2004.

"Stop" Hormones

In their quest for causes, scientists have long concentrated on metabolic hormones. In 1994 Jeffrey M. Friedman of the Rockefeller University discovered that adipose tissue, or fat, possesses a feedback mechanism by which it can block additional eating. Indeed, fat cells secrete a protein that passes through the blood to the hypothalamus in the brain, where it suppresses feelings of hunger. Friedman dubbed the substance leptin, from the Greek *leptos,* meaning "thin."

When researchers genetically engineered mice in which leptin could not function, the animals rapidly became obese. The results led some to speculate that obesity might stem from little more than a faulty feedback mechanism—and not human behavior. On closer examination, however, this interpretation turned out to be too

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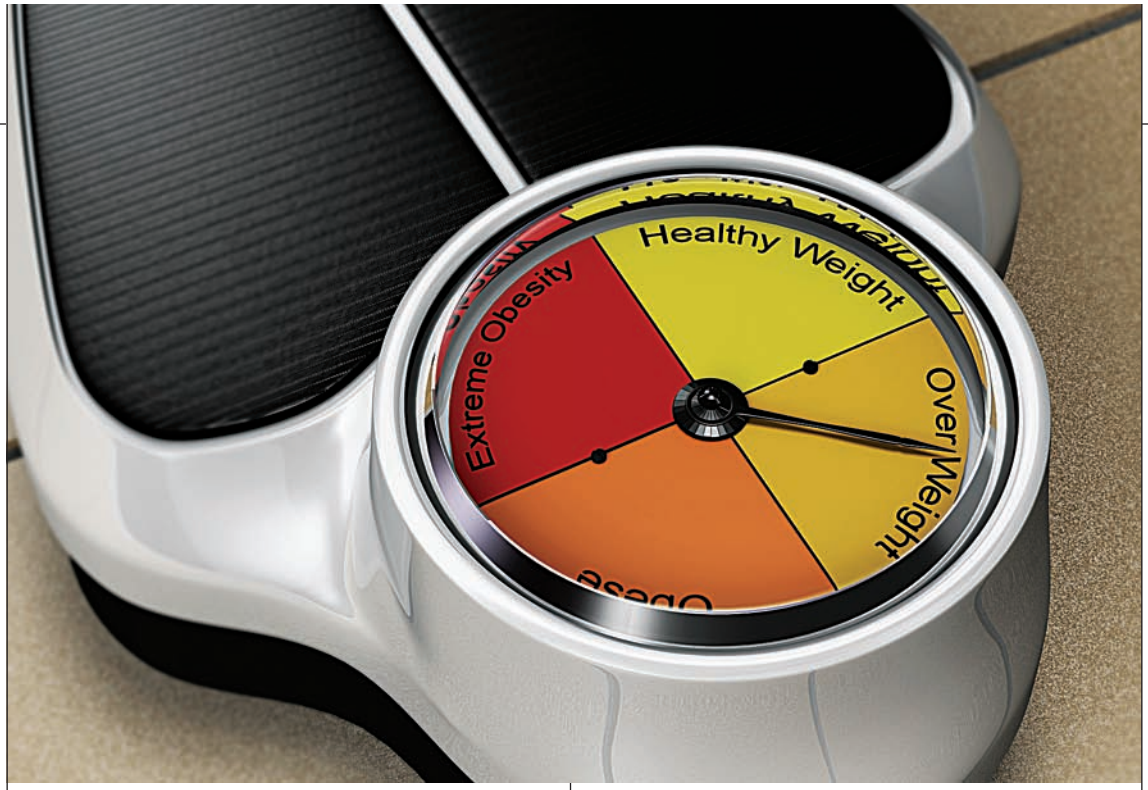

Hunger is a potent, if temporary, physical condition that can overpower our very best nutritional intentions. When our stomach begins to growl, too often it drowns out any good advice coming from our brain.

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Insatiable hunger for food is caused by our biological need to survive

one-sided. Leptin, we now know, also plays an important role in addictive behavior. Heroin-addicted lab animals suffer even more during withdrawal if they are kept hungry. Perhaps this satiety hormone suppresses cravings not only for food but for certain drugs as well.

Is Food a Drug?

Anyone who has ever dieted knows how hard it is to kick old habits. Should we view overweight people as addicts of a sort? The comparison seems far-fetched at first glance. After all, a person who eats too much does not develop a food tolerance, and overweight dieters certainly do not suffer the terrible physical symptoms of withdrawal. But obese people do show some hallmarks of dependency, among them a strong drive to eat and a loss of control to the point of neglecting other needs.

As it turns out, drug addiction and binge eating are not dissimilar in neurobiological terms. Bundles of nerve fibers that run from the midbrain to a structure called the nucleus accumbens secrete unusually large amounts of the neurotransmitter dopamine whenever we experience something surprising or pleasant. If a hungry lion, for example, spots a nice piece of meat, its nucleus accumbens is flooded with dopamine. Likewise, cocaine and amphetamines cause dopamine levels in the nucleus accumbens to rise at least 10-fold, delivering a rush of pleasure.

This reward system further controls the hypothalamus, which, among other things, regulates eating behavior. Mice that have been genetically modified so that they no longer produce dopamine reveal just how important this connection is. The animals lose all desire to consume anything and simply starve. Once provided with dopamine, however, their eating behavior returns to normal.

In 2001 Gene-Jack Wang of Brookhaven National Laboratory and Nora Volkow of the National Institute on Drug Abuse confirmed the important role dopamine plays in eating. Using positron-emission tomography (PET), they measured the quantity of dopamine receptors in the striatum of overweight volunteers and found that this amount correlated closely to BMI. The higher the subject's BMI, the fewer dopamine receptors he or she had. The researchers concluded that, like drug addicts, extremely overweight individuals suffer from a dopamine shortage, causing them to constantly seek new rewards in the

FAST FACTS

Addiction and Obesity

1» Obesity is associated with about 112,000 deaths a year in the U.S. By some estimates, annual medical spending on overweight and obese patients constitutes 9.1 percent of U.S. health expenditures.

2» Drug addiction and binge eating are not dissimilar in neurobiological terms. Recent research makes it clear that the brain's reward systems play a key role in the control of eating behaviors.

3» Neurobiology is showing why it can be so hard for overweight people to lose weight: for all their differences, drug addiction and obesity may be two sides of the same coin.

The brain processes stimuli related to eating in much the same way it responds to addictive substances.

form of food. But their brain then compensates for the excess dopamine that follows by reducing its number of dopamine receptors—a mechanism known to occur among cocaine addicts.

In a 1930s experiment that targeted a different brain system, apes became eating machines. German neuroscientist Heinrich Kluever and his American colleague, Paul C. Bucy, destroyed the animals' amygdala, a brain region involved in arousal and emotional responses. The finding suggested that it plays a role in satiety. Kevin LaBar of Duke University picked up this thread of research in 2001, taking magnetic resonance imaging (MRI) scans of the amygdala in nine human subjects as they looked at pictures of either food or nonfood items, such as cars or tools. The test subjects were healthy but hungry, having fasted for eight hours before the experiment. Once tested, they were given a meal of their choice and then put back inside the scanner.

In this way, LaBar was able to compare the brain activity of a hungry person to that of a sated one. He found that a hungry subject's amygdala became active the instant he or she saw anything edible. Once the person had eaten, though, this brain region no longer responded. Clinton Kilts and his colleagues at Emory University carried out similar experiments on cocaine addicts at roughly the same time. As PET scans revealed, the amygdala also reacted immediately when these subjects were shown images sure to excite them, including thin lines of white powder. Apparently the amygdala acts as a kind of alarm bell. Anytime it detects something important to the organism's survival—be it a big snake or a tempting sandwich—it rings.

Overeating as Habit

Yet another brain region, the orbitofrontal cortex (OFC), is involved in human addiction. The OFC, which lies in the frontal lobes just above the orbits of the eyes, seems to function as a control center monitoring our behavior. People with an OFC that has been damaged by accident or disease, for example, are frequently unable to control themselves. They act impulsively and demonstrate some degree of addictive behavior. And the OFC is significantly less active in drug addicts than it is in healthy people.

In 2001 Dana M. Small, now at Yale University, demonstrated that the OFC also processes food-related pleasures and aversions. She took PET scans of nine subjects while they let their favorite chocolate melt on their tongues. Brain activity increased in areas associated with sensory inputs but even more so in the OFC. Next the researchers asked their subjects to eat chocolate until their enjoyment turned to disgust. At that point, the central part of the OFC suddenly switched off, and activity increased instead in the adjacent region, the lateral OFC.

All these experiments support a single idea: the brain processes stimuli related to eating in very much the same way it responds to other addictive stimuli. So although some obese patients can trace their problem directly to hormonal imbalances, behavioral control plays a considerable role.

We hope that as we gain a better understanding of how the brain handles feelings of hunger and satiety, we will be able to develop more effective therapies for overeating and obesity. Medications developed to treat drug addiction already show some promise. For instance, patients who take naltrexone, an opiate antagonist that blocks the pleasure associated with opiate narcotics, typically stop gaining weight. Another drug called rimonabant, which blocks a receptor of the endogenous cannabinoid system, helps some patients lose weight, though often not much.

Of course, counseling, exercise and healthy eating habits give better results than anything else. But neurobiology now shows just why that route can be so hard: for all their differences, drug addiction and obesity seem to be two sides of the same coin. M

(Further Reading)

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- **Increasing Leptin Precedes Craving and Relapse during Pharmacological Abstinence Maintenance Treatment of Alcoholism.** Falk Kiefer, Holger Jahn, Christian Otte, Cueneyt Demiralay, Karsten Wolf and Klaus Wiedemann in *Journal of Psychiatric Research,* Vol. 39, No. 5, pages 545–551; 2005.
- **Individual Differences in Reward Drive Predict Neural Responses to Images of Food.** John D. Beaver, Andrew D. Lawrence, Jenneke van Ditzhuijzen, Matt H. Davis, Andrew Woods and Andrew J. Calder in *Journal of Neuroscience,* Vol. 26, No. 19, pages 5160–5166; May 2006.