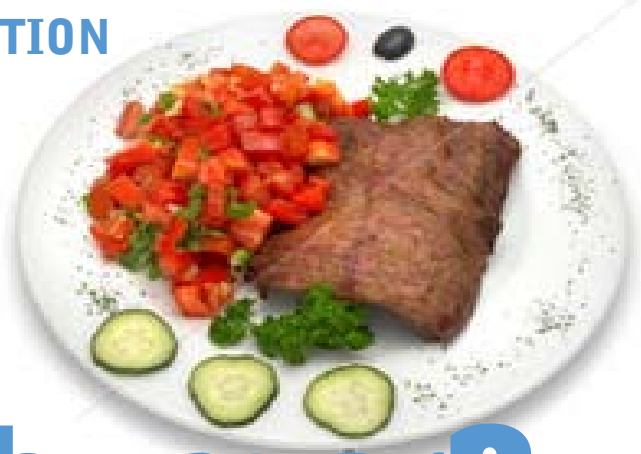


NUTRITION



What is hunger?



When people given the hunger stimulating hormone were shown images of delicious foods, an area of the brain associated with addiction – one of its pleasure centres – lit up on scans more than it did with those not given extra ghrelin

We still have the urge to hunt, gather and consume food – even though we are lucky enough to have plenty to go around, writes

Erika Gabel

Grumble. That's the sound your belly makes to let you know it's chow time. Ever wonder what triggered that hunger in the first place? Maybe you haven't eaten since breakfast and it's (gasp) 7:30pm. Or it's 10am and, even though you had a hearty bowl of steel-cut oatmeal just two hours ago, you find yourself facing a tray of richly glazed doughnuts.

Whatever the reason, hunger is real – and difficult to withstand, even when you

know you don't "need" to eat. Driven by the increasing rates of obesity and the demand for weight-loss help among the non-obese, scientists are studying the biochemistry behind hunger, in some cases moving closer to creating drugs that can help people divert its relentless drive.

Evolutionarily speaking

Back when people lived in caves, hunger was an essential motivator for grabbing a spear and embarking on a potentially dangerous hunt. In this case, hunger was the result of the body's energy stores being low and in need of replenishment. And yet even after a massive prehistoric feast, hunger could still be triggered by, say, the sight of some ruby-red berries. This kind of hunger encouraged our ancestors to "eat 'em if you got 'em" because there might not be food around the next time they needed it.

These Stone Age scenarios illustrate the two kinds of hunger: one driven by

internal desire and one sparked by external opportunity. Unfortunately, modern human beings are still motivated by the same biochemistry as our ancestors, even though food abounds for most of us. The pleasure-seeking hunger of early humans has translated into an obesity and diabetes epidemic in modern times.

"The cause of the obesity epidemic has to do with the brain," says Alain Dagher, MD, an associate professor at McGill University in Montreal, Canada. "The treatment of obesity will have to target the brain."

Scientists are hard at work figuring out what causes feelings of hunger or fullness and using this knowledge to develop anti-obesity drugs. As it turns out, the interactions between hormones sent to the brain from metabolically important parts of the body - like fat cells or the stomach - seem to be at the root of eating behavior and perhaps the answer to the epidemic.

The hunger hormone

“Most likely, feeding is controlled by multiple systems. It is the most important function in animals,” says Dr Dagher. “There are people who go so far as to say that [eating] is why we have a brain.”

So far, scientists have found only a single hormone that stimulates hunger in people, though they are eagerly seeking more. That hormone, called ghrelin, seems to orchestrate not only pleasure-seeking and physiological hungers but “stress eating” as well.

Ghrelin is released from cells in the stomach and travels to the brain, where it interacts with both the hypothalamus – the brain’s physiological eating centre – and the brain’s pleasure centres to stimulate hunger. Over the course of a day, ghrelin levels naturally change dramatically, rising steeply before a meal and then plummeting after eating.

In experiments, people who got injections of ghrelin before a buffet meal ate 30% more than a group of eaters not given extra ghrelin. Interestingly, ghrelin levels rise when people go on calorie-restriction diets – which may explain why dieting is so difficult.

Hooked on eating

Ever feel as if you’re addicted to food? Well, you just might be.

“The brain circuits that control feeding behavior are very similar to the ones involved in drug abuse,” says Dr Dagher, who was the principal investigator on a May 2008 study of ghrelin.

When people who had been administered the hormone were shown images of delicious foods, an area of the brain associated with addiction – one of its pleasure centres – lit up on scans more than it did with those not given extra ghrelin.

We already know that many people overeat when they are feeling stressed or because it satisfies a longing that has nothing to do with rebuilding the body’s energy stores.

Some research has shown that during times of trouble, ghrelin levels rise and, through its interaction with the brain’s pleasure centres, may help with coping.



Obese people tend to already have increased levels of circulating leptin, compared with thin people. However, they are resistant to its appetite-suppressing effects (not unlike the way type 2 diabetes is, partly, caused by resistance to insulin)

But those soothing feelings come with a price.

“As a side effect, you have an increase in body weight from stress-induced eating,” says Jeffrey Zigman, MD, PhD, an assistant professor of internal medicine at the University of Texas Southwestern Medical Center. Dr Zigman demonstrated that ghrelin has antidepressant and anti-anxiety effects in rodents.

Sweet satisfaction

When you think about it, there are two sides to every meal: hunger and satiety. We’ve covered hunger, but what about that hands-on-belly contentment that follows a meal? As it turns out, even though scientists have found only one hunger hormone, they’ve discovered a whole bunch of satiety hormones. The most well understood is a hormone called leptin.

Leptin is produced naturally by the body’s fat cells, travels through the blood to the hypothalamus in the brain, and suppresses appetite. When leptin was first identified, many scientists thought they had hit the jackpot: the skinny hormone.

“There was an explosion of research and data about these hormones,” says Zigman. But upping leptin levels didn’t help people shed pounds. Obese people tend to already have increased levels of circulating leptin, compared with thin people. However, they are resistant to its

appetite-suppressing effects (not unlike the way type 2 diabetes is, in part, caused by a resistance to insulin).

Not all hope is lost, though, for a leptin-based weight-loss drug.

“There are tricks around to potentially use leptin as a drug,” Dr Zigman says. And researchers now have several satiety hormones in their tool kit, like obestatin and peptide tyrosine-tyrosine (PYY). According to Dagher, PYY is being tested in clinical trials as a hunger suppressant.

Dagher also says that many companies are developing ghrelin blockers for weight loss. In recent studies, drugs that block the action of ghrelin in mice have shown promise as weight-loss agents. However, researchers must approach these agents with caution after a lesson learned from another weight-loss drug: rimonabant. It worked by interfering with one of the brain’s cannabinoid receptors – the contact point for cannabis (marijuana) and part of the brain circuitry that regulates mood – causing people to lose weight through the diminishment of appetite.

“Ghrelin makes the food more pleasurable,” says Dagher. “But if you block pleasure centres, you run the risk of having side effects, especially those that involve mood.”

Rimonabant worked very well as a weight-loss agent, but it could also cause severe depression, sometimes leading to suicide. Never approved in the United States, rimonabant was approved for use in the EU in June 2006, but in October 2008 the European Medicines Agency recommended that doctors stop prescribing it.

Although the study of appetite hormones is still quite young, new members of this hormone class are being discovered all the time. It’s possible that a medication that could help combat the obesity epidemic and the spread of diabetes may already be in the pipeline. And even if not, scientists believe this line of research may yet hold the answer to overeating.

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