How the brain senses fatty food

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As you gorge on food this holiday season, you might not want to think about the fat content of all the goodies you've indulged in. Nevertheless, your brain will be keeping tabs directly, suggests a report in the November 26th issue of the journal *Cell*, a Cell Press publication.

Researchers have discovered in studies of rats that one type of lipid produced in the gut rises after eating fatty foods. Those so called N-acylphosphatidylethanolamines or NAPEs enter the bloodstream and go straight to the brain, where they concentrate in a brain region that controls food intake and energy expenditure.

The good news is that the most abundant form of NAPE doesn't seem to lose its effectiveness even when it is artificially administered over the course of several days. That means treatments designed to boost NAPE levels might offer a new way to fight obesity.

" A lot of gut hormones have an effect on food, but when you give them chronically they lose their effectiveness," said Gerald Shulman of Yale University School of Medicine. Or, for instance, another nutrient-sensing, gut-derived peptide known as CCK leads animals and people to eat smaller meals, but they eat them more often, yielding no change in the overall calories consumed, he said.

" Here, we gave rats NAPE for five days and saw a continuous reduction in food intake and a decline in body weight," Shulman said. "It suggests NAPE or long-acting NAPE analogs may treat obesity." For that, however, much work remains to extend the new findings in rats to

humans, he added.

The researchers focused in on NAPEs potential role as a fat intake signal after screening the blood for lipids that rise after a high-fat feeding. Among the increased metabolites was a class of phospholipids, the NAPEs, of previously unknown physiologic function in plasma.

Now, they show that NAPEs are secreted into circulation from the small intestine in response to ingested fat and that systemic administration of the most abundant circulating NAPE, at doses naturally found in the bloodstream, lowers food consumption in rats without making food unappealing to the animals.

By injecting radiolabeled NAPE into the animals, they found that the lipid enters the brain and is particularly concentrated in the hypothalamus. Infusions of NAPE directly into the brain also led the animals to cut back on calories, supporting the notion that its effects may be mediated through direct interactions with the central nervous system. Curiously, they also found that NAPE left the animals in what is sometimes described as a food coma.

Animals fed a high-fat diet for 35 days lose the normal increases in circulating NAPE after a fatty meal. That suggest that derangements in NAPE secretion associated with chronic high-fat feeding may contribute to diet-induced obesity precipitated by overexposure to triglyceride-rich foods. However, those animals still responded to NAPE treatment.

" These results suggest that chronic C16:0 NAPE treatment is capable of generating a state of negative energy balance over multiple days and merits longer-term studies in rodents and nonhuman primates to examine its potential for treatment and prevention of diet-induced obesity," the researchers wrote. "In conclusion, these data support the hypothesis that circulating NAPEs, synthesized in the small intestine from ingested fat,

may be part of an important physiologic negative feedback loop that serves to reduce food intake and arousal after a fat-containing meal."

Source: Cell Press