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Scientists identify stomach's timekeepers of hunger

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(PhysOrg.com) -- New York collaborators at Columbia and Rockefeller Universities have identified cells in the stomach that time the release of a hormone that makes animals anticipate food and eat even when they are not hungry. The finding, which has implications for the treatment of obesity, marks a landmark in the decades-long search for the timekeepers of hunger. The work reveals what the stomach "tells" the brain.

Rae Silver, head of the Laboratory of Neurobiology and Behavior at Columbia University and Helene L. and Mark N. Kaplan Professor at Barnard College, Joseph LeSauter, senior research scientist at Barnard, and their colleague Donald W. Pfaff, at Rockefeller University, are the first to show that these cells, which release a hormone called ghrelin, are controlled by a circadian clock that is set by mealtime patterns. They also show that the hormone's release whets the appetite of mice, spurring them to actively search for and consume food, even when they are not hungry.

"Circadian clocks allow animals to anticipate daily events rather than just react to them," notes LeSauter, first author of the paper. "The cells that produce ghrelin have circadian clocks that presumably synchronize the anticipation of food with metabolic cycles."

The scientists show that the stomach cells release ghrelin into the general circulation before mealtime. The hormone triggers a flurry of food-seeking behavior such as digging in the bedding around the food hopper,

and it also stimulates eating. These behaviors are part of the subjective experience of hunger.

LeSauter, who spearheaded the project, studied genetically engineered mice that lack the receptor that recognizes ghrelin and compared them with normal mice on identical feeding schedules. He found that the mice that lack the ghrelin receptor had normal overall activity throughout the day but began to forage for food much later and to a lesser extent than their normal counterparts. However, when foraging and other anticipatory behaviors actually began, foraging increased in a remarkably predictable manner in both sets of mice.

Pfaff believes that ghrelin, which is released from stomach cells and travels through the bloodstream to the brain, influences a decision-making process in brain cells. These brain cells are constantly deciding whether or not to eat and, as mealtime draws near, the presence of ghrelin increases the proportion of “yes” decisions. “We applied mathematics to precise behavioral data and then interpreted them in the context of neurobiology,” says Pfaff. “And that’s very, very rare.”

Previous studies have shown that people given ghrelin injections feel voraciously hungry and eat more at a buffet than they otherwise would. The new research suggests that the stomach tells the brain when to eat, and establishing a regular meal schedule will regulate the stomach’s release of ghrelin. “If you eat all the time, ghrelin secretion will not be well controlled,” says Silver. “It’s a good thing to eat meals at a regularly scheduled time of day.”

The research also suggests that ghrelin, the only known natural appetite stimulant made outside the brain, is a promising target for drug developers. Unlike drugs that focus on satiety, those that target ghrelin could help curb appetite before dieters take that first bite.

More information: *PNAS* 106(32): 13582-13587 (August 11, 2009); Stomach ghrelin-secreting cells as food-entrainable circadian clocks; Joseph LeSauter, Nawshin Hoque, Michael Weintraub, Donald W. Pfaff and Rae Silver

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