How excess holiday eating disturbs your 'food clock'

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(Medical Xpress)—If the sinful excess of holiday eating sends your system into butter-slathered, brandy-soaked overload, you are not alone: People who are jet-lagged, people who work graveyard shifts and plain-old late-night snackers know just how you feel.

All these activities upset the body's "food clock," a collection of interacting genes and molecules known technically as the foodentrainable oscillator, which keeps the human body on a metabolic even keel. A new study by researchers at UCSF is helping to reveal how this clock works on a molecular level.

Published this month in the journal Proceedings of the National Academy of Sciences, the UCSF team has shown that a protein called PKCγ is critical in resetting the food clock if our eating habits change.

The study showed that normal laboratory mice given food only during their regular sleeping hours will adjust their food clock over time and begin to wake up from their slumber, and run around in anticipation of their new mealtime. But mice lacking the PKCγ gene are not able to respond to changes in their meal time – instead sleeping right through it.

The work has implications for understanding the molecular basis of diabetes, obesity and other metabolic syndromes because a desynchronized food clock may serve as part of the pathology underlying these disorders, said Louis Ptacek, MD, the John C. Coleman Distinguished Professor of Neurology at UCSF and a Howard Hughes Medical Institute Investigator.

It may also help explain why night owls are more likely to be obese than morning larks, Ptacek said.

"Understanding the molecular mechanism of how eating at the "wrong" time of the day desynchronizes the clocks in our body can facilitate the development of better treatments for disorders associated with night-eating syndrome, shift work and jet lag," he added.

Resetting the Food Clock

Look behind the face of a mechanical clock and you will see a dizzying array of cogs, flywheels, reciprocating counterbalances and other moving parts. Biological clocks are equally complex, composed of multiple interacting genes that turn on or off in an orchestrated way to keep time during the day.

In most organisms, biological clockworks are governed by a master clock, referred to as the "circadian oscillator," which keeps track of time and coordinates our biological processes with the rhythm of a 24-hour cycle of day and night.

Life forms as diverse as humans, mice and mustard greens all possess such master clocks. And in the last decade or so, scientists have uncovered many of their inner workings, uncovering many of the genes whose cycles are tied to the clock and discovering how in mammals it is controlled by a tiny spot in the brain known as the "superchiasmatic nucleus."

Scientists also know that in addition to the master clock, our bodies have other clocks operating in parallel throughout the day. One of these is the food clock, which is not tied to one specific spot in the brain but rather multiple sites throughout the body.

The food clock is there to help our bodies make the most of our nutritional intake. It controls genes that help in everything from the absorption of nutrients in our digestive tract to their dispersal through the bloodstream, and it is designed to anticipate our eating patterns. Even before we eat a meal, our bodies begin to turn on some of these genes and turn off others, preparing for the burst of sustenance – which is why we feel the pangs of hunger just as the lunch hour arrives.

Scientist have known that the food clock can be reset over time if an organism changes its eating patterns, eating to excess or at odd times, since the timing of the food clock is pegged to feeding during the prime foraging and hunting hours in the day. But until now, very little was known about how the food clock works on a genetic level.

What Ptacek and his colleagues discovered is the molecular basis for this phenomenon: the PKCγ protein binds to another molecule called BMAL and stabilizes it, which shifts the clock in time.

More information: The article, "PKCγ participates in food entrainment by regulating BMAL1" is authored by Luoying Zhang, Diya Abrahama, Shu-Ting Lin, Henrik Oster, Gregor Eichele, Ying-Hui Fu, and Louis J. Ptácek and appears in the *Proceedings of the National Academy of Sciences*. www.pnas.org/content/109/50/20679.abstract

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