

Brain plays key role in appetite by regulating free radicals

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Researchers at Yale School of Medicine have found the brain's appetite center uses fat for fuel by involving oxygen free radicals—molecules associated with aging and neurodegeneration. The findings, reported in the journal *Nature*, suggest that antioxidants could play a role in weight control.

The study's lead authors were Sabrina Diano and Tamas Horvath, who are an associate professor and professor, respectively, in the Departments of Obstetrics, Gynecology & Reproductive Sciences and Neurobiology. Horvath is also chair of the Section of Comparative Medicine.

"In contrast to the accepted view, the brain does use fat as fuel," said Horvath. "Our study shows that the minute-by-minute control of appetite is regulated by free radicals, implying that if you interfere with free radicals, you may affect eating and satiety."

The results also imply, added Horvath, "that each time a feeling of fullness or satiety is reached during a meal, you may be chipping away some time from your maximum lifespan as the most free radicals are produced when satiety-promoting brain cells are active."

Diano, Horvath and colleagues conducted the study in mice to better understand how the brain mediates neuronal activation in response to ghrelin, a hormone produced in the stomach and previously associated with growth hormone release, appetite, learning and memory.

They found that ghrelin-induced increase in appetite is driven by burning fat in hypothalamic mitochondria, which produces free radicals that are scavenged by a mitochondrial protein called uncoupling protein 2 (UCP2).

"The timing of taking antioxidants may be critical for the control of appetite," said Diano. "If taken on an empty stomach antioxidants may further increase appetite, however when taken with food, they may affect satiety. Further studies are needed to determine whether any regiment of orally taken antioxidants could be used to control appetite in animals and humans."

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