

METABOLISM

## CILIA LENGTH—ROLE IN ENERGY BALANCE

The length of the cilia at the surface of hypothalamic neurons is important in the regulation of energy balance, suggest the findings of a new study in mice. Ciliary length seems to be controlled, at least in part, by leptin signalling.

Mammalian cells typically have one nonmotile primary cilium. Previous studies have established a link between genetic ciliopathies and obesity in humans and mice. The researchers sought to clarify the precise role of primary cilia in the maintenance of energy homeostasis by comparing the length of cilia in hypothalamic neurons of obese and nonobese mice and in mice deficient in leptin and the leptin receptor. They also analysed the effects of leptin treatment on the brains of live mice and on hypothalamic mouse neurons grown in culture. Finally, they investigated the metabolic effects of artificially shortening the cilia of hypothalamic neurons of live mice.

The length, surface area and volume of the cilia in the hypothalami of diet-induced obese mice (which are leptin-resistant), leptin-deficient mice and leptin-receptor-deficient mice were substantially reduced compared with those in lean mice. “Interestingly, obesity-associated ciliary changes are specific to the hypothalamic neurons that primarily sense metabolic signals from the periphery to modulate ingestive behaviour and energy metabolism,” comments Min-Seon Kim (University of Ulsan College of Medicine, South Korea).

Leptin injections to leptin-deficient mice and leptin treatment of hypothalamic neurons in culture increased cilia length, whereas artificial shortening of hypothalamic cilia impaired the ability of mice to generate satiety responses in response to leptin, insulin and glucose.

“Our findings describe a novel phenomenon whereby leptin dictates the ability of hypothalamic neurons to sense metabolic signals through control of cilia length,” says Kim. “Our study suggests that ciliary defects in hypothalamic neurons may be closely related to impaired satiety generation, leading to overeating in individuals with obesity. Thus, regulation of ciliogenesis in hypothalamic neurons could be a potential target in the development of anti-obesity drugs.”

**Joana Osório**

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