

Understanding how a fly modulates its feeding behavior could help fight obesity

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Turning various neural circuits on and off in the brain of the vinegar fly could help A*STAR researchers develop new treatments for obesity, diabetes, and heart disease.

In changing external environments, animals, including humans, maintain a steady physiological energy state by altering both their internal metabolism and feeding behavior. If energy supplies are low, for example, the brain produces hunger signals to drive food-seeking behavior to replenish the animal's reserves.

In a recent study, Adam Claridge-Chang, and colleagues from A*STAR's Institute of Molecular and Cell Biology and the Singapore Institute of Manufacturing Technology looked at how inhibiting neuromodulator cells that release dopamine and serotonin would affect feeding and metabolic functions1.

"When we started this project, I expected to find a lot of studies in this important area, but was surprised to find just three papers with five experiments. Our study more than doubles the available information."

"We wanted to know: if we turn off these different circuits, what will happen to the feeding behavior?" Claridge-Chang says. "If we see a dramatic impact on feeding, could that be a pathway for treating the compulsive eating related to obesity?"

To find out, the research team silenced five different neuromodulator systems in genetically manipulated vinegar flies, Drosophila melanogaster. "We used transgenes that combine the fly's own gene switch with a protein that silences electrical activity in neurons. This way, we can shut off specific modulator circuits and examine the effect this has on feeding."

The insects were then assessed by monitoring 11 parameters: activity, climbing ability, individual

feeding, group feeding, food discovery, both fed and starved respiration, lipid content, and body weight.

Claridge-Chang says the results from these experiments indicate that individual neuromodulatory system effects on <u>feeding</u> <u>behavior</u>, motor activity and metabolism are not related to each other. As an example, in one experiment, oxygen intake—which should have mirrored food intake—actually decreased while food intake increased.

The group's original hypothesis was that disrupting neuromodulators would have coordinated effects on feeding and other aspects of physiology, but this was refuted—an outcome that Claridge-Chang says could lead to important new insights. "The dissociation of phenotypes implies that different modulatory <u>circuits</u> have disconnected or even oppositional effects on different physiological functions. We will test this hypothesis in future experiments."

More information: Anders Eriksson et al. Neuromodulatory circuit effects on Drosophila feeding behaviour and metabolism, *Scientific Reports* (2017). DOI: 10.1038/s41598-017-08466-0

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