

XL SAN

meeting

e-book

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S-014

Antagonistic Monoaminergic Control of State-Dependent Foraging in *C. elegans*

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The perception of food as more rewarding after deprivation is an evolutionarily conserved phenomenon, yet its underlying neural mechanisms remain poorly understood. We dissect this process using the nematode *C. elegans*, a model organism with a well-defined nervous system and conserved neurochemistry that provides universal insights into state-dependent behaviors.

In *C. elegans*, fasting triggers an enhanced slowing response upon food re-encounter, ensuring efficient exploitation of the source. We demonstrate that this behavior is governed by an antagonistic relationship between serotonin (5-HT) and tyramine (TA, the invertebrate analog of noradrenaline). The fasting-induced decline in TA disinhibits serotonergic signaling, which primes serotonergic neurons for a heightened response. Consequently, upon encountering food, these neurons release a surge of 5-HT that dramatically slows locomotion to ensure efficient feeding. This mechanism is confirmed in TA-deficient mutants, which exhibit hyperactive serotonergic neurons and an exaggerated slowing response. We further establish that TA directly inhibits the NSM neuron through the activation of two adrenergic-like GPCRs.

This defines a neural switch where fasting reduces inhibitory monoamines, disinhibiting 5-HT to ensure feeding. Conservation of these neurotransmitters suggests similar principles govern state-dependent decisions across species, providing insight into foraging and appetite.