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The Pharyngeal I2 Neurons Are Multifunctional Command Neurons that Respond to Noxious Stimuli by Reducing Food Intake via Inhibition of Feeding and Stimulation of Spitting

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How neuromuscular systems encode context-appropriate behaviors is an important problem in neuroscience. One simple system for the study of this problem is the pharynx of *C. elegans*, which contracts rhythmically (pumps) to ingest food. In nature, the pharynx interfaces with bacteria that range from nutritious to toxic and to which it must respond appropriately.

Recently our laboratory showed that pharyngeal pumping is interrupted by noxious stimuli such as hydrogen peroxide and ultraviolet light (UV). Using UV as a tool to analyze the response of pharyngeal circuits to noxious insults, we found that UV activates the pharyngeal I2 neurons, which likely act as light-detectors and directly inhibit pharyngeal muscles via glutamate release (Bhatla and Horvitz, Neuron, 2015). After inhibiting pumping, UV subsequently stimulates pumping, and these pumps induce spitting of food (Bhatla *et al*., Current Biology, 2015). While ordinary feeding pumps retain bacteria in the pharynx, spitting pumps open a filter in the anterior pharynx such that relaxation of the pharynx ejects food into the environment. Spitting depends on the pharyngeal M1 neuron.

Here we report that in addition to inhibiting overall pumping, the I2 neurons also stimulate spitting pumps via M1. I2 activation increases M1 calcium levels and drives M1-dependent spitting. The observation that the I2s inhibit overall pumping while promoting spitting pumps via M1 seems counterintuitive. However, these apparently antagonistic outputs both cause a rapid reduction of food intake: inhibiting pumping reduces food ingested through feeding pumps, while stimulating spitting causes those pumps that do occur to expel pharyngeal contents.

Thus the I2s act as multifunctional motor-command neurons that are activated by noxious stimuli and reduce food intake via parallel behavioral strategies. Our work identifies a basic pharyngeal circuit motif and also highlights the importance of analyzing neural circuits in the ethological context of the behaviors they produce.