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Sensory integration and neuromodulatory feedback facilitate *Drosophila* mechanonociceptive behavior

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ABSTRACT: Nociception is an evolutionarily conserved mechanism to encode and process harmful environmental stimuli. Like most animals, *Drosophila melanogaster* larvae respond to a variety of nociceptive stimuli, including noxious touch and temperature, with stereotyped escape responses through activation of multimodal nociceptors. How behavioral responses to these different modalities are processed and integrated by the downstream network remain poorly understood. By combining trans-synaptic labeling, ultrastructural analysis, calcium imaging, optogenetics and behavioral analyses, we uncovered a circuit specific for mechanonociception but not thermonociception. Notably, integration of mechanosensory input from innocuous and nociceptive sensory neurons is required for robust mechanonociceptive responses. We further show that neurons integrating mechanosensory input facilitate primary nociceptive output by releasing short neuropeptide F, the *Drosophila* neuropeptide Y homolog. Our findings unveil how integration of somatosensory input and neuropeptide-mediated modulation can produce robust modality-specific escape behavior.

STATEMENT:

Our works sheds light on how a specific response to a nociceptive cue, in this case mechanical but not thermal stimulation, is encoded within the network. Both heat and mechanical noxious stimuli are detected by the same neurons (i.e. nociceptors), however specific circuit elements and neuropeptide-mediated signaling are recruited in a modality-specific manner. Our data show the importance of neuromodulation to select for a specific behavioral action.

BACKGROUND:

This work was performed at the Center for Molecular Neurobiology (ZMNH) in the Neuronal Patterning and Connectivity laboratory headed by Dr. Peter Soba, in collaboration with the ZMNH electron microscopy group (Dr. Michaela Schweizer) and Duke University researchers (Dr. Ananya Guntur and Prof. Dr. Chung-Hui Yang).

It was part of a lab-wide effort headed by Dr. Chun Hu, Meike Petersen and Dr. Nina Hoyer.

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