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DEVELOPMENTAL BIOLOGY:

Flipping the Light Switch

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The behavior of animals is flexible and can change dramatically in response to the environment, nutritional state, or even age, among other factors. However, the neural basis of how external and internal cues modify innate behavior is not clearly understood. For example, the fruit fly *Drosophila melanogaster* is inherently either attracted or repelled by vinegar depending on its concentration (1). And age changes the innate light avoidance behavior of young *Drosophila* larvae into light preference in older larvae (2). The behavioral switch may be an adaptation that occurs as older larvae leave their food source—and thus darkness—to search for a suitable population site in the light. On page 499 of this issue, Gong *et al.* (3) identify two pairs of neurons in the *Drosophila* larval brain that control behavioral switch.

Conceptually, a behavioral switch can be implemented in different ways. For instance, two independent neuronal pathways could control behavioral extremes (attraction or repulsion), with the strength of each pathway determining the final outcome. Alternatively, a single neuron or pathway could switch between two different outputs depending on the sensory inputs received, on previous experience, or on intrinsic factors. Separate processing in two distinct pathways occurs in the adult fly's innate response to vinegar (1). In the olfactory system, sensory neurons express different odorant receptors and project to different glomeruli in the antennal lobe (4,5), which pass information to higher brain centers. Vinegar odor activates several glomeruli, two of which are necessary and sufficient for attraction to low vinegar concentrations. At higher concentrations, an additional glomerulus is recruited, which changes the behavioral response to repulsion (1). Both responses are mediated by the same sensory neuron, but the mechanism that drives the behavioral switch has yet to be identified.

How do older *Drosophila* larvae switch from light avoidance to light preference? Gong *et al.* have identified a pair of neurons called NP394 in each central brain hemisphere that are required to maintain light avoidance in young larvae. When the function of these neurons was inhibited, either by interfering with synaptic transmission or through hyperpolarization, even young larvae were attracted to light. By contrast, continuous hyperactivation of these neurons caused older larvae to avoid light instead of moving toward it. Thus, the activity of these neurons appears necessary and sufficient for controlling larval behavior in response to light.

The NP394 neurons most likely receive signals from ventral lateral neurons in the central brain through direct connections (synapses). The latter neurons develop into the master pacemaker that controls circadian rhythms in adult flies, but also have been implicated in controlling larval light avoidance (6). Ventral lateral neurons are innervated by photoreceptors of the Bolwig's organs, the visual system of the fly larva (7). When ventral lateral neurons were ablated in young larvae, the time course of light-induced Ca^{2+} influx

into NP394 neurons changed, thus demonstrating a functional connection. Surprisingly, this ablation resulted in faster and slightly stronger Ca^{2+} influx into NP394 neurons upon light stimulation. This suggests that ventral lateral neurons block NP394 neuron function and that light releases this block. It also indicates that ventral lateral neurons are not the only light information input to NP394 neurons. This is consistent with the morphology of an NP394 neuron, which exhibits two postsynaptic arborizations—one close to the terminals of ventral lateral neurons and another close to midline neurons of the central nervous system.

The mechanism by which NP394 neurons control the behavioral switch from light avoidance to preference remains unclear. It is unlikely that these neurons change signaling properties over time because their hyperactivation in older larvae still results in avoidance. Perhaps NP394 neurons participate in aversive signaling, whereas a parallel neuronal circuit signals attraction (see the figure). In this scenario, NP394 neurons would become less active during development, thus reducing light avoidance. This agrees with current data, but further studies are needed to characterize NP394 function. For instance, it is important to determine if their activity decreases in older larvae. If this reduction is due to decreased input from ventral lateral neurons, then Ca^{2+} imaging of NP394 neurons in older larvae would be informative. However, if it is the output of NP394 neurons that decreases with age, it will be necessary to perform Ca^{2+} imaging in downstream neurons, which have not yet been identified.

Another question regards the cues that change the output of the NP394 circuit during development. An intrinsic developmental timer could measure the age of the larva and change the properties of the neuronal circuit accordingly. Alternatively, the metabolic state of the animal could indicate when it is time to stop feeding (in the dark) and to enter pupation (in the light). This change could be linked to the developmental pathway controlled by the hormone ecdysone. Ecdysone triggers larval wandering and entry into pupation, and may affect the activity of NP394 neurons (8,9). In *Drosophila*, ecdysone controls another dramatic sensory switch: In the adult Bolwig's organ, green-sensitive photoreceptors die, while blue sensitive photoreceptors form an extraocular structure (the eyelet), but only after expression of blue opsin is turned off, and green opsin expression is turned on (10).

The finding of Gong *et al.* advances our understanding of how the animal brain interprets visual cues. It is also a step toward determining the neural basis of how both environmental and intrinsic cues modify innate behaviors.

References and Notes

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1. . Behavior circuits

The circuit shown depicts how parallel neuronal pathways may control the innate behavioral response of an animal (fly larva) to a stimulus (light).