

Dispatches

Escape Behavior: Linking Neural Computation to Action

A new study uses a combination of physiological and optogenetic techniques to identify visual neurons in fruit flies that detect approaching objects, and whose activation is integral in escaping an oncoming threat.

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When an animal needs to escape or defend itself from an impending collision, reaction time is paramount, but distinguishing between a benign stimulus and one requiring immediate evasion can involve complicated neural processing. For instance, a very different reaction is required when one walks past a basketball sitting upon a shelf compared to when the ball is heading directly at you — yet the visual inputs the ball produces at the retina might differ only subtly between these two cases. This challenge of scanning the visible world for oncoming threats and taking defensive measures when needed is nearly universal to sighted animals, yet much remains unknown about the underlying sensory-motor mechanisms. A study reported in this issue of *Current Biology* [1] takes advantage of genetic techniques to demonstrate that a handful of neurons in each optic lobe of fruit flies both sense approaching objects and initiate escape away from the threat.

Nearly all animals endowed with spatial vision display escape or defensive behaviors to objects approaching on a collision course or their two-dimensional simulation, referred to as looming stimuli. Both human adults [2] and infants as young as two weeks [3] display such avoidance responses. Further, studies on primates [4], rodents [5], fish [6], birds [7], amphibians [8], crustaceans [9], and insects [10] have all revealed behavioral responses specific to looming stimuli.

Fruit flies exhibit two distinct visually evoked jumping escape behaviors, one in response to a sudden visual flash and the other in response to a looming stimulus [11]. The response to a sudden flash more closely resembles escape behaviors evoked by mechanical stimulation that produce immediate escape mediated by a giant fiber neuron, like those seen in fish and crustaceans [12]. The escape from

a looming stimulus, however, involves a ‘planning’ stage in which wings are raised to prepare for flight and posture is adjusted to direct the animal away from the oncoming object [13]. This behavior can be aborted at different stages in its production and is probabilistic, unlike the giant-fiber-evoked escapes, which are stereotypically produced when the command neuron fires a single action potential and are unaffected by further sensory input once the behavior has been initiated.

Individual neurons or small networks tuned to looming stimuli have been discovered in almost as many species as show behavioral response to looming stimuli, including rodents [14], felines [15], birds [7], fish [6], amphibians [8], crustaceans [9], and insects [16]. In mice, looming-sensitive neurons occur as early in the visual system as the retina [14]. The most extensively studied looming-sensitive neuron has been the Lobula Giant Movement Detector (LGMD) of locusts. First described by O’Shea and Williams in 1974 [17], the LGMD and its downstream neurons involved in escape behavior [18] have been studied for four decades.

The LGMD integrates inputs from an entire visual hemifield in a large, retinotopically organized dendritic field [19]. As an object approaches the animal, the LGMD’s firing rate increases until the object reaches a threshold size, and then decreases as the object continues to expand on the retina. In this manner the timing of the neuron’s peak firing rate encodes when the object reaches the threshold size, and the firing rate matches a function of the angular speed of the object’s edges multiplied by a negative exponential of the object’s angular size [20]. If the animal jumps to escape the looming stimulus, take-off occurs a consistent delay after the LGMD’s peak firing rate is reached [10].

These visually evoked escape behaviors require precise computations performed on the retinal input to determine whether an object is

approaching and requires avoidance. Study of looming-sensitive neurons allows researchers to pursue neural mechanisms underlying these computations and to address questions about the initiation of complex, multistage behaviors. These studies have been previously limited by the inability to stimulate looming-sensitive neurons in unrestrained animals, to directly determine if the activity of these neurons alone can produce a multistage escape response.

Such stimulation experiments have been attempted in mammals, and can produce avoidance-like behavior [5]. However, as the targeted area is involved in sensory-motor integration of many types, it was not possible to test which neurons were responsible for the observed output. In the locust nervous system, looming-sensitive neurons can be stimulated directly, but only in a restrained animal, and this fails to produce escape behavior [18]. The genetic tools available to study fruit flies have now provided a more elegant test.

The starting point of this recent work was a genetic enhancer trap line allowing de Vries and Clandinin [1] to visualize five identifiable neurons in each fly’s optic lobe potentially involved in the generation of collision avoidance behaviors (Figure 1A). A series of electrophysiological recordings confirmed that they were indeed tuned to looming stimuli and that their properties were similar to those of the locust LGMD and analogous neurons in other systems [19]. With the advent of optogenetic methods, de Vries and Clandinin [1] were able to stimulate or silence these five neurons in an unrestrained fly. Silencing them demonstrated a clear reduction of escape behavior in response to looming stimuli (Figure 1B,D). That the escape behaviors were not prevented entirely is not surprising, as redundant and complementary systems often control escape.

De Vries and Clandinin [1] were also able to create a blind fly expressing Channelrhodopsin within the looming-sensitive neurons. Direct stimulation of these cells, in the

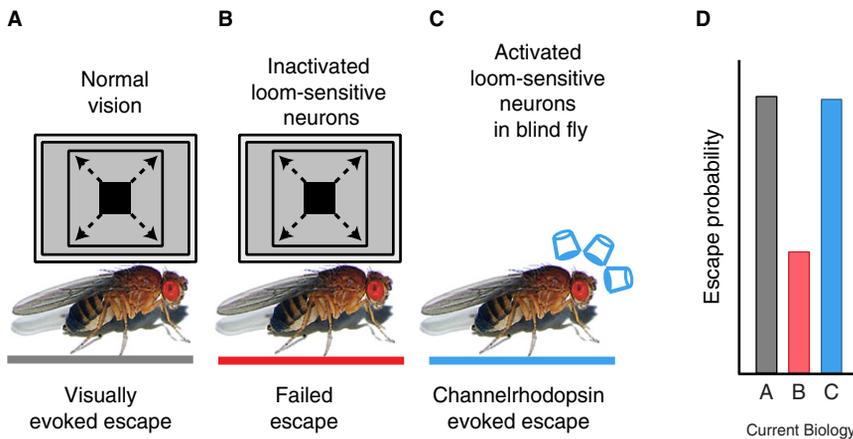


Figure 1. Genetic manipulations were used to test the role of looming-sensitive neurons in escape behavior.

(A) Wild-type flies show a stereotypical escape jump when presented with an expanding square to simulate a directly approaching object. (B) When just five looming-sensitive neurons were silenced, flies were much less likely to attempt escape. (C) Optogenetic stimulation with blue LEDs of only these neurons in the absence of any visual inputs produced escape behavior in the animals, indicating that the activity of these neurons alone was often sufficient to initiate the behavior. (D) Relative probability of escape behavior in the three conditions. Letters and colors match conditions in A–C. Based on [1].

absence of visual input, was often sufficient to produce the characteristic looming evoked escape behavior (Figure 1C), including the ‘planning’ stage preceding a directed jump. Further, activation of the neurons upstream of the looming detectors, which are not tuned to approaching objects, produced no increase in escape behavior. This confirmed that the looming-sensitive neurons are sensing the object’s approach and initiating the escape.

Refinement of these techniques will allow further research to address even more detailed questions, including whether all five of the neurons need to be activated, or whether the escape may be initiated by just one or a few of them on its own. It also remains unknown if the particular duration or activity pattern of the neurons produced by optogenetic stimulation matter for the behavior. Future investigations, along with the present

work, will continue to reveal the mechanisms used by nervous systems to make the complex evaluations of sensory inputs necessary to produce appropriate behavioral responses in the face of an impending threat.

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Meiosis: Mouse Eggs Do Their Anaphase Topsy-Turvy

The meiotic separation of sister chromatids in mature metaphase II mouse eggs is observed to depend initially on spindle lengthening (Anaphase B), then on microtubule shortening (Anaphase A). Having Anaphase B precede