This Week in The Journal

Regulation of Wallerian Degeneration in *Drosophila*

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(see pages 8457–8470)

When peripheral axons are severed, the distal parts remain intact for several hours, then rapidly degenerate in a process called Wallerian degeneration. Mutations that slow Wallerian degeneration have led to the discovery of several molecular events that set the process in motion. One early step is the depletion of nicotinamide adenine dinucleotide (NAD^+) as a result of increased degradation triggered by SARM1 and reduced synthesis stemming from loss of the NAD^+-synthesizing enzyme NMNAT2. Activation of SARM1 and/or depletion of NAD^+ lead to activation of a mitogen-activated protein kinase cascade that involves DLK and JNK and is thought to promote disassembly of the cytoskeleton in the disconnected axon. At the same time, however, activation of DLK and JNK proximal to the injury leads to activation of the transcription factors *fos* and *jun*, which promote regeneration of the proximal axon stub (Girouard et al., 2018, Dev Neurobiol 78:978).

While investigating whether a caspase that contributes to apoptosis is also involved in Wallerian degeneration, Hao et al. encountered a spontaneous mutation that slowed axonal degeneration after nerve crush injury in *Drosophila*. They localized the protective mutation to the *raw* gene, which was previously shown to restrain JNK-mediated signaling. The missense mutation resulted in a partial loss of function, which could be replicated by knocking down *raw* and, as expected, resulted in increased JNK signaling. Expressing a dominant-negative form of JNK accelerated axon degeneration in *raw* mutants, and dominant-negative forms of *fos* and *jun* eliminated the protective effects of the *raw* mutation, suggesting these effects are mediated by the JNK–*fos/jun* pathway. In contrast, the *raw* mutation did not alter the level of Nmnat, and reducing either Nmnat or DLK did not reduce the protective effect of the mutation.

These results indicate that the propensity for *Drosophila* axons to degenerate after nerve crush is influenced by *raw*-dependent regulation of JNK activity and downstream regulation of *fos* and *jun*. This transcriptional effect likely occurs before the axon is severed, when the targets of *fos* and *jun* are still able to reach the distal axon. Further exploration of this pathway might provide additional clues about the mechanisms of axon stabilization, which might then be targeted to slow degeneration.

Dragonflies have a neuron, CSTMD1, that exhibits selective visual attention. See Lancer et al. for details. Flickr photo by Donald Hobern (creativecommons.org/licenses/by/2.0/legalcode).

Selective Attention in a Single Dragonfly Neuron

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(see pages 8497–8509)

The ability to focus on one object in a crowded visual field is essential for many activities in humans and other species. When dragonflies hunt, for example, they must focus their attention on a single insect in a swarm. Remarkably, this selective attention can be detected at the level of a single neuron, named CSTMD1, in the dragonfly optic lobes and midbrain. Although CSTMD1 can respond to objects anywhere in the dragonfly's visual field (preferably small, dark, fly-like specks moving upward against a bright background), its spiking can be driven by a single target in the field.

Lancer et al. used frequency tagging to investigate the selective-attention properties of CSTMD1 *in vivo*. Because the spike rate of CSTMD1 varies with stimulus contrast, modulating the contrast at a given frequency causes CSTMD1 spiking to vary at the same frequency. Lancer et al. found that when the contrasts of two simultaneously presented targets were modulated at different frequencies, spiking in CSTMD1 oscillated at one frequency or the other, suggesting that the spiking was driven by only a single target. Nonetheless, modulation in CSTMD1 sometimes switched from one target frequency to the other, suggesting that the focus of attention had switched.

The authors also showed that CSTMD1 can be primed to attend to a specific target: they first presented an unmodulated priming stimulus moving along an upward trajectory, then presented one frequency-modulated target that continued along the primed trajectory and another frequency-modulated target that moved along a different trajectory. CSTMD1 exhibited response modulation at the same frequency as the target that followed the primed trajectory, even if the other target had a higher contrast and was therefore expected to generate a larger-amplitude response. Although response modulation in CSTMD1 often switched to match the frequency of the high-contrast target, it sometimes continued to match the frequency of the low-contrast-target throughout the trial, without any change in response amplitude. This suggests that the mechanism of selective attention in CSTMD1 differs from that hypothesized to occur in primate visual cortex, where selective attention increases response amplitude. How selective attention develops in CSTMD1 and how it aids prey capture are intriguing topics for future research.

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