This Week in The Journal

Homeostatic Plasticity in Somatosensory Interneurons

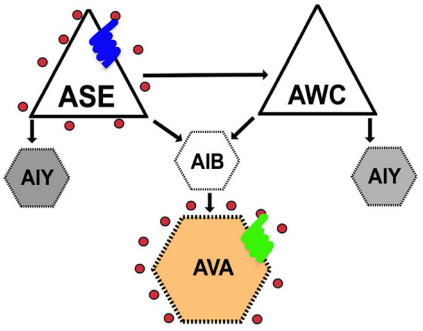
Melanie A. Gainey, Joseph W. Aman, and Daniel E. Feldman

(see pages 4749–4761)

Synapses are strengthened when presynaptic spikes precede postsynaptic spikes; otherwise, they are weakened. This so-called Hebbian plasticity works with homeostatic plasticity—which maintains neuronal spiking in a preferred range—to optimize information processing in the brain. When primary sensory cortex is deprived of afferent input, Hebbian mechanisms weaken synapses from inactive afferents, whereas homeostatic processes make neurons more responsive to remaining inputs. The latter synapses are eventually strengthened through Hebbian processes, so neurons' response properties change. Thus, when individual whiskers are removed in rodents, neurons in primary somatosensory cortex that responded to those whiskers ultimately become more sensitive to movement of adjacent whiskers. This shift occurs gradually, however. In fact, whisker-evoked spiking in layer 2/3 (L2/3) pyramidal neurons of rat somatosensory cortex remains unchanged for up to 7 d after whiskers are trimmed, despite decreased excitatory afferent input. The enhanced responsiveness results from a rapid decrease in inhibitory input to the cells (Li et al., 2014 Proc Natl Acad Sci U S A 111:1616).

Gainey et al. now report that excitatory and inhibitory inputs to L2/3 pyramidal cells decrease within 1 d of whisker removal in young mice. Inhibition was reduced more than excitation, however. The loss of inhibition stemmed from a decrease in the ability of L4 excitatory neurons to evoke spiking in L2/3 parvalbumin-expressing (PV) interneurons. Excitatory and inhibitory conductances evoked in PV cells were indistinguishable in whisker-deprived and control brains, however, indicating that synaptic input from L4 to these cells was unchanged. But the spike threshold of deprived PV cells was more depolarized than that of controls. Moreover, a given amount of current injection produced fewer spikes in deprived cells, and the latency to the first spike was increased. These effects were likely mediated by increases in two types of voltage-sensitive potassium currents: a delayed-rectifier current and the transient A-type current.

These results suggest that the excitability of L2/3 PV neurons in rat somatosensory cortex decreases within 1 d of whisker deprivation, helping to maintain normal firing in L2/3 pyramidal cells. Future work should explore the molecular mechanisms underlying this circuit-level homeostatic plasticity and determine how reductions in inhibitory and excitatory input are coordinated to maintain normal responses to whisker deflection.



FLP-18 (red), which is upregulated during starvation, acts on NPR-1 receptors in ASE sensory neurons and NPR-4 receptors in AVA command neurons to reduce the length of reversals. See Bhardwaj et al. for details.

How Food Deprivation Shapes Nematode Locomotion

Ashwani Bhardwaj, Saurabh Thapliya, Yogesh Dahiya, and Kavita Babu

(see pages 4641–4654)

While foraging for food, nematodes are guided by numerous cues. These cues act by changing the frequency and duration of basic locomotor patterns: forward undulations, reverse undulations, slight turns, and sharp omega turns. When food is abundant, *Caenorhabditis elegans* move slowly forward and make frequent short reversals that are often followed by a small-angle turn. This behavior ensures that worms take full advantage of a food source before moving on. When worms are removed from food, their forward speed and the duration of reversals increase, and reversals are often followed by omega turns, leading to large changes in direction that promote local exploration. If this strategy fails to yield food, worms change direction less frequently and disperse over a larger area (Gray et al., 2005 Proc Natl Acad Sci U S A 102:3184). Although previous work has identified the sensory, motor, and interneurons that control nematode locomotion, how environmental cues influence these circuits to alter behavior is only partially understood.

Bhardwaj et al. have discovered some of the molecular mechanisms and neural pathways through which food deprivation alters nematode locomotion. They found that levels of the neuropeptide FLP-18 increased after 24 h of food deprivation. At the same time, the duration of reversals was decreased. Similar effects occurred in mutants lacking functional CREB1/CRH-1, a transcription factor that likely regulates FLP-18 expression.

The effect of food deprivation was absent in *flp-18* mutants, as well as in mutants lacking two FLP-18 receptors, NPR-1 and NPR-4. Notably, the duration of reversals was greater in *flp-18*, *npr-1*, and *npr-4* mutants than in controls even when worms were well fed. Moreover, calcium levels in AVA neurons, which were previously shown to control reversals, were higher during reversals in mutant worms than in controls. Finally, the increased reversal duration in *npr-1*/*npr-4* double mutants was partially rescued by expressing *npr-1* in ASE sensory neurons or expressing *npr-4* in AVA neurons.

Together, these results suggest that food deprivation alters nematode locomotion by increasing expression of FLP-18, possibly by altering the activity of CREB1/CRH-1. Through actions on NPR-1 and NPR-4 in ASE and AVA neurons, FLP-18 reduces the activity of AVA, and thus limits reversal duration. This might facilitate the worm's search for food.

This Week in The Journal was written by Teresa Esch, Ph.D.