This Week in The Journal

Purkinje-Cell Complex Spikes Alter Simple-Spike Encoding

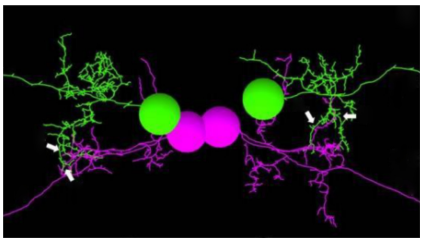
Martha L. Streng, Laurentiu S. Popa, and Timothy J. Ebner

(see pages 1997–2009)

The cerebellum is essential for motor learning and coordinating ongoing behaviors. To perform these functions, the cerebellum is thought to monitor the effects of motor commands and provide a signal to adjust these commands when an error occurs. A long-standing hypothesis proposes that complex spikes, which are evoked in Purkinje cells by climbing fibers, signal motor errors and alter the temporal pattern of simple spikes, partly by driving plasticity at parallel-fiber synapses. The change in simple-spike pattern is thought to modulate motor output to improve performance. Although much evidence supports this hypothesis, doubts have been raised, for example, by data showing that complex spikes are absent on some error trials. Therefore, the relationships between motor errors, complex and simple spikes, and error correction remain unclear.

To investigate these relationships, Streng et al. recorded from Purkinje cells as monkeys manually tracked a pseudo-randomly moving target. They then asked how complex spikes influenced the representation of cursor position, velocity, and error by simple spikes. Their analyses revealed that complex spikes typically preceded changes in the strength and sensitivity of simple-spike encoding of these three parameters. For example, a cell that weakly represented velocity along the *y*-axis before a complex spike occurred strongly encoded that parameter after the spike. In some cases, complex spikes were followed by a decrease in the strength of encoding for one parameter and an increase in encoding of another. For example a cell that strongly encoded *x*-axis position before the complex spike might instead encode *y*-axis position afterwards. In many cells, an increase in encoding strength for a particular parameter was followed by a significant change in that parameter at the behavioral level. In contrast, significant behavioral changes rarely preceded complex spikes and the associated changes in simple-spike patterns.

These results suggest that during ongoing tasks that require constant monitoring and updating of motor output, climbing fibers modulate Purkinje cell responses to parallel-fiber inputs. In particular, complex spikes appear to change which kinematic parameters are encoded by Purkinje-cell simple spikes, and this often precedes behavioral changes in that parameter. Such changes might serve to reduce movement errors, but this needs to be confirmed with future research.



Pairs of motor neurons in the first (green) and second (purple) abdominal segments of a *Drosophila* larva. Arrows indicate contact sites where gap junctions might occur. See Matsunaga et al. for details.

Motor Neuron Feedback Influences Locomotor Rhythms

Teruyuki Matsunaga, Hiroshi Kohsaka, and Akinao Nose

(see pages 2045–2060)

Locomotion is driven by central pattern generators that activate motor neurons in regular sequences. In *Drosophila* larvae, locomotion involves waves of motor-neuron activity and muscular contraction that travel along the nerve cord from back to front. Propagation of these waves depends on interneurons that project between segmental ganglia. Increasing evidence suggests that motor neurons can also influence the generation and/or propagation of locomotor activity in various species. In *Drosophila* larvae, for example, Inada et al. (2011 PLoS One 6:e29019) found that locally inhibiting motor neurons stopped the progression of muscular contraction during locomotion.

To determine how motor neurons influence locomotor rhythms, Matsunaga et al. expressed light-sensitive proteins in these neurons and manipulated their activity in isolated nerve cords. Inhibition of motor neurons in middle hemisegments reduced the frequency of locomotor waves. Inhibiting neurons in anterior or posterior hemisegments had no effect, however. In contrast, stimulating motor neurons in posterior hemisegments increased wave frequency. Because sensory feedback was absent in these experiments, the effects must have been mediated by direct communication between motor neurons and the locomotor circuit.

Inhibiting middle-segment motor neurons caused calcium levels to decrease in motor neurons along the entire contralateral nerve cord. Conversely, stimulating posterior motor neurons increased calcium levels. When gap junctions were blocked pharmacologically, neither inhibition nor stimulation of motor neurons altered locomotor wave frequency or calcium levels. But experiments in larvae lacking the gap junction proteins ShakB or Ogre indicated that motor neurons did not regulate wave frequency by changing calcium levels. In mutant larvae, inhibiting or stimulating motor neurons failed to affect wave frequency despite changing calcium levels as usual. Finally, knocking down ShakB selectively in motor neurons blocked the effects of inhibition on locomotor-wave frequency, but restricted knockdown of Ogre did not.

Together, these data indicate that motor neurons can influence locomotor circuits via multiple types of gap junctions. To modulate the frequency of locomotor waves, motor neurons must express ShakB and form gap junctions with cells that express Ogre (most likely interneurons). Gap junctions composed of other proteins enable motor neurons to influence each others' calcium levels. If and how widespread changes in motor-neuron calcium levels affect behavioral output remains unclear.

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