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The Problem

Organisms from ants to horses to humans all get around the same way—walking. But what happens when a spinal cord injury or disease like Parkinson’s damages nerve cells leading to the limbs and makes walking difficult or impossible? And what causes mysterious pain in the limbs, such as those experienced in fibromyalgia or phantom limb pain? Scientists want to create ways to repair or regenerate these nerve cells and restore walking ability or prevent patients from losing coordinated walking as a disease progresses. And they hope to develop better therapies for chronic pain that involves the neural circuitry of the spinal cord and limbs. But there’s a big hurdle: They don’t have a good understanding of how the nerve cells that allow walking and pain sensation develop in the first place, or even all the cells involved.

The Approach

Martyn Goulding developed a specialized experimental setup that let him pinpoint in mice the subset of neurons required for locomotion. Neurons called V0 neurons, he discovered, mediate the alternating left-right pattern of walking, while V1 neurons set pace and a third set of neurons controls muscle activity.

Armed with this technique and the new knowledge of important neuron types, Goulding has been able to delve into the genetics and development of these walking neurons. He can introduce genetic mutations into mice and observe the effect on their walking ability, uncovering which genes are important for locomotion. In other experiments, Goulding also studies how

neuron cells implicated in walking grow, develop and connect muscles to the right spots in the brain in fetal mice. The knowledge of what neurons are needed for smooth walking might help scientists develop drugs or techniques that prevent diseases like Parkinson’s from affecting walking, or restore walking ability in people with spinal cord injuries. Goulding has also leveraged his expertise in spinal neural circuitry to explore the causes of mysterious chronic pain.

The Innovations and Discoveries

- Goulding’s lab identified an important neural mechanism in the spinal cord that appears capable of sending erroneous pain signals to the brain. By charting the spinal circuits that process and transmit pain signals in mice, the study lays the groundwork for identifying ways to treat pain disorders that have no clear physical cause.
- Goulding’s team mapped the neural circuitry of the spinal cord that processes the sense of light touch. A better understanding of these circuits should eventually aid in developing therapies for spinal cord injury and diseases that affect motor skills and balance, as well as the means to prevent falls for the elderly.
- Goulding discovered the role of V3 neurons in walking—the neurons, he showed, help coordinate movement between the two sides of the body.

For more information, please visit:
www.salk.edu/scientist/martyn-goulding

Genetics, Neurological Disease, Locomotion,
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