Spinal cord findings could help explain origins of limb control

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We might have more in common with a lamprey than we think, according to a new Northwestern University study on locomotion. At its core, the study of transparent zebrafish addresses a fundamental evolution issue: How did we get here?

Neuroscientists Martha W. Bagnall and David L. McLean have found that the spinal cord circuits that produce body bending in swimming fish are more complicated than previously thought.

Vertebrate locomotion has evolved from the simple left-right bending of the body exemplified by lampreys to the appearance of fins in bony fish to the movement of humans, with the complex nerve and muscle coordination necessary to move four limbs.

Bagnall and McLean report that differential control of an animal's musculature—the basic template for controlling more complex limbs—is already in place in the spinal networks of simple fish. Neural circuits in zebrafish are completely segregated: individual neurons map to specific muscles.

Specifically, the neural circuits that drive muscle movement on the dorsal (or back) side are separate from the neural circuits activating muscles on the ventral (or front) side. This is in addition to the fish being able to separately control the left and right sides of its body.

Ultimately, understanding more about how fish swim will allow scientists to figure out how humans walk.

"Evolution builds on pre-existing patterns, and this is a critical piece of the puzzle," McLean said. "Our data help clarify how the transition from water to land could have been accomplished by simple changes in the connections of spinal networks."

The findings will be published Jan. 10 in the journal *Science*. McLean, an assistant professor of neurobiology in the Weinberg College of Arts and Sciences, and Bagnall, a postdoctoral fellow in his research group who made the discovery, are authors of the paper.

"This knowledge will put us in a better position to devise more effective therapies for when things go wrong with neural circuits in humans, such as spinal cord damage," McLean said. "If you want to fix something, you have to know how it works in the first place. Given that the fish spinal cord works in a similar fashion to our own, this makes it a fantastic model system for research."

McLean and Bagnall studied the motor neurons of baby zebrafish because the fish develop quickly and are see-through. They used state-of-art imaging techniques to monitor and manipulate neuronal activity in the fish.

"You can stare right into the nervous system," McLean said. "It's quite remarkable."

The separate circuits for moving the left and right and top and bottom of the fish allow the animal to twist its body upright when it senses that it has rolled too far to one side or the other.

"This arrangement is perfectly suited to provide rapid postural control during swimming," Bagnall said. "Importantly, this ancestral pattern of spinal cord organization may also represent an early functional template for the origins of limb control."

Separate control of dorsal and ventral muscles in the fish body is a possible predecessor to separate control of extensors and flexors in human limbs. By tweaking the connections between these circuits as they elaborated during evolution, it is easier to explain how more complicated patterns of motor coordination in the limbs and trunk could have arisen during dramatic evolutionary changes in the vertebrate body plan, the researchers said.

"We are teasing apart basic components of locomotor circuits," McLean said. "The molecular mechanisms responsible for building spinal circuits are conserved in all animals, so this study provides a nice hypothesis that scientists can test."

More information: The paper is titled "Modular Organization of Axial Microcircuits in Zebrafish." www.sciencemag.org/content/343/6167/197.abstract

Provided by Northwestern University