Parallel brainstem circuit discovery suggests new path in Parkinson's research

19 May 2010

Chicago and Montreal researchers studying the lowly lamprey eel have identified an overlooked nervous system pathway running parallel to known brainstem locomotor command circuitry in vertebrates such as birds, fishes and mammals.

The finding is reported in Nature Neuroscience, online May 16, and highlighted in the magazine's "news and views" section.

Simon Alford, University of Illinois at Chicago professor of biological sciences and the article's corresponding author, said the role of a neurotransmitter associated with this parallel pathway may also suggest new research directions for treating Parkinson's disease.

Alford, along with his former graduate student and lead author Roy Smetana, now a University of Pittsburgh resident in psychiatry, worked with Université de Montréal and Université de Québec à Montréal neurobiologist Réjean Dubuc and his post-doctoral researcher Laurent Juvin in trying to sort out how the neurotransmitter analog muscarine modifies sensory information going to the brain.

Their work determined that muscarine stimulated neural activity, leading to locomotion in the laboratory lampreys.

The group focused its attention on a collection of brainstem neurons that tell the spinal cord to generate motor output that enables walking and other locomotion.

"We started looking at this group of neurons, which in the lamprey are conveniently very large, so they're easy to plant electrodes and record from," said Alford. "We discovered the muscarinic excitation was not working on these cells, but on a previously unknown group of cells within the brainstem."

What's more, these newly discovered brainstem neurons showed what Alford called a "very odd response" to the muscarine.

"Instead of just turning on -- like a synapse turns on a neuron and makes it fire -- when you put muscarine on these cells, they turn on and stay on" for a minute or longer which he said for a neurological reaction can be a very long time.

The researchers discovered the actual brain neurotransmitter that activates muscarine receptors -- another chemical, acetylcholine -- sends a signal to these newly discovered brainstem neurons, switching them on for the lengthy minute or so durations.

Alford said the finding opens up new insights into animal locomotion.

"It's a system for turning on your locomotor system and making you walk or run in a very coordinated, straight-line fashion sustaining locomotion for a considerable time," he said. "This simply was not known to exist before we discovered it."

The role of the neurotransmitter acetylcholine may ultimately suggest new Parkinson's disease treatments. While a key Parkinson's symptom is tremor, an advanced stage symptom is the inability to start a movement, such as walking. Symptoms associated with Parkinson's can be helped by reducing acetylcholine-mediated neurotransmission in the brain, but little work has focused on brainstem muscarine receptors in this disease.

"This may be a backdoor finding into a secondary effect of Parkinson's disease that's not well studied because most research emphasis has been on dopamine and the basal ganglia, a different neurotransmitter and region of the brain," Alford said.

Provided by University of Illinois at Chicago