MedicalXpress

Researchers Disprove 15-year-old Theory about the Nervous System

February 3 2009

(PhysOrg.com) -- A delay in traffic may cause a headache, but a delay in the nervous system can cause much more. University of Missouri researchers have uncovered clues identifying which proteins are involved in the development of the nervous system and found that the proteins previously thought to play a significant role, in fact, do not. Understanding how the nervous system develops will give researchers a better understanding of neurological diseases, such as multiple sclerosis and Charcot-Marie-Tooth disorders.

“Speed is the key to the nervous system,” said Michael Garcia, investigator in the Christopher S. Bond Life Sciences Center and assistant professor of biological sciences in the MU College of Arts and Science. “The peripheral nervous system ‘talks’ to muscles through nerve impulses in response to external stimuli. When babies are born, they do not have fully developed nervous systems, and their systems run slower. Eventually, the nervous system matures. Our study tried to understand that maturation process.”

The process of nerve cells maturation is called myelination. During myelination, a layer of myelin (electrically insulating material) wraps or forms around the axons (part of the nerve cell that conducts electrical impulses). Nerve impulses travel faster in myelinated nerve cells.

“Myelination is important for signal transmission because it increases nerve conduction velocity,” Garcia said. “The relationship between axons and myelinating cells is a reciprocal one, with each cell type sending and

receiving signals from the other cell. One signal originates from myelinating cells and results in a large increase in axonal diameter."

When nerve cells are unmyelinated, the axon has a smaller diameter and contains neurofilaments that are less modified and are more compact. Neurofilaments are a group of proteins that are essential for diameter growth. The protein group includes neurofilament subunits that are classified as light, medium and heavy. Loss of all neurofilaments in the axon results in myelinated axons with slowed conduction velocities.

For the last 15 years, the proposed underlying mechanism for an axon's diameter growth has focused on myelin-dependent modification of regions of neurofilaments that are located within the heavy and medium subunits. In a previous study, genetically removing the region of the medium subunit that is modified impaired growth and slowed nerve conduction. However, this did not directly test if the proposed modification was required as a much larger region was genetically removed. In the current study, researchers genetically altered the neurofilament medium subunit such that it could no longer be modified in response to myelination. Surprisingly, Garcia found that prevention of what was thought to be an extremely important modification did not affect axonal diameter.

"It is now clear that the basic mechanism for how neurofilaments affect axonal diameters remains unanswered," Garcia said. "This discovery introduces a lot of new questions."

The study, "Phosphorylation of Highly Conserved Neurofilament-M KSP Repeats Is Not Required for Myelin-Dependent Radial Axonal Growth," was published in *The Journal of Neuroscience*. The research was funded by the National Institutes of Health.

Provided by University of Missouri