Proteins important in Alzheimer's, Parkinson's disease travel in the slow lane

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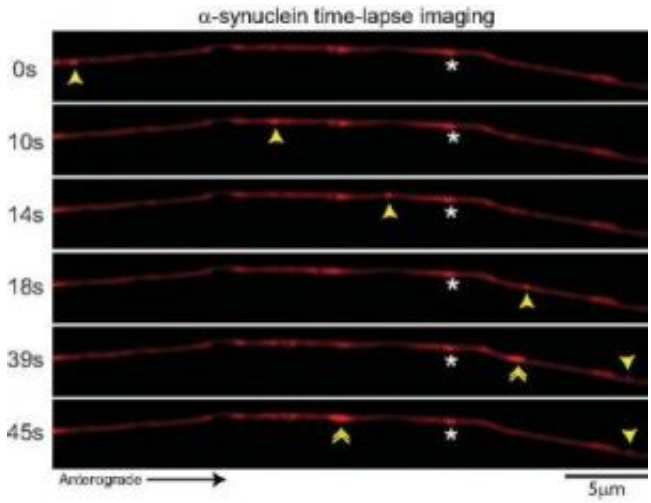

Slow transport protein alpha-synuclein moving along an axon (arrowheads mark movement). Credit: Subhojit Roy, MD, PhD, University of Pennsylvania School of Medicine

Using a novel video-imaging system, researchers at the University of Pennsylvania School of Medicine have been able to observe proteins important in Alzheimer's and Parkinson's disease moving along axons, extensions of nerve cells that carry proteins away from the cell body. Understanding this process of axonal transport is important for studying many neurodegenerative diseases. The study appeared in the *Journal of Neuroscience*.

Axonal transport often breaks down and many neurodegenerative

diseases are characterized by defects in this process. Of particular interest is a group of transported proteins called slow component-b that includes synuclein and tau, disease proteins involved in Parkinson's and Alzheimer's disease, respectively, in addition to many other proteins critical for axonal growth and regeneration.

"There are two basic transport groups called fast and slow components, with a 200 to 300 fold difference in average velocities," says first author Subhojit Roy, MD, PhD, a neuropathologist and Research Associate in the Department of Pathology and Laboratory Medicine. "While scientists have seen proteins in the fast component move rapidly to the tip of the axon, until now, mechanisms of the slow movement of these disease-related proteins have been unclear as their transport had not been directly visualized."

Roy devised a system to simultaneously visualize the transport of two labeled slow-component-b proteins in living cultured mouse axons. This clarified unique aspects of slow-protein transport. He found that the "slow" proteins actually showed rapid bursts of movement followed by pauses. This intermittent transport behavior of individual cargoes made the overall population slow and suggests that fast and slow proteins use the same basic mechanisms for transport.

Surprisingly, the videos also revealed that multiple slow proteins are transported together as "packets," essentially piggy-backing on each other, possibly on the same specialized proteins called molecular motors. "It makes sense when you think about it – why would the neurons spend so much energy transporting proteins separately when they're going to the same place anyway, like car pooling" speculates Roy.

"Our study reveals novel aspects of axonal transport of an important class of proteins, namely the slow component-b proteins, and also opens up new avenues for investigating axonal transport defects in

neurodegenerative diseases," concludes Roy.

Source: University of Pennsylvania