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Investigating the Role of Dystrophin in Neuronal Homeostasis

Authors : Samantha Shallop, Hakinya Karra, Tytus Bernas, Gladys Shaw, Gretchen Neigh, Jeffrey Dupree, Mathula Thangarajh

Abstract : Abnormal neuronal homeostasis is considered a structural correlate of cognitive deficits in Duchenne Muscular Dystrophy. Neurons are highly polarized cells with multiple dendrites but a single axon. Trafficking of cellular organelles are highly regulated, with the cargo in the somatodendritic region of the neuron not permitted to enter the axonal compartment. We investigated the molecular mechanisms that regular organelle trafficking in neurons using a multimodal approach, including high-resolution structural illumination, proteomics, immunohistochemistry, and computational modeling. We investigated the expression of ankyrin-G, the master regulator controlling neuronal polarity. The expression of ankyrin G and the morphology of the axon initial segment was profoundly abnormal in the CA1 hippocampal neurons in the mdx52 animal model of DMD. Ankyrin-G colocalized with kinesin KIF5a, the anterograde protein transporter, with higher levels in older mdx52 mice than younger mdx52 mice. These results suggest that the functional trafficking from the somatodendritic compartment is abnormal. Our data suggests that dystrophin deficiency compromised neuronal homeostasis via ankyrin-G-based mechanisms.

Keywords : neurons, axonal transport, duchenne muscular dystrophy, organelle transport
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