The development, plasticity and pathology of myelinated CNS axons.

https://neurodegenerationresearch.eu/survey/the-development-plasticity-and-pathology-of-myelinated-cns-axons/

Name of Fellow

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Institution
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Research Abstract

CNS white matter transmits information rapidly between grey matter computational nodes. Its function depends on oligodendrocytes wrapping myelin around axons to speed action potential

propagation. Myelinated axons are poorly understood, which is surprising, given that: (i) the white matter is half of the human brain, (ii) development of myelin is crucial for normal brain function, (iii) white matter plasticity is increasingly invoked as a learning mechanism, and (iv) myelinated axon dama ge disrupts cognitive and motor function in cerebral palsy, multiple sclerosis, stroke, spinal cord injury and age-related vascular dementia. We will address the following key problems in our understanding of CNS myelinated axons. How is oligodendrocyte development regulated to set axonal conduction speed? The roles of neurotransmitter- and voltage-gated ion channels in oligodendrocyte precursors, provision of N-acetyl-aspartate from neurons (a pathway revealed by human mutations), and mole cules assembling the node of Ranvier, are poorly understood. What are the mechanisms of white matter plasticity? Diffusion tensor imaging has demonstrated structural plasticity of myelinated axons during learning, perhaps reflecting addition of myelin to adjust axonal conduction speed and thus promote synchrony of action potential arrival at target neurons. Simulations suggest that altering node geometry and periaxonal space width, as well as myelination, could tune conduction speed. We will develop an in vitro model to study white matter plasticity. How is the oligodendrocyte-axonal unit disrupted in pathology? How are the node of Ranvier and the internodal myelin affected, what signalling pathways are involved, and how do microglia survey oligodendrocytes to assess their health?

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