

Experience-Dependent Myelination: Neuropeptides as Axonal Signals for Oligodendrocyte Differentiation and Myelination

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Live Webinar
via Zoom Conference



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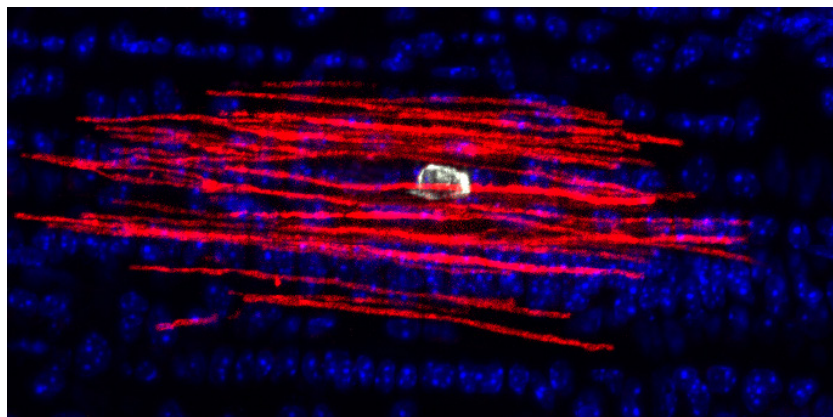
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Abstract

Emerging evidence implicates experience-dependent myelination in learning and memory. However, the specific signals underlying this process remain unresolved. We demonstrate that the neuropeptide dynorphin, which is released from neurons upon high levels of activity, promotes experience-dependent myelination. Following forced swim stress, an experience that induces striatal dynorphin release, we observe increased striatal oligodendrocyte precursor cell (OPC) differentiation and myelination, which is abolished by deleting dynorphin or blocking its endogenous receptor, kappa opioid receptor (KOR). We find dynorphin also promotes developmental OPC differentiation and myelination and demonstrate that this effect requires KOR expression specifically on OPCs. We characterize dynorphin-expressing neurons and use genetic sparse-labeling to trace their axonal projections. Surprisingly, we find they are unmyelinated normally and following forced swim stress. We propose a new model whereby experience-dependent and developmental myelination is mediated by unmyelinated, neuropeptide-expressing neurons that promote OPC differentiation for the myelination of neighboring axons.



1. Preservation of a remote fear memory requires new myelin formation. *Nat Neurosci.* 2020 04; 23(4):487-499. Pan S, Mayoral SR, Choi HS, Chan JR, Kheirbek MA. PMID: 32042175.
2. Myelin degeneration and diminished myelin renewal contribute to age-related deficits in memory. *Nat Neurosci.* 2020 04; 23(4):481-486. Wang F, Ren SY, Chen JF, Liu K, Li RX, Li ZF, Hu B, Niu JQ, Xiao L, Chan JR, Mei F. PMID: 32042174.
3. Initiation of CNS Myelination in the Optic Nerve Is Dependent on Axon Caliber. *Cell Rep.* 2018 10 16; 25(3):544-550.e3. Mayoral SR, Etxeberria A, Shen YA, Chan JR. PMID: 30332636.

