



556.20 / B99 - Regulation of oligodendrocyte exploratory behavior and sampling of axons by neural activity

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Abstract

Oligodendrocytes (OLs), the myelinating cell type of the CNS, interact with a plethora of diverse neuronal subtypes but only wrap a select subset with myelin sheaths. Prior to initiating axon wrapping, OLs dynamically extend and retract membrane processes in order to contact and sample numerous axons. Whether neural activity-dependent mechanisms regulate exploratory axon sampling, target axon recognition, and stabilization of OL-axon interactions prior to initial axon wrapping is unknown. To test this, we directly observed interactions between pre-myelinating OL processes and individually labeled target axons in larval zebrafish using time-lapse confocal microscopy. In control larvae anesthetized with the neuromuscular blocker pancuronium bromide, we observed dynamic axon sampling characterized by frequent formation and turnover of OL-axon interactions. In contrast, treatment with the neural activity blocker tricaine methanesulfonate (MS-222) caused reduced frequency of new interaction formation, increased interaction duration, and reduced frequency of interaction retraction. Time-lapse imaging revealed differential effects on OL-axon interactions at axon varicosities and thin, intervening segments. Specifically, the destabilizing effects of neural activity on OL-axon interactions were heightened at axon varicosities. MS-222 increased contact durations at varicosities but not at neighboring intervening segments. Neural activity manipulations also influenced the dynamics of axon varicosity formation, lifetime, and turnover, raising the possibility that changes to axon morphology or local properties could direct OL-axon interactions and subsequent myelination. Taken together, we conclude that neural activity negatively regulates the duration of OL-axon interactions prior to initial axon wrapping and myelination. These findings support a mechanism whereby neural activity plays opposing roles on OL-axon interactions before and after initial myelin ensheathment. Prior to ensheathment, neural activity destabilizes interactions, which may serve to facilitate increased overall sampling of potential wrapping sites. After successful ensheathment, neural activity stabilizes OL-axon adhesion in order to promote continued growth and maturation of the myelin sheath. Current and future studies aim to understand the reciprocal effects between OL processes and axon morphology, and the effects of synaptic vesicle release during initial OL-axon interactions.

Abstract Citation