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Oligodendroglial responses to neuronal activity in the developing and adult CNS

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Human neuroimaging studies and animal models suggests that neuronal activity can influence myelination in an adaptive manner, potentially allowing for strengthening or synchronization of specific connections and circuits. The degree to which dynamic changes to myelin really serve as a physiologically relevant form of neuroplasticity in the nervous system is unknown, however. In particular, it is not clear whether neural activity can modulate myelination at the level of individual axons, which would presumably be a requirement for adaptive modulation of circuitry. We investigate this by manipulating neural activity in the postnatal mouse brain using a pharmacogenetic approach (the DREADDs). Enhancement of neural activity in a small subset of collosally projecting neurons increased the proliferation and subsequent differentiation of OPCs within the white matter of both the developing and adult CNS, albeit with slower kinetics in the adult. In addition to these relatively broad lineage changes, neural activity resulted in selective changes to the myelination of activated axons, within increased thickness of the myelin surrounding DREADD expressing axons and preferential myelination of these axons by newly formed oligodendrocytes. These results underscore that highly specific changes to myelin are a feasible form of neuroplasticity in the intact adult nervous system. We are currently using a number of genetic approaches to study the *in vivo* transcriptional responses of oligodendroglia to neuronal activity to better understand the genetic pathways mediating adaptive myelination.