

Role of TrkB Deletion from NG2+ Cells following Cuprizone-Induced Demyelination in Mice

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Brain-derived neurotrophic factor (BDNF) is a growth factor known to be involved with oligodendrocyte differentiation following a demyelinating lesion. BDNF binds with high affinity to tropomyosin receptor kinase B (TrkB) receptors. However, these receptors are present on multiple cell types. Recent studies in the Dreyfus lab have revealed that deletion of the receptors on mature oligodendrocytes (OLGs) within the lesion site reduces myelin and myelin protein. On the other hand, little is known about the direct effect of BDNF on oligodendrocyte progenitor cells (OPCs) in such lesions. Here, we examine the role of the TrkB pathway on OPCs following a demyelinating lesion. Male C57BL/6 mice with TrkB deleted from NG2+ OPCs (NG2Cre-floxed TrkB) were injected with 1 mg tamoxifen intraperitoneally (IP) twice daily for 5 days. Afterwards, the mice were fed 0.2% cuprizone feed or control feed for 5 weeks. The mice then were sacrificed, and the corpus callosum overlying the hippocampus was collected. Western blots for myelin basic protein (MBP), proteolipid protein (PLP), myelin-associated glycoprotein (MAG), Neural/glial antigen 2 (NG2), platelet-derived growth factor receptor- α (PDGFR α), and TrkB were performed and analyzed, with Glyceraldehyde 3-phosphate dehydrogenase (GAPDH) and beta-tubulin (β Tub) used as loading controls. Preliminary staining for PDGFR α was used to count OPC populations between experimental groups. TrkB deletion in the cuprizone group had a decrease in NG2, PDGFR α , and PLP proteins compared to mice without TrkB deleted. Interestingly, there was no effect on MBP and MAG between mice with TrkB and without TrkB following cuprizone treatment. One explanation for these observations is that PLP is expressed in OPCs as well as mature OLGs. In addition, the TrkB deletion reduced the number of PDGFR α cells. This data suggests that BDNF has a direct effect on OPCs by influencing the number of cells and decreasing their ability to mature. Additional studies are required to confirm deletion of TrkB from NG2+ cells and to determine effects on mature cell numbers. Supported by NIH R25ES020721.

