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Role of astrocytic MeCP2 in regulation of CNS myelination by affecting oligodendrocyte and neuronal physiology and axo–glial interactions

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Abstract

Astrocytes perform several critical functions such as promoting neuronal maturation, neuronal survival, maintaining and supporting neurons and oligodendrocytes. Astrocytes participate in the formation of nodes of Ranvier. Recently, studies emphasizing on the role of astrocytes in regulating myelination by secreting pro-myelinating factors like growth factors, neurotrophins and ECM proteins, have been investigated by many researchers. Methyl-CpG-Binding Protein 2 (MeCP2), an epigenetic protein, binds to CpG islands in the genome and induces multiple gene regulatory functions by conforming changes in the chromatin structure and resulting in cell-specific gene expression. MeCP2 deficient astrocytes have been linked with abnormal neuronal function including decreased dendritic arborization and decreased dendritic outgrowth. However, role of astrocytic MeCP2 in central nervous system myelination is largely not known. The data from the current study indicate altered mRNA levels (*Lif, Cntf, Pdgfa, Cxcl10*) of astrocyte-secreted factors involved in myelination. *Bdnf* and *Ngf* mRNA levels were also altered in MeCP2 knockdown astrocytes. Moreover, the secreted BDNF levels were significantly altered whereas there were no significant changes in NGF secretion. We also observed that astrocytic MeCP2 affects the morphology, physiology and survival of oligodendrocytes and neurons—two of the key players in myelination. Further, we report that some of the axo–glial interaction genes, namely *Caspr, Notch1, Nf155* and *Nrg1* are under the regulation of astrocytic MeCP2 along with key myelin genes and proteins.

Keywords : myelinating; neurotrophins; CpG; arborization; *Caspr*