

## **Cerebrospinal Fluid of Primary Progressive MS Patients Impairs Remyelination in an Experimental Model of Multiple Sclerosis**

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**Objective:** To investigate whether primary progressive MS (PPMS), relapsing-remitting (RRMS), and secondary progressive (SPMS) cerebrospinal fluid (CSF) differentially affect remyelination after lysolecithin-induced demyelination.

**Background:** In PPMS disease progression from clinical onset is characteristic and is a result of a failure of remyelination, which is distinct from the features seen in RRMS and in early inflammatory SPMS. To further investigate these differences and to better understand the failure of remyelination in PPMS, we used the spontaneously and temporally predictable remyelinating model of lysolecithin-induced demyelination.

### **Design/Methods:**

Mice underwent a laminectomy at cervical level 5 (C5). 1µl of 1% lysolecithin was injected into the dorsal column. Five days post injection, 3µl CSF from untreated PPMS, RRMS, and SPMS patients was injected into the subarachnoid space at C5. Control mice were injected with saline or CSF obtained from healthy individuals. Motor deficits were assessed at 1, 3, and 7 days post CSF injection (DPI). Mice were perfused at 12DPI and pathology was assessed in the cervical region.

### **Results:**

Only PPMS CSF-injected mice exhibited significantly impaired forelimb function and increased tail flaccidity compared to all other experimental groups. Luxol fast blue staining revealed a significantly greater extent of demyelination in PPMS CSF-injected mice as compared to controls, RRMS and SPMS CSF-injected mice. Immunostaining revealed significantly greater microglial activation (Iba1) and astrogliosis (GFAP) for PPMS CSF-injected mice as compared to RRMS and SPMS CSF-injected mice. No significant differences were found among groups for numbers of proliferating oligodendrocyte progenitor cells (NG2/Ki67) or mature oligodendrocytes (APC/Olig2).

### **Conclusions:**

Intrathecal delivery of PPMS CSF, but not RRMS or SPMS CSF at the site of a lysolecithin-induced lesion yielded larger lesions, greater microglial activation and reactive astrogliosis, as compared to controls. This suggests that as yet unidentified factors present in PPMS CSF, but not RRMS or SPMS CSF can impede remyelination.