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Evaluating the relation of NfL, GFAP and Contactin-1 in serum and CSF with clinical and MRI measures in Progressive MS

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Introduction:

NfL, GFAP and Contactin-1 are soluble biomarkers of CNS tissue injury that are potential prognostic and treatment response biomarkers in MS. Their relationship to clinical and imaging measures of tissue injury in progressive MS is under study. SPRINT-MS was a phase 2 trial in progressive MS, and baseline serum, CSF, clinical, and imaging measures provide an opportunity to explore these relationships.

Objectives/Aims:

Evaluate the correlation between serum and CSF measures of NfL, GFAP, and Contactin-1 with clinical and imaging measures of tissue injury in progressive MS.

Methods:

255 patients (mean age 55.6 yrs; 53.3% female) with either PPMS (n=134) or SPMS (n=121) underwent clinical and MRI assessments. Serum samples and CSF (from a subset, n=70) were analyzed for NfL by SIMOA, GFAP by SIMOA, and Contactin-1 by Luminex. Clinical measures included EDSS, 9-hole peg test (9HPT), 25-foot timed walk (25FW), and low contrast visual acuity (LCVA). MRI measures included whole brain atrophy (BPF), cortical atrophy (CLADA), and MTR in normal-appearing brain tissue. Relationships were explored through Spearman rank correlations and linear regression models of the log transformed fluid biomarker values.

Results:

Serum NfL correlated with BPF (r=-0.193, p=0.002), CLADA (r=-0.198, p=0.002), EDSS (r=0.211, p<0.001), and 25FW (r=0.217, p<0.001), but not MTR, 9HPT or LCVA. Serum GFAP correlated with BPF (r=-0.301, p<0.001) and CLADA (r=-0.357, p<0.001), and LCVA (-0.157, p=0.01). Serum Contactin-1 did not correlate with any MRI or clinical measure. Most correlations of CSF measures with MRI and clinical measures were weaker than their serum counterparts and not significant, although the smaller sample size limits direct comparison. After adjusting for age and sex, the log-linear regression models found significant relationships between serum GFAP and BPF (p<0.001) and CLADA (p<0.001), and LCVA (p=0.05); CSF GFAP and MTR (p<0.001); serum NfL and CLADA (p=0.03), EDSS (p=0.01), and 25FW (p=0.03), but not CSF NfL or serum or CSF Contactin-1.

Conclusion:

In this progressive MS population, both serum NfL and serum GFAP correlated with MRI measures of tissue injury, although GFAP showed somewhat stronger correlations with MRI measures than NfL. In general, CSF measures correlated less well than serum measures, which suggests that serum may be sufficient to estimate these biomarkers and CSF sampling is unnecessary. These analyses support serum GFAP as a clinically relevant biomarker of tissue injury in progressive MS.

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