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CSF markers of blood-brain barrier integrity forecast disease progression in early MS

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Background and aim: Cortical atrophy, reflecting neuronal loss, is highly associated with long-term disability in patients with multiple sclerosis (MS). In this longitudinal study we link cerebrospinal fluid (CSF) markers of blood-brain barrier (BBB) integrity to longitudinal cortical atrophy and clinical disability.

Methods: 71 relapsing-remitting multiple sclerosis (RRMS) patients (31.2 ± 9.4 (mean ± SD), 25 males) were included in this longitudinal study. CSF and serum samples were obtained from each patient at the time of first clinical event. We analyzed CSF levels of albumin (AlbCSF), immunoglobulin A (IgACSF), IgG (IgGCSF) and IgM (IgMCSF). All patients underwent MR imaging twice with the same standardized protocol (follow-up after 12 ± 1 months) at 3T (Siemens Magnetom Trio). Longitudinal changes of cortical thickness (CT) were extracted using the FreeSurfer processing stream. The Expanded Disability Status Scale (EDSS) score at follow-up was used as a clinical outcome measure to quantify clinical disability. The rate of cortical atrophy was assessed in relation to CSF variables.

Results: Baseline AlbCSF and IgACSF were highly associated with the rate of cortical atrophy over one year. Significant correlations were found in the precuneus (PrC), rostral middle frontal, precentral and inferior parietal gyri of both hemispheres. The regions with the highest atrophy rates were the right PrC ($R = 0.604$, $p < 0.001$) and left fusiform gyrus ($R = 0.539$, $p < 0.001$). IgACSF and IgMCSF (IgA: 1.67 ± 0.69 mg/l vs 2.03 ± 0.71 mg/l, IgM: 9.87 ± 2.38 mg/l vs 11.5 ± 2.03 mg/l; $p = 0.04$ and $p = 0.003$, respectively) significantly differed between patients with no disability (EDSS 0 - 1.5) and those with mild to moderate disability (EDSS 2 - 6) at the second time point.

Conclusion: Our data show that widespread cortical atrophy is highly associated with increased baseline CSF Albumin and IgA mirroring a permeable BBB. Patients with this BBB pattern showed higher functional disability at follow-up. These parameters could be addressed to dichotomize patients at risk of rapid disease progression.

Disclosure

Julia Kroth: nothing to disclose