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Background: Chronic fatigue has a major impact on quality of life in MS patients. Its pathogenesis is still poorly understood. MS-related tissue damage of different brain structures has been related to fatigue. Alternatively, the inflammatory milieu within the CNS compartment itself may contribute to fatigue. Therefore, we related both volumes from structural brain magnetic resonance imaging (MRI) and measures of cerebrospinal fluid (CSF) to fatigue in patients with MS.
Methods: We determined CSF cell count, intrathecal IgG-, IgM- and IgA-synthesis and oligoclonal bands in 84 MS patients at time of diagnosis. In a subset of 31 patients, CSF was additionally analysed by flow cytometry. We performed brain MRI after a mean follow-up period of 3 years and determined volumes of grey matter, white matter, white matter lesions, thalamus, putamen, caudate nucleus, hippocampus, amygdala and nucleus accumbens. Fatigue was quantified by the Fatigue Scale for Motor and Cognitive Functions (FSMC) at the time point of MRI. We performed correlation analyses and a multiple regression analysis with fatigue as dependent variable and CSF and MRI parameters as independent variables controlling for age and total intracranial volume (TIV).
Results: No significant correlation was found between fatigue and any of the MRI parameters. In contrast, the CSF CD4/CD8-ratio and the percentage of CD8+ T cells at the time of MS diagnosis was associated with the development of fatigue ($r=-0.57$, $p=0.001$; $r=0.55$, $p=0.001$). Correlation of the CSF CD4/CD8-ratio with fatigue persisted even after correction for the EDSS as a global marker for disease severity ($r=-0.57$, $p=0.005$). In a multiple regression analysis with fatigue as dependent variable and all CSF and MRI parameters, age and TIV as independent variables, the overall model was significant ($p=0.035$; adjusted $R^2=0.46$) and confirmed the significant correlation of the CD4/CD8-ratio with fatigue ($p=0.005$).
Conclusion: Our data lend support to the idea that the inflammatory milieu in the CNS itself may contribute to the development of fatigue in MS.

Disclosure

Viola Biberacher has nothing to disclose.
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Chasing the driver of fatigue in multiple sclerosis: brain MRI versus CSF.

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Bernhard Hemmer has served on scientific advisory boards for Roche, Novartis, Bayer Schering, Merck Serono, Biogen Idec, GSK, Chugai Pharmaceuticals, Micromet, Genentech and Genzyme Corporation; serves on the international advisory board of Archives of Neurology and Experimental Neurology; has received speaker honoraria from Bayer Schering, Novartis, Biogen Idec, Merck Serono, Roche, and Teva Pharmaceutical Industries Ltd; and has received research support from Biogen Idec, Bayer Schering, Merck Serono, Five prime, Metanomics, Chugai Pharmaceuticals and Novartis. He has been filed a patent for the detection of antibodies and T cells against KIR4.1 in a subpopulation of MS patients and genetic determinants of neutralizing antibodies to interferon-beta.
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