

Definition of Regional Distribution of Gray Matter Loss in MS Patients With Fatigue: A Voxel-Based Morphometry Study

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Introduction. Fatigue is one of the most frequent and disabling symptoms in multiple sclerosis (MS) patients. MS-related fatigue has been associated with metabolic, hormonal and neurotransmitter disturbances, and, more recently, to dysfunction of cortico-subcortical networks, measured using functional magnetic resonance imaging (MRI).

Objective. The main objective of this study is to define the topographical distribution of gray matter (GM) atrophy, if present, in MS patients with fatigue, in comparison to MS patients without fatigue and matched healthy volunteers, using voxel-based morphometry (VBM).

Methods. This study included twenty-four patients with relapsing-remitting (RR) MS and fourteen healthy volunteers (mean ages: 38.4 ± 8.0 and 38.7 ± 8.4 , respectively). MS patients were divided into two groups according to the presence/absence of fatigue. In all the subjects a high-resolution T1-weighted scan was acquired using a 1.5 Tesla scanner. VBM analysis was performed using SPM5 and an ANCOVA model (p value < 0.001 uncorrected; $k > 100$).

Results. Compared to healthy volunteers and to MS patients without fatigue, patients with fatigue had significant reduced GM volume in several areas of the left frontal lobe, including the middle frontal gyrus (MFG) (BA6 and 9), the precentral gyrus (BA4), the superior and inferior frontal gyrus (BA8 and 47), and the cingulate gyrus (BA31). Compared to MS patients with fatigue and to healthy volunteers, MS patients without fatigue showed GM atrophy in the left MFG (BA6) only. In the whole group of MS patients, FSS was significantly correlated with atrophy of the left precentral gyrus ($r = -0.76$, $p < 0.001$).

Conclusions. Patients with fatigue exhibit a more severe GM atrophy than healthy controls or MS patients without fatigue in several frontal lobe areas of the left hemisphere, which are part of the sensorimotor network.