REVERSIBLE MOVEMENT-ASSOCIATED FMRI CHANGES IN RELAPSING-REMITTING MS PATIENTS COMPLAINING OF FATIGUE AFTER WEEKLY IFNB-1A INJECTION

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Introduction. In fatigued MS patients, PET and fMRI studies (1, 2) have shown an altered recruitment of several brain regions, supporting the hypothesis of a central origin of MS-related fatigue. The correlation found in one study (2) between the extent of activity of some of these regions and the severity of fatigue suggests that an altered activation of specific brain regions might be associated with the appearance of clinical symptoms in MS. In order to verify this hypothesis, we evaluated the movement-associated short-term changes of brain pattern of cortical activations in a group of patients treated with interferon beta 1a (IFNb-1a) (AVONEX, 30 μgr i.m. weekly) complaining of fatigue after drug administration. We reasoned that if fatigue in MS is related to an abnormal activation of specific brain regions, the activity of these regions should vary with varying fatigue complaint.

Patients and methods. Among the MS population treated with intramuscular IFNb-1a once a week attending the Outpatient Clinic of our Department, we selected 10 patients with no side effects after IFN injection and 12 patients complaining of fatigue as the unique adverse reaction. Each patient underwent three fMRI examinations: 1) before IFN injection, on the same day (entry); 2) the day after IFN injection (time1), and 3) four days after IFN injection (time2). In all occasions, they performed a simple motor task with the right, clinically unaffected, upper limb. FMRI data were analysed using the statistical parametric mapping (SPM99) software, as previously described (2). During the first fMRI session, dual-echo, magnetization transfer (MT) MRI and diffusion tensor (DT) MRI sequences of the brain were also acquired and T2-lesion loads and MT and DT MRI histograms of the normal-appearing white (NAWM) and gray (NAGM) matter were derived (3).

Results. No differences were found between the two groups of patients for any of the brain structural MRI derived metrics. Compared with entry and time2, at time1, fatigued MS patients had increased activations of the thalamus, bilaterally. On the contrary, in non-fatigued MS patients this structure was more activated at entry than at time1. Furthermore, in both groups at entry the primary sensorimotor cortex (SMC) and the supplementary motor area (SMA) were significantly more activated than at time1 and time2. At entry and time1, compared with fatigued patients, non-fatigued patients had more significant activations of the secondary sensorimotor cortex and SMA. Conversely, fatigued patients had more significant activations of the left thalamus and of several regions located in the frontal lobes, bilaterally.

Conclusions. An abnormal recruitment of the fronto-thalamic circuitry seems to be the main factor associated to reversible fatigue in patients in MS. This recruitment may be modulated negatively by IFNb-1a. Whether other therapies, specifically aimed at ameliorating fatigue, may modulate favourably this cortico-basal network has now to be investigated.

References.

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