Efficacy of an executive function intervention programme in MS: a placebo-controlled and pseudo-randomized trial

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Abstract
We evaluated a rehabilitation programme for executive deficits in multiple sclerosis patients by comparing outcome scores of a cognitive intervention group (CIG; n = 11) with those of a placebo group (n = 14) and an untreated group (n = 15). Executive functioning and verbal learning improved significantly more in the CIG. The treatment effect on verbal learning was still present at 1-year follow-up. Baseline brain atrophy, quantified by the brain parenchymal fraction, was associated with treatment effects for one aspect of executive functioning. Consequently, cognitive intervention may be beneficial and baseline brain atrophy has some predictive value in determining treatment outcome for executive functioning.

Keywords
brain atrophy, cognitive intervention, executive functioning, multiple sclerosis

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Introduction
Existing studies on rehabilitation methods for improving executive functioning in multiple sclerosis (MS)¹,² show some promising results, but suffer from methodological limitations such as a limitation in scope or an implementation of outcome measures that are sensitive to other cognitive processes such as deductive reasoning.

We evaluated a programme for rehabilitation of executive deficits³ in patients with relapsing–remitting MS (RRMS). According to our model⁴ executive functioning has three distinctive features: preference shifting, response shifting and working-memory. Preference shifting requires the adaptation of an object preference in face of changing contingencies. In response shifting a subject has to adapt his response strategy to the same stimulus, depending on the context. The formation of those associations relies on a working memory system, enabling the association of different circumstances with concurring responses and the internal up-dating of task-relevant information throughout the conditional tasks.

In the present study, tasks measuring these aspects of executive functioning were used as outcome measures. The efficacy in the cognitive intervention treatment group (CIG) was contrasted with the enhancement in executive functioning in a placebo group (PG; computer controlled exercises⁵) and an untreated group (UG). The long-term effects of treatment were evaluated at 1-year follow-up. Moreover, we correlated treatment effects with degree of baseline brain atrophy.⁶

Methods
Patients
Fifty RRMS patients (41 women and nine men, mean age: 44.8 (±8.2) years, mean disease duration: 92.4

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