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Research Article

Repeated Working Memory Training Improves Task Performance and Neural Efficiency in Multiple Sclerosis Patients and Healthy Controls

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Background/Objective. To explore the effectiveness of a specific working memory (WM) training program in MS patients and healthy controls (HC). **Method.** 29 MS patients and 29 matched HC were enrolled in the study. MS and HC were randomly split into two groups: nontraining groups (15HC/14 MS) and training groups (14 HC/15 MS). Training groups underwent adaptive n-back training (60 min/day, 4 days). Functional magnetic resonance imaging (fMRI) was used to monitor brain activity during n-back performance (conditions: 0-back, 2-back, and 3-back) at 3 time points: (1) baseline, (2) post-training (+7days), and (3) follow-up (+35days). **Results.** In post-training and follow-up fMRI sessions, trained groups (HC and MS patients) exhibited significant reaction time (RT) reductions and increases in Correct Responses (CRs) during 2-back and 3-back performance. This improvement of task performance was accompanied by a decrease in brain activation in the WM frontoparietal network. The two effects were significantly correlated. **Conclusions.** After WM training, both cognitively preserved MS patients and HC participants showed task performance improvement made possible by neuroplastic processes that enhanced neural efficiency.

1. Introduction

Cognitive impairment is present in 40–65% of Multiple Sclerosis (MS) patients [1]. Although the neuropsychological profile varies among patients, there is evidence that the functions mainly affected in this clinical population, even in the early stages of the disease, are information processing speed, attention, and working memory (WM) [2, 3]. A decline in cognitive functions has a negative impact on patients' daily lives and quality of life [3]. Consequently, numerous studies have been carried out in recent years to explore the potential effects of cognitive interventions focused on improving cognition in MS patients.

In this regard, several studies using functional Magnetic Resonance Imaging (fMRI) have provided positive evidence about the presence of neural plasticity in MS patients that

helps to conceal the disease's clinical expression, at least in some phases of the disease [4–6]. However, the counteracting effects of spontaneous neuroplasticity are limited and transitory, and they are ultimately overcome by the disease's progression [7].

As initial evidence of this concept, Sastre Garriga et al. [8] showed that neuropsychological training resulted in general cognitive improvement in MS patients, with an increase in activity in cerebellar areas. After this initial study, other researchers showed the efficacy of neuropsychological interventions in improving memory [9–11], attention, processing information speed, and executive functions [12–17] in MS patients. In general, the results of these studies revealed greater cerebral activation or higher functional connectivity in MS patients after completing the training program, which in some cases was positively correlated with improvements in

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