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The effects of default mode network functional connectivity modulation on cognition and quality of life of people with relapsing-remitting multiple sclerosis.

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Background: Cognitive impairment has been increasingly recognised as a common manifestation of multiple sclerosis (MS). Its detrimental effects, which are best observed by assessing memory and speed of information processing, have been reported to negatively impact on patients' quality of life (QoL). Moreover, changes in brain activity, particularly in the default mode network (DMN), appear consistently linked to cognitive impairment in patients with MS. However, this wealth of knowledge has been neglected when designing cognitive rehabilitation interventions for patients with MS which have mainly relied on symptomatic approaches.

Objectives: This study investigated the impact of a cognitive stimulation programme designed to modulate the DMN functional connectivity on cognitive performance, QoL and neuroplasticity in a cohort of people with relapsing remitting multiple sclerosis (RRMS).

Methods: Forty-five patients with RRMS (Expanded Disability Status Scale ≤ 6, age = 44.6 ± 8.8, disease duration = 9.1 ± 6.5) were randomised to three groups: standard cognitive stimulation (CS), processing-speed-loaded cognitive stimulation (PS-CS) or non-intervention control group. The CS consisted of 20 sessions of computerised multi-domain exercises aimed at inducing co-activation of DMN areas. The PS-CS was developed by limiting the amount of time for response. Participants underwent cognitive and magnetic resonance imaging (MRI) assessments at baseline and after treatment completion. Mixed repeated-

measure models were used to investigate group-by-time effects both on clinical and MRI outcome measures.

Results: Significant improvements in memory and QoL were observed in the CS compared to the other two groups. No differential effects emerged when the PS-CS and the control group were compared. However, both active treatment groups induced functional up-regulation of the posterior DMN. Moreover, the CS programme was associated with greater decoupling between the DMN and the anterior cingulate than the PS-loaded version. No microstructural diffusivity changes occurred across the three groups.

Conclusions: Cognitive stimulation focussed on the DMN induced neuroplastic changes and parallel improvements in cognitive performance. There was significant improvement in of patients' perceived QoL. This hypothesis-based treatment approach appears to benefit significantly people with RRMS experiencing cognitive impairment and should be further developed for home-based settings.