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Mechanisms of Network Changes in Cognitive Impairment in Multiple Sclerosis

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Study Question

How is functional connectivity affected in cognitively impaired patients with multiple sclerosis (MS)?

What Is Known and What This Paper Adds

While abnormalities in functional connectivity have been associated with cognitive impairment in MS, mechanisms behind these remain unclear. This study explains how functional network regions can be prone to alterations, highlighting their potential applications as biomarkers of cognitive impairment in MS.

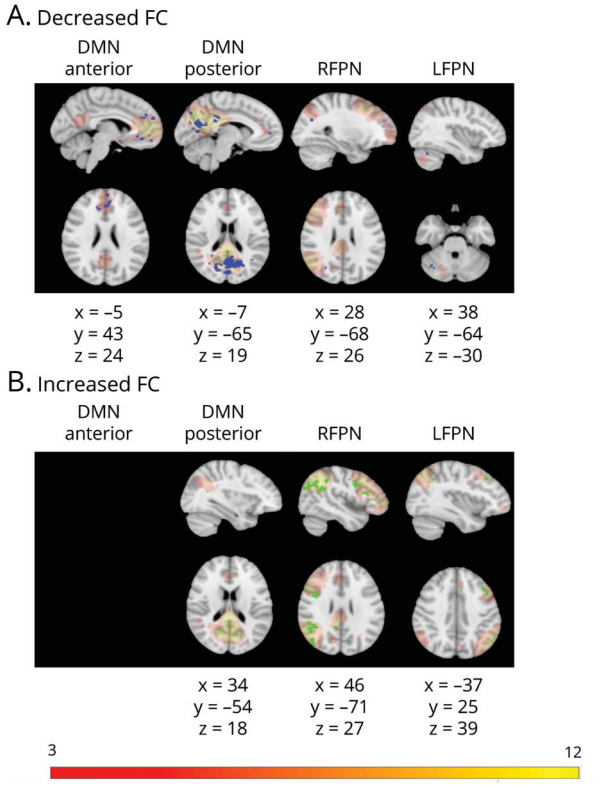
Methods

Data from 102 patients diagnosed with relapsing-remitting MS (RRMS) and 27 healthy controls (HCs) aged between 18 and 60 years were used in this study. Patients could not have other neurologic comorbidities or psychiatric disease and no changes in treatment for 3 months prior to imaging. Functional connectivity, structural connectivity, and blood flow were evaluated with 3T MRI. The MS Functional Composite (MSFC) was used to assess arm and leg function and cognitive ability. Neuropsychological assessment was done using the Brief Repeatable Battery of Neuropsychological Tests (BRB-N). Independent component analysis was used to identify resting state networks relevant to cognitive function in MS: the default mode network (DMN anterior and posterior), left and right frontoparietal networks (LFPN, RFPN) and the salience network. Diffusion MRI and arterial spin labeling was then used to assess whether any changes in these resting state networks were accompanied with local changes in anatomical connectivity and blood flow.

Results and Study Limitations

Fifty-five participants had cognitive impairment (CI) and 47 had preserved cognition. Abnormal functional connectivity was seen in all participants with RRMS compared to HCs across all the resting state networks analyzed, suggesting the pathogenic role of altered functional connectivity (FC) in MS. Further analysis revealed that patients with CI had FC abnormalities across DMN anterior and posterior, LFPN, and RFPN compared to those with preserved cognition in the absence of group differences in lesion load or gray matter volume. These resting state networks also had alterations in anatomical connectivity and cerebral blood flow, but these changes did not overlap with the regions of FC abnormalities. These findings suggest that functional connectivity of resting state networks may be particularly sensitive to CI in MS, but that the mechanisms underlying FC changes likely do not involve simple structural connectivity or metabolic changes. Limitations of this study include inclusion of a control group that was younger and more educated than the patient cohort and investigation of overall cognition and not individual cognitive domains.

Figure Functional Connectivity Abnormalities in Cognitively Impaired Compared to Cognitively Preserved Patients With MS



Study Funding and Competing Interests

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A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The corresponding author(s) of the full-length article and the journal editors edited and approved the final version.

