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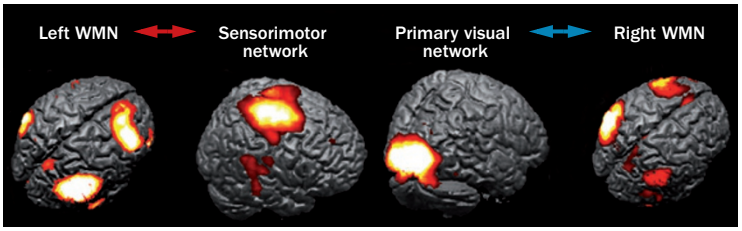
DISEASE MECHANISMS IN MS

Neuronal network connectivity is altered in multiple sclerosis

Brain functions, such as working memory and vision, are subserved by specific neuronal networks. Now, two studies published in *Neurology* have shown alterations in these brain networks in patients with multiple sclerosis (MS) under resting-state conditions.

One study, conducted by Massimo Filippi and colleagues, involved 85 patients with relapsing–remitting MS (RRMS) and 40 matched controls. The researchers used functional MRI (fMRI) to measure functional connectivity in 10 resting-state networks including, for example, sensorimotor and visual networks. "Analysis of resting-state fMRI has the advantage of not being influenced by task performance, which can vary considerably between patients," explains Filippi.

Compared with controls, patients with RRMS showed significant decreases in resting-state functional connectivity in numerous networks underlying sensory and cognitive functions. Moreover, the extent of this abnormality correlated with disability and T2 lesion volume. Increases in resting-state functional connectivity in the executive control network and auditory network were also observed in patients. Building on these within-network studies, Filippi and colleagues also found altered connectivity between the various brain networks in patients with RRMS. "Our results show a distributed pattern of abnormalities in the efficiency of brain networks in patiens with RRMS," says Filippi.



Resting-state brain networks in multiple sclerosis. Red arrow indicates increased network connectivity compared with controls. Blue arrow indicates decreased network connectivity compared with controls. Abbreviation: WMN, working memory network. Image courtesy of M. Filippi.

In another study, Antonio Gallo *et al.* focused on the visual resting-state network (V-RSN) in 30 patients with RRMS. As demyelinating lesions in MS often occur in the optic nerve as acute episodes of optic neuritis (ON), the researchers further subdivided the patient group into those who had previously experienced ON, and those who had not.

Compared with healthy controls, the group of patients with RRMS had decreased functional connectivity in the peristriate visual cortex. Importantly, patients who had previously experienced ON showed different connectivity patterns in the V-RSN compared with patients without a history of ON, including stronger functional connectivity in the extrastriate cortex. "This finding might represent a potential compensatory mechanism in patients who have recovered after ON," suggests Gallo. As such, the results point towards an ability of the brain to recover at the functional level, independently of repair of structural MS-related damage.

Both groups are aiming to conduct longitudinal studies to determine whether the observed changes in functional network connectivity represent an aspect of MS pathology or a protective response to disease.

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Original articles Rocca, M. A. *et al.* Large-scale neuronal network dysfunction in relapsing–remitting multiple sclerosis. *Neurology* doi:10.1212/WNL.0b013e31826d5f10 | Gallo, A. *et al.* Visual resting-state network in relapsing–remitting MS with and without previous optic neuritis. *Neurology* doi:10.1212/WNL.0b013e31826d5eea