Abnormalities of the brain connectome in patients with multiple sclerosis
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Purpose. Topology-based analysis of human brain networks provides a novel way to characterize functional disconnection and loss of efficiency in several neurological conditions [1]. Aim of this study was to investigate, using graph theoretical analysis [2], the functional organization of large-scale brain networks (connectome) in patients with multiple sclerosis (MS) using resting state functional MRI (RS fMRI).

Methods. RS fMRI data were acquired from 246 MS patients (121 relapsing-remitting [RR] MS, 80 secondary progressive [SP] MS, and 45 benign [B] MS) and 55 matched healthy controls. Whole-brain networks were constructed using graph theory and the Brain Connectivity toolbox [2]. The global topology of functional networks was examined by computing the average clustering coefficient (C), the characteristic path length (L), and the global and local efficiencies (Eg and El). Small-worldness properties [3] were tested by comparison with matched random networks. Hubs were defined as regions having either degree or betweenness centrality one standard deviation greater than the average over the network. Between-group differences of global network metrics were investigated with a Mann-Whitney or a Kruskal-Wallis test, as appropriate.

Results. Small-worldness (i.e., high clustering and short paths) was verified in both controls and MS patients. All global network parameters were significantly altered in MS patients vs. controls (Figure 1). No differences were found among MS phenotypes, except for a lower El in SPMS vs. RRMS. The left precuneus, the bilateral middle cingulate cortex, middle and inferior temporal gyri, and the cerebellum (crus I-II) were hubs in both controls and MS patients (Figure 2). RRMS had a trend towards an increased number of cortical hubs in the frontal lobe (including the middle frontal gyrus and the anterior cingulate cortex). This trend was maintained in BMS patients, whereas in SPMS all frontal hubs were lost (Figure 2).

Discussion and conclusions. The large-scale functional network organization is significantly altered in MS patients vs. controls, suggesting a loss of efficiency in information exchange between brain areas.


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