Abnormalities of the brain connectome in patients with multiple sclerosis

Massimo Filippi[1], Paola Valsasina[1], Sara Sala[1,2], Alessandro Meani[1], Andrea Falini[3], Giancarlo Comi[4], and Maria A. Rocca[1]

[1]Neuroimaging Research Unit, Institute of Experimental Neurology, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, MI, Italy, [2]Department of Statistics, University of Milano-Bicocca, Milan, MI, Italy, [3]Department of Neuroradiology, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, MI, Italy, [4]Department of Neurology, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, MI, Italy

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 (E_g and E_l). Small-worldness properties [3] were tested by comparison with matched random networks. Hubs were defined as regions having either degree or betweeness centrality one standard deviation greater than the average over the network. Between-group differences of global network metrics were investigated with a Mann-Withney 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 E_l 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).

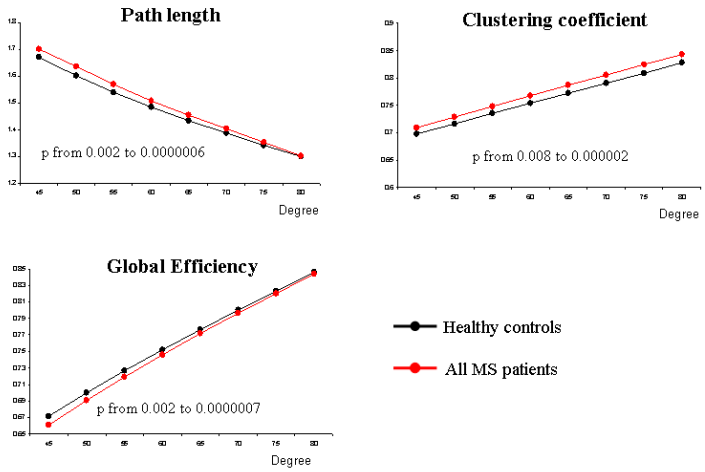

Figure 1 (above). *Plots of the global network parameters in healthy controls (black) and patients with multiple sclerosis (red) over a range of network degrees.*

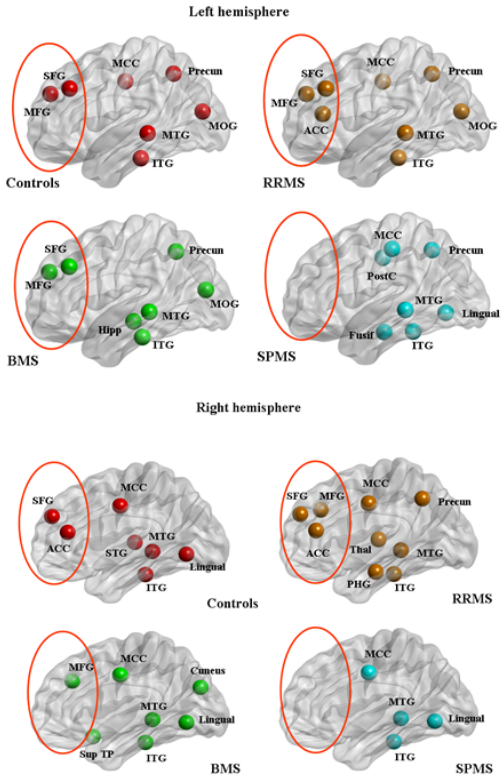

Figure 2 (right). *Brain cortical hubs in the functional networks of healthy controls, patients with relapsing remitting (RR) multiple sclerosis (MS), benign (B) MS, and secondary progressive (SP) MS. Hubs were identified as brain regions having either integrated nodal degree or betweenness centrality one standard deviation greater than network average.*

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.

References. [1] Bullmore E, Sporns O. Nat Rev Neurosci 2009;10:186-198. [2] Rubinov M, Sporns O. Neuroimage 2010;59:1059-1069. [3] Watts D, Strogatz S. Nature 1998;393:440-442.

This work has been partially supported by a grant from Fondazione Italiana Sclerosi Multipla (FISM/2011/R/19).