THALAMIC DYSFUNCTION IS ASSOCIATED WITH FATIGUE IN PATIENTS WITH MULTIPLE SCLEROSIS: A GRAPH THEORY STUDY

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Target Audience. Neurologists and Neuroradiologists.

Purpose. To explore abnormalities of large-scale brain networks (connectome) in patients with multiple sclerosis (MS) and fatigue, using resting state (RS) functional MRI (fMRI) and graph theory.[1]

Methods. Graph theoretical analysis was applied to RS fMRI data from 64 MS patients with fatigue (F) according to the Fatigue Severity Scale. As control groups, 60 MS patients without fatigue (NF) matched for disease duration and brain T2 lesion volume with F-MS patients and 59 gender and age-matched healthy controls (HC) were included. Functional connectivity between 116 cortical and subcortical brain regions was estimated using a bivariate correlation analysis. Small-worldness properties were tested by comparison with matched random networks. Hubs were defined as regions having either degree or betweeness centrality one standard deviation greater than network average. Between-group differences of global and local network metrics were investigated using ANOVA models.

Results. Small-worldness (i.e., high clustering and short paths) was verified in all study groups. All global network parameters were significantly altered in F-MS patients and NF-MS patients compared with HC, with no significant differences between F- and NF-MS patients. The cerebellum (right lobule VI and bilateral crus I), and bilateral middle and inferior temporal gyri were hubs in all study groups. F- and NF-MS patients lost hubs in the bilateral anterior cingulate cortex and cerebellar regions (lobule VII-VIII, crus II). F-MS patients also lost hubs in the thalami and middle cingulate cortex (*Figure 1*). Compared to HC, F- and NF-MS patients had a decreased degree in the bilateral caudate nucleus. F-MS patients also experienced a decreased degree in the bilateral thalamus.

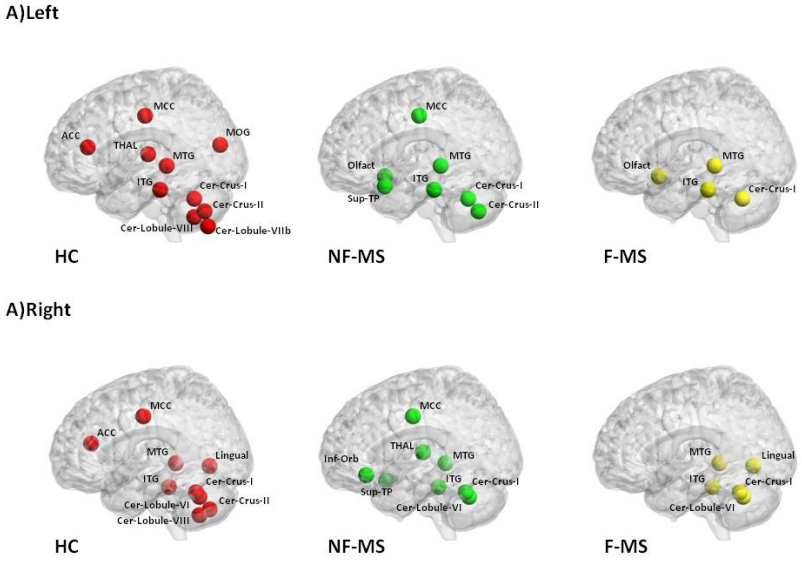

Figure 1. Hubs in HC, NF-MS and F-MS patients

Discussion. In this study we applied graph theoretic analysis to explore the relationship between abnormalities of large-scale brain networks (connectome) and fatigue in patients with MS to better understand the substrates of such a disabling and common symptom. Fatigue in MS was associated to the loss of hubs in the talami and middle cingulated cortex and to decreased degree in the bilateral thalamus.

Conclusion. Fatigue in MS is related to a functional disruption of the thalamic connector, which should be the target of potential therapeutic interventions.

References.

1. Bullmore E and Sporns O. Complex brain networks: graph theoretical analysis of structural and functional systems. Nat Rev Neurosci 2009;10(3):186-198.

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