Connectivity-based parcellation of the thalamus in multiple sclerosis and its implications for cognitive impairment: a multicenter study

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Target audience. Neuroradiologists, radiologists, neurologists.

Background. Several studies have consistently detected a high vulnerability to damage of the thalamus in patients with multiple sclerosis (MS) from the earliest stages of the disease. The study of the whole thalamus could be inadequate to explain deficits of specific cognitive functions.

Purpose. To investigate the relationship between thalamic connectivity abnormalities and cognitive impairment in MS.

Methods. Brain dual-echo, 3D T1-weighted and diffusion tensor (DT) MRI scans were collected from 52 relapsing-remitting MS patients and 57 healthy controls from six European centers. Patients underwent an extensive neuropsychological assessment. Thalamic connectivity defined regions (CDRs) were segmented based on their cortical connectivity using Diffusion Tractography-Based Parcellation[1] (Figure 1). DT-derived metrics were averaged within thalamic CDRs and cortico-thalamic tracts, before entering statistical analysis. A vertex analysis of thalamic shape was also performed[2]. Between-group differences were assessed. A random forest analysis was run to identify the best imaging predictor of global cognitive impairment and deficits of specific cognitive domains.

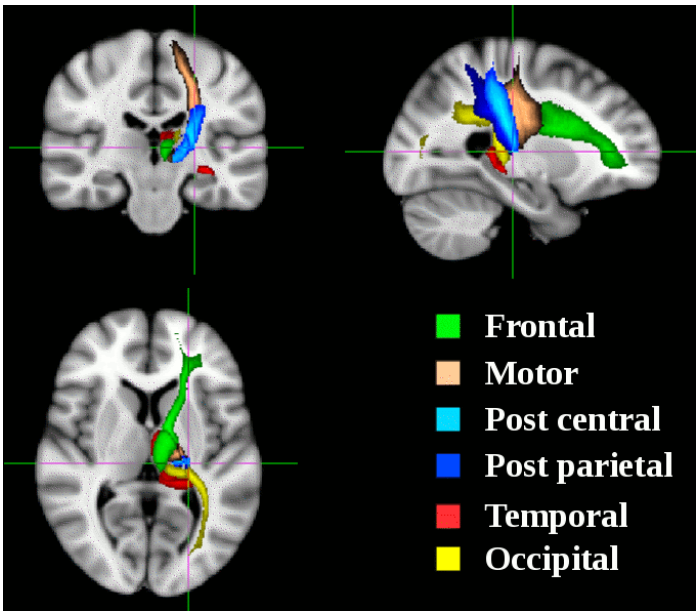

Figure 1. Probability maps of thalamic connectivity defined regions (CDRs) and cortico-thalamic tracts obtained from healthy controls.

Results. Twenty-two (43%) MS patients were cognitively impaired (CI). Compared to cognitively preserved (CP), CI MS patients had: 1) increased fractional anisotropy (FA) of motor, post-central and occipital connected CDRs ($0.003<p<0.05$) and 2) decreased FA of temporal connected CDRs ($0.01<p<0.02$). They also experienced more pronounced atrophy in anterior thalamic regions and abnormal DT-derived indices of all cortico-thalamic tracts. Damage of specific cortico-thalamic tracts explained global cognitive dysfunction and impairment of selected cognitive domains better than all other MRI variables. Thalamic CDR DT MRI abnormalities were correlated with abnormalities of the corresponding cortico-thalamic tracts.

Discussion. Regional and side differences of FA behaviour can be explained by the complex structure of the thalamus. The decreased FA observed in temporal connected CDR could reflect intrathalamic white matter damage or a higher proportion of white matter at this level. Conversely, the increased FA detected in other regions can be expression of a more prominent gray matter damage (or a greater effect of damaged gray matter due to its proportion in interested areas).

Conclusions. Decreased FA of temporal connected CDR is likely related to white matter damage, present in all MS patients, that worsens with the evolution of the disease. Conversely, increased FA of other thalamic sub-regions could reflect prominent gray matter damage, more relevant in CI MS patients. Cortico-thalamic disconnection is, at various levels, implicated in cognitive dysfunction in MS.

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References. [1] Behrens TE, Johansen-Berg H, Woolrich MW, et al. Non-invasive mapping of connections between human thalamus and cortex using diffusion imaging. Nat Neurosci 2003;6:750-757. [2] Patenaude B, Smith SM, Kennedy DN, Jenkinson M. A Bayesian model of shape and appearance for subcortical brain segmentation. Neuroimage 2011;56:907-922.