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Structural and functional magnetic resonance imaging correlates of fatigue and dual-task performance in progressive multiple sclerosis

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Introduction: Damage of frontal cortico-subcortical networks contributes to fatigue and dual-task impairment in multiple sclerosis (MS). However, the mechanisms underlying these clinical deficits in progressive (P) MS still need to be fully explored.
Objectives and Aims: In this study, we investigated the associations between structural and functional MRI abnormalities of frontal cortico-subcortical circuits and fatigue and dual-task performance in PMS.
Methods: Brain structural and functional MRI scans, Modified Fatigue Impact Scale (MFIS) and dual-task performances were obtained from 57 PMS patients with impaired processing speed from 4 centers and 10 healthy controls (HC). The associations of thalamic, caudate nucleus and dorsolateral prefrontal cortex (DLPFC) atrophy, microstructural abnormalities of their connecting tracts and their resting state effective connectivity (RS EC) with fatigue, single- and dual-task performances were investigated.
Results: Compared to HC, PMS patients had higher fatigue ($p \leqslant 0.027$) and worse dual-task performance ($p < 0.001$). Compared to non-fatigued (MFIS$<$38), PMS patients with fatigue (MFIS$\geqslant$38) had lower RS EC from left-caudate nucleus to left-DLPFC ($p=0.007$). In PMS, higher MFIS-physical and MFIS-psychosocial scores were predicted by lower RS EC from left-caudate nucleus to left-DLPFC ($R^2=0.112$, $p=0.027$) and higher RS EC from right-thalamus to right-DLPFC ($R^2=0.102$, $p=0.046$), respectively. Dual-task motor performances were predicted by lower RS EC from left-DLPFC to left-thalamus ($R^2 \geqslant 0.137$, $p \leqslant 0.032$). Several structural MRI measures independently predicted dual-task correct response rates ($R^2=0.307$, $p \leqslant 0.010$) and dual-task cognitive cost ($R^2=0.188$, $p=0.002$). Fatigue impact was not associated with single- and dual-task performances.
Conclusions: Frontal cortico-subcortical structural and functional MRI abnormalities differently contribute to fatigue impact and single- and dual-task performance in PMS.
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Scientific Session 12: The earliest events in MS

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MS as an inside-out disease – insights using spectral pathology

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Introduction: The pathology of MS has been extensively studied using traditional histochemical stains (e.g. H&E, LFB) and more specific immunohistochemical methods aimed at a broad range of protein targets. However, these techniques are limited in their ability to report subtle but potentially important lipid derangements, particularly in myelin. Moreover, immunohistochemistry is largely agnostic to the misfolded character of a number of important proteins underpinning most neurodegenerative diseases, and would therefore fail to report protein misfolding pathology if this were an important component of MS pathogenesis.

Objectives & Results: This presentation will describe novel approaches for interrogating myelin lipid abnormalities using spectral microscopy and the solvatochromic fluorescent probe Nile Red. Results indicate a widespread alteration of myelin polarity in non-lesional white matter that may have important implications for conduction velocity disturbances in the brain, and could underpin important non-focal symptoms such as fatigue, cognitive impairment and depression. Consistent with pathological abnormalities using conventional methods, these abnormalities are more pronounced in periventricular regions suggesting that a circulating factor in the CSF may be responsible.