Structural disconnectivity secondary to white matter lesions in MS-related tremor

B. Alonzo[1], J. Jimenez[1], A. Bayoumi[1], J. Thomas[1], K. Hasan[2], J. S. Wolinsky[1], J. A. Lincoln[1]
[1]Neurology, McGovern Medical School at UTHealth, Houston, TX, [2]Radiology, McGovern Medical School, Houston, TX

Background:

Tremor affects up to 50% of patients with MS (pwMS). Effective management has yet to be achieved due to incomplete understanding of its pathophysiology and anatomic involvement.

Objective:

To investigate lesion-driven structural disconnectivity in MS-related tremor.

Methods:

This prospective case-control study included patients with MS (pwMS) with tremor (MS-T) and without tremor (MS-C) recruited from an academic MS center. Inclusion criteria were confirmed MS diagnosis and unilateral or limb-predominant MS-related tremor. 3.0 T MRI scans, including 3D T1-w and T2-FLAIR sequences were performed on subjects, as well as clinical evaluation of tremor severity using a previously validated scoring system, The Essential Tremor Rating Assessment Scale (TETRAS). On the T2 FLAIR-weighted images, white matter (WM) hyperintense lesions were manually segmented and validated. Lesion maps were normalized to standard space using linear and non-linear transforms. Network Modification Tool was used to estimate structural disconnectivity due to T2 lesions, providing subjects' regional grey matter (GM) change in connectivity (ChaCo) scores. Group mean differences in regional ChaCo were estimated using Welch's t-test, and p-values were adjusted for false discovery rate (q). In MS-T, we used Spearman's partial correlation coefficients (r_{sp}) between regional ChaCo scores and TETRAS to determine the correlation between WM lesions and clinical tremor severity.

Results:

Greatest group differences were observed in deep GM structures, notably in the left caudate (MS-C – MS-T= -33.4 %, $q<0.001$) and right hippocampus (-33.9%, $q<0.001$), while greatest ChaCo changes in cortical GM were observed in the left hemisphere in the insula (-22.2%, $q<0.001$) and entorhinal (-21.7%, $q<0.001$), and in the right hemisphere in the entorhinal (-20.9, $q<0.001$) and insula (-20.4, $q<0.001$).

Significant correlations with TETRAS were found in the precentral gyrus ($r_{sp}= 0.4$, $p= 0.01$), amygdala ($r_{sp}= 0.4$, $p= 0.03$), and entorhinal cortex ($r_{sp} = 0.4$, $p= 0.04$) on the left side, meanwhile on the right, strong correlations were observed in the nucleus accumbens area ($r_{sp}= 0.5$, $p= 0.004$), caudal anterior cingulate ($r_{sp}= 0.5$, $p= 0.004$), as well as the precentral gyrus ($r_{sp}= 0.45$, $p= 0.008$).

Conclusions:

Widespread changes in structural connectivity were observed in the tremor group, with specific regions correlating to tremor severity, proposing a role of lesion-driven structural disconnectivity in the emergence of MS-related tremor.