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Abnormal thalamic functional connectivity correlates with cardiorespiratory fitness and physical activity in progressive multiple sclerosis

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Introduction: Patients with progressive multiple sclerosis (PMS) have insufficient levels of physical activity (PA) and cardiorespiratory fitness (CRF), which showed some associations with measures of structural MRI damage. Functional MRI (fMRI) correlates of reduced PA/fitness have never been explored. Given the role of

thalamus in motor planning, sensory processing and cognition, abnormal thalamic resting state (RS) functional connectivity (FC) might explain PA/fitness levels in these patients.

Objectives: To assess thalamic structural and functional MRI alterations and investigate their correlations with PA/CRF levels in PMS patients.

Methods: Ninety-one PMS patients performed a cardiopulmonary exercise test and wore an accelerometer for 7 days to assess PA/CRF levels. They also underwent, together with 37 matched healthy controls (HC), a structural and RS fMRI acquisition at 3.0T, which was used to derive whole-brain and thalamic atrophy and thalamic RS FC. Between-group comparisons of MRI measures and their correlations with PA/CRF variables were assessed.

Results: PMS patients had significant whole-brain and subcortical atrophy compared to HC (all $p < 0.001$). Patients also showed decreased intra- and inter-thalamic RS FC, decreased RS FC of the thalamus with caudate nucleus, cerebellum and bilateral anterior cingulate cortex (ACC), and increased thalamic RS FC with the bilateral hippocampus and some occipital regions. Lower CRF levels correlated with lower normalized white matter volume ($r = \text{range } 0.28; 0.31$, $p = \text{range } 0.003; 0.01$), with decreased thalamic RS FC with the left ACC ($r = \text{range } 0.22; 0.28$, $p = \text{range } 0.01; 0.04$), and with increased thalamic RS FC with the left hippocampus, left calcarine cortex, and right lingual gyrus ($r = \text{range } -0.26; -0.21$, $p = \text{range } 0.01; 0.04$). Lower PA correlated with decreased inter-thalamic RS FC ($r = 0.27$, $p = 0.02$), and with increased thalamic RS FC with the right hippocampus ($r = -0.3$, $p = 0.01$) and left lingual gyrus ($r = -0.23$, $p = 0.04$).

Conclusions: Only white matter atrophy correlated with CRF variables. Conversely, abnormal RS FC in the thalamic network showed various maladaptive associations with PA and fitness status in people with PMS. Given its extensive correlation with PA and CRF, thalamic RS FC might be used as an outcome to monitor physical impairment and efficacy of rehabilitative and disease-modifying treatments in PMS patients.

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Disease-modifying effect of circuit class therapy in patients with relapsing-remitting multiple sclerosis

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Introduction: Physical therapy plays an essential role in the long-term multidisciplinary management of patients with multiple sclerosis (MS) and has shown to be beneficial in improving gait impairment and alleviating fatigue. Recent evidence suggests that physical exercise in MS is not just a symptomatic therapy but seems to have also a disease-modifying effect.

Aims: Our study aimed to assess the efficacy of 12-week intensive circuit class therapy (ICT) on MS progression by comparing 2 years before and after the ICT in relapsing-remitting MS patients with lower disability (EDSS up to 4).

Methods: Twenty-two MS patients underwent 12-week circuit class therapy (1 hour once a week) and were motivated to continue exercising on regular basis in their home environment for the next two years. Median EDSS 2.5 (0 to 4). Twenty-four MS patients served as a control group. Median EDSS 1 (1 to 3.5). All patients were treated with disease-modifying therapies.

Patients were clinically evaluated at three-month intervals for 4 years (2 years before and after the ICT in the exercising group) to assess any further clinical attacks or EDSS progression. The brain MRI was performed once a year.

Results: Significant improvement was found in the annualized relapse rate (ARR) in the exercising group: 0.5 (0 to 1.5) before and 0 (0 to 1.5) after the ICT ($p=0.01$). No significant AAR change was found in the control group: 0 (0 to 0.5) both in the first and second 2-years interval ($p=0.30$).

The prevalence of new or enlarging T2 lesions after the ICT in the therapy group (24%) was significantly lower than before ICT in the same patients (61%; $p=0.001$). No significant difference was found between the first (27%) and second 2-years interval (32%) in the control group ($p=0.37$).

No significant differences in EDSS change were found between the first and second 2 years in either ICT ($p=0.29$) or the control group ($p=0.32$).