EPR-168 | Aerobic and cognitive training effects on insular functional connectivity in progressive multiple sclerosis: CogEx trial

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Background and aims: The anterior insula (AI) is crucial for cognitive attentional processes, while the posterior insula (PI) is related to somatosensory properties. CogEx trial (NCT03679468) investigated the effects of aerobic exercise (EX) and cognitive rehabilitation (CR) on cognitive impairment in progressive multiple sclerosis (MS). The aim of this study was to assess the effects of rehabilitation on resting state functional connectivity (RSFC) of AI and PI exploiting CogEx data.

Methods: CogEx participants were randomized to: 'CR+EX', 'CR+sham EX (EX-S)', 'EX+sham CR (CR-S)' and 'CR-S+EX-S'. We selected all subjects ($n=87$) who underwent the 12-week intervention period and completed baseline and 12-week physical/cognitive and RS-fMRI assessments. RSFC of AI and PI was assessed using a seed-based approach.

Results: At week-12 compared to baseline, groups performing CR were both characterized by increased RSFC between AI and the left temporal pole, while groups performing EX were both characterized by increased RSFC between AI and the left hippocampus. Conversely, 'CR-S+EX-S' patients were characterized by decreased RSFC of AI/PI with cingulate cortex and frontoparietal regions. In the 'EX+CR-S' group, increased RS FC between AI and left hippocampus tended to be associated with concomitant increase in California Verbal Learning Test score ($p=0.063$). In contrast, in 'CR-S+EX-S' group, over time modifications of insular RSFC with cingulate and parieto-temporal regions were associated with concomitant worsening of visuospatial memory performance ($p<0.047$).

Conclusion: EX and CR modulated RSFC of anterior and posterior insular regions in patients with progressive MS. Adaptive compensatory mechanisms occurring in insular RSFC seem to support cognitive mnemonic function.

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