

Brain Functional Connectivity is modulated by Resistance Training and is associated with Blood Biomarkers in Mild Cognitive Impairment

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- Resistance Training improved cognition and increased functional connectivity in older adults with mild cognitive impairment.
- Functional connectivity correlates with blood biomarkers of neurodegeneration and Alzheimer disease pathology.

INTRODUCTION

Mild cognitive impairment (MCI) refers to cognitive decline beyond that expected for age and educational level, with preservation of functional independence. In this diagnosis, alterations in plasma biomarkers of Alzheimer’s disease (AD) and reductions in functional connectivity (FC) of brain networks may occur, leading to an increased risk of developing dementia. The practice of physical exercise is associated with a reduced risk of dementia in individuals with MCI.

It remains unclear whether resistance training (RT), which has already been associated with improvements in cognition and protection against cerebral atrophy, can modulate FC in brain networks in this population. In addition, understanding the relationship between plasma biomarkers and FC of brain networks contributes to the knowledge regarding the clinical performance of these blood biomarkers. This study aimed to evaluate the effects of RT on cognition and brain network FC, as well as to investigate the associations between FC and AD blood biomarkers.

METHODS

This study was approved by the local ethics committee under the number: 4.337.553.

Sixty-one older adults with MCI were allocated to a RT group (RTG; 24 weeks, n=19) or a control group (CG, n=42).

The participants were assessed for global cognition using MoCA, functional magnetic resonance imaging, and AD blood biomarkers, including p-tau181, p-tau217, p-tau181/Aβ42, p-tau217/Aβ42, Aβ42/40, and neurofilament light chain (NfL), measured using Simoa.

Functional Connectivity was assessed using UF2C (<https://www.lnunicamp.com/uf2c>), a software in Matlab that allow us to measure FC inter networks and between networks.

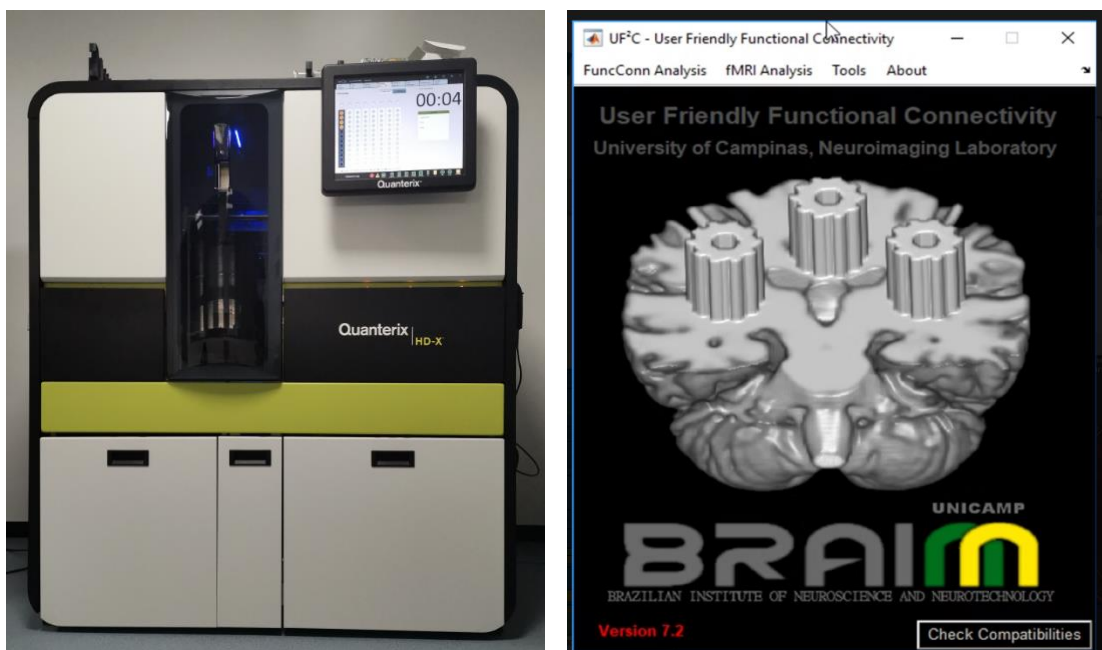


Figure 1. Simoa HD-X Quanterix and UF2C main interface.

RESULTS

The RTG showed a significant increase in global cognition (p = 0.015) and increased FC in the posterior salience network (p = 0.03, FDR-corrected).

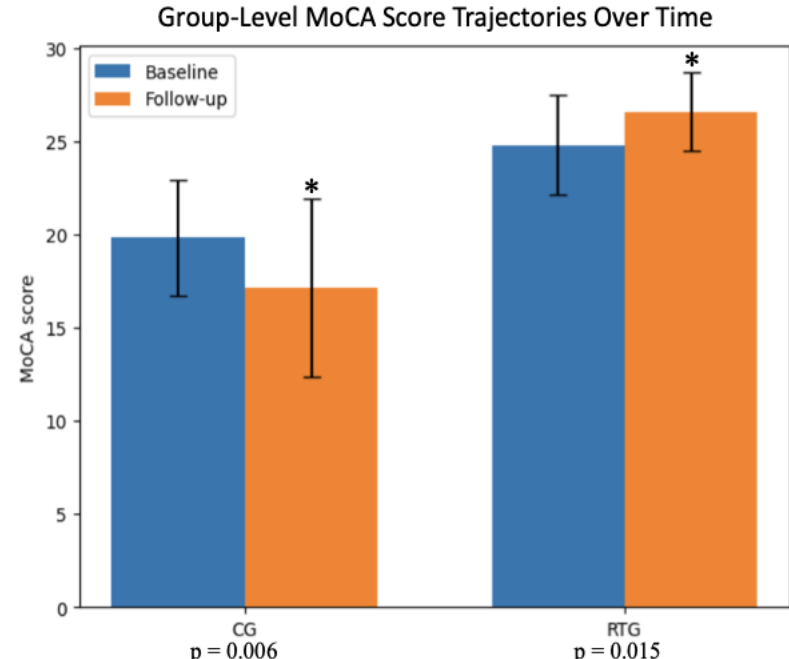


Figure 2. Group-level trajectories of MoCA scores across time.

In contrast, the CG showed a reduction in global cognition (p = 0.006) and no significant changes in FC (p > 0.05). Aβ42/40 showed negative correlations with FC in ROIs of the posterior salience network (r = -0.462, p = 0.030; r = -0.561, p = 0.002) and RECN (r = -0.444, p = 0.022).

NfL showed negative correlations with FC in RECN (r = -0.578, p < 0.001), dorsal DMN (r = -0.456, p = 0.029; r = -0.455, p = 0.029), and the visual network (r = -0.357, p = 0.015; r = -0.513, p < 0.001; r = -0.483, p = 0.001).

Timepoint comparisons (Baseline vs Follow-up)

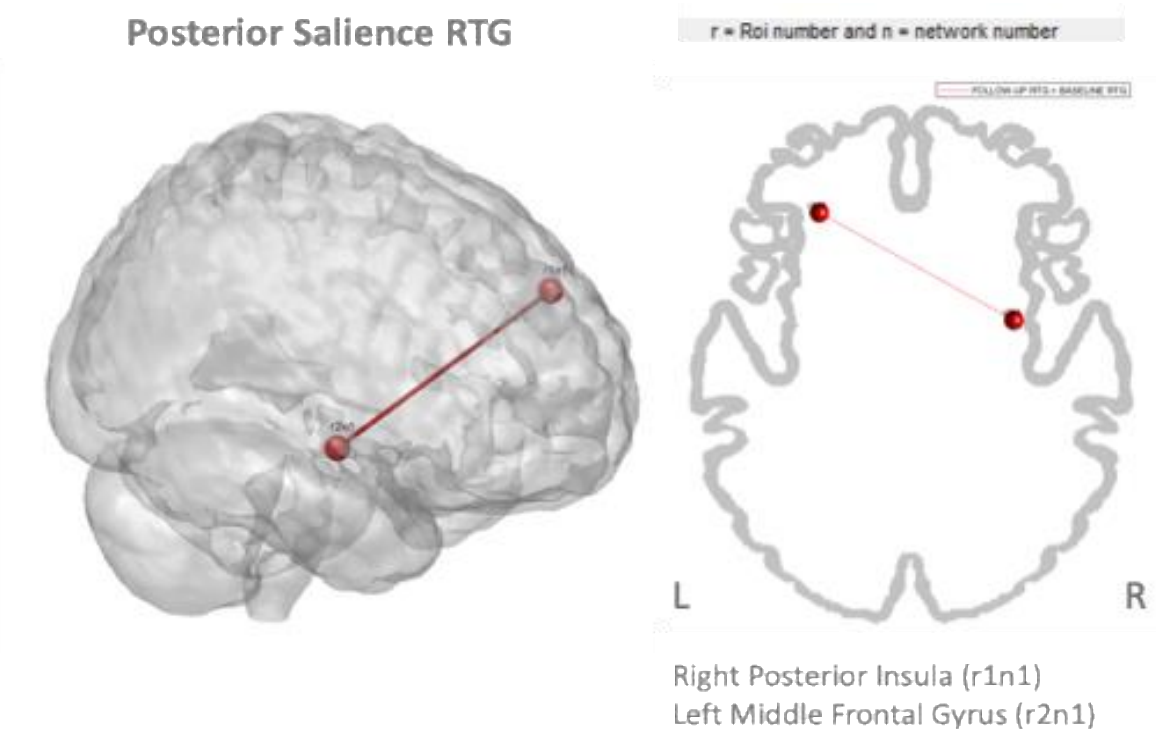


Figure 3. Functional connectivity comparisons across timepoints.

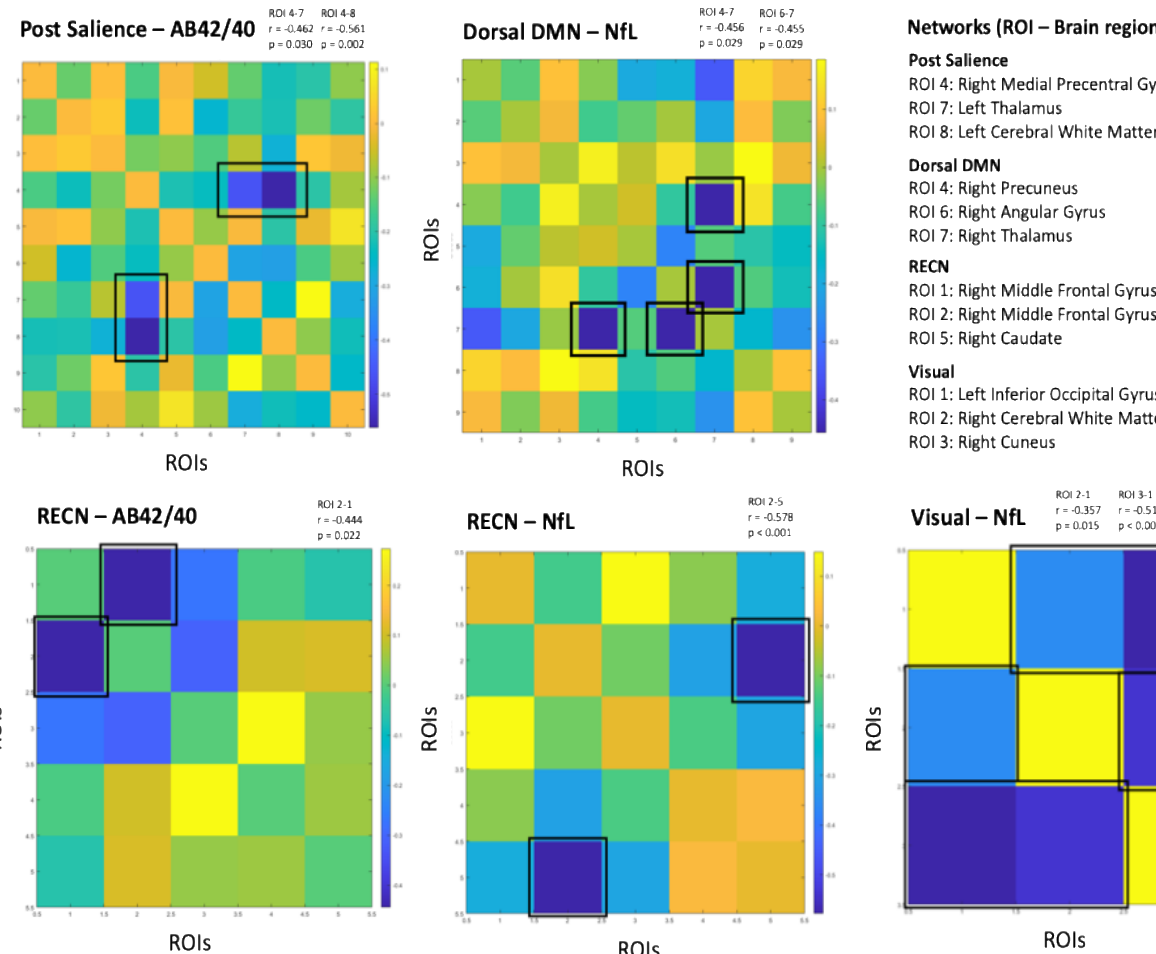


Figure 4. Correlation matrix between functional connectivity and blood biomarkers per network. ROIs: Region of Interest. r: Pearson correlation, p: p-value.

CONCLUSIONS

RT improves cognition and FC in a population at increased risk of developing dementia. The correlation between FC and Aβ42/40 may reflect a compensatory process of hyperconnectivity in the brain in MCI, whereas the correlation between FC and NfL reinforces that higher NfL concentrations are related to neurodegenerative processes that influence brain network connectivity. Therefore, Aβ42/40 and NfL levels may influence FC in MCI.

