**Hippocampal Volume and Functional Connectivity Predicts Functional Decline in Mild AD and aMCI**

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**INTRODUCTION / HYPOTHESIS**

The study of biomarkers in mild Alzheimer's disease dementia (AD) and amnestic mild cognitive impairment (aMCI) is essential for the improvement of early diagnosis. However, it is not completely known the usefulness of different biomarkers for tracking the progression of the disease. The aim of this study is to evaluate if cerebrospinal fluid (CSF) biomarkers (Aβ42, p­tau and t­tau), hippocampal volumes (HV) and Default Mode Network (DMN) functional connectivity (FC) could predict the cognitive and functional evolution of mild Alzheimer’s disease dementia and amnestic mild cognitive impairment patients.

**OBJECTIVE**

**-** Compare the dosage of beta-amyloid, total tau and phosphorylated tau proteins in patients with AD and aMCI at the onset of the disease;

- Compare the hippocampal volume in patients with AD and aMCI at the onset of the disease;

**-** Compare the Default Mode Network (DMN) functional connectivity (FC) in patients with AD and aMCI at the onset of the disease;

- Verify if the biomarkers described are correlated with the progression of cognitive (MMSE) and functional (Pfeffer Questionnaire and CDR sum of boxes) measures;

**METHOD**

We evaluated 32 mild AD and aMCI due to AD during 9 months. All subjects underwent neuropsychological assessment, MRI at 3 Tesla for structural and FC evaluation, and CSF biomarkers. All aMCI subjects had evidence of AD pathophysiology (hippocampal atrophy and/or low CSF Aβ42 and/or low Aβ42/ptau). HV was obtained by Freesurfer software. We performed the FC analysis using the UF²C toolbox (http://www.lni.hc.unicamp.br/app/uf2c/). We estimated an average DMN map that was divided in eight DMN subparts: the prefrontal cortex; medial parietal cortex; left and right parietal lobe, left and right temporal lobe, left and right hippocampus. The average values were converted to z­scores that were used for statistical analysis. Dosages of Aβ42, t­Tau and p­Tau were obtained from INNOTEST® kits (Fujirebio).We performed multiple regressions considering changes (Δ) in cognition (Mini Mental Status Examination ­ MMSE) and in functional status (Pfeffer's Questionnaire of daily living) as dependent variables and, age, sex, education, CSF biomarkers, HV and DMN subparts FC as independent variables. **Preliminary Results**: We did not find any significant result concerning these variables and changes in MMSE over time. However, we found that hippocampal volume and FC predicted changes in Pfeffer's Questionnaire: left HV (adjusted R2= 0.79, F= 5.75; t = ­5.73, p=0.029); right hippocampal FC: (adjusted R2= 0.84, F= 12.06 ; t = 5.13, p=0.004). All testes were corrected for multiple comparisons.

**RELEVANCE**

Hippocampal structure and functional connectivity (but not CSF biomarkers) predict changes over time in functional activities in patients with mild AD and aMCI. Interestingly, we found a direct relationship between hippocampal FC and the worsening of our patients, what could mean that initial high connectivity might be compensatory.