MEG functional network disorganization associates with cerebrospinal fluid biomarkers in early Alzheimer's disease

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Purpose: To determine whether functional connectivity patterns, as an index of synaptic dysfunction, associate with cerebrospinal fluid (CSF) biomarkers (i.e., phospho-tau and amyloid beta -A42- levels) in patients with Mild Cognitive Impairment due to Alzheimer's disease. We also assessed orrelations of aberrant functional connections with structural connectivity abnormalities and with cognitive deficits.

Methods: Resting-state magnetoencephalography was recorded in twelve patients with Mild Cognitive Impairment. Neuropyschological tests, including the MMSE and the Recall test were evaluated. Phase-locking value was used to analyze functional connectivity, and diffusion tensor imaging for structural connectivity.

Results: One third of the patients converted to Alzheimer's disease during a follow-up of 2.5 years. Patients with abnomal CSF phospho-tau and A42 levels exhibited both reduced and increased functional connectivity affecting limbic structures such as the anterior/posterior cingulate cortex, orbitofrontal cortex, or medial temporal areas in different frequency bands. A reduction in posterior cingulate functional connectivity mediated by phospho-tau associated with impaired axonal integrity of the hippocampal cingulum. Phospho-tau and A42–related connectivity abnormalities correlated with cognitive scores.

Conclusions: CSF markers of amyloid deposition and neuronal injury in early Alzheimer's disease associate with a dual pattern of cortical network disruption, affecting key regions of the Default Mode Network and fronto-temporal circuits. Magnetoencephalography may represent a potential "non-invasive" tool to detect early synaptic dysfunction associated with Alzheimer's disease brain pathology.