

# A COMBINED RS-EEG/RS-fMRI CHARACTERIZATION OF THE ALZHEIMER CONTINUUM

Giordano Cecchetti,<sup>1,2,3</sup> Silvia Basaia,<sup>3</sup> Camilla Cividini,<sup>3,4</sup> Marco Cursi,<sup>2</sup> Roberto Santangelo,<sup>1,4</sup> Francesca Caso,<sup>1</sup> Fabio Minicucci,<sup>2</sup> Giuseppe Magnani,<sup>1</sup> Massimo Filippi,<sup>1,4</sup> Federica Agosta<sup>3,4</sup>

<sup>1</sup>Neurology Unit, and <sup>2</sup>Neurophysiology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy;

<sup>3</sup>Neuroimaging Research Unit, Institute of Experimental Neurology, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy;

<sup>4</sup>Vita-Salute San Raffaele University, Milan, Italy

## INTRODUCTION AND AIMS

Alzheimer's disease (AD) is the most prevalent cause of dementia. Unavailability of a reliable and reproducible early diagnostic process compromises the prompt management of the disease and the success of disease-modifying therapies.

The aim of this study was to evaluate electroencephalogram (EEG) performances alone or combined with resting state functional MRI (rs-fMRI) in order to characterize amnesic mild cognitive impairment (MCI) subjects with an AD-like cerebrospinal fluid (CSF) biomarkers profile within the Alzheimer Continuum.

## METHODS

✓ Thirty-nine AD, 86 amnesic MCI and 86 healthy controls (HC) underwent EEG and/or rs-fMRI. MCI subjects were divided according to their CSF profile: those with phosphorylated tau/β-amyloid-42  $\geq 0.13$  (MCI-ATpos) and those with the ratio  $< 0.13$  (MCI-ATneg).

✓ Current source density (CSD) analysis was applied to EEG data at a lobar level. To combine the two techniques, networks mostly affected by AD pathology were identified using Independent Component Analysis (ICA) applied to rs-fMRI data. Afterwards, EEG CSD and graph analyses were focused on these networks (Fig. 1).

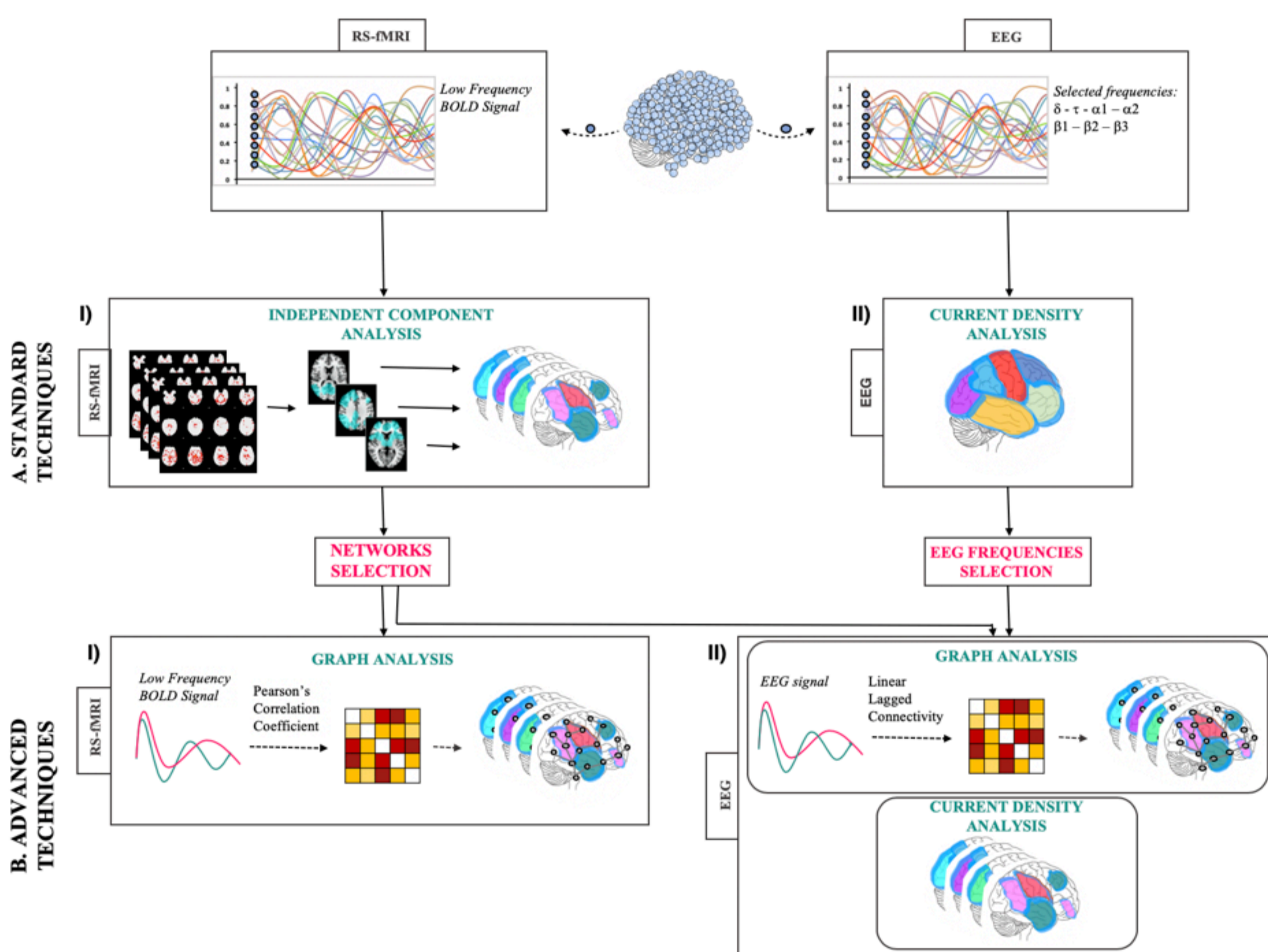


Figure 1. Graphical representation of methodological framework.

## RESULTS

✓ When compared to healthy subjects, Alzheimer's disease patients showed decreased functional connectivity within default mode network (DMN), primary visual network (PVN), visual-associative network (VISASS) and right frontal-parietal network (RFP) (Fig. 2).

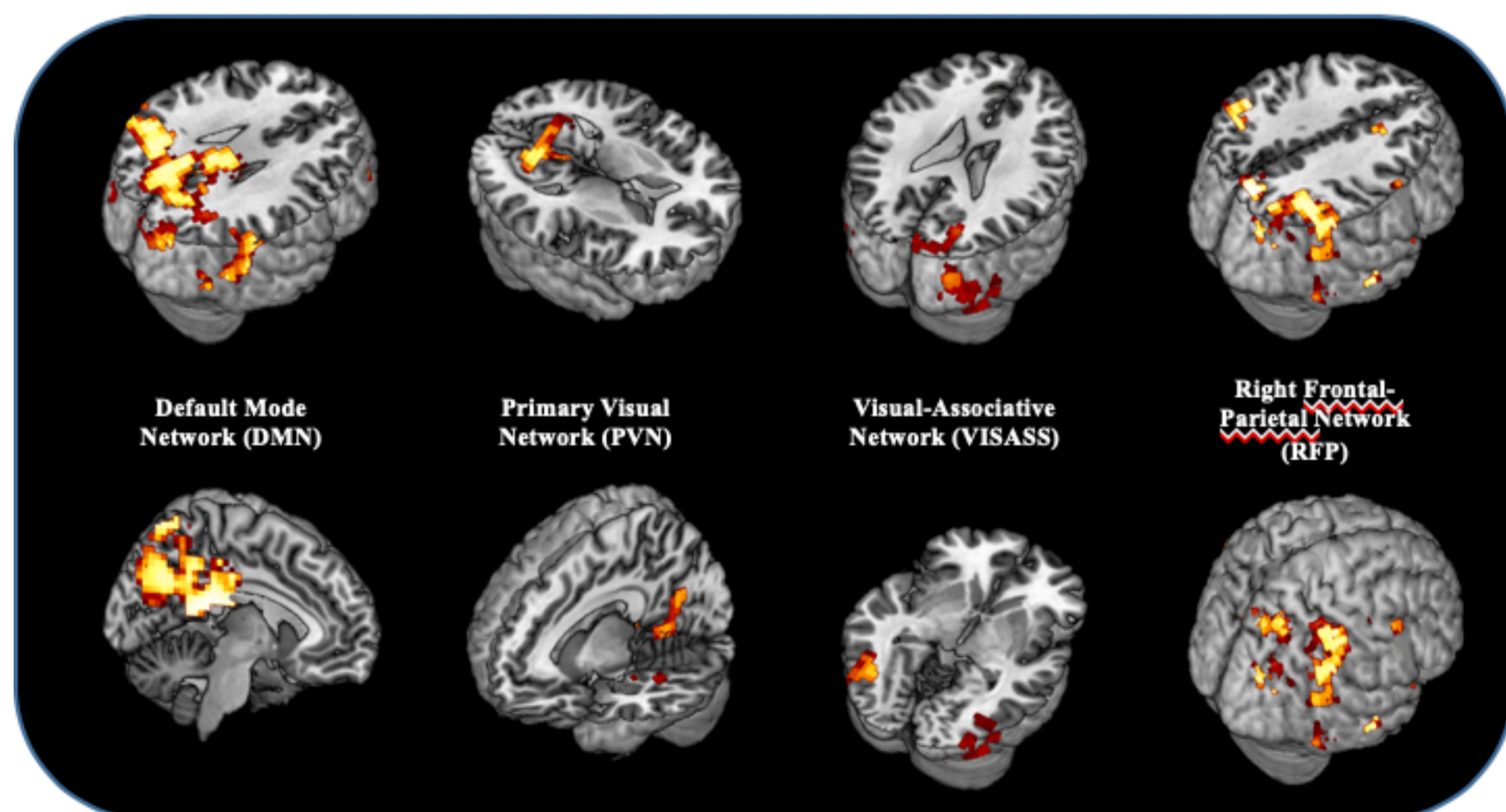


Figure 2. Independent component analysis.

Supported by: Italian Ministry of Health (GR-2011-02351217)

## RESULTS

✓ AD patients showed an increase of delta and theta and a decrease of alpha2 and beta1 densities. MCI-ATpos showed higher theta density than MCI-ATneg patients (Fig. 3-A,B). After the application of rs-fMRI networks to CSD analysis, alpha2 band distinguished MCI-ATpos patients from MCI-ATneg, AD and HC (Fig. 3-B).

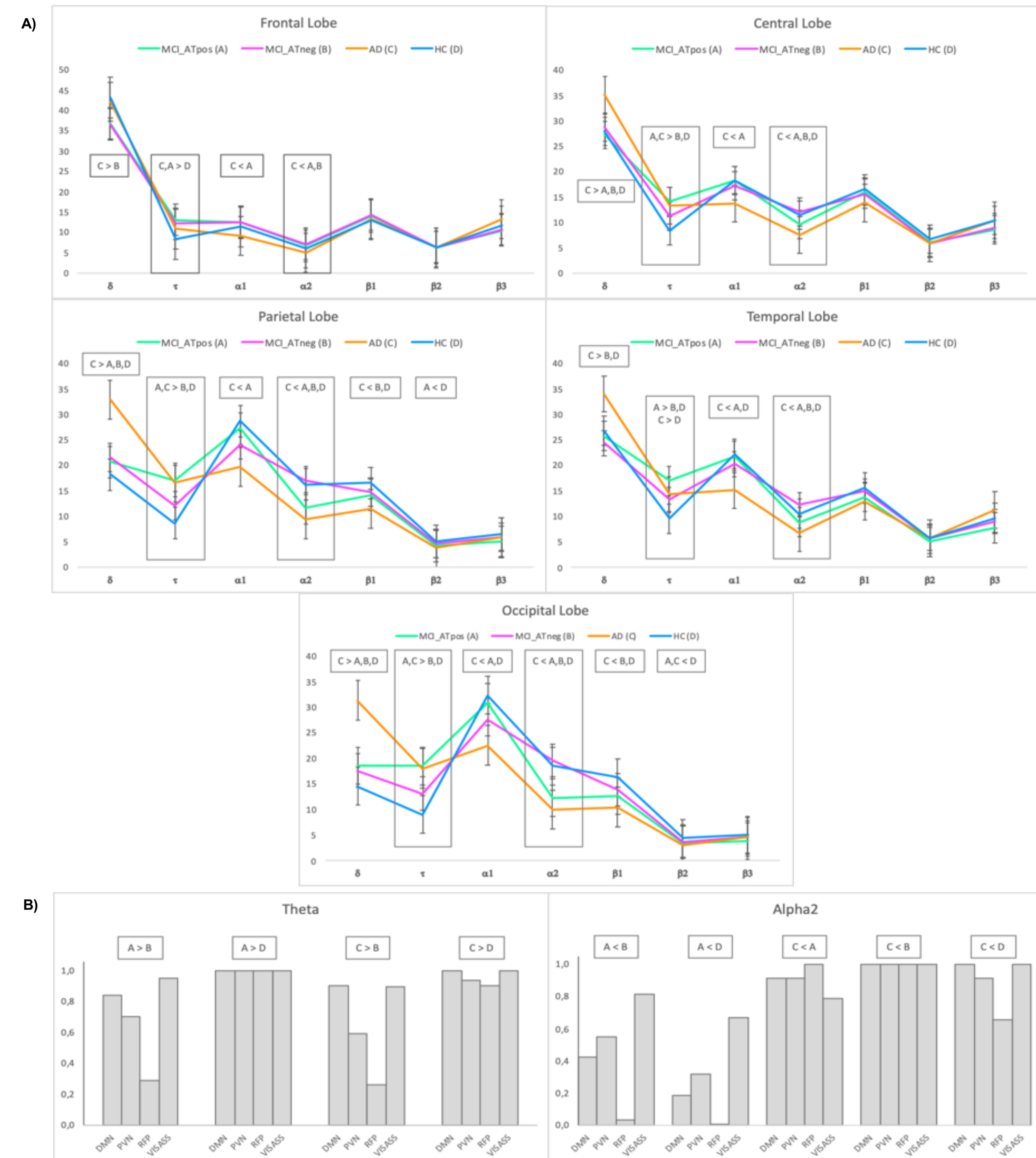


Figure 3. A) Mean values and error bars of lobar CSD. B) Percentage of voxels belonging to each extracted network that showed differences at CSD analysis at selected frequencies. Abbreviations: A=MCI-ATpos, B=MCI-ATneg, C=AD, D=HC, DMN=Default-mode network, PVN=Primary visual network, RFP=Right frontal-parietal network, VISASS=Visual-associative network.

✓ Graph analysis from rs-fMRI data and EEG data at theta frequency allowed to distinguish MCI-ATpos and AD from MCI-ATneg and healthy subjects at network level (Fig 4-A,B). Graph analysis from EEG data at alpha2 frequency showed a trend of progressive alteration of network metrics throughout the Alzheimer continuum (Fig. 4-C).

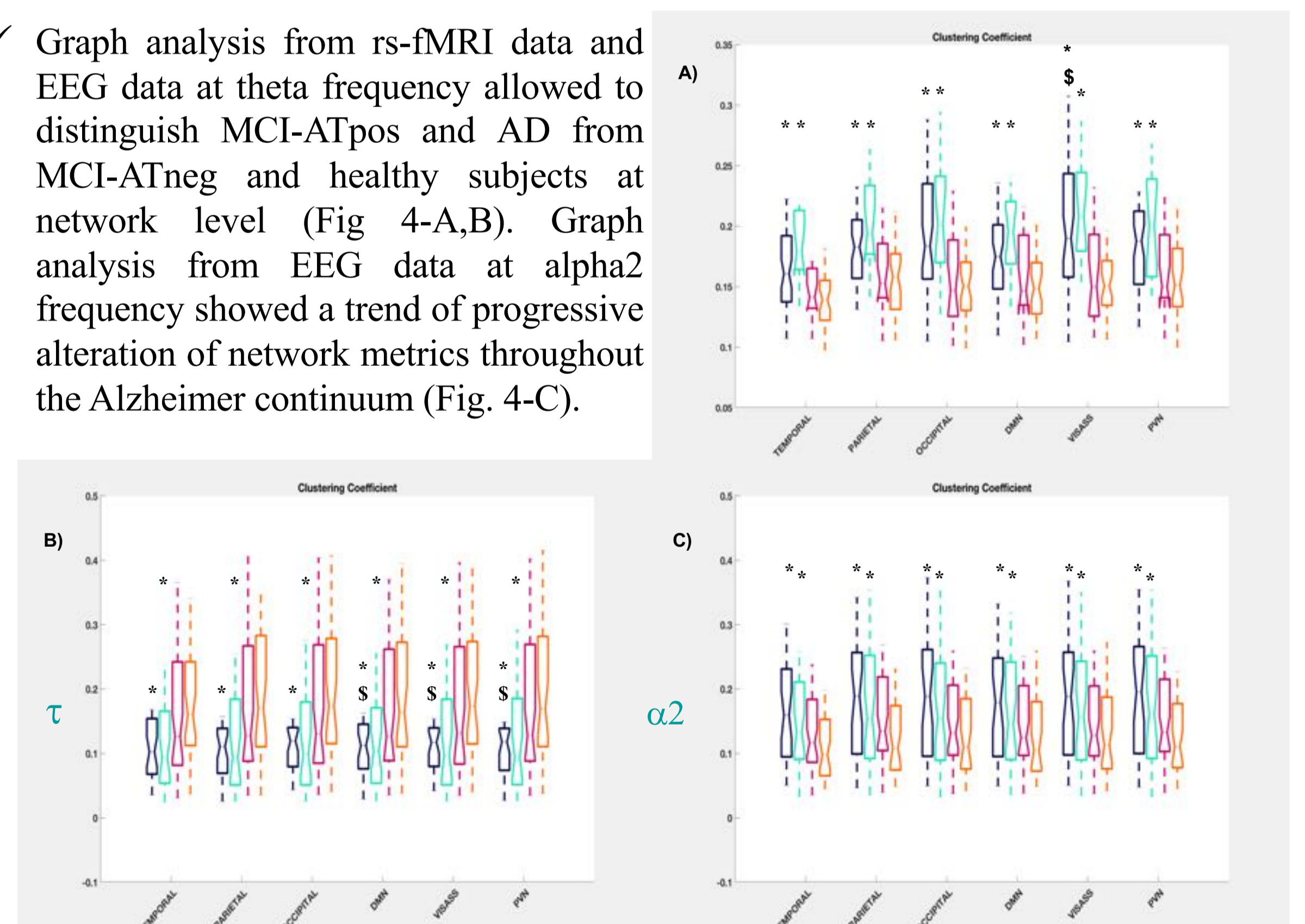


Figure 4. Network metrics from rs-fMRI (A) and EEG at theta (B) and alpha2 (C) frequencies (AD: orange, HC: blue, MCI-ATpos: violet, MCI-ATneg: light blue). \*  $p < 0,05$  vs AD, \$  $p < 0,05$  vs MCI-ATpos. Abbreviations: DMN=Default-mode network, PVN=Primary visual network, VISASS=Visual-associative network,

## CONCLUSIONS

✓ **Theta** frequency band is sensitive to AD-like CSF biomarker profile and it is therefore a promising early noninvasive marker of AD.

→ Biomarker category: Amyloidopathy (A) and Tauopathy (T)

✓ **Alpha2**, as highlighted by the integration of EEG and rs-fMRI, correlates with disease progression within the Alzheimer Continuum.

→ Biomarker category: Neurodegeneration (N)