

A NEW NEUROPHYSIOLOGICAL PREDICTIVE CANDIDATE BIOMARKERS FOR FRONTOTEMPORAL AND ALZHEIMER'S DISEASE DEMENTIA: A LONGITUDINAL MULTICENTER EEG STUDY

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Background

EEG studies of functional connectivity have provided new measures of brain organization in neurodegenerative diseases, especially Alzheimer's disease (AD).

We aim to study the macroscale modifications occurring along the course of the disease in Frontotemporal dementia (FTD), in comparison with AD.

Methods

Mutual information (MI) (measure of functional connectivity) were measured in a longitudinal study on resting state EEG signals recorded on 18 FTD (13 behavioural variant and 5 with primary progressive aphasia), 18 AD, 20 healthy controls. EEG were recorded at the prodromal stage of the diseases, at onset of cognitive symptoms and at 2-3 years follow-up.

Results

MI resulted to be higher in FTD and AD patients as compared to HC at the prodromal stage of the disease (Fig.1). With more spatial detail, MI was higher in left and right local anterior connections in FTD patients as compared to HC and in left local anterior connections as compared to AD patients. Furthermore, MI was higher in left and right local posterior in AD patients as compared to HC (Fig.2).

Discussion

Both FTD and AD groups in the prodromal stage showed a higher strength in the functional connectivity, as measured by MI at electrode pairs. This allowed to define hyperconnectivity as a biomarker of the prodromal stage of both dementia groups. (Fig.3)

Furthermore, in a regional based analysis, hyperconnectivity was more evident in anterior regions in FTD patients, whereas it was more evident in posterior regions in AD patients.

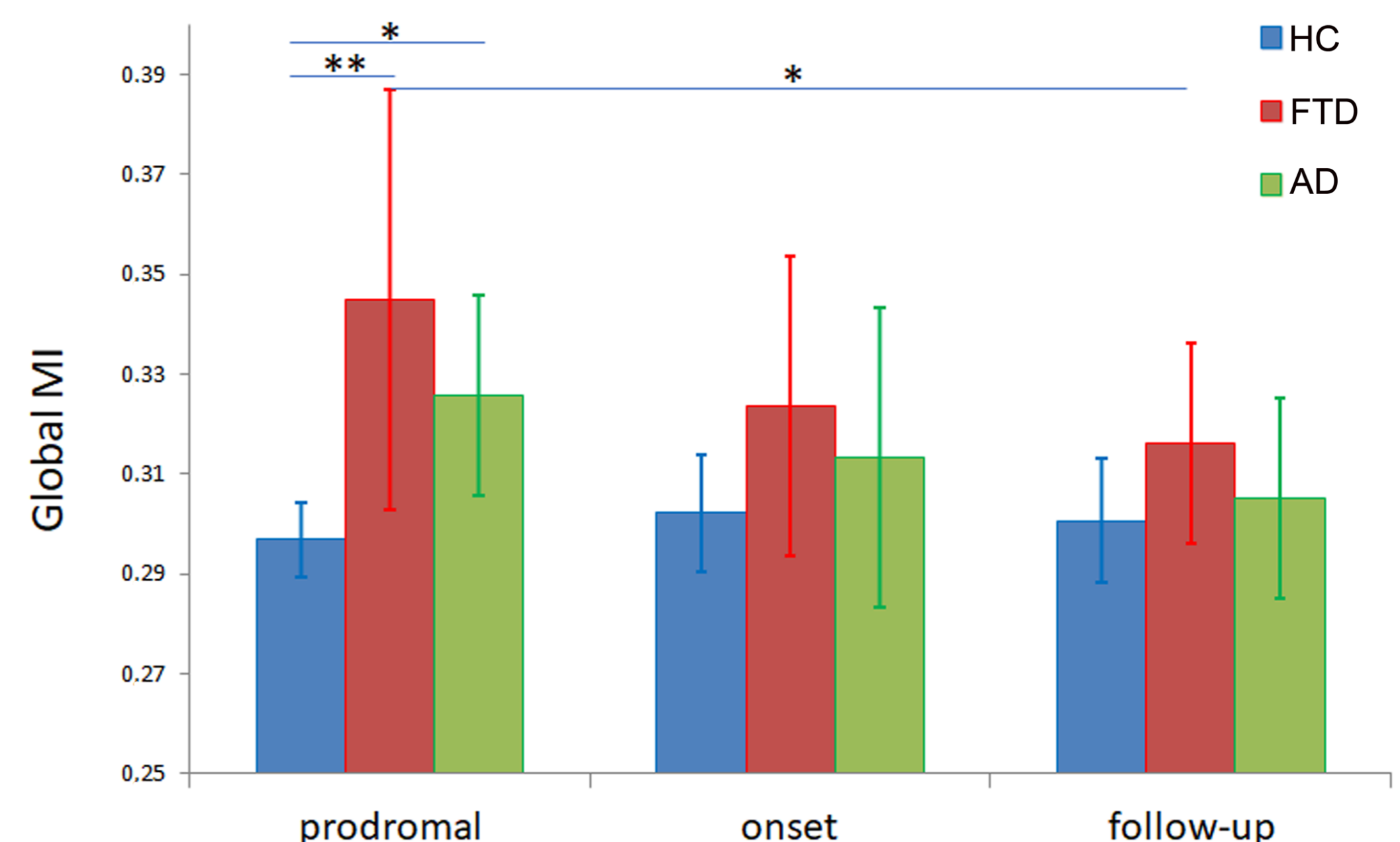


Fig.1

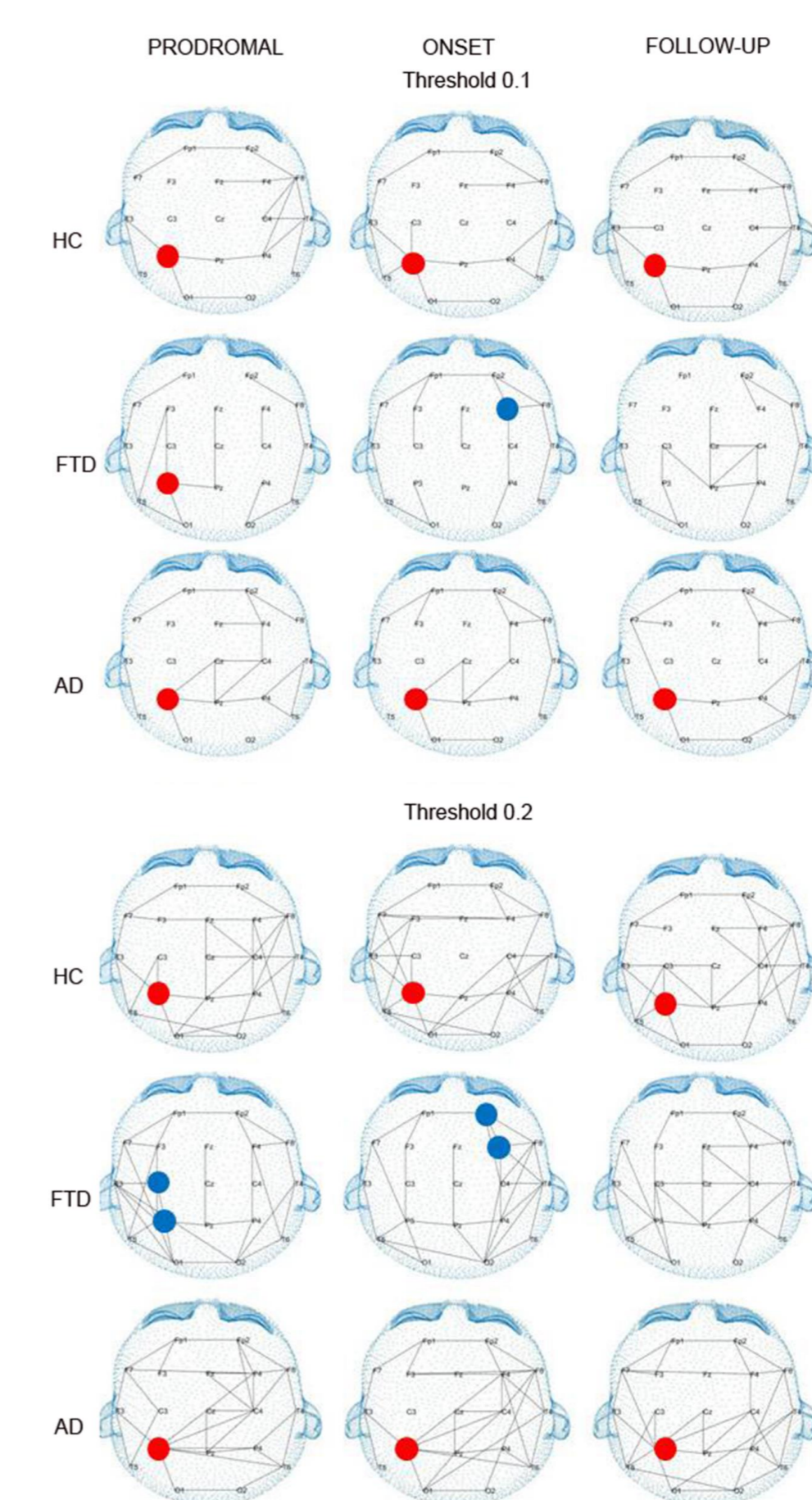


Fig.2

Comparisons	Variables at prodromal stage > Cut-off value	Sens	Spec	PPV	NPV	AUC
FTD and AD vs. Controls	Global MI > 0.30	92%	90%	94%	86%	0.95
	MI in left local anterior connection > 0.30	89%	90%	89%	90%	0.94
FTD vs. Controls	MI in right local anterior connection > 0.44	72%	95%	93%	79%	0.83
	Global efficiency at 0.1 threshold > 0.26	44%	95%	89%	66%	0.67
	Global clustering coefficient at 0.1 threshold > 0.35	67%	85%	80%	74%	0.79
	Global clustering coefficient at 0.2 threshold > 0.31	94%	40%	59%	89%	0.68
	small world propensity at 0.2 threshold > 0.44	100%	35%	58%	100%	0.61
AD vs. Controls	MI in left local posterior connection > 0.30	100%	85%	86%	100%	0.94
	MI in right local posterior connection > 0.30	89%	100%	100%	91%	0.96
FTD vs. AD	MI in left local anterior connection > 0.31	89%	44%	62%	80%	0.71
	Global efficiency at 0.1 threshold > 0.23	56%	94%	91%	68%	0.62
	Global clustering coefficient at 0.1 threshold > 0.34	67%	100%	100%	75%	0.80
	Global clustering coefficient at 0.2 threshold > 0.38	67%	61%	63%	65%	0.65

Fig.3

References

- Rascovsky K, Hodges JR, Knopman D, Mendez MF, Kramer JH, Neuhaus J, et al. Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. Brain 2011; 134: 2456-77.
- Supekar K, Menon V, Rubin D, Musen M, Greicius MD. Network analysis of intrinsic functional brain connectivity in Alzheimer's disease. PLoS Comput Biol 2008; 4: e1000100.
- Wang ZJ, Lee PWH, McKeown MJ. A novel segmentation, mutual information network framework for EEG analysis of motor tasks. Biomed Eng Online 2009; 8: 9.