Brain network topology in hereditary spastic paraparesis: a magnetoencephalography study

R. Rucco[1], A. Antenora[2], F. Jacini[1], F. Baselice[3], G. De Michele[2], C. Criscuolo[2], C. Granata[4], G. Sorrentino[1], P. Sorrentino[3]

1 Department of Motor Sciences and Wellness, University of Naples Parthenope, Napoli, Italy
2 Department of Neurosciences, Reproductive and Odontostomatological Sciences, Federico II University, Naples, Italy
3 Department of Engineering, University of Naples Parthenope, Napoli, Italy
4 National Research Council – Institute of Applied Sciences and Intelligent Systems, via Campi Flegrei 34, 80074 Pozzuoli (Napoli)

Objective

Hereditary spastic paraplegias (HSPs) are a group of neurodegenerative disorders characterized by progressive spasticity and weakness of the lower limbs. HSPs can be classified into "pure" and "complicated" forms depending on the presence of other neurological or systemic abnormalities. The most frequent HSP is SPG4, an autosomal dominant form caused by mutations in the *SPAST* gene. Despite the fact that SPG4 is considered a "pure" form of HSP, a more widespread involvement of the CNS has been reported in both clinical and neuroimaging studies. In this exploratory study, we studied in SPG4 the features of brain network through magnetoencephalograpy (MEG).

Materials

Ten patients (8 males and 2 females) from 7 families were included, as well as ten matched controls. The mean age of our cohort was 53,6 years ± SD 11,6 (range 40-74 years), and the mean age at onset of symptoms was 36,2 ± SD 10,3 (range 18-50 years). All treatments that might interfere with brain connectivity had been suspended. The patients underwent a five – minutes, eyes – closed MEG acquisition as well as a clinical rating performed by SPRS.

Methods

The signals were cleaned from environmental noise, physiological and system related artifacts using principal component analysis, supervised independent component analysis and visual inspection. Nine patients had enough clean data. Subsequently, time series of neuronal activity were reconstructed in regions of interests (ROIs) using an AAL atlas-based beamforming and then filtered in the classical frequency bands (delta, theta, alpha1, alpha2, beta, gamma). The phase lag index (PLI) estimated the connectivity between ROIs. Interpreting the ROIs as nodes of a network and the PLI values as its links, we obtained frequency-specific minimum spanning trees (MST). Finally, we compared topological parameters in patients and controls using permutation testing corrected for multiple comparisons. The compromise parameters were correlated to clinical disability.

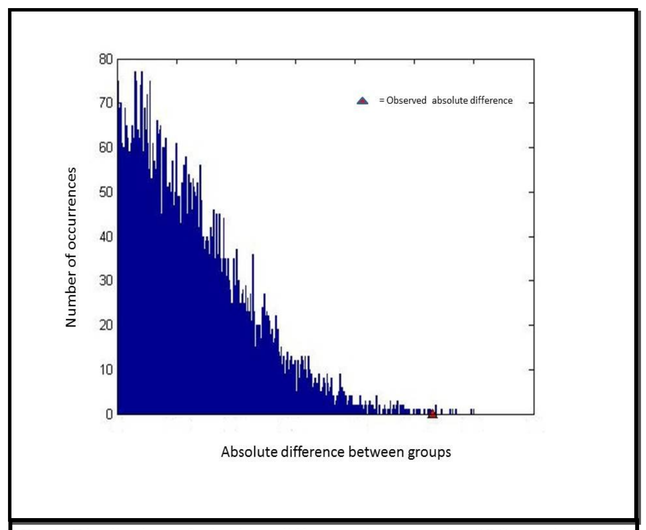

Fig.1 Distribution of absolute difference between the SPG4 and Control group

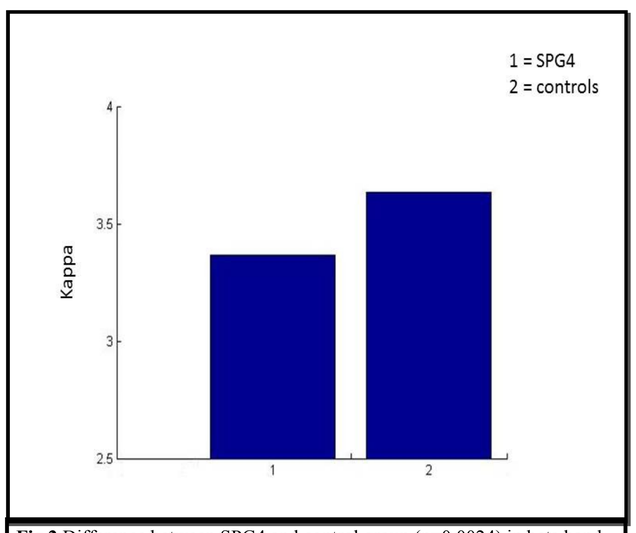

Fig.2 Difference between SPG4 and control group (p=0.0024) in beta band of Kappa parameter.

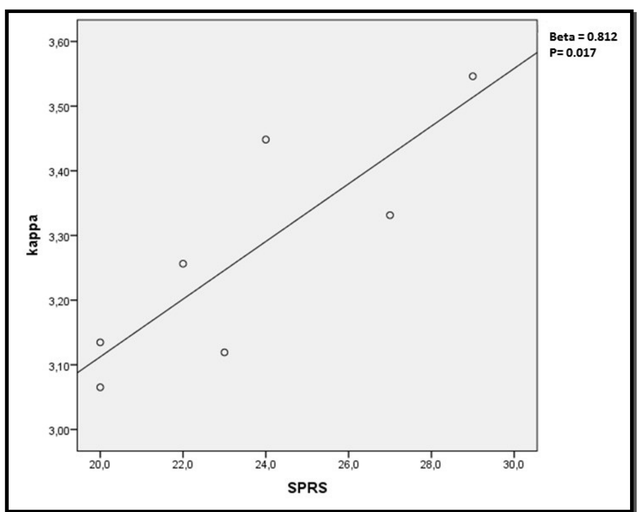

Fig.3 Correlation between Kappa parameter (in beta band) and SPRS. B=0.812, p=0.017

Results

Our results showed no difference in betweenness centrality between groups (after correction for multiple comparisons). Comparing the broadness of the degree distribution (k), a loss of hubs was evident in the networks of patients as compared to controls, specifically in the beta band (p = 0.0004, after multiple comparison correction p=0.0024). Furthermore, this metric related to the clinical disability in the patients (standardized beta 0.812, p=0.017).

Discussion

Our exploratory study shows a change in the functional network assessed by MEG in HSP patients. This observation may be useful in further understanding the multifaceted pathophysiology of disease.

References

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