Exploring Graph-derived Metrics from Functional Brain Connectivity Analyses from PDC and DTF Connectomes as VNS Outcome Predictors

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ABSTRACT

In 1/3 of epilepsy patients, medication may be insufficient, and respective surgery may be offered whenever the seizure onset is localized and situated in a non-eloquent brain region. When surgery is not possible, vagus nerve stimulation (VNS) therapy can be used as an add-on treatment to reduce seizure frequency and/or duration. However, screening tools or methods for predicting patient response to VNS and avoiding unnecessary implantation of VNS in non-responders (NR) are unavailable, and confident biomarkers of clinical efficacy are unclear.

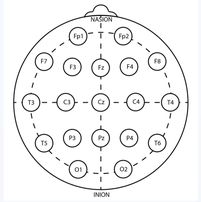
OBJECTIVES

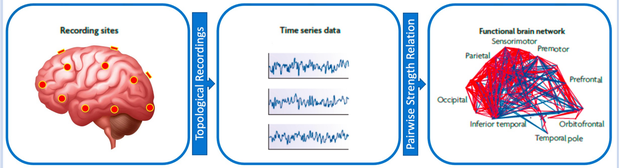
This study aims to identify graph-derived measurements from functional brain connectivity analyses that may be used as new VNS outcome predictors

MATERIALS & METHODS

Thirty-seven refractory epilepsy patients were retrospectively studied, calculating five functional brain connectivity indexes (Global Efficiency, Average Clustering Coefficient, Modularity, Global Reaching Centrality, and Degree Assortativity) per frequency band (Delta, Theta, Alpha, Beta, and Broadband) upon partial directed coherence (PDC) and direct transform function (DTF) connectivity matrices from EEG recordings. Data were separated into awake and sleep conditions, where ten epochs of 10 seconds were selected from the resting state awake condition and non-rem sleep stage II. Graph measurements were calculated upon three thresholding methods: non-thresholded, surrogate data test, and thresholded binarized connectomes.

Classification	Number of patients
VNS Outcome	
Responders	22
Non-Responders	15
Epilepsy Type	
Focal	20
Bi-focal	1
Multi-focal	4
Generalized	9
Unknown	3





Data -> MVAR Model

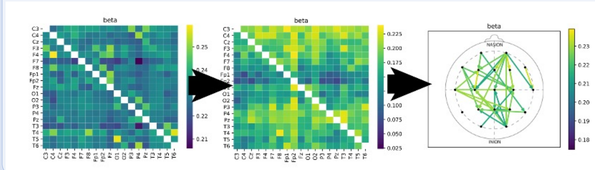
$$X(t) = \sum_{m=1}^{p} A(m)X(t-m) + E(t)$$

Partial Directed Coherence

$$\pi_{ij}(f) = \frac{A_{ij}(f)}{\sqrt{\sum_{m=1}^{k} |A_{mj}(f)|^2}}$$

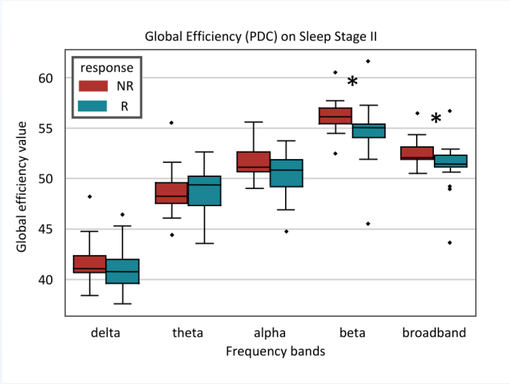
Direct Transfer Function

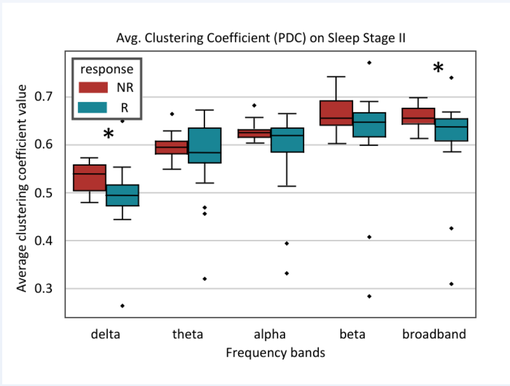
$$\gamma_{ij}^2(f) = \frac{H_{ij}(f)}{\sqrt{\sum_{m=1}^{k} |H_{im}(f)|^2}}$$

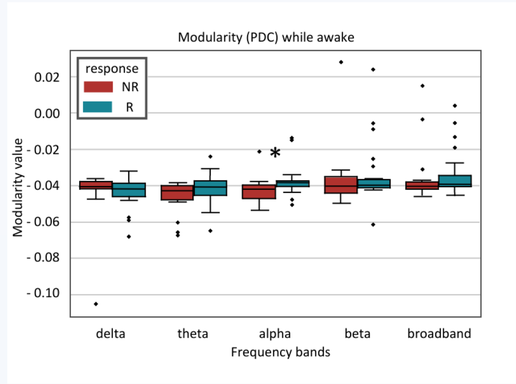


RESULTS

We found some graph measures from the PDC connectome were statistically different between responders (R) and non-responders (NR) using the Mann-Whitney U test with Benjamini-Hochberg correction procedure and a false discovery rate of 5% ($p<0.05$). Specifically, global efficiency and average clustering coefficient in beta/broadband and delta/broadband, respectively, during non-rem sleep stage II had a higher value in non-responders. Also, the modularity on the alpha band in the wakefulness state had lower values in non-responders.







CONCLUSIONS

Our study showed that global efficiency, average clustering coefficient, and modularity calculated from PDC connectomes might discriminate between R and NR based on EEG analysis before VNS implantation.

ACKNOWLEDGEMENTS

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