

Abstracts

EEG Connectivity Analysis of Vns-dose-dependency in Refractory Epilepsy

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Rationale: Epilepsy is characterized by hypersynchronization in brain networks, resulting in higher global brain network efficiency [Carboni M. et al.,2020]. Vagus Nerve Stimulation (VNS) is an established treatment for refractory epilepsy, yet clinical response remains variable and stimulation parameters are determined empirically. A major mechanism of action of VNS is cortical desynchronization, and dose-dependent patterns of EEG power topographic allocation and brain desynchronization have previously been reported [Germany E. et al., 2024]. This study aims to investigate the acute effects of different VNS doses on brain network connectivity, which may help identify the optimal intensity ranges for effective patient treatment.

Methods: Twenty-eight VNS-implanted patients (17 responders (R), 11 non-responders (NR)) participated in the study. A 64-channel resting state EEG in an eyes-open condition was recorded. VNS was programmed with a 14s ON/40s OFF duty cycle, with first increasing VNS intensities until reaching the clinical programmed intensity (CI) plus an additional 0.25 mA, and thereafter at decreasing intensities. EEG data were analyzed using the weighted phase lag index (wPLI) to measure pairwise electrode connectivity. The acute VNS effect on connectivity was assessed by calculating the wPLI OFF/wPLI ON pairwise ratio matrices per intensity and frequency band. Global efficiency (GE) and global reaching centrality (GRC) were computed as network metrics. Results were averaged in function of the CI and compared between R and NR. Individual intensities were compared using t-tests, while the dose-response effects on GE and GRC were examined with a mixed-effect model.

Results: In the alpha band, GE was significantly higher in R than NR at 0.25 mA above CI, as revealed by the t-test ($p = 0.03$). The mixed-effect model showed significantly higher GE at increasing intensities in R in contrast to NR ($p = 0.05$). In the theta band, the t-test indicates that GRC was significantly higher in R than NR at 1 mA

below CI ($p = 0.01$). The mixed-effect model suggested that R had a higher GRC at lower intensities compared to NR, and increasing intensities significantly decreased the GRC in R ($p = 0.04$).

Conclusions: Our study indicates that increasing VNS intensities modulates brain connectivity differently in R compared to NR. Increasing VNS intensities in R recruits neural networks progressively, potentially leading to a higher cortical desynchronization as demonstrated by an increase in GE. This may result in a decrease in local active seizure foci, which is reflected by a progressive decrease in centrality.

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