Abstracts

A Longitudinal Vagus Nerve Stimulation Study: Effects on EEG Synchronization Using a Clinical-research Response Scale

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Rationale: Previous studies have shown that Vagus Nerve Stimulation (VNS) induces acute electroencephalogram (EEG) desynchronization. No reliable biomarkers for predicting and assessing VNS response exist up till today. Additionally, a longitudinal evaluation of VNS-induced EEG desynchronization is lacking. We performed a prospective study investigating EEG synchronization before and after VNS implantation and correlated it with a newly developed clinical research response scale (CRRS).

Methods: Adult patients with drug-resistant epilepsy, candidates for VNS implantation, were prospectively recruited. A 64-channel cap EEG was recorded 1 month before surgery (V1) and at 1-(V2), 3-(V3), and 6-(V4) months post-implantation. Clinical stimulation parameters (intensity, pulse width, frequency) were kept stable and 180s of resting state EEG with eyes open (EO) and eyes closed (EC) were recorded. The global weighted Phase Lag Index (wPLI – a connectivity metric) was computed from the 64x64 channels matrices in each frequency band (delta, theta, alpha, beta and broadband) with VNS ON and OFF. At V2, V3, and V4, the acute response to VNS was evaluated based on the magnet effect to (1) stop seizure; (2) reduce (2.1) seizure duration, (2.2) seizure intensity, and/or (2.3) post-ictal duration. Chronic VNS effects were assessed based on: (1) seizure frequency reduction - >80%, >50%, or >30%; (2) reduction of (2.1) seizure duration, (2.2) seizure intensity, and/or (2.3) post-ictal duration. A CRRS based on these items was built, ranging from 0 (no response) to 15 (maximum response), and compared to the usual binary classification (responders (R): >50% seizure frequency reduction/non-responders (NR): < 50% seizure frequency reduction). Linear mixed models

were computed: $WPLI_{band}$~ $Response_{CRRS/binary}$ + $Visits_{V1\text{-}4}$ + $Response_{CRRS/binary}$: $Visits_{V1\text{-}4}$ + $(1|id_{subject})$ with ID used as a random variable. In addition, a linear regression was built using wPLI at V1 to predict VNS response based on CRRS scores.

Results: Eleven patients were included. In the delta band in VNS OFF in EC condition, a significant effect of patient's *Response* on wPLI (p_{CRRS}= 0.003**, p_{binary}= 0.006**) was found, while the *Visit* variable was significantly related to wPLI at V4 -using CRRS score only (p_{CRRS}= 0.004**, p_{binary}= 0.1). The interaction between *Response* and *Visit* was significant using CRRS only (p_{CRRS}= 0.002** - Fig.1, p_{binary}= 0.06 - Fig.2). Linear regression showed a positive correlation between the wPLI at V1 and CRRS scores (p_{CRRS}= 0.024, R^2 = 0.4) (Fig.1-V1).

Conclusions: (i) VNS efficacy is correlated with a higher EEG desynchronization in resting-state EC condition while the VNS is OFF. (ii) A decreased wPLI over time is correlated with higher CRRS scores. (iii) A higher pre-implantation wPLI predicts future VNS response. Overall, VNS may positively influence specific brain states, with a time-dependent evolution of EEG synchronization, which could reflect therapeutic efficacy improving throughout the treatment. Moreover, CRRS may better characterize VNS response compared to a binary classification. Further validation of the CRRS on a larger sample is warranted.

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