Feasibility study on the use of pre-implantation MEG to identify predictive biomarkers of response to vagus nerve stimulation in patients with drug-resistant epilepsy (PREVEDeRE)

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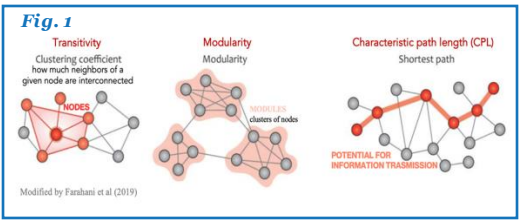
Objectives: Evaluate the feasibility of using pre-implantation resting-state magnetoencephalography (MEG) to identify **functional connectivity biomarkers predictive of clinical response** to vagus nerve stimulation (VNS) in patients with drug-resistant epilepsy (DRE). The aim is to support development of a predictive model to improve **patient selection** and personalize neuromodulatory strategies.

Materials: Retrospective, single-center, observational study. 38 patients, treated at Gent University Hospital (Belgium), with DRE underwent VNS implantation and pre-operative MEG between 2008 and 2024. Most patients had focal epilepsy (n = 29, 78.4%), followed by generalized epilepsy (n = 6, 16.2%) and combined focal/generalized (n = 2, 5.4%). Etiology was structural in 19 patients (52.8%), unknown in 10 (27.8%), genetic in 4 (11.1%), and infectious in 3 (8.3%). At baseline, all patients were on antiseizure polytherapy.

Methods: Pre-implantation MEG data were preprocessed (1–100 Hz bp, Notch filtered, ICA for artifacts, resampled to 250 Hz). **Source reconstruction** was performed with MRI-based 3-shell BEM, LCMV beamforming, and parcellation using the Brainnetome Atlas (246 regions). Resting-state functional connectivity was estimated with **weighted Phase Lag Index (wPLI)** across multiple bands. Graph-theoretical metrics (modularity, clustering coefficient, characteristic path length) were extracted from thresholded networks (20% density). Responders were defined as ≥50% seizure reduction at follow-up. EEG before and 1 year after VNS was visually inspected (normal/abnormal epoch ratio), and ASM regimen changes were documented. *[Fig. 1]*

Fig. 1

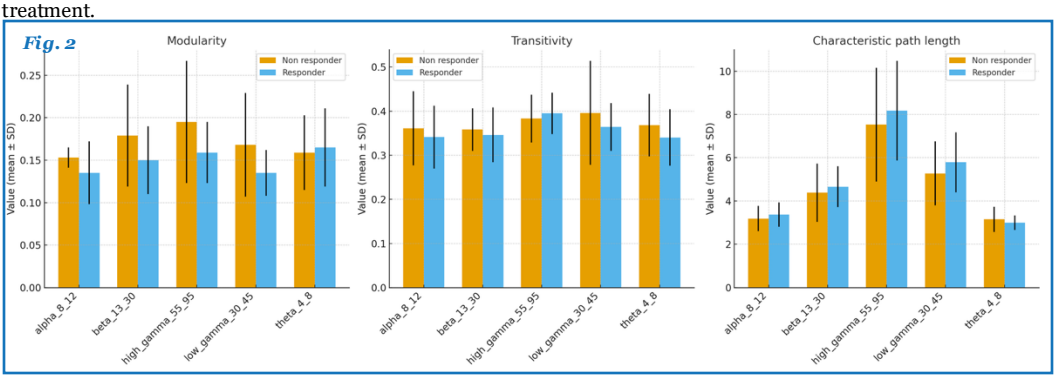


Results: No statistical outcomes are presented. Based on previous literature, we expect that VNS responders will display higher modularity and lower clustering (4,6). Preliminary data for 10 patients (5 responders, 5 non-responders) are presented in *Figure 1.* and revealed distinct network patterns. **Modularity** was consistently higher in non-responders across alpha, beta, and gamma bands, with the only exception in the theta band, where responders showed slightly higher values. **Transitivity** was generally lower in responders (theta, alpha, beta, low gamma), indicating less clustered networks, but this trend reversed in the high-gamma band. **Characteristic path length (CPL)** showed no consistent directionality: responders exhibited longer CPL in alpha, beta, and gamma bands, while shorter CPL was observed in theta.

Discussion: While VNS is widely used for DRE, response variability is high (1–3), and reliable biomarkers are still lacking and debated (5). Preliminary findings suggest that reduced transitivity may represent a potential marker of clinical response to VNS, whereas modularity and CPL did not show consistent discriminatory power across frequency bands. However, these results remain inconclusive due to the limited sample size and require validation in larger cohorts.

Conclusions: This study evaluates the feasibility of integrating MEG-derived connectivity measures into pre-surgical VNS assessment. Our preliminary data partially support this hypothesis. Reduced transitivity emerged as a potential marker of response, whereas modularity and CPL showed less consistent patterns. Although inconclusive these findings suggest potential RS-MEG contribution for the development of predictive models for individualized treatment.

Fig. 2



Ref.: 1. Brodie et al (2012) 2. Hödl et al (2020) 3. Larsen et al (2016) 4. Babajani-Feremi et al (2018) 5. Pourmotabbed at al (2021) 6. Clifford at al (2024).

No conflict of interest to disclose.