Methodologies for Vagus ElectroNeuroGram (VENG) analysis

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Background

- 30% of epileptic patients are **refractory** to medication and not eligible to resective surgery [1]
- **VNS therapy** can be an adjunctive treatment but **1/3** of patients are **not responders** [2]
- The response can be **improved** by stimulating at the **seizure onset** [3]
- **Seizures** are **associated** with **autonomic symptoms** [4]
- **Vagus Nerve** (VN) transmits **parasympathetic** information [5]
- **GAERS** is a robust animal model of **absence** seizures[6]
- Epileptic patients and GAERS have **autonomic dysfunctions** [7]
- Autonomic system **might evolve** over age in GAERS[8]

Results

➢ **Vagus Nerve Activity increases during absences**

The detection of this modulation could be used as a biomarker for seizure detection and development of closed-loop VNS.

➢ **Parasympathetic response decreases with age**

Vagus nerve modulation during seizures in GAERS **decreases with age** and becomes **less variable.**

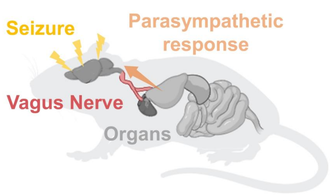
BUT a subset of seizures does not exhibit RMS modulation.

❖ **Is the vagus nerve activity modulated during absences ?**
❖ **Does this modulation evolve with age linked to seizure occurrence?**

New question: does vagus nerve activity lack parasympathetic cues during these seizures, or is our methodology insufficient to detect subtle or different modulations?

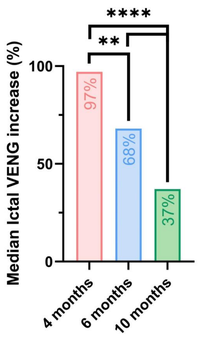
Vagal Parasympathetic activity is modulated by spontaneous seizures in Genetic Absence Epilepsy Rats from Strasbourg

Vagus nerve activity increases during seizures

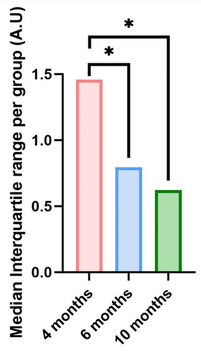


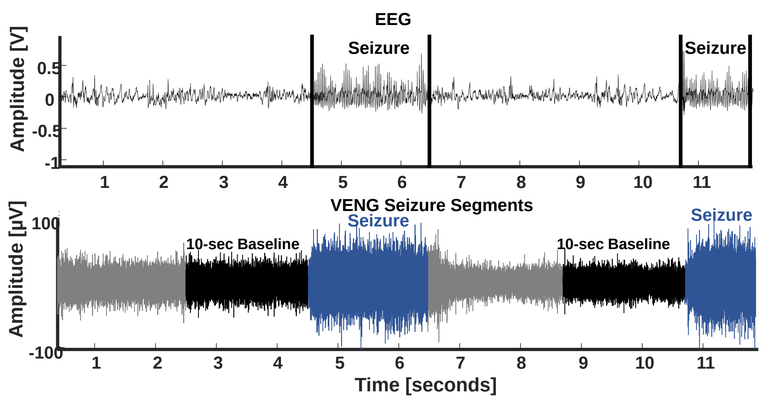
+ 60% in 620 seizures
N=11

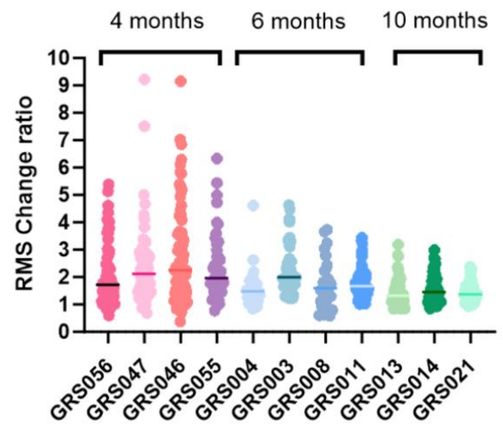
Ictal VENG* decreases with age



Individual ictal VENG variability decrease with age







Methodology

For all figures: *Comparison of different methods between **A**. Big amplitude VENG changes during seizures and **B.** Low amplitude VENG changes during seizures.*

Root Mean Square analysis

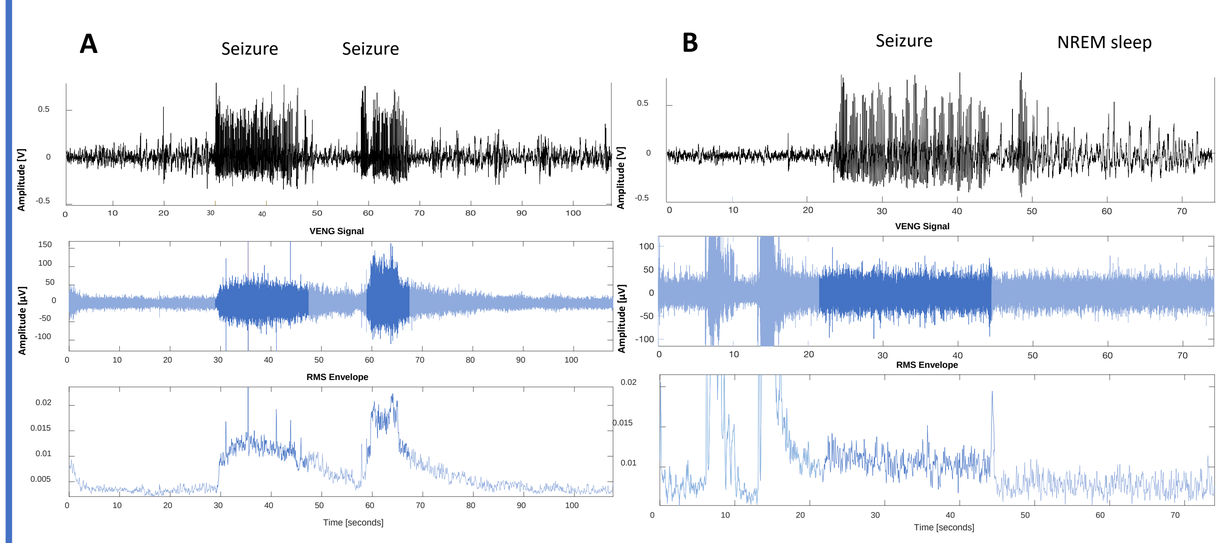


Fig1. The root mean square value (RMS) is a statistical measure used to evaluate the amplitude and energy of a signal in the time domain. RMS provides a single value representing the magnitude of a varying signal and reflects the energy contained within the signal, helping to assess the power and intensity over defined time periods.

Fuzzy Entropy Analysis

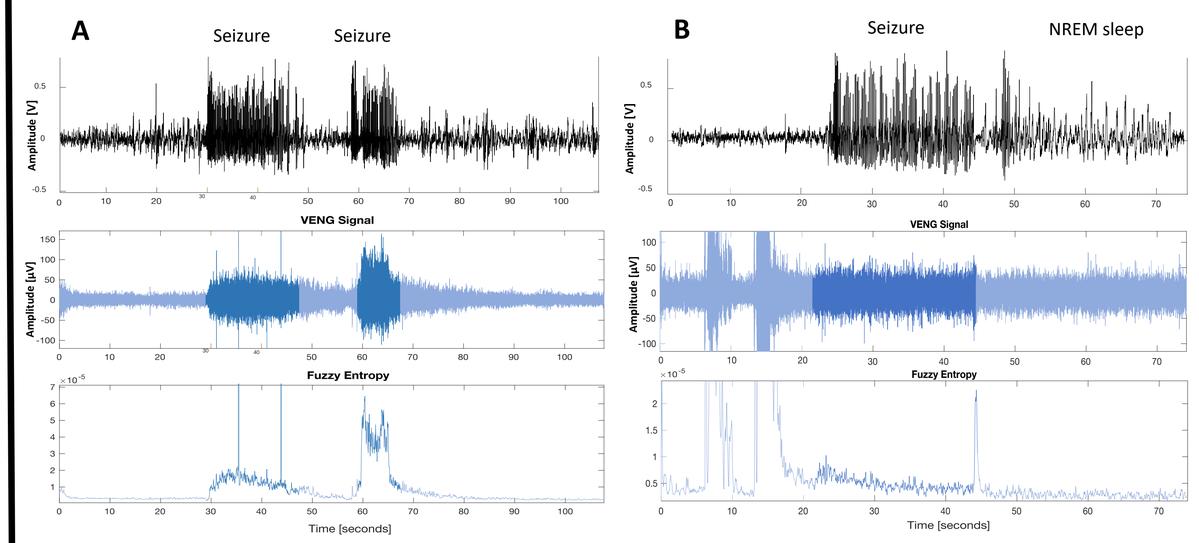


Fig2. Entropy measures serve as features for signal processing by **quantifying the complexity, irregularity, or unpredictability of signals.** These features can be used to distinguish between different states or conditions of the system being analyzed. Fuzzy entropy (FuzEn) measures signal complexity by evaluating the similarity of embedded vectors with fuzzy sets. Unlike traditional entropy measures, FuzEn accounts for soft, continuous boundaries between classes, making it more robust for short or noisy signals. This method overcomes sample entropy (SampEn) limitations, offering better continuity and reduced sensitivity to data length.

Spike Frequency analysis

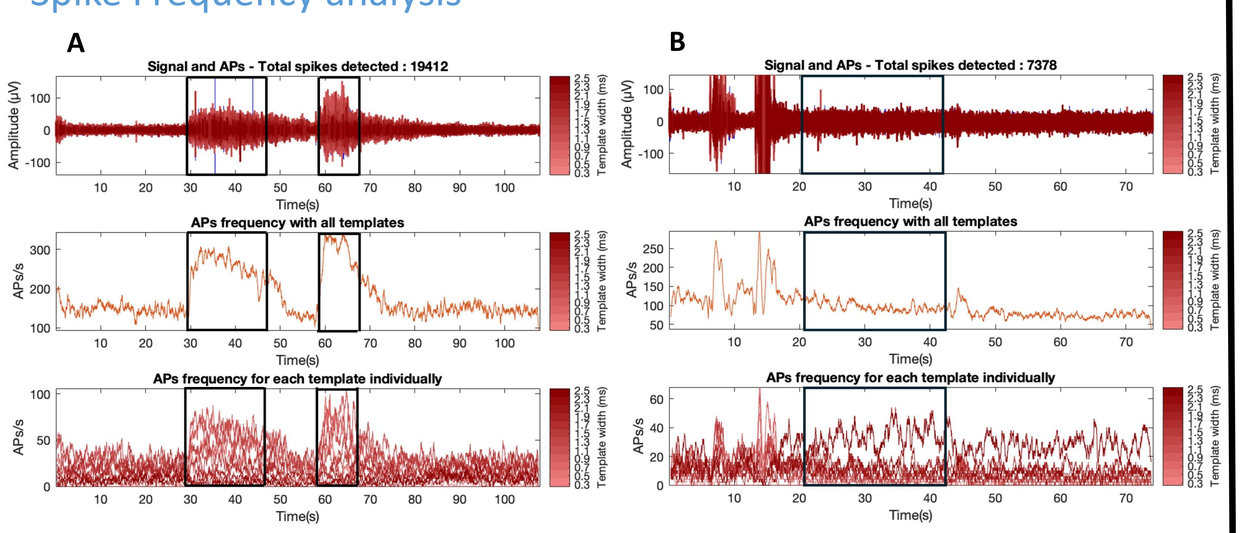


Fig3. Spike detection methods are techniques used to identify transient, high-amplitude events in extracellular recordings of compound action potentials, which are crucial for analyzing and diagnosing neural function. Detecting and time-sorting these spikes are essential for evaluating dynamic changes in neural signals, as they allow for the precise measurement of the timing and patterns of neural activity, which is necessary for understanding the underlying physiological processes and detecting abnormalities or dysfunctions in the nervous system.

Merging RMS and Entropy

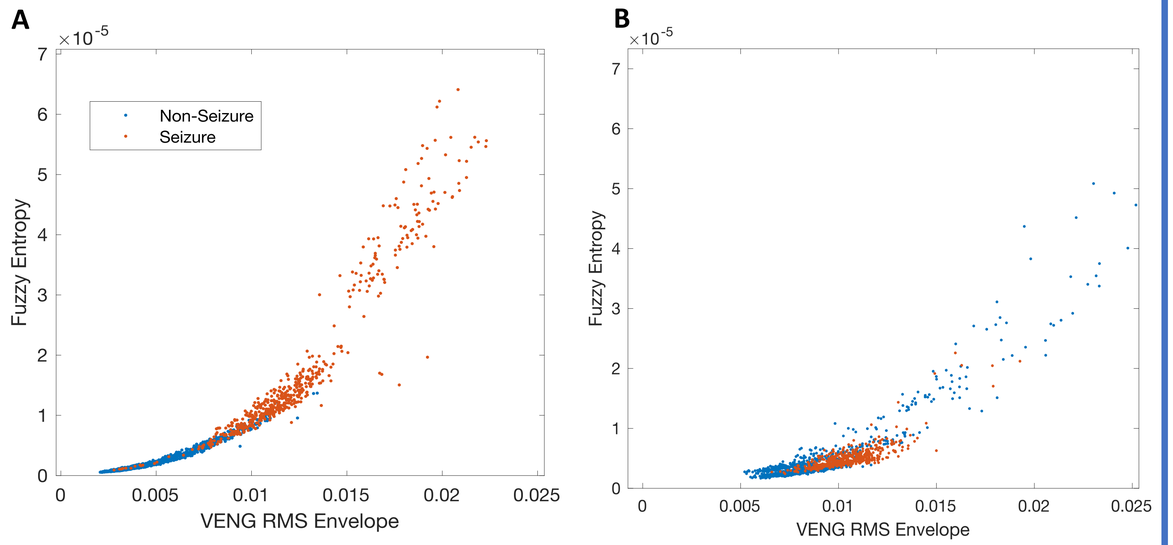


Fig4. Scatter plot displaying the 2D dispersion of Fuzzy Entropy and RMS Envelope features. Seizure segments are color-coded in red, while non-seizure segments are color-coded in blue. The plot highlights the clustering patterns of the seizure and non-seizure data points.

Conclusion: Vagus nerve activity represents a complex and noise-sensitive signal. Employing a combination of signal analysis methods such as RMS, fuzzy entropy or spike frequency analysis may facilitate the identification of specific features during seizures, potentially advancing detection capabilities.

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References:[1]Sanchez-Alvarez (2002) ; [2] Martorell-Llobregat (2022) ; [3] Boon (2001) ; [4] Devinsky (2004) ; [5] Yuan(2016) ; [6] Danober (1998) ; [7] Mamalyga (2014) ; [8] Myers (2018).

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