Fractal dimension and clinical neurophysiology fusion to gain a deeper brain signal understanding: A systematic review

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Background

Fractal Geometry

- Fractals are structures that repeat patterns at different scales (*self-similarity*).
- Basis for measuring complexity in nature and biological systems.

Fractal Dimension (FD)

- FD quantifies **irregularity and complexity** of a signal or structure.
- Higher FD = greater complexity and variability.
- Applied to **time series signals** to capture dynamics beyond linear methods.

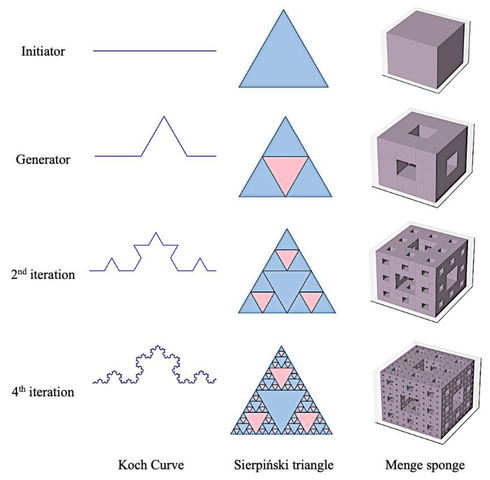
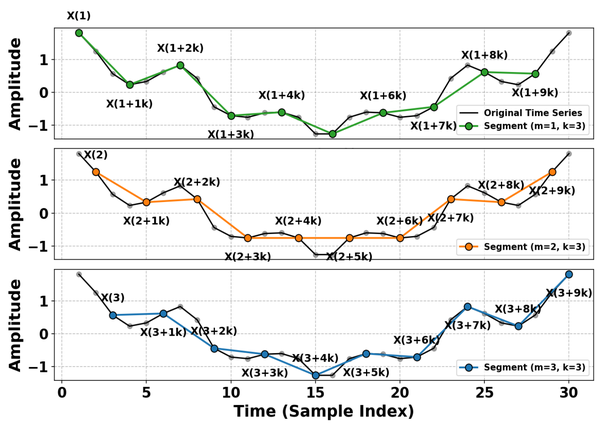


Fig1. Fractal Geometry (Koch curve, Sierpiński triangle, Menger sponge).

FD Calculation Methods

- Multiple algorithms exist: **sPSD** (Slope of Power Spectral Density), **DFA** (Detrended Fluctuation Analysis), **HE** (Hurst Exponent), **HFD** (Higuchi's Fractal Dimension), **KFD** (Katz's Fractal Dimension).



Higuchi Fractal Dimension (HFD)

- Estimates FD **directly in the time domain**.
- Well suited for **short, noisy, non-stationary signals** (e.g., EEG).
- **Method**: Split signal into subseries→ compute curve lengths → average → slope of log–log plot gives HFD.

Fig 2. Higuchi algorithm: the signal is segmented into subseries with different offsets (m) and step sizes (k) to compute curve lengths.

FD in Neurophysiology

- Brain signals (EEG, MEG, fMRI) are **non-linear and non-stationary**, making them difficult to analyze with classical linear methods. FD provides a mathematical measure of their complexity.

Objectives

- To systematically review applications of **FD** in clinical neurophysiology.
- To identify how FD has been used across neurological conditions.
- To evaluate the potential of FD as a **biomarker**.
- To summarize **meta-analysis findings** (Alzheimer's disease, stroke).

Methods

Database: PubMed was queried for the past 20 years using "fractal dimension" and "clinical neurophysiology" keywords. 499 articles identified.

Screening Process:

- Excluded duplicates (n=2) and abstracts without full text (n=2).
- Removed studies on animals, retina, structural imaging (PET, CT), or brain morphology.
- Excluded cases where "fractal" was not used as a measure of signal complexity.
- Review papers were excluded but screened for relevant citations.

Citation search: added 9 additional studies.
Final Selection: 59 studies included in the review.
Trend: > 60% of studies were published in the last 5 years

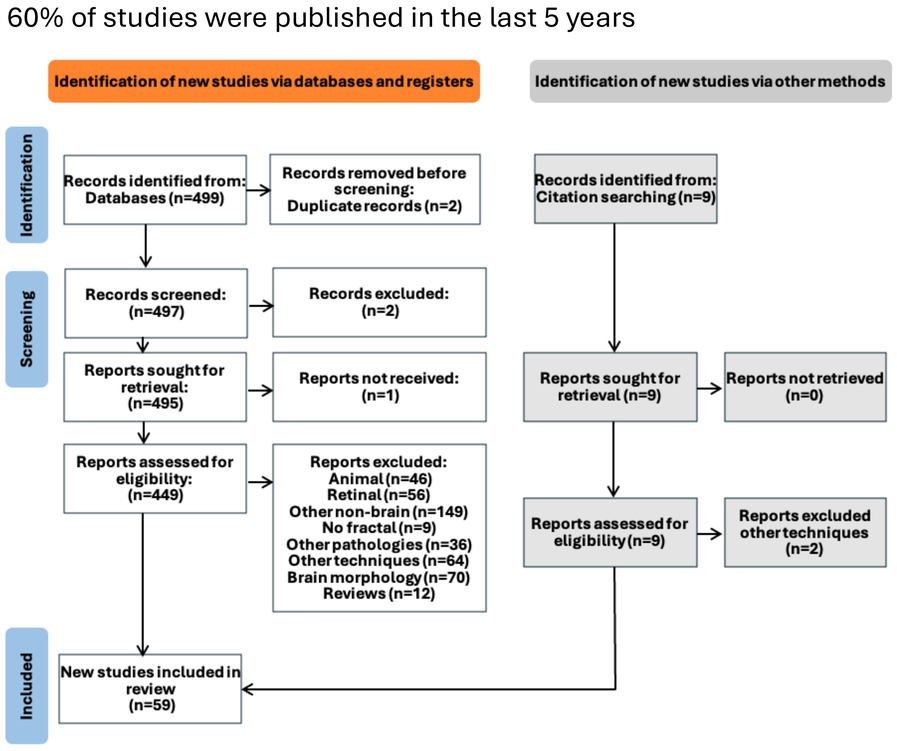


Fig3. PRISMA flow diagram of study selection

Findings Across Neurological Conditions

- Based on 59 studies included in this systematic review, FD shows disease-specific changes across several neurological conditions.
- Forest plots display the mean effect size (Hedges' g) with 95% confidence intervals, where negative values indicate a reduction in FD compared to healthy controls (HC).

Alzheimer's Disease (AD)

- FD is consistently **reduced** across EEG, MEG, and fMRI studies.
- This reduction is robust across multiple independent cohorts.
- **Meta-analysis shows a significant overall decrease in FD** (summary effect size < 0, CI not overlapping zero), supporting FD as a reliable biomarker for AD detection and monitoring.

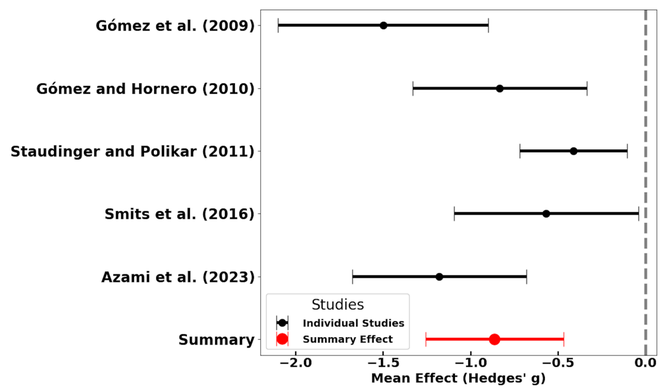


Fig4. Forest Plot of HFD Differences AD and Healthy Controls for meta analysis

Parkinson's Disease (PD)

- FD alterations correlate with **cognitive decline**.
- Suggests FD as a marker of disease-related brain dynamics.

Stroke

- FD shows a pronounced **reduction in the acute phase**.
- Demonstrates sensitivity to sudden neural damage.
- Meta-analysis supports FD reduction during acute and early subacute stages.

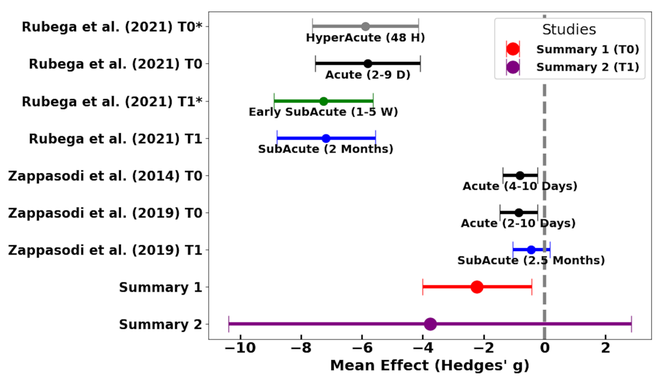


Fig5. Forest Plot of HFD Differences Stroke and Healthy Controls for meta analysis

Multiple Sclerosis (MS)

- FD is **altered** and responds to **stimulation paradigms**.
- Highlights FD's potential to track neuroplastic changes.

Schizophrenia (Scz)

- FD alterations and **multifractality** indicate disrupted network complexity.
- *Meta-analysis shows significant FD reduction compared to controls.*

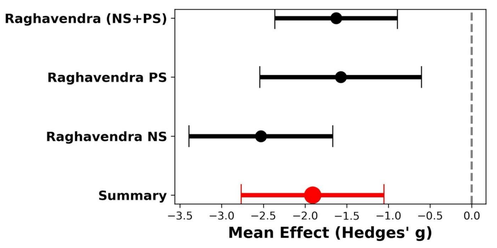


Fig6. Forest Plot of HFD Differences Scz and Healthy Controls for meta analysis

Aging

- FD follows an **inverted U-shaped trajectory**: higher in midlife, declining with older age.
- Reflects age-related reductions in brain signal complexity.
- *Meta-analysis confirms FD decline with aging.*

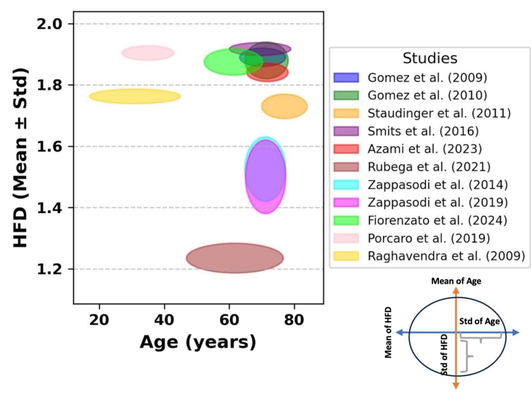


Fig7. HFD of HC subjects with different ages from different studies

Conclusion and Outlook

- FD provides a robust framework to capture **brain signal complexity**.
- Across **59 studies**, **Meta-analyses confirm significant FD reductions** in Alzheimer's disease, stroke, schizophrenia, and aging.
- **HFD** is the most widely applied method for clinical signals.
- FD shows strong promise as a **biomarker** for diagnosis, monitoring.

Future Directions

- Standardize FD estimation methods across studies.
- Explore **longitudinal and real-time applications** in clinical practice.

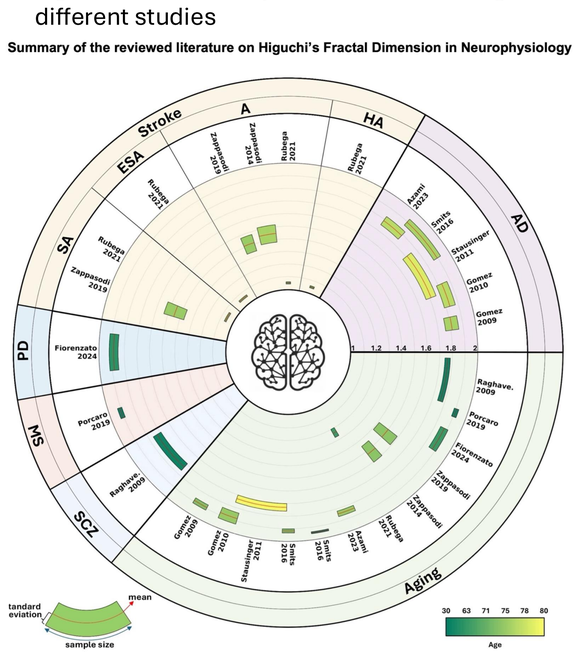


Fig8. Summary of the reviewed literature on HFD in neurophysiology across neurological conditions, showing sample size, variability, and age distribution.

Acknowledgement

This work was supported by:
HORIZON-ERC SyG (Grant No. 101071900) – *NEMESIS: Neurological Mechanisms of Injury and Sleep-Like Cellular Dynamics* (to MC, ALB, CP)
PRIN – MUR (Grant No. 20228ARNXS) (to CP and SM)

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