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DBS/L-dopa condition in a Parkinson's patient with a subthalamic nucleus implant: An evaluation using rms $\Delta \log F_{DFA}$ function

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Keywords: Parkinson's; Levodopa (L-dopa); Subthalamic Nucleus (STN); rms ΔlogF_{DFA}.

Abstract

Introduction: The mechanism by which low- or high-frequency Deep Brain Stimulation (DBS) attenuates tremor and other symptoms of Parkinson's disease remains unknown, especially in patients with electrodes implanted in the subthalamic nucleus.

Objective: To quantitatively evaluate the differences in the amplitudes of atypical DBS-L-dopa interaction fluctuations in resting tremor in a Parkinson's disease patient undergoing DBS of the subthalamic nucleus, considering two stimulation conditions (on-off) and two pharmacological conditions (L-dopa on-off).

Methods: Tremor was recorded for approximately 60 seconds in eight experimental conditions: DBS on/off × medication (L-dopa) on/off; and at four time points (15, 30, 45, and 60 minutes) after DBS was turned off for 60 minutes (without medication). Detrend Fluctuation Analysis (DFA) was applied to assess auto-correlation, and the rms function Δ log F_{DFA} was used to evaluate differences in amplitude variations.

Results: DFA revealed antipersistence (α_{DFA}<0.5), noise $1/f$ (α_{DFA}≈1), and nonstationarity (α_{DFA}>1) under the ren, ref, ron, and rof conditions. The Δ log F_{DFA} metric captured subtle differences at 15, 30, 45, and 60 minutes, complementing the traditional analysis.

Conclusions: The combined DFA-rms approach Δ log F_{DFA} provides an objective measure of the effects of DBS and levodopa, adding value to the clinical scales (UPDRS and TRS) used in the postoperative evaluation of subthalamic implants.

Introduction

Parkinson's disease is considered a systemic disease that begins with the death of nerve cells specialized in producing and releasing dopamine, a neurotransmitter fundamental to various functions of the central nervous system [1,2]. One of the main characteristics of this disease is related to the progressive loss of dopaminergic neurons in the substantia nigra of the midbrain and is associated with motor symptoms, including resting tremor, bradykinesia, and rigidity [3,4].

Depending on the stage of Parkinson's disease, the tremor becomes more harmonic, its frequency shifts to a lower range (4-6 Hz), its amplitude increases, the oscillation pattern changes, and it exhibits fluctuations on an atypical time scale [5]. The changes are subtle and intermittent, disappearing in cycles and tending to become more evident as the disease progresses [6,7].

For patients with this disease who have been diagnosed for more than 4 years, have a good response to levodopa, refractory

symptoms with optimized medication, preserved cognitive functions, and favorable general clinical conditions, Deep Brain Stimulation (DBS) surgery is recommended https://www.nice.org.uk/guidance/ipg382/informationforpublic. Since it is not a cure but a therapeutic option, the response to the invasive procedure is effective and safe, improving motor response and achieving its main objective, which is to improve the patient's quality of life [2,7,8].

Even after Parkinson's disease, patients undergoing DBS surgery may still require the use of Levodopa (L-dopa). The combination of DBS and L-dopa stimulation improves motor control, reduces fluctuations and dyskinesias, and eventually eliminates the need for high medication doses. To achieve this control, monitoring is conducted using the subjective Unified Parkinson's Disease Rating Scale (UPDRS) and Tremor Rating Scale (TRS), which are balanced by the expertise of a neurologist seeking the best combination of DBS and L-dopa stimulation [2].

A recent study evaluated the resting tremor velocity of the index finger in 16 individuals with Parkin-son's disease who received high-frequency electrical deep brain stimulation, unilaterally and bilaterally, in three targets: Ventro-Intermediate thalamus (Vim), internal globus pallidus (GPi), and Subthalamic Nucleus (STN) [6]. Two groups were analyzed: High-Amplitude (HAT) and Low-Amplitude (LAT). The study considered eight possibilities: deep brain stimulation on with medication on, deep brain stimulation on with medication off, deep brain stimulation off with medication on, deep brain stimulation off with medication off, and especially deep brain stimulation off for 15, 30, 45, and 60 minutes with medication off [6,9,10].

The methodology employed was the association of the Detrended Fluctuation Analysis (DFA) method with Shannon Entropy (H). Two points were verified in the study, the first identifying behavioral transitions with a typical time scale and the second providing information about the uncertainty in the tremor's position.

Even though it is an innovative research study [9] with important methodological contributions, the difference in fluctuation amplitude between the eight possibilities mentioned, considering two conditions (on/off) mentioned above for the same self-affinity scaling process, had not yet been explored. Given this gap, in this study we propose to investigate, in a reduced domain, the fluctuation amplitude via the rms function $\Delta logF_{DFA}$ with the aim of quantifying the relationship between Levodopa (L-dopa) combined with DBS electrical brain stimulation in the Subthalamic Nucleus (STN) target.

Methods

For the test performed with the rms function, we will use the publicly available database, available at:

https://physionet.org/content/tremordb/1.0.0/

The database provides recordings of resting tremor velocity data from the index finger of 16 individuals diagnosed with Parkinson's Disease (PD) who received high-frequency chronic Deep Brain Stimulation (DBS), unilaterally and bilaterally.

Since this is a statistical test, and a pioneering one for this subject (DBS/L-dopa) with the rms function ($\Delta logF_{DFA}$), we will only use patient (S016). The reason for the choice is associated with tremor patterns with good signal quality and low noise, as well as temporal stability when compared to other patients in the group who receive chronic high-frequency deep brain stimulation targeting the Subthalamic Nucleus (STN). A priori, this is a patient with rigidity and dyskinesias. Figure 1 illustrates, in red dots, the candidate region for the surgical procedure of the subcortical electrode in the structure of the Subthalamic Nucleus (STN).

Detailed information and descriptions of all patients in the database, such as: subject, age of the group, gender, target stimulation frequencies, intensity (volts), and other patient-specific parameters, can be found in PhysioNet [11]. Details of the original signal with minimum, maximum, and average values can also be viewed in Figure 2.

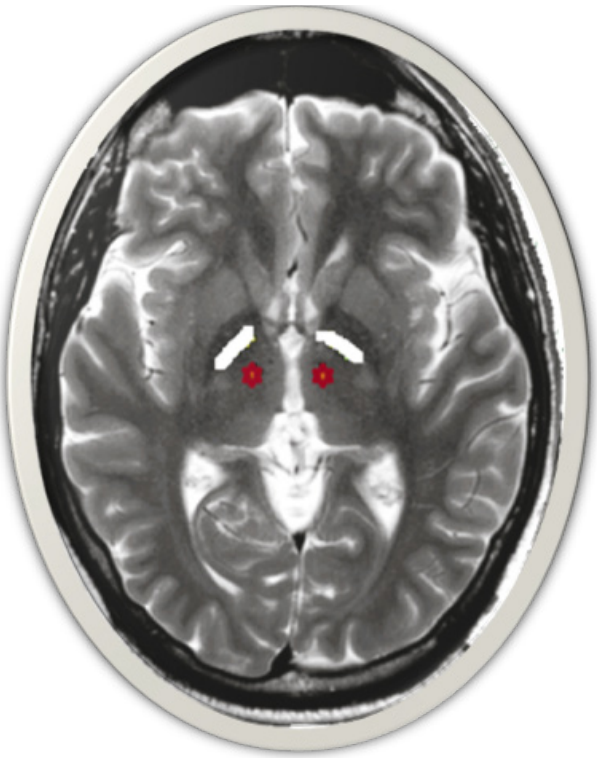

Figure 1: Horizontal cross-section of the human brain, in superior view, highlighting the region of high synaptic density that received the implant, specifically the Subthalamic Nucleus (STN).

The subthalamic nucleus (STN)

Described by Jules Bernard Luys in 1865, the Subthalamic Nucleus (STN), also known as the Corpus Luysii, is an ovoid diencephalic structure located ventrally to the thalamus [12]. The STN plays a fundamental role in the functioning of the basal ganglia circuits [12-14]. From a physiopatholog-ical perspective, it is considered a key structure, as its dysfunction is directly associated with several neurological disorders [15,16].

Over the past decades, the STN has become a relevant target for Deep Brain Stimulation (DBS) in the treatment of Parkinson's disease, with the aim of modulating neuronal firing patterns and, consequently, improving both the understanding of the disease and its clinical manifestations. Its activity is essential for the regulation of motor function and is also involved in cognitive and emotional processes through its connections with associative and limbic circuits. Furthermore, the STN plays a critical role in the modulation of neural circuits, particularly within the indirect and hyper direct pathways of the basal ganglia [17,18].

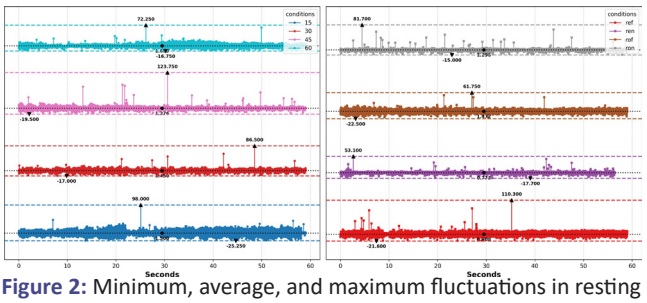

Figure 2: Minimum, average, and maximum fluctuations in resting tremor velocity of the index finger of individual S016 with PD, low amplitude, under DBS (*on–off*) and L-dopa (*on–off*) conditions.

Patient: S016 - DBS / L-dopa

- Patient S016 (age 37, female, with disease latency between 1981-1992) has a recording of approximately 60 seconds of resting tremor of the left index finger. Medication on, implies 150% of her morning dose of L-dopa and receiving effective stimulation in the STN, categorized into eight conditions:
- **res**: Deep brain stimulation on (DBS), L-dopa medication on (samples = 6300).
- **ref**: Deep brain stimulation on (DBS), L-dopa medication off (samples = 7128).
- **ron**: Deep brain stimulation off (DBS), L-dopa medication on (samples = 6696).
- **rof**: Deep brain stimulation (DBS) off, L-dopa medication off (samples = 6594).
- **15**: Deep brain stimulation (DBS) off for 15 minutes, L-dopa medication off (samples = 6486).
- **30**: Deep brain stimulation (DBS) off for 30 minutes, L-dopa medication off (samples = 6588).
- **45**: Deep brain stimulation (DBS) off for 45 minutes, L-dopa medication off (samples = 6744).
- **60**: Deep brain stimulation (DBS) off for 60 minutes, L-dopa medication off (samples = 7302).

Detrended fluctuation analysis (DFA)

For the purpose of analyzing the time series of resting tremor velocity in the index finger, here specifically in high-frequency chronic deep brain stimulation (DBS), unilaterally or bilaterally, we will provide a brief description of the DFA method and the Fluctuation Function - rms (Δlog).

To understand the method proposed by Peng [19], consider a sample of correlated signal $u(i)$ (DBS signal), where $i = 1, \cdots, N$, where N is the total number of points in the time series. We integrate the signal $u(i)$ and obtain $y(k)=\Sigma k\ [u(i)-<u>]$, where $<u>$ is the mean of $u(i)$.

The integrated signal $y(k)$ is divided into boxes (without overlap) of the same size n (time scale). For each box of size n, we fit $y_n(k)$ in each box using a first-order linear regression, which represents the trend. The entire process is obtained by the least squares method. The integrated series $y(k)$ is subtracted from the fitted series $y_n(k)$ in each box size n. Then, for each box of size n, the root mean square will be calculated, that is,

$$F_{DFA}(n) = \sqrt{\frac{1}{N_{max}} \sum_{k=1}^{N_{max}} [y(k) - y_n(k)]^2}; \quad (1)$$

The procedure is repeated for a wide range of scales, that is, $4 \leq n \leq N/4$. Next, the function $F_{DF\,A}$ characterizes a power law of the type $F_{DFA} \sim n^{\alpha DFA}$, where $\alpha_{DF\,A}$ will be the long-range correlation indicator.

The interpretation of the relationship is given as follows: $\alpha_{DF\,A}$<0.5 (antipersistent signal), $\alpha_{DF\,A}$ = 0.5 (uncorrelated white noise), $\alpha_{DF\,A}$>0.5 (persistent signal - long-range correlation), $\alpha_{DF\,A} \simeq 1$, (1/*f* noise), α_{DFA}>1 (non-stationary) and $\alpha_{DFA} \simeq 3/2$ (Brownian noise).

The DFA method enables the detection of long-range correlation and embedded self-affinity in appar-ently non-stationary time series and, above all, avoids the spurious detection of long-range correlations [9,20,21,22,23].

Rms function $\Delta LogF_{DFA}$

The root mean square fluctuation function (*rms*) arises with the intention of measuring the difference in amplitude fluctuation between two EEG channels [20]. The tool is an enhancement given to the DFA method and has proven to be very useful in the application of electrophysiological signals. Through this function (*rms*), we can study how much two brain regions are correlated to the same scale (temporal coherence) [9,21,22,23].

The first step consists of calculating the DFA of two time series and their logarithms individually.

Then, subtract the result from the logarithms. See equation 2.

$$\Delta logF_{DFA_{x,y}} = logF_{DFA_x} - logF_{DFA_y} \quad (2)$$

From the function $\Delta logF_{DF\,A}x,y$ we can infer that the amplitude of the fluctuation relative to *rms*

- can be viewed through three conditions:If $\Delta logF_{DFA_{x,y}} > 0$, then the amplitude of the rms fluctuation function around *x* with respect to y is greater;
- If $\Delta logF_{DFA}x,y=0$, then the amplitude of the rms fluctuation function around *x* with respect to y is zero;
- If $\Delta logF_{DFA}x,y<0$, then the amplitude of the rms fluctuation function around *x* with respect to y is smaller.

Results

To test the effects of Deep Brain Stimulation (DBS) combined with L-dopa medication in a patient diagnosed with Parkinson's disease, using resting tremor velocity of the index finger with an implant in the STN target, bilaterally, we applied the Detrended Fluctuation Analysis (DFA) method and the rms function $\Delta logF_{DFA}$. For this, we used time series of approximately 60 seconds, with the patient classified as having low-amplitude tremor. We began by investigating the DFA results for the case where patient S016 tested the following conditions: DBS on and L-dopa on (ren), DBS on and L-dopa off (ref), DBS off and L-dopa on (ron), and DBS off and L-dopa off (rof). Following the same procedure, we evaluated the results: DBS off for 15, 30, 45, and 60 minutes, all with L-dopa interrupted for 60 minutes (without medication).

For both conditions, we calculated the autocorrelation exponent α_{DFA}. The results are presented in tables 1 and 2. For the first condition, table 1, described in Figure 3(a), three conditions were verified: ref showed non-stationary behavior ($\alpha_{DF\,A}>1.0$) accompanied by antipersistence ($\alpha_{DF\,A}<0.5$). rof showed non-stationary behavior ($\alpha_{DFA}>1.0$) accompanied

by antipersistence ($\alpha_{DF\ A}<0.5$) followed by persistence ($\alpha_{DF\ A}>0.5$). ren showed antipersistence behavior ($\alpha_{DF\ A}<0.5$) for all scales. ron, on the other hand, showed persistent behavior ($\alpha_{DF\ A}>0.5$) for all scales. For the second condition (b), three behaviors were also verified: 15 showed non-stationarity ($\alpha_{DF\ A}>.0$) accompanied by antipersistence ($\alpha_{DF\ A}<0.5$). 30 repeats condition 15, non-stationarity ($\alpha_{DF\ A}>1.0$) accompanied by antipersistence ($\alpha_{DF\ A}<0.5$). [45] also follows the condition of 15 and 30. 60 showed persistence ($\alpha_{DF\ A}>0.5$) accom-panied by antipersistence ($\alpha_{DFA}<0.5$), and finally persistence ($\alpha_{DF\ A}>0.5$). So far, the results are consistent with the literature presented in [9].

With an analysis not yet presented in the literature for this type of study (effect: DBS / L-dopa), we calculated the amplitude of the fluctuation via the rms function $\Delta logF_{DF\ A}$. In figure 4(c), we verified that the difference for ref-ren, ref-rof and ren-rof, on small scales (n=4), showed fluctuations below zero while for ron-ref, ron-ren and ron-rof the fluctuations are positive and above 0.2.

Still in (c), it is observed that, as the scale *n* increases, all conditions tend to decrease. The com-binations ron–ref and ron–ren remain positive, whereas ron–rof exhibits a negative behavior after n=100, following the patterns observed for the pairs ref–ren, ref–rof, and ren–rof. In (d), the same behavioral pattern is also observed. The combinations 15–30, 15–45, and 15–60 show differences at small scales (n=4), with positive fluctuation amplitudes exceeding 0.2, whereas 30–45, 30–60, and 45–60 exhibit amplitude differences with values below zero. Thus, as the scale *n* increases, these differ-ences tend to decrease. Special attention is given to the pair 15–60, which, after n=100, follows the same behavior as the pairs 30–45, 30–60, and 45–60.

Even with a well-defined and known pattern and behavior, converging with what the literature shows in terms of autocorrelation with the DFA method [19, 9], in this study we focus on understanding this combination in three characteristic time scales $4<n<10$, $10<n<100$ and $100<n<1000$. The reasons for choosing the scales are related to the phase transitions in the fluctuations and how they vary around $\Delta logF_{DFA}$=0 (Figure 4).

We observed that the L-dopa (on–off) and DBS (on–off) combinations exhibit similarities in both the waveform shape and the overall curve behavior, although subtle differences may be identified depending on the specific combination analyzed. To investigate these small variations, we compared the values reported in Tables 5 and 7. It is worth noting that the differences observed in these tables arise from the calculations associated with the α_{DFA} exponent (Table 4) and the rms function $\Delta \log F_{DFA}$ (Table 6).

Discussion

Consistently and innovatively combining Levodopa/DBS with DFA autocorrelation and Shannon entropy (H) in resting tremor velocity recordings in Parkinson's disease patients undoubtedly demonstrates a fantastic contribution, especially as a methodological complement to the UPDRS and TRS scales. However, the subtlety of the fluctuations and intermittent differences remains a point of discussion in scientific communities investigating chronic and progressive neurodegenerative disorders.

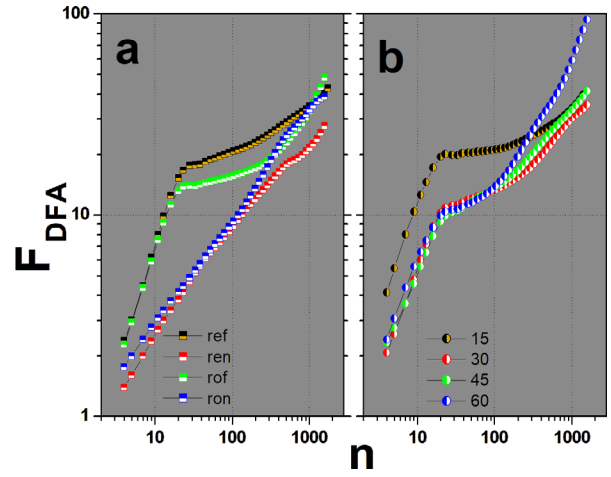

Figure 3: Autocorrelation via DFA method of patient S016 with Low-Amplitude Tremor (LAT) who received deep brain stimulation. In **(A)**, we have: ref (DBS on / L-dopa off), ren (DBS on / L-dopa on), rof (DBS off / L-dopa off), ron (DBS off / L-dopa on). In **(B)**, we have deep brain stimulation off for 15, 30, 45 and 60 minutes with medication off (interrupted for 60 minutes (without medication)).

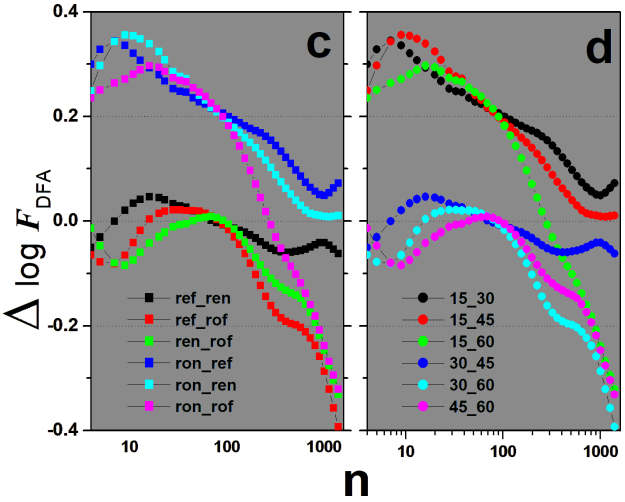

Figure 4: Difference in amplitude of fluctuation of resting index finger tremor velocity using the *rms* $\Delta logF_{DFA}$ function. In **(C)** we have four possibilities for deep brain stimulation [DBS (on/off) - L-dopa (on/off)] and four possibilities for deep brain stimulation off for 15, 30, 45 and 60 minutes and L-dopa off (interrupted for 60 minutes (without medication)).

Table 1: Results for subject S16 in the three ranges of α_{DFA} and four conditions: ref, ren, rof, and ron.

	$4 < \alpha_1 < 23$	$24 < \alpha_2 < 223$	$\alpha_3 > 223$
S16 ref	1.15 ± 0.02	0.21 ± 0.02	0.21 ± 0.02
S16 ren	0.47 ± 0.02	0.47 ± 0.02	0.47 ± 0.02
S16 rof	1.12 ± 0.02	0.10 ± 0.01	0.56 ± 0.01
S16 ron	0.53 ± 0.01	0.53 ± 0.01	0.53 ± 0.01

Table 2: Results for subject S16 in the extended ranges of αDFA with four conditions: 15, 30, 45 and 60.

	4 < α1 < 60	60 < α1 < 135	*α3 > 135*
S16 15	1.03 ± 0.03	0.07 ± 0.01	0.29 ± 0.01
S16 30	1.02 ± 0.02	0.15 ± 0.01	0.43 ± 0.01
S16 45	0.87 ± 0.01	0.23 ± 0.01	0.43 ± 0.01
S16 60	0.93 ± 0.01	0.22 ± 0.01	0.71 ± 0.01

Based on this gap, this preliminary study presents, in a reduced domain (eight conditions), the analysis of the response in a candidate with an electrode implanted in the subcortical structure in the Subthalamic Nucleus (STN). We show that it was possible to quantify, compare, and differentiate all L-dopa (on-off) x DBS (on-off) conditions of the tremor suppression mechanism based on resting tremor velocity data of the index finger.

The analysis takes into account how each combination is associated given the stimulus/medication relationship. We recorded the conditions in the table 3. In this table, we verified the behavior of the combination and observed that the influence of the L-dopa or DBS medication changes as the scale (n) increases. To understand this relationship, also described in the table 3, we took: ref (DBS on / L-dopa off) - ren (DBS on / L-dopa on). We observed at this point that for small scales ($4 < n < 10$) and large scales ($100 < n < 1000$), ren (DBS on / L-dopa on) responds better than ref, while for medium scales ($10 < n < 100$) ref (DBS on / L-dopa off) responded better. The response can also be verified when we calculate DBS off 15 L-dopa off - DBS off 30 L-dopa off. Regardless of the scale (n), it is observed that the response, DBS off 15 L-dopa off (interrupted for 60 minutes (without medication)), prevails, revealing that the medication acts for the entire observed period.

Another piece of information seen in Figure 4 is that, regardless of the condition (on/off) for DBS and L-dopa, the curves decrease with increasing scale (n) for all situations presented: ref, ron, rof, ren, 15, 30, 45, and 60. Situations also associated with the two conditions: ref-ren ≈ 30-45; ref-rof ≈ 15-60; ren-rof ≈ 15-60; ron-ref ≈ 15-30; ron - ren ≈ 30-60 and ron - rof ≈ 45 - 60. Details of these differences can be found, for comparison purposes, in the spreadsheets presented in the supplementary material: 4,5, 6 and 7.

Conclusion

In this study, we aimed to evaluate, by means of the Detrended Fluctuation Analysis (DFA) method and the rms function $\Delta \log F_{DFA}$, still open questions regarding the response to the combination of Levodopa and Deep Brain Stimulation (DBS) in a patient with Parkinson's disease. The patient received an implant in the Subthalamic Nucleus (STN) with the objective of suppressing tremor and reducing other PD-related symptoms.

Table 3: Comparison of pairs of conditions at different n scales. Patient S016 with chronic high-frequency electrical deep brain stimulation in the Subthalamic Nucleus (STN).

S016	$4 < n < 10$	$10 < n < 100$	$100 < n < 1000$
ref (DBS on / L-dopa off) ren (DBS on / L-dopa on)	ren	ref	ren
ref (DBS on / L-dopa off) rof (DBS off / L-dopa off)	rof	ref	rof
ren (DBS on / L-dopa on) rof (DBS off / L-dopa off)	rof	rof	rof
ron (DBS off / L-dopa on) ref (DBS on / L-dopa off)	ron	ron	ron
ron (DBS off / L-dopa on) ren (DBS on / L-dopa on)	ron	ron	ron
ron (DBS off / L-dopa on) rof (DBS off / L-dopa off)	ron	ron	rof
DBS off 15 L-dopa off DBS off 30 L-dopa off	15	15	15
DBS off 15 L-dopa off DBS off 45 L-dopa off	15	15	15
DBS off 15 L-dopa off DBS off 60 L-dopa off	15	15	60
DBS off 30 L-dopa off DBS off 45 L-dopa off	45	30	45
DBS off 30 L-dopa off DBS off 60 L-dopa off	60	30	60
DBS off 45 L-dopa off DBS off 60 L-dopa off	60	60	60

To understand the increased amplitudes and atypical temporal fluctuations, we evaluated eight possible combinations for the conditions L-dopa (on–off) and DBS (on–off). We analyzed the autocorrelation of each response and identified that, depending on the scale ($4<n<10$, $10<n<100$, and $100<n<1000$), the responses may exhibit distinct regimes, such as reference behavior, non-stationarity ($\alpha_{DFA}>1$), and anti-persistence ($\alpha_{DFA}<0.5$). These characteristics were also observed in the conditions ren, rof, and ron. Similar results were found for the 15-, 30-, 45-, and 60-minute intervals with DBS interrupted for 60 minutes (medication off).

To investigate subtle and intermittent changes, we computed the differences between the conditions ref, ren, rof, ron, and 15, 30, 45, and 60. Depending on the scale and specific time periods, these differences allow a better understanding of the shared contributions of Levodopa and DBS. In this context, we identify a differential feature that has not yet been explored using the rms function $\Delta \log F_{DFA}$. Another observed result was the similarity of responses across the different cases analyzed.

This study should be considered preliminary, since the analysis was conducted on a single patient. The most widely used clinical assessment tools for this type of analysis are the Unified Parkinson's Dis-ease Rating Scale (UPDRS) [1,5] and the Tremor Rating Scale (TRS) [3,5]. Both scales focus on rest, posture, intentional movements, and functional impact, and therefore do not capture the level of sub-tlety and detail provided by the DFA technique and the rms function $\Delta \log F_{DFA}$ presented in this study.

As future work, we will reproduce the model presented here using the rms function $\Delta \log F_{DFA}$ for all patients available in the database at https://physionet.org/content/tremordb/1.0.0/ who received chronic high-frequency electrical deep brain stimulation, either unilaterally or bilaterally, targeting one of the following structures the Ventro-Intermediate nucleus of the thalamus (Vim), the internal globus pallidus, or the subthalamic nucleus.

Declarations

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Author contributions statement: All researchers participated in all aspects of the manuscript construction.

Abbreviations

DP: Parkinson's disease; DBS: Deep brain stimulation; ECP: Deep brain stimulation; STN: Subthalamic nucleus; VIM: the internal Globus pallidus; GPi: the internal Globus pallidus; DFA: Detrended Fluctuation Analysis; L-dopa: Levodopa; LAT: Low Amplitude Tremor; HAT: High amplitude tremor; ren: Deep Brain Stimulation on, Medication on; ref: Deep Brain Stimulation on, Medication off; ron: Deep brain stimulation off, Medication on; rof: Deep Brain Stimulation off, Medication off; UPDRS: Unified parkinson's disease rating scale; TRS: Tremor rating scale; EEG: Electroencephalogram.

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Supplementary material

Tables 4, 5, 6, and 7 present the values of the α_{DFA} exponents calculated for the data sets ron, ref, ren, and rof across different scales n. These tables also report the values of the differences obtained using the rms function $\Delta \log F_{DFA}$, allowing the assessment of structural variations among the series at each scale. In addition, we provide the values of α_{DFA} and the corresponding differences $\Delta \log F_{DFA}$ for the data sets 15, 30, 45, and 60, likewise computed over multiple scales. This set of supplementary information offers the reader a comprehensive description of the dynamic behavior of the analyzed series, contributing to the transparency and reproducibility of the results presented in the main article.

Table 4: Values of the α_{DFA} exponents calculated for ron, ref, ren, and rof across different scales.

ron	ref	ren	rof
1.758427	2.381365	1.392812	2.276340
1.994957	2.997046	1.602547	2.938193
2.413662	4.462556	1.997995	4.360600
2.776846	6.173197	2.365422	5.916822
3.094949	8.018048	2.699957	7.563506
3.378833	9.887874	2.995806	9.177574
3.756643	12.523118	3.374883	11.297335
4.178379	15.316707	3.817479	13.209646
4.457149	16.689012	4.144757	13.877591
4.906014	17.677427	4.687005	14.020888
5.338249	17.757508	5.180290	13.953300
5.744361	17.864107	5.608449	14.204326
6.268677	18.486946	6.104168	14.527079
6.739714	18.936890	6.507226	14.605025
7.223702	19.192484	6.915526	14.828795
7.711211	19.660808	7.348576	15.016292
8.207742	19.992401	7.808517	15.218115
8.759397	20.413190	8.330310	15.445467
9.321936	20.759070	8.863748	15.676770
9.982137	21.138985	9.459337	15.926839
10.722506	21.495289	10.070828	16.192672
11.596621	21.914597	10.726406	16.482465
12.481047	22.373993	11.344032	16.757964
13.540498	22.946024	12.022363	17.089719
14.648528	23.533880	12.653287	17.453163
15.910052	24.213543	13.331796	17.930301
17.314633	24.965719	14.066124	18.547800
18.802708	25.729495	14.824622	19.248228
20.422713	26.512231	15.630182	20.054449
22.036149	27.310858	16.459176	20.942208
23.573056	28.152444	17.271872	21.917298
24.971753	29.031965	17.957071	23.012183
26.170689	29.911318	18.418902	24.217573
27.326950	30.838641	18.758172	25.586069
28.623667	31.790324	19.244367	27.103843
30.122326	32.723507	19.909041	28.769465
31.796075	33.727886	20.779900	30.687994
33.471271	34.872453	21.643893	32.958738
35.156438	36.051946	22.622838	35.758537
36.784065	37.313169	23.980960	39.194223
37.959335	38.690744	25.707443	43.419046

Table 5: Values of the α_{DFA} exponents calculated for 15, 30, 45, and 60 across different scales.

15	30	45	60
4.125903	2.071228	2.325451	2.403078
5.454697	2.564800	2.753647	3.065636
8.027586	3.633444	3.642698	4.378003
10.386536	4.793947	4.577747	5.563925
12.559158	6.003255	5.554782	6.590957
14.564747	7.186671	6.533667	7.490248
17.194669	8.757557	7.879813	8.682351
19.477438	10.239218	9.246892	9.904238
20.049924	10.829290	9.872728	10.380099
19.893985	11.117273	10.309014	10.593978
19.818628	11.203817	10.496258	10.686680
20.238566	11.478047	10.819331	10.969566
20.402223	11.874358	11.351571	11.346863
20.393811	12.075087	11.718290	11.576551
20.652870	12.337016	12.131257	11.946861
20.681619	12.577942	12.545643	12.307930
20.878505	12.818153	12.920100	12.754253
21.005544	13.088185	13.321357	13.284439
21.159864	13.377102	13.719051	13.913584
21.384663	13.705868	14.170488	14.694019
21.647324	14.059644	14.658008	15.577974
21.978712	14.470477	15.222949	16.680949
22.355583	14.880508	15.818760	17.899690
22.841070	15.356032	16.564182	19.426959
23.335362	15.853834	17.361854	21.051971
23.874603	16.442974	18.276795	22.904884
24.427119	17.146399	19.316724	24.868784
24.986340	17.941745	20.404811	26.820937
25.610150	18.863584	21.569565	28.854599
26.293387	19.870247	22.775280	30.890155
27.009825	20.978686	24.029869	32.924970
27.745623	22.173388	25.318332	35.023823
28.489593	23.408187	26.630925	37.371906
29.312649	24.732592	27.969350	40.282942
30.271663	26.120124	29.280501	43.709811
31.416040	27.585559	30.576313	47.718710
32.678419	29.082749	31.923808	52.740079
34.057643	30.431966	33.418135	58.955794
35.738106	31.597510	35.096599	66.239813
37.665506	32.615064	36.899162	74.223985
39.817937	33.728218	38.894769	83.407812

Table 5: Values of the differences calculated using the rms function $\Delta \log F_{DFA}$ for ron, ref, ren, and rof across different scales *n*.

n	ron-ref	ron-ren	ron-rof	ref-ren	ref-rof	ren-rof
4	-0.131701623	0.101231844	-0.112112786	0.232933466	0.019588836	-0.213344630
5	-0.176759870	0.095122764	-0.168146781	0.271882633	0.008613089	-0.263269544
7	-0.266907226	0.082082056	-0.256869797	0.348989282	0.010037429	-0.338951853
9	-0.346958341	0.069643163	-0.328536709	0.416601505	0.018421632	-0.398179873
11	-0.413415155	0.059296649	-0.388069659	0.472711804	0.025345496	-0.447366308
13	-0.466336196	0.052253041	-0.433961168	0.518589237	0.032375029	-0.486214209
16	-0.522912547	0.046541204	-0.478176082	0.569453751	0.044736466	-0.524717286
20	-0.564157575	0.039231173	-0.499883349	0.603388748	0.064274225	-0.539114523
23	-0.573373474	0.031558079	-0.493256931	0.604931553	0.080116543	-0.524815010
28	-0.556690269	0.019833366	-0.456046737	0.576523636	0.100643532	-0.475880103
33	-0.521983192	0.013044755	-0.417278104	0.535027946	0.104705087	-0.430322859
38	-0.492739586	0.010398950	-0.393178906	0.503138536	0.099560680	-0.403577856
45	-0.469689280	0.011549415	-0.365002405	0.481238695	0.104686874	-0.376551820
52	-0.448667189	0.015245577	-0.335860837	0.463912766	0.112806352	-0.351106414
60	-0.424371366	0.018934603	-0.312346040	0.443305969	0.112025326	-0.331280643
69	-0.406478775	0.020919397	-0.289440118	0.427398172	0.117038657	-0.310359515
79	-0.386641258	0.021655136	-0.268137165	0.408296394	0.118504092	-0.289792302
91	-0.367436668	0.021813047	-0.246326834	0.389249715	0.121109834	-0.268139881
104	-0.347701776	0.021888717	-0.225750470	0.369590493	0.121951307	-0.247639186
119	-0.325860605	0.023362828	-0.202906064	0.349223433	0.122954541	-0.226268892
135	-0.302046991	0.027231119	-0.179022221	0.329278110	0.123024770	-0.206253340
154	-0.276402025	0.033877233	-0.152690698	0.310279257	0.123711326	-0.186567931
174	-0.253492479	0.041483576	-0.127970235	0.294976055	0.125522245	-0.169453810
198	-0.229072806	0.051644801	-0.101100284	0.280717607	0.127972522	-0.152745085
223	-0.205899549	0.063590627	-0.076080159	0.269490176	0.129819390	-0.139670786
252	-0.182386742	0.076782940	-0.051915981	0.259169682	0.130470761	-0.128698921
285	-0.158930787	0.090238849	-0.029879114	0.249169636	0.129051674	-0.120117963
321	-0.136210861	0.103236773	-0.010170353	0.239447634	0.126040508	-0.113407126
362	-0.113332841	0.116149399	0.007902700	0.229482240	0.121235541	-0.108246699
407	-0.093199644	0.126727611	0.022113232	0.219927255	0.115312875	-0.104614380
457	-0.077100215	0.135076477	0.031628875	0.212176692	0.108729091	-0.103447602
513	-0.065427401	0.143213531	0.035491212	0.208640932	0.100918613	-0.107722319
575	-0.058020393	0.152551419	0.033684539	0.210571813	0.091704933	-0.118866880
645	-0.052504069	0.163400648	0.028587595	0.215904718	0.081091665	-0.134813053
723	-0.045569683	0.172421640	0.023694398	0.217991324	0.069264081	-0.148727242
809	-0.035971337	0.179838163	0.019956719	0.215809500	0.055928055	-0.159881445
905	-0.025615609	0.184730059	0.015405012	0.210345668	0.041020621	-0.169325047
1011	-0.017810294	0.189336826	0.006701630	0.207147119	0.024511924	-0.182635196
1130	-0.010923845	0.191457781	-0.007374876	0.202381626	0.003548970	-0.198832656
1261	-0.006202414	0.185793157	-0.027562338	0.191995570	-0.021359924	-0.213355495
1407	-0.008288485	0.169259714	-0.058361681	0.177548199	-0.050073196	-0.227621395