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Fractal measures of video-recorded trajectories can classify motor subtypes in Parkinson's Disease

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HIGHLIGHTS

- The power-spectral distribution can be used to separate patients with different motor subtypes.
- The Hurst exponent present different values for patients with and without tremor.
- Differences are also clearly identifiable between patients and control subjects.
- The Box-Counting Dimension presents different values between patients with Parkinson's Disease and healthy subjects.

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ABSTRACT

Parkinson's Disease is one of the most prevalent neurodegenerative diseases in the world and affects millions of individuals worldwide. The clinical criteria for classification of motor subtypes in Parkinson's Disease are subjective and may be misleading when symptoms are not clearly identifiable. A video recording protocol was used to measure hand tremor of 14 individuals with Parkinson's Disease and 7 healthy subjects. A method for motor subtype classification was proposed based on the spectral distribution of the movement and compared with the existing clinical criteria. Box-counting dimension and Hurst Exponent calculated from the trajectories were used as the relevant measures for the statistical tests. The classification based on the power-spectrum is shown to be well suited to separate patients with and without tremor from healthy subjects and could provide physiotherapists with a tool to aid in the diagnosis of patients in an early stage of the disease.

1. Introduction

In the past few years, the development of new technologies has provided different methods to quantify objectively the extent and the characteristics of the motor symptoms that are present in Parkinson's Disease. The aim of this innovation effort is to provide quantitative measured data that can be used by professionals in the health sciences to support clinical diagnosis. These quantities can be combined with the subjective functional clinical scales such as the Hoehn & Yahr scale (H&Y) [1], or the Unified Parkinson's Disease Rating Scale (UPDRS) [2] to provide further information on the disease.

Parkinson's Disease is a neurodegenerative disease characterized by many motor symptoms such as slowness of movements, rest tremor (4–7 Hz), postural instability, neuromuscular rigidity, difficulty to swallow and severe functional

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incapability in its later stages [3,4]. Its symptoms, despite being known since the 19th century [5], are still not fully understood and there are many different physiological models to explain the generation and the wide variability of their expression [6].

The existence of two different motor subtypes has been recently considered in the literature in an attempt to account for this symptom variability [7,8]. One motor subtype presenting tremor as the main symptom was defined as the *Tremor Dominant* (TD) subtype, while the *Posture Impairment*/*Gait Difficulty* (PIGD) subtype presented posture related impairments without tremor [9]. Other subtypes have been identified by clustering analysis methods, such as the Young Onset (YOPD) and Late Onset (LOPD) subtypes [10,11]. It is already known that Parkinson's Disease is a condition with multiple causes [12] and these different subtypes might be associated with different causes and different physiological mechanisms within the disease. Another possibility is that these subtypes could be associated with different stages of the disease [13]. This work focuses on TD and PIGD subtype classification, for their major prevalence and for the direct relation they bear with motor measurements.

The majority of quantitative experimental methods of assessment for tremor measurement has been based on indirect time-series measurements generated from accelerometry [14,15] and electromyography [16,17], as reviewed by Ref. [18]. Both these indirect methods are subject to noise from important sources, such as numerical integration and mechanical noise in the case of accelerometry [19] and background neuromuscular activity in the case of electromyography [20]. Furthermore, the studies that encompassed electromyographic measures of tremor in Parkinson's Disease did not address the issue of variability inside the disease, with the presence of different subtypes [21,8,22]. An interesting recent study [23] have used spirogram tests with touch screen sensors and has been able to establish the frequency and amplitude of tremor and the correlation of these measures with well known tremor rating scales. Yet the need for new and precise quantitative assessment tools that can assist clinical diagnosis is still a matter of relevance in the context of Parkinson's Disease.

The data processing methods used for the evaluation of the symptoms of the disease are perhaps as important as the experimental procedures used to register them. The use of nonlinear measurements is a natural possibility, considering the nonlinear and variable nature of biological signals. These methods can also provide important information in situations where regular time–frequency analysis alone is not sufficient to describe the studied behavior.

In this regard, the Hurst exponent H [24] is a statistical index that quantifies temporal correlations in a time-series and is widely used in areas such as hydrology, time-series and stock market analysis [25]. It can take values between 0 and 1. For $0 < H < 0.5$, the fluctuations are said to be *anti-persistent*, implying that a period of growth is soon followed by a period of decrease, and vice versa. Anti-persistent correlations are often related to negative feedback control mechanisms, extensively found on regulation mechanisms in the human body [26,27]. For $0.5 < H < 1$, the correlations are said to be *persistent*. A period of growth is likely to be followed by another period of growth and a period of decrease is likely to be followed by another period of decrease. Hence the index H provides a method to evaluate statistical fluctuations in a time-series. Complex systems such as human biological signals and the climate often do not present a single value for the Hurst index, but instead present different scaling relationships in different time scales, associated with different phenomena. Specifically, stochastic series modulated by periodical oscillations present a decreasing region in slope that is associated with the wavelength of the periodic signal [28,29].

Another important measure used in biological signals analysis is the Box-Counting dimension [30]. The box-counting dimension D of a given two-dimensional trajectory provides a measure of the roughness or irregularity of the profile and, perhaps more importantly, the occupation pattern of space by the trajectory being considered. The value of D can vary between 0 and 2 in a plane, reflecting the way that a given structure fills the space in which it is embedded. It has been used to describe irregular structure that appears in a wide range of natural systems [31,32] and most notably in human physiology [33]. As will be discussed throughout this work, both these nonlinear measurements can be applied to the study of human movement with important results.

2. Methods

The experimental procedures conducted in this work were approved by the research ethics committee of the Professor Edgar Santos University Hospital of the Federal University of Bahia and registered under the number 118/2012, in accordance with the Declaration of Helsinki (1964). All participants signed a written informed consent term.

The experimental procedure aimed to test the existence of measurable features that could, under the same conditions, separate control individuals from TD and PIGD motor subtypes, considering the intersubject variability of symptom expression. It also intended to test for measurable features that could separate controls from individuals with Parkinson's disease.

2.1. Patients

The trials involved 7 healthy control individuals, in a group of 4 women (mean age 72.5[min 63, max 81]) and 3 men (mean age 68[min 67, max 70]), and 14 patients in a group of 6 women (mean age 67.17[min 58, max 79]) and 8 men (mean age 74.12[min 67, max 84]) with idiopathic Parkinson's Disease enrolled in the Parkinson Ferrol Association (Galicia, Spain). All patients were receiving medical and physical therapeutic treatment. All the patients were in the active (*on*) phase of the medication, as for the moment of the data acquisition. None of the patients had been subject to surgical intervention,

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