Heart Rate Variability in Parkinson Disease and Essential Tremor During Physical and Mental Stress

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Summary

The autonomic nervous system (ANS) plays a vital role in maintaining homeostasis through its sympathetic and parasympathetic branches. This study investigates sympathetic activation in PD and ET patients by analyzing heart rate variability (HRV) during physical and cognitively stressful tasks, using electrocardiography (ECG) data. Subjects alternate rest conditions with physical and mental stress. Preliminary data from Parkinson disease (PD) and Essential Tremor (ET) patients suggest altered ANS responses in PD. Specifically, PD subjects exhibit reduced changes in the low to high frequency (LF/HF) power ratio, with respect to ET patients, who show the expected increases and decreases during stress and rest transitions, respectively. On the other hand, respiratory rate estimation through ECG lead movement revealed that in most cases, respiration fell below or exceeded the classical high-frequency (HF) HRV band (0.15Hz to 0.4Hz) for significant portions of the recordings, compromising LF/HF metric interpretability. These findings support existing clinical evidence of autonomic dysfunction in PD and highlight the need for improved ANS assessment methods in motor disorders.

1. Introduction

The autonomic nervous system (ANS) is a crucial part of the nervous system, being responsible for regulating involuntary functions essential for maintaining homeostasis. It is divided into two main branches: the sympathetic and parasympathetic systems, which work in a complementary manner. Roughly, the sympathetic system is activated during stressful situations, while the parasympathetic system predominates during states of rest and recovery [1].

In neurodegenerative diseases such as Parkinson's disease (PD), autonomic dysfunctions have been documented [2, 3]. They can manifest in several forms, including urological, gastrointestinal, and psychiatric disorders, among others [4], and have a significant impact on patients' quality of life.

However, these autonomic disturbances have received limited research attention. There have been attempts at basic heart rate variability (HRV) analysis. Respiration is known to have a big effect on HRV, usually within its high frequency (HF) band, through a phenomenon known as respiratory sinus arrythmia (RSA). RSA remains a modulation that is not always within HF band, making respiratory frequency an interesting parameter in HRV analysis [9].

In this work, we are recording electrocardiography (ECG) signals in PD patients during a controlled, stress inducing, experimental protocol and then analyzing their HRV and ECG-derived respiration.

Furthermore, possible ANS alterations in essential tremor (ET) disease have not been systematically studied. With the aim of contributing to knowledge in this little-explored area, we apply a similar experimental protocol in patients with ET.

2. Materials and methods

2.1. Subjects

5 (2 female) patients diagnosed with Parkinson Disease aged 58.5 ± 8.5 yrs and 5 (2 female) patients diagnosed with Essential Tremor aged 61 ± 8 yrs were recruited.

2.2. Experimental protocol

We recorded the ECG of subjects for the whole experiment using a Bittium Pharos 180 Holter device in single lead configuration (RA-LA) with a sampling rate of 1000Hz. The protocol is composed of 5-minute conditions as shown in Figure 1.



Figure 1: Diagram of the experimental protocol.

The standing position for 5 minutes serves to induce physical stress, while the Serial Subtraction Task (SST) is designed to induce cognitive load and psychological stress. Both techniques have been previously used to induce stress in the literature. The latter consists of asking the subject to repeat-

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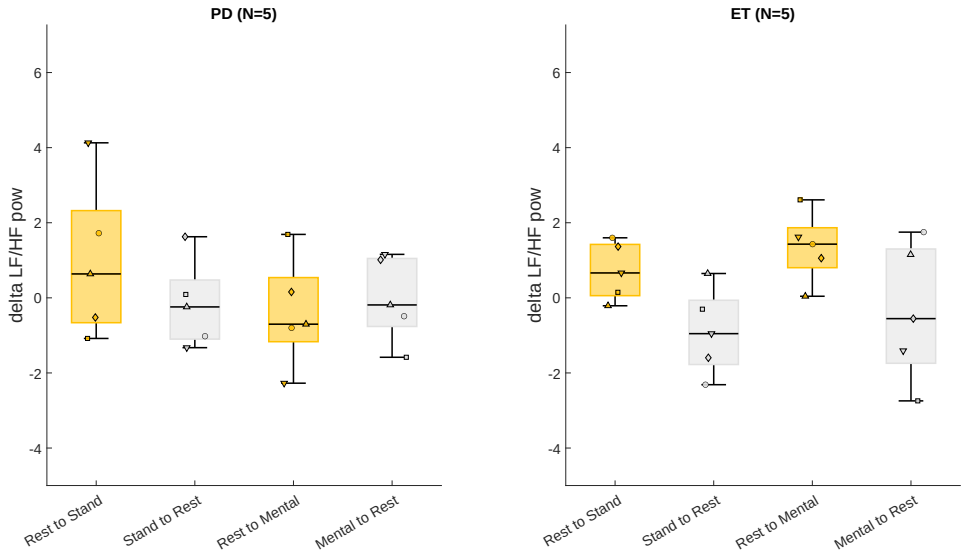


Figure 2: Deltas of the low power-high power ratio of the HRV. Left: PD patients, right: ET patients. The yellow boxes correspond to the transitions from rest to a stressful task. Gray boxes, the transition from stress to rest.

edly subtract a fixed number (*e.g.*, 13) from a starting number (*e.g.*, 1022) as quickly and accurately as possible.

2.3. Analysis

2.3..1 HRV analysis

QRS complexes were detected from the ECG by using an algorithm based on variable-frequency complex demodulation [5]. The HRV signal was derived from QRS detections by using a time-varying integral pulse modulation model, which takes into account possible missdetections and ectopic beats [6]. Then, the powers within low frequency (LF, [0.03 Hz, 0.15 Hz]) and high frequency (HF, [0.15 Hz, 0.4 Hz]) bands were computed, as well as the ratio LF/HF (denoted $R_{\text{LF/HF}}$ in this paper).

The variations of the $R_{\text{LF/HF}}$ between consecutive stages ($\Delta_{\text{LF/HF}}$) were computed by subtracting the corresponding values of such stages. This leads to 4 indices per subject: from first rest to stand, from stand to second rest, from second rest to mental task, and from mental task to third rest.

A positive $\Delta_{\text{LF/HF}}$ between a given stage A and a given stage B indicates more sympathetic dominance in stage B with respect to stage BS. In the same way, a negative $\Delta_{\text{LF/HF}}$ indicates a lower sympathetic dominance in stage B with respect to stage A.

2.3..2 Respiratory rate estimation

Respiratory sinus arrhythmia (RSA) is a key contributor to the HF component of the HRV [7]. In some cases, the respiratory frequency may be higher (*e.g.*, doing exercise or in stressful situations) than the classical HF band (0.15-0.4 Hz). When this happens, the parasympathetic activity is underestimated by the classical HF parameter. On the other hand, the respiratory frequency can be lower than 0.15 Hz, leading to an underestimation of parasympathetic activity by the classical HF parameter and to an overestimation of the sympathetic activity by the classical LF parameter. In order to take into account these situations, respiratory frequency was estimated from the ECG by a method based on morphological changes in the QRS slopes and in the R-wave angle [8].

This way, we obtain a continuous signal representing the instantaneous frequency of the subjects' respiration, as it varies during the experimental condition. Thus, we can check whether the respiratory rate is within the HF band, and how often this is the case. Specifically, in this work we plot the Smoothed Pseudo Wigner-Ville Distribution of the HRV signal and, superimposed, the aforementioned instantaneous estimated respiratory frequency. Then, we visually inspect and calculate the percentage of the time that respiratory frequency is outside the HF band.

3. Results and discussion

Table 1 contains the four computed $\Delta_{\text{LF/HF}}$, for each disorder. Figure 2 shows their distributions. In the absence of ANS dysfunction, a greater sympathetic dominance is expected during stressful tasks. This means higher $\Delta_{\text{LF/HF}}$ values from rest stages to stressful stages (colored in yellow in Figure 2). On the contrary, lower $\Delta_{\text{LF/HF}}$ values are expected from stressful stages to rest stages (colored in gray in Figure 2).

$\Delta_{\text{LF/HF}}$	$rest \rightarrow stand$	$stand \rightarrow rest$	$rest \rightarrow SST$	$SST \rightarrow rest$
PD	0.9765 ± 1.8486	-0.1748 ± 1.0361	-0.3858 ± 1.2987	-0.0181 ± 1.0144
ET	0.7126 ± 0.6907	-0.9034 ± 1.0235	1.3514 ± 0.8321	-0.3611 ± 1.6468

Table 1: Variations of $R_{\text{LF/HF}}$ between consecutive experimental conditions, for both PD and ET.

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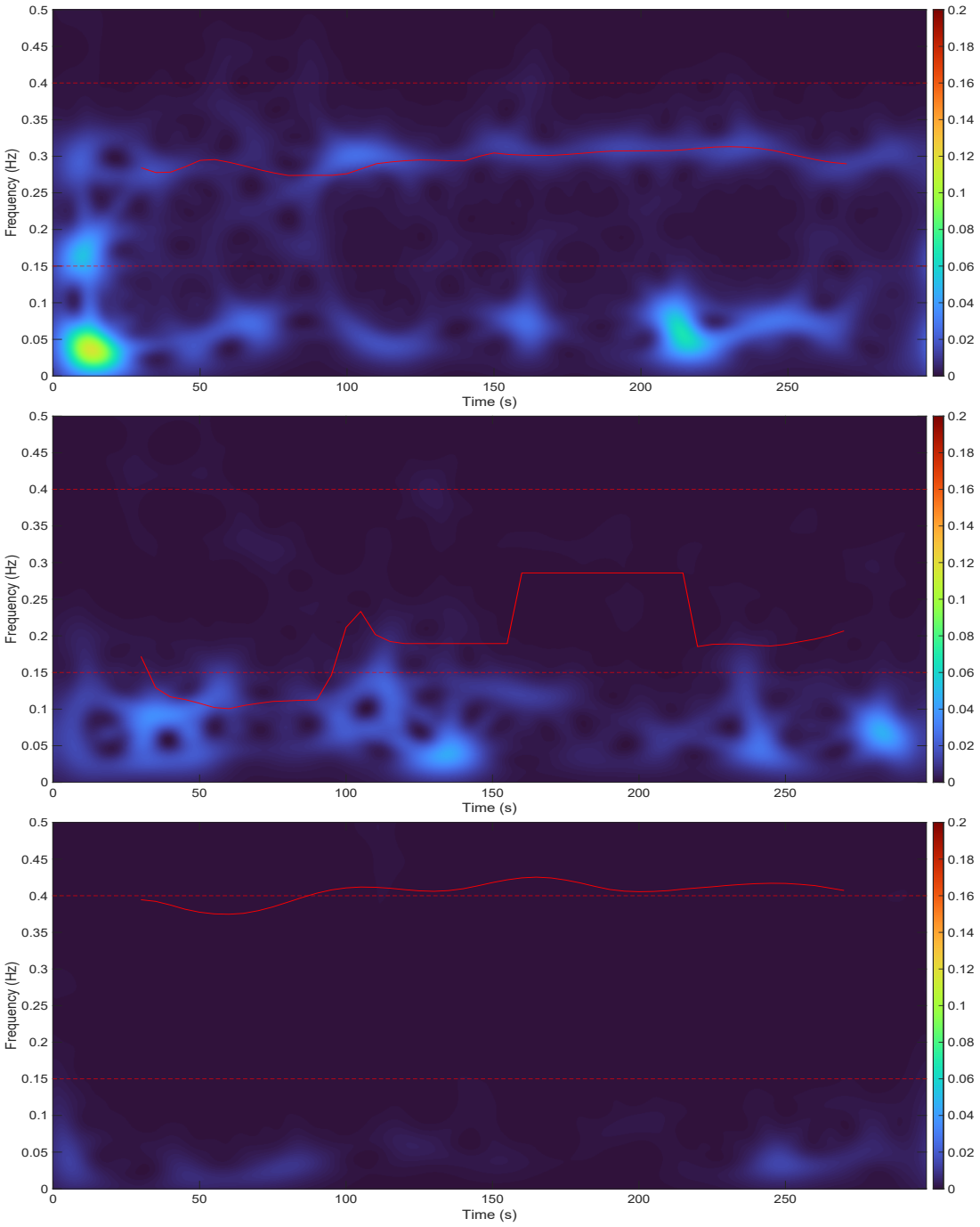


Figure 3: Example smoothed pseudo Wigner-Ville time-frequency distributions and the estimated respiratory rate (red line). On top, the respiratory rate is inside the classical band. In the middle, a case where it falls below 0.15Hz (bottom red dotted line), overlapping with the classical LF band. In the bottom, a case where it gets over 0.4Hz (top red dotted line), thus outside the classical HF band.

The results for ET suggest that there is a sympathetic activation during both the stand-up task and the mental task, as expected. Meanwhile, for Parkinson's patients, there is less difference (means of $\Delta_{LF/HF}$ are closer to zero), which is consistent with the clinical observation of the existence of disautonomies in PD. [8].

On the other hand, we found that 40% of the subjects had respiratory frequencies below the classical HF band at some point during the experiment. In average, this occurred for 6.8% of the total recording duration. At the same time, 60% of the subjects had respiratory rates above the classical HF band at some point during the condition, with an average duration of 7.8% of the recording. Figure 3 shows examples where the respiratory frequency is at some point outside the classical HF band.

4. Conclusions and future work

Our first experimental results are consistent with the fact that ANS impairment has been reported in patients with PD and

not in patients with ET.

However, these results are very preliminary due to the low sample size, high subject variability (particularly seen for PD), and the unreliability of the $R_{\text{LF/HF}}$ metric due to the fact that in some patients the RSA frequency was outside the classical HF band.

To advance in this field, it is important to include larger samples, so that stronger conclusions can be reached.

Also, further analysis comparing the disorders to age-matched control subjects could be useful to better understand the nature of the disautonomy in PD and to further confirm whether ET patients do indeed not present alterations in ANS function.

Additionally, more reliable metrics could be obtained, including respiratory information. There are several approaches in the literature [9, 8]. For the cases where the respiratory rate is above the HF band, it would be necessary to redefine the band around the actual respiratory frequency. For the cases where the respiratory rate is below the HF band, *i.e.*, overlapping with the LF band, the simplest option is to discard them if it is an uncommon occurrence. However, since recruiting PD patients is a difficult endeavor, it might be preferable to separate the respiratory influence from the HRV signal. For example, through orthogonal subspace projection [8].

Finally, more sophisticated metrics such as HRV complexity markers could be explored with the ECG of PD and ET patients.

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