Measures of Heart Rate Variability in Patients with Idiopathic Parkinson’s Disease

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Abstract
The aim of this study was to verify measures of heart rate variability in patients with idiopathic Parkinson’s disease. Seventy-two male participants volunteered for the study, 36 with diagnosed Parkinson’s disease and 36 asymptomatic individuals. We conducted ambulatory recordings of 10 minutes in orthostatic position after five minutes of rest. Data was collected with POLAR RS800CX cardiac monitor and then analyzed by Kubios HRV 2.0 software to obtain measures of time and frequency domains. We found reductions in most part of collected indexes without correlation with disease duration or drugs dosage. The reduced indexes reinforce the idea that Parkinson’s disease alters the autonomic nervous system modulation.

Keywords: Parkinson’s disease; Heart rate; Autonomic nervous system

Abbreviations: NN: NN Interval (Inter-Beat Interval); RMSSD: Root Mean Square of Differences Between NN Intervals; SDNN: Standard Deviation of NN Intervals; PNN50: Percentage of NN Intervals Greater than 50 ms (Milliseconds); FFT: Fast Fourier Transform; LF: Low Frequency; HF: High Frequency; LF/HF: LF An HF Ratio; ECG: Electrocardiogram; HRV: Heart Rate Variability

Introduction
Parkinson’s disease is a neurodegenerative morbidity that leads to motor, psychiatric and sleep disorders. In terms of motor symptoms, postural instability, shaking, rigidity, and slowness of movements are the most common symptoms. There is loss of dopamine production in midbrain neurons, resulting in loss of dopaminergic innervations in the striatum [1]. In addition to an extra pyramidal motor dysfunction, patients frequently show Autonomic Nervous System (ANS) disorders, even in early phases of the disease [2].

This disease can promote autonomic dysfunction by damage in hypotalamus, basal ganglia, formatio reticularis, cerulean and nerve vagus dorsal nuclei [3-5]. Besides those pre-ganglia structures, post-ganglia sympathetic neurons and other ANS structures are also affected [6,7].

There are assumptions that the neurodegenerative characteristics of the disease may be associated with indexes of Heart Rate Variability (HRV). Changes in ANS in Parkinson’s patients include perturbations in cardiovascular regulation, hypotension, especially in orthostatic position, and sexual dysfunction [8-10].

HRV indexes in time and cardiac frequency domains have proven useful measures in predicting cardiac arrhythmias, mortality risk by cardiac artery disease and various central nervous system disturbs, such as stroke, epilepsy, brain damages and other degenerative brain disease [11].

Recently, authors evaluated the cardiovascular autonomic regulation in patients in different disease stages using short duration measures and reinforced the method efficacy as non-invasive strategy [6]. Thus, the aim of this study was to verify measures of HRV in patients with idiopathic Parkinson’s disease.

Materials and Methods
Seventy-two volunteer male participants were randomly selected in a university clinical center (UNP/Brazil). The sample included 36 patients with diagnosed Parkinson’s disease (Parkinson Group PG) and 36 healthy individuals (Control Group=CG). We conducted measures of HRV using ambulatory recordings with 10 minutes of duration in orthostatic position, after a 5-minute rest period. The CG did not have any kind of neurologic or cardiac disorder. In addition, they did not use any kind of medication and had no genetic relation with the patients.

Heart rate variability (HRV)
We used POLAR RS800CX cardiac monitors to collect data, as there are close correlations with data obtained with electrocardiogram (ECG) [12,13]. Then, we analyzed the dataset with Kubios HRV 2.0 software. Analysis of time domain included NN intervals, SDNN, pNN50 and RMSSD. The frequency domain was analyzed by Fast Fourier Transform (FFT) and included Total Power (TP, 0-0.4 Hz), High Frequency (HF, 0.15-0.4 Hz), Low Frequency (LF, 0.04-0.15 Hz), LF and HF ratio (LF/HF), and Very Low Frequency (VLF, 0.003-0.04 Hz) [14]. The TP express the magnitude of the HRV in a global manner. HF an LF reflect the interaction between parasympathetic, sympathetic and vagal tonus, respectively.

Statistical analysis
All measures are presented by means and standard deviation. The comparisons were conducted with t Student test for independent values (p<0.05). Pearson's r was used for correlations analysis (p<0.05).

Results and Discussion
Table 1 shows participant's anthropometric and clinical
characteristics. There was no evidence of peripheral or autonomic neuropathy, including postural hypotension. Rest heart rate, Systolic Blood Pressure (SBP) or Diastolic Blood Pressure (DBP) did not differ between groups. Body weight was significantly different between groups but we have no reason to believe that it interfered with the dependent variables [15,16].

The time domain of HRV in patients revealed accentuated reductions in RMSSD, SDNN, NN, pNN50 in comparison with CG in accordance with the literature [17]. The frequency domain revealed consistent reductions in LF, HF and LF/HF in PG, in contrast with elevations on the same indexes in the CG. There was no correlation between age and time or frequency domains in any group (Table 2).

Parkinson’s is a slow-progression disease and is, in general, related with shaking, rigidity in body members, as long as rigidity in muscles and slowness of movements. Some evidences suggest that a combination between genetic and environmental factors may be placed as causes of those symptoms [18,19].

In addition, the deregulation of cardiovascular control may be related with the peripheral or central physiopathology of the Parkinson’s disease [20]. Our findings support this hypothesis, once there were significant differences in HRV indexes between groups, denoting dysfunctions in this system. Orthostatic hypotension itself could contribute for susceptibility for falling, and other traumatic accidents in patients, and its treatment, after an early diagnosis, may be important for Parkinson’s disease patient’s quality of life [27].

Here we advocate that HRV test is a valid, noninvasive, method that seems to be useful to evaluate autonomic dysfunctions as soon as they appear. We also demonstrate that HRV analysis, using time and frequency domains, in short duration (10 minutes), represents an alternative to more expensive and time demanding 24h analysis using ECGs.

### Conclusions

Reductions in HRV indexes, associated with the disease, reflect loss of sympathetic and parasympathetic balance, which may be result of structural damage caused by Parkinson’s disease. HRV, as non-invasive technique, might represent a strong indicator of neuronal regulatory activity. Its use can represent a useful tool, not only for research, but also for early diagnosis and clinical behavior of Parkinson’s disease.

### References


