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Short communication

Heart rate variability in patients with essential tremor: A cross sectional study

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ABSTRACT

Objective: To investigate heart rate variability (HRV) in patients with Essential Tremor (ET) in comparison with patients with Parkinson's Disease (PD).
Methods: This is a cross sectional control study including 10 patients with ET, 10 patients with PD and 10 age-sex-matched controls. In patients and controls, we measured the components of HRV analysis in the frequency domain during a daytime period of 12-h. Selected HRV variables were low-frequency (LF) and high-frequency (HF), conventionally considered to be influenced by the sympathetic system and the parasympathetic system respectively.
Results: HRV variables, in patients with ET, were significantly different from those detected in PD patients and similar to those of controls while in PD patients, they were significantly different from those of controls. At cut off level of 654 ms^2, LF component correctly distinguished ET patients versus PD with sensitivity, specificity, PPV and accuracy of 100%. By contrast, at cut off level of 737 ms^2, HF component showed sensitivity, specificity, PPV and accuracy of 80%, 100%, 100%, and 86.67% respectively. DAT-SPECT and cardiac MIBG uptake were both normal in ET patients whereas they were markedly decreased in those with PD.
Conclusions: In our study, the LF component of HRV analysis distinguishes ET patients from those with PD on an individual basis, thus representing a valid help in everyday clinical practice for differentiation between these patients in absence of scintigraphic investigations.

1. Introduction

Essential tremor (ET) is defined as a kinetic/postural tremor affecting hand, head, or other parts of the body without other clinical signs of parkinsonism [1].

Heart rate variability (HRV) analysis is a simple and non-invasive measure of cardiac impulses thus representing one of the most promising quantitative markers of cardiac autonomic balance [2].

Previous studies [3,4] have shown that HRV parameters were reduced in patients with Parkinson's disease (PD) while no evidence has been reported in ET patients. Several reports demonstrated that patients with PD show cardiac sympathetic denervation [5] a condition that is lacking in patients with ET [6,7]. Evidence suggests the reduction of HRV parameters observed in patients with PD may be related to cardiac sympathetic denervation that typically occur in these patients.

Indeed, distinguishing clinically between these disorders may be difficult especially in early phase of the disease and in absence of DAT-scan investigation, a highly invasive and costly diagnostic procedure. Thus, the aim of this study was to differentiate patients with ET from those with PD by using of HRV analysis.

2. Patients and methods

2.1. Participants

We enrolled 10 patients with a diagnosis of ET according to established criteria [8], 10 patients with a diagnosis of PD according to UK Parkinson's Disease Society Brain Bank clinical diagnostic

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Table 1
Demographic, clinical and neuroimaging features of patients and control subjects.

Description	ET (n = 10)	PD (n = 10)	Controls(n = 10)	P-value
Age (y)	58.7 ± 13.4	60.9 ± 6.0	59.7 ± 16.4	0.92[a]
Gender (M/F)	4/6	6/4	6/4	0.72[b]
Age at onset (y)	51 ± 11.6	54.6 ± 6.6	–	0.37[c]
Duration of the disease (y)	8.0 ± 4.5	6.3 ± 3.6	–	0.36[c]
Family history of tremor (Y/N)	6/4	4/6	–	0.66[b]
Tremor characteristics (n.%)				
Head	4(40)	0(0)	–	0.087[b]
Jaw	3(30)	0(0)	–	0.21[b]
Voice	2(20)	0(0)	–	0.47[b]
Upper limb	10(100)	10(100)	–	1[b]
Upper limb tremor unilateral or asymmetrical	4(40)	6(60)	–	0.66[b]
Aggravation: specific position	8(80)	0(0)	–	0.0007[b]
Aggravation: specific tasks	4(40)	0(0)	–	0.0867[b]
Resting tremor	0(0)	6(60)	–	0.01[b]
Postural tremor	10(100)	3(30)	–	0.003[b]
Kinetic tremor	10(100)	0(0)	–	0.00001[b]
Re-emergent tremor	0(0)	4(40)	–	0.0867[b]
Other characteristics (n.%)				
Hypomimia	0(0)	10(100)	–	<0.0001[b]
Increased Tone	1(10)	10(100)	–	0.0001[b]
Slowness	2(20)	10(100)	–	0.003[b]
Reduced arm swing	2(20)	9(90)	–	0.0055[b]
Gait Disturbance	0(0)	2(20)	–	0.4737[b]
UPDRS-ME	–	24.7 ± 6.8	–	–
H&Y	–	2.6 ± 0.62	–	–
Fahn-Tholosa scale	26.1 ± 12.6	–		–
MMSE	27.5 ± 2.2	27.6 ± 1.5	–	0.88[d]
DAT-SPECT[e]				
Left Putamen	4.71 ± 0.49	2.39 ± 0.47	–	<0.0001[c]
Right Putamen	4.56 ± 0.29	2.29 ± 0.47	–	<0.0001[c]
Cardiac MIBG scintigraphy[f]				
H/M ratio early	1.81 ± 1.51	1.24 ± 0.13	–	0.000003[c]
H/M ratio delayed	1.84 ± 1.55	1.16 ± 0.07	–	0.000001[c]

Data are given as mean values ± standard deviations. Abbreviations: ET: Essential Tremor; PD: Parkinson's Disease.
[a] ANOVA followed by pairwise *t*-test.
[b] Fisher's exact test.
[c] *t*-test.
[d] Mann-Witney *U* test.
[e] Put/Cau right (n.v: mean ± SD, 4.29 ± 0.34) and Put/Cau left (n.v: mean ± SD, 4.19 ± 0.39).
[f] H/M ratio: mean ± SD, 1.94 ± 0.18 early; 2.02 ± 0.19 delayed. n.v (normal values).

criteria [9] and 10 age-sex-matched controls. Each patient underwent an accurate clinical history and neurological evaluation. Fahn-Tolosa [10] and motor portion of the Unified Parkinson's disease (UPDRS-ME, section III) [11] scales were used for clinical evaluation of ET and PD patients respectively. Cognitive status was assessed through Mini-Mental State Examination. Imaging protocol including brain magnetic resonance imaging, DAT-SPECT and cardiac MIBG scintigaphy was performed in all patients. Before inclusion in the study, written informed consent was obtained from all participants and the study was approved by the institutional review board.

2.2. HRV analysis

Autonomic control of heart rate (HR) was obtained in all our patients by heart rate variability (HRV) analysis [12]. R-R intervals were taken from 24-h ambulatory ECG recording (ECG/HRV device: Mega Electronics Emotion Faros 180°, 2-leads wearable ECG- HRV monitor). Sampling rate for ECG was set at 500 Hz. The electrodes were placed approximately along the electrical axis of the heart. The optimal placement of the electrodes followed the locations of electrodes RA and V5 in the Mason-Likar modification of the standard 12 lead ECG: the negative electrode was placed in the right infraclavicular fossa (just below the right clavicle), and the positive electrode on the left side of the chest, below the pectoral muscle in the left anterior axillary line. The RR signal (tachogram) was processed using PhysioNet HRV Toolkit base functions, integrated in the Matlab® computing environment. Time series acquisition was then divided into 10-min epochs, with an overlapping of 5 min, for frequency analysis. In particular, each epoch was processed with means of the Lomb-Scargle algorithm, which computes the power spectrum of unevenly sampled data. LF (low frequency, sympathetic system) power was taken in the 0.04–0.15 Hz frequency band, while HF (high frequency, parasympathetic system) power is taken in the 0.15–0.4 Hz band.

Detrended fluctuation analysis, information-based similarity, estimate of largest Lyapunov exponent, multiscale entropy analysis and multifractal analysis were performed by means of the PhysioNet open source libraries for the nonlinear analysis of time series. Filtering of artifacts and ectopic beats was accomplished using Physionet HRV Toolkit functions for the removal of outliers.

We also performed some time-domain measures such as the standard deviation of normal to normal intervals (SDNN) and the root mean square of successive differences (rMSSD) using PhysioNet HRV Toolkit libraries embedded in our custom Matlab code.

2.3. Heart rate variability study design

HRV analysis was performed in all patients and controls. During the registration the patients were independent in their activities. The mean values of the spectral components of HRV were calculated for a daytime period of 12 h (from 09 a.m. to 9 p.m.). The

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