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Assessment of QT variability in Parkinson's Disease and REM Sleep Behaviour Disorder during REM phase

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***Abstract*—QT interval variability (QTV) is a marker of ventricular repolarization variability, frequently associated with sympathetic outflow and cardiovascular risk. This study explores QTV in drug-naïve ten Parkison's disease (PD), ten PD with Rapid Eye Movement (REM) Sleep Behavior Disorder (PD-RBD) subjects, and ten control (CG) participants. Five minutes of ECG data from polysomnographic recordings during REM sleep were used for analysis. To assess QTV, both time domain and frequency domain indexes were calculated. The results indicated higher QTV in PD groups compared to both CG and RBDpd, suggesting significant cardiac autonomic dysregulation in PD patients.**

Keywords— QT interval variability (QTV), Parkinson's disease (PD), REM Sleep Behavior Disorder (RBD), sleep

I. Introduction

Parkinson's disease (PD) is a neurodegenerative disorder characterized by motor symptoms such as tremors, rigidity, and bradykinesia. However, non-motor symptoms, particularly cardiac autonomic dysfunction, also significantly impact the life quality of affected people. Some works have shown that autonomic dysfunction is common in PD, with heart rate variability (HRV) analysis being a key method for its assessment. However, some studies report contrary findings [1], which could be due to HRV analysis primarily capturing only autonomic modulation of the sinoatrial (SA) node [2]. Therefore, while HRV could provide valuable insights into autonomic function, it does not offer a complete picture of the autonomic regulation of other cardiovascular aspects.

To gain a more comprehensive understanding of cardiac autonomic dysfunction in PD, it is useful to also consider QT variability (QTV) measures. QTV measures ventricular repolarization variability and it is usually associated with sympathetic ventricular outflow, especially the part that is not related to HRV [2]. This is crucial because irregularities in ventricular repolarization are linked to increased risk of arrhythmias and sudden cardiac death, which PD patients are prone to [3]. PD presents in different phenotypes with varying outcomes and prognoses, such as the coexistence of Rapid Eye Movement (REM) Sleep Behavior Disorder (RBD). RBD is a parasomnia, that is characterized by the loss of muscle atonia during REM sleep. This condition can lead to physical acting out of dreams, and it is commonly observed in PD patients and identifies as a more malignant subtype of PD [4].

Previous studies have analyzed prolongation of QT interval in PD patients due to PD severity, autonomic dysfunction or due to the pharmacological therapies such as antidepressants, antiemetics, and atypical antipsychotics [5]. While PD patients experience QT interval prolongation, it is important to differentiate this from QTV. Although both QT duration and QTV are related to ventricular repolarization, there has been no research analyzing QTV specifically in PD patients. Therefore, understanding how QTV is affected by PD is crucial for comprehensively assessing and managing the cardiac risks in PD patients which is not addressed previously.

Thus, this work aims to explore the QTV in drug-naïve PD and PD-RBD patients compared to a control group (CG) during REM sleep, as the impact of RBD is more prominent during this phase. By investigating differences in QTV, we seek to enhance our understanding of cardiovascular dysregulation in PD and its subtypes, ultimately contributing to better risk stratification and management strategies for these patients.

II. Materials and Methods

Three groups of participants were included in this study: 10 CG (55±7 y.o., 70% females), 10 PD (65±10 y.o., 30% females) and 10 PD-RBD (66±7 y.o., 30% females). Inclusion criteria were the compliance to full-night polysomnographic (PSG) exam, the absence of any further cardiological or neurological disorder, and the absence of dopaminergic treatment and other treatments affecting HR. The diagnosis of PD and RBD was done following the international guidelines. Ethical approval was obtained from the Ethics Committee at University Hospital of Cagliari (PG/2018/11699) and the IRB at Policlinico San Martino in Genova (IRB approval n. 105/2023 – DB id 13027).

To perform QTV analysis, the electrocardiographic (ECG) signal during REM phase was extracted from PSG data. To maintain homogeneity, a single 5-minute ECG epoch was examined for all participants. The detection of Q-wave onset, R-peak and T-wave end were performed by a wavelet-based ECG delineator [6], followed by automatic R-peak position refinement, ectopic beat correction followed by outlier rejection in QT series. To measure QTV, time and frequency domain indexes were computed. The time-domain indexes included the corrected QT interval (QTc) with the Bazett's formula, the average of normal RR intervals (RRmean), the average of normal QT intervals (QTmean), standard deviation of QT interval (SDQT), normalized QT interval variance (QTVN), the short-term QT interval variability (STVQT), the QTV index (QTVi), and the QTV ratio (VR). Frequency-domain indexes included the power of QT-based tachograms (in ms^2) in three frequency bands, i.e., the total power (QTV_{TOT}) in [0.04-0.4 Hz], the power at low frequencies (QTV_{LF}), in [0.04-0.15 Hz], and the power at high frequency (QTV_{HF}), in [0.15-0.4 Hz] [2].

To assess any potential statistical difference in QTV parameters, statistical analysis was carried out by using the pairwise, non-parametric Wilcoxon rank sum test across populations, i.e. CG vs. PD, CG vs. PD-RBD and PD-RBD vs. PD. Results were considered significant for $p < 0.05$.

III. Results and Discussion

Figure 1 shows the time and frequency domain QTV analysis across the three groups. There were no significant differences in RRmean, QTmean and QTc values across the three groups. In comparison with CG, PD subjects exhibited higher STVQT, QTV_{LF} and QTV_{HF}. This indicates increased variability in ventricular repolarization and suggests heightened autonomic dysfunction. Additionally, PD subjects had higher SDQT, QTVN, STVQT, QTVi, QTV_{LF}, QTV_{HF}, and QTV_{TOT} compared to PD-RBD, further indicating greater autonomic instability. In contrast, the PD-RBD group showed no significant differences from CG except for significantly lower SDQT and QTVN, suggesting a distinct pattern of autonomic regulation possibly due to the impact of RBD on autonomic control during REM sleep. In conclusion, these findings suggest that QTV measures provide valuable insights into autonomic dysfunction in PD and its subtypes, offering a preliminary understanding that is still in development. This study has some limitations, including the small dataset and the analysis of only one 5-minute ECG epoch per subject. Additionally, respiratory information and QTV adjustment for confounding factors was not considered, which may impact the comprehensiveness of the findings.

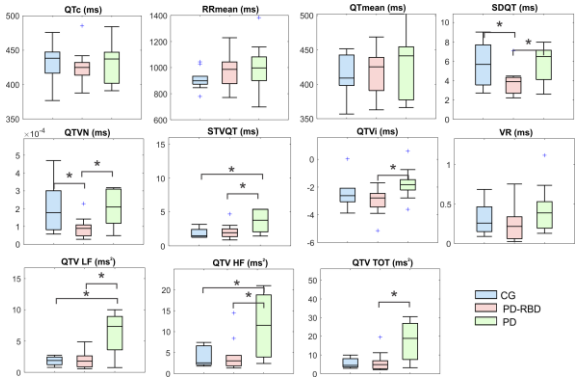

Fig.1. Time and frequency domain QTV indexes. The statistically significant results are marked by *.

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