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Heart rate variability in evaluation of autonomic dysfunction in idiopathic REM-sleep behaviour disorder

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ABSTRACT

Introduction. Nearly 80% of people diagnosed with idiopathic REM sleep behaviour disorder (iRBD) via video-polysomnography (v-PSG) are expected to be in the prodromal stage of an alpha-synucleinopathy. Signs of autonomic dysfunction can appear earlier than motor or cognitive alpha-synucleinopathy symptoms. Heart rate variability (HRV) can potentially be an objective measurement of autonomic dysfunction, and furthermore can be obtained directly from v-PSG.

Objectives. The aim of this study was to evaluate dysautonomia in iRBD subjects using HRV obtained during different sleep stages and wakefulness from v-PSG.

Material and methods. Subjects positively screened by an RBD screening questionnaire (RBD-SQ) underwent v-PSG to diagnose RBD. HRV obtained from v-PSG recordings was correlated to dysautonomia evaluated from a Non-Motor Symptoms Scale (NMSS) questionnaire. Optimal cut-off values of HRV parameters to predict dysautonomia were calculated using receiver operating characteristics (ROC) — area under the curve (AUC) analysis. The effect of confounder variables was predicted with binomial logistic regression and multiple regression analyses.

Results. Out of 72 positively screened subjects, 29 subjects were diagnosed as iRBD (mean age 66 ± 7.7 years) by v-PSG. Eighty-three per cent of the iRBD subjects in our cohort were at the time of diagnosis classified as having possible or probable prodromal Parkinson's disease (pPD) compared to zero subjects being positively screened in the control group. The iRBD-positive subjects showed significant inverse correlations of NMSS score, particularly to log low-frequency (LF) component of HRV during wakefulness: $r = -0.59$ ($p = 0.001$). Based on ROC analysis and correlation between NMSS score, log LF during wakefulness (AUC 0.74, cut-off 4.69, sensitivity 91.7%, specificity 64.7%, $p = 0.028$) was considered as the most accurate predictor of dysautonomia in the iRBD group. Apnoea-hypopnoea index (AHI) negatively predicted dysautonomia in the iRBD group. None of the HRV components was able to predict the presence of iRBD in the full cohort. Age, gender, and PSG variables were significant confounders of HRV prediction.

Conclusions. The presented study did not confirm the possibility of using HRV from v-PSG records of patients with iRBD to predict dysautonomia expressed by questionnaire methods. This is probably due to several confounding factors capable of influencing HRV in such a cohort.

Key words: idiopathic REM sleep behaviour disorder, dysautonomia, heart rate variability, RBD Screening Questionnaire

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Introduction

Consistent evidence indicates that RBD is the most specific clinical prodromal marker of alpha-synucleinopathies — neurodegenerative disorders characterised by the pathological accumulation of alpha-synuclein, such as Parkinson's disease (PD), dementia with Lewy bodies and multiple system atrophy [1, 2]. The presence of RBD is also currently being studied in tauopathies, such as progressive supranuclear palsy [3] and Alzheimer's disease [4]. Several studies have demonstrated that c.80% of v-PSG proven RBD patients eventually develop alpha-synuclein-induced neurodegeneration [2, 5, 6], with a nearly 6.3% phenoconversion rate per year [7], and thus it can be effectively used as a substitute for pPD in research studies of other potential biomarkers [1].

Such a predictor is dysfunction of the autonomic nervous system (ANS). Signs of autonomic dysfunction are estimated to start developing as much as 15 years before the diagnosis of PD [8]. Orthostatic hypotension in PD involves a combination of sympathetic denervation and baroreflex failure, and occurs in 20–50% of patients with PD, according to the different diagnostic criteria used [9]. Other signs of dysautonomia are constipation, with a prevalence ranging from 24.6–63% [10], and lower urinary tract dysfunction, mostly characterised by overactivity of the detrusor muscle leading to an overactive bladder, occurring in 27–80% of PD patients [11].

It has been recognised that the presence of RBD identifies a specific PD subtype characterised by a higher prevalence of autonomic dysfunction [12]. A recent proposal [13] divides PD into two subtypes, according to the phenotypes seen in the prodromal stage. One is the 'body-first' subtype, clearly associated with the presence of RBD, appearing during the prodromal stage and with significant damage to the ANS preceding measurable damage to the nigrostriatal dopamine system. The other subtype is designated 'brain-first', which in its prodromal stage is without RBD or quantifiable dysfunction of the ANS, but already with evident damage to the nigrostriatal dopamine system [13].

Questionnaires and rating scales are currently the gold standard for assessing most aspects of autonomic dysfunction; however, these are subjective, and few objective measures are available, e.g. HRV. HRV measures the fluctuation of the time intervals between consecutive heartbeats, revealing the dynamic interactions between the sympathetic and parasympathetic functions. HRV has been suggested as a possible biomarker for dysautonomia in conditions such as diabetes mellitus type 2 [14] and ischaemic stroke [15]. Having the advantage of being directly obtained from diagnostic v-PSG, HRV is an inexpensive measure of cardiac dysautonomia compared to examinations such as 123 I-MIBG-scintigraphy [16], and could potentially be an objective measure of autonomic dysfunction in subjects at risk of developing an alpha-synucleinopathy. In this study, we tested the hypothesis that HRV can predict subjective autonomic dysfunction in iRBD patients.

Material and methods

Study participants were recruited in a single Movement Disorder Centre in Kosice, Slovakia, between 2018 and 2021 after a nationwide media campaign, followed by a multistage screening described previously [17]. Patients were screened using the REM Sleep Behaviour Disorder Single-Question Screening [18], followed in the case of positive findings by the RBD-SQ [19]. Patients with ≥ 5 points on the RBD-SQ underwent v-PSG. All involved subjects signed informed consent forms prior to their enrolment. The investigation protocol was approved by the local ethics committee, and the work was carried out in accordance with the Declaration of Helsinki.

A full night v-PSG examination was performed over the course of one or two nights using Sleepware G3 version 3.9.5. software to guarantee an appropriate amount of REM sleep for the evaluation. The v-PSG scoring used was according to the American Academy of Sleep Medicine's recommendation [20]. REM sleep muscle tone was recorded and scored according to the SINBAR group's recommendations [21]. Subjects were considered as RBD-positive patients in the presence of REM-sleep without atonia (RWA) in PSG and complex motor behaviour in the REM phase based on the synchronised v-PSG recording or patient history, according to the International Classification of Sleep Disorders — 3rd edition [22].

All patients were evaluated by a movement disorder specialist to exclude the presence of clinically established parkinsonism and also by a level 2 neuropsychological assessment to exclude the presence of cognitive dysfunction [23]. Patients presenting with severe autonomic dysfunction and age below 50 were also excluded in the initial visit [24]. After performing v-PSG analysis, those patients who were observed to have severe OSA (apnoea-hypopnea index (AHI) over 30 per hour of total sleep time), and those with cardiac arrhythmia or artefacts affecting ECG signal were excluded from the study as well. Subjects included in the study were then divided into an iRBD group and an RBD-negative group based on the presence of RBD (Fig. 1).

The likelihood ratio (LR) of a given subject being in pPD at the time of examination was also calculated based on the updated Movement Disorder Society (MDS) Research Criteria for prodromal Parkinson's disease [24], using all risk factors and prodromal markers, excluding genetic testing, plasma urate levels in men, and physical inactivity, as described previously [17].

HRV analysis came from a 5-min interval with stable ECG taken from v-PSG in three distinct sleep and wake stages: pre-sleep relaxed wakefulness, NREM (especially stage N2 but occasionally also N1 and optimally from the first sleep cycle), and REM. Intervals did not contain arousals, motor or respiratory events. For each interval, HRV was analysed in the frequency domains using Kubios HRV Premium software version 3.5.0 (University of Eastern Finland, Kuopio, Finland).

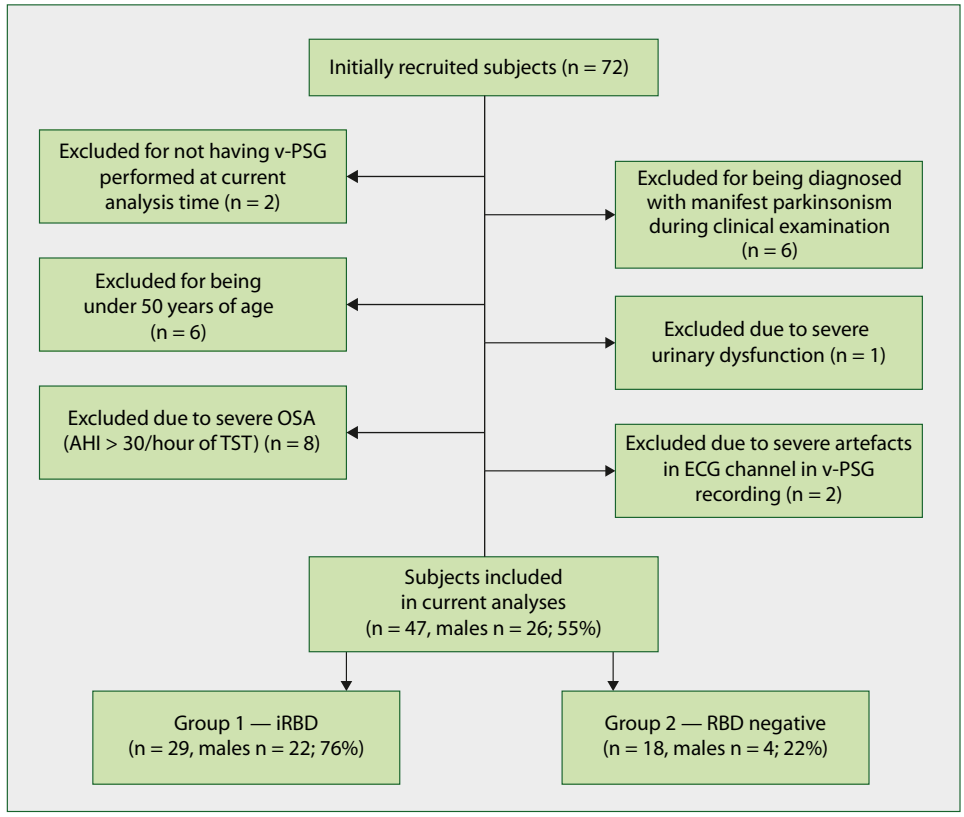

Figure 1. Flow chart of study population. AHI — Apnoea-Hypopnoea Index; iRBD — idiopathic rapid eye movement (REM) sleep behaviour disorder; n — number; OSA — obstructive sleep apnoea; v-PSG — video-polysomnography; TST — total sleep time

HRV analysis provided several different metrics: the frequency-domain metric LF is a measure of the low-frequency band (0.04–0.15 Hz) traditionally associated with both sympathetic and vagal influence and reflects baroreflex sensitivity [25]. Parasympathetic activity is considered to be a major contributor to the high-frequency (HF) band (0.15–0.4 Hz). The LF/HF ratio is used to estimate the relation between the influence of the sympathetic and parasympathetic systems under controlled conditions, also known as the sympathovagal balance [26]. In our analysis, the following frequency-domain spectral components of HRV were obtained, as quantified by a fast Fourier transform decomposition algorithm available in the software: absolute power of LF — LF ms^2, natural logarithm of LF — log LF, absolute power of HF — HF ms^2, natural logarithm of HF — log HF, and the LF/HF ratio.

Lastly, the Non-Motor Symptoms Severity Scale (NMSS) questionnaire was selected in this study based on MDS recommendations [27] to reflect multidomain autonomic dysfunction due to its cross-validity with other scales [28]. Items regarding autonomic function were selected (Nos. 1, 2, 19–24 and 30) [29]. Each item is evaluated based on the severity of the symptoms (0–3 points) and frequency (1–4 points). The final score for each NMSS item is the result of the severity multiplied by the frequency.

The NMSS total in the study represents the sum of the scores for the items concerning autonomic function, and the separate domains of autonomic dysfunction — the cardiovascular (CVS), gastrointestinal (GIT), urinary domains or sweating, were quantified by a set of NMSS items regarding specific domain.

We defined significant dysautonomia if the subject scored at least one severity score of 2 or 3 points that represents symptoms which were a moderate or major source of disturbance for the patient.

Data analysis

Statistical analysis was performed using IBM SPSS Statistics 22 and managed by spreadsheet software. The one-tail unequal variance t-test (Welch's t-test) was used when assessing the differences in demographic, v-PSG and autonomic parameters between the two study groups.

Correlations between the values of NMSS total, as well as of separate autonomic dysfunction in the CVS, GIT, urinary and sweating domains, with the LF (ms^2), log LF, HF (ms^2), log HF and the LF/HF ratio components of HRV obtained separately during wakefulness, NREM and REM sleep, were calculated using Pearson's correlation coefficient (r) in the full cohort and in iRBD subjects. The correlations were considered to be significant if $r > 0.5$ or $r < -0.5$.

Table 1. Description of study groups. Values are expressed as averages followed by standard deviations (in brackets)

	All individuals n = 47, age [years] = 63.8 (7.7)		
	Group 1 (iRBD) n = 29	Group 2 (RBD negative) n = 18	Statistical significance – p-value
Age [years]	66 (7.7)	60.4 (6.6)	0.006
MDS-UPDRS-III total evaluation score	7.1 (6)	6.5 (6.1)	0.379
TST —total sleep time [min]	375.7 (106.4)	407.8 (62.3)	0.1
Sleep efficiency [%]	76.7 (13.5)	82.4 (7.8)	0.039
AHI index (/h TST)	11.9 (8.1)	9.8 (7.3)	0.19
PLMS index (/h TST)	20.7 (19)	12.1 (12.9)	0.035
Arousal index (/h TST)	9.6 (5.5)	10.7 (8.6)	0.311
NMSS total autonomic score	11.1 (10.2)	10.2 (15.8)	0.416

AHI — Apnoea-Hypopnoea Index; MDS-UPDRS-III — Movement Disorder Society-Unified Parkinson's Disease Rating Scale part III; N — number; NMSS — Non-Motor Symptoms Severity Scale; PLMS — periodic Limb movements of sleep; TST — total sleep time

We performed ROC analysis, from which the AUC (values 0–1) was calculated, using HRV components as the diagnostic test and significant dysautonomia as the outcome.

The ROC analysis was performed to obtain a cut-off value for different components of HRV that predict whether or not a given subject has a significant autonomic dysfunction, with a given sensitivity and specificity. Using the AUC calculation, we obtained a cut-off value for each of the studied HRV components, predicting if a given subject had a significant autonomic dysfunction.

Binomial logistic regressions were performed to ascertain the effects of independent variables — age, gender, AHI index and PLMS index on the prediction of HRV changes, having iRBD, and the presence of significant autonomic dysfunction. The Nagelkerke r^2 coefficients and correct prediction — overall percentage of the final binary regression model for the prediction of the dependent variables were calculated. The magnitude of association between the dependent and the independent variables was measured by the odds ratio (OR). A 95% confidence interval (CI), was used in the study, with a p-value of under 0.05 considered statistically significant.

Results

Demographic, v-PSG, autonomic parameters and HRV components

Seventy-two initially recruited patients with positive RBD-SQ (average age 62.6 ± 9 years, 29 females and 43 males) were eventually included in the study (Fig. 1). Due to technical problems, two of the 72 subjects did not undergo v-PSG. Six patients were excluded because of the presence of parkinsonism. From the remaining 64 subjects, six were excluded from further analysis due to age under 50 years, plus one because of severe urinary dysfunction (associated with a complication of surgery), plus 10 due to severe OSA or severe artefacts in ECG (Fig. 1). For the further analysis of HRV, we used 47 patients (average age 63.8 ± 7.7 years, 21 females and 26 males), 29 of them diagnosed with iRBD (Tab. 1). Thirty-five (50%) positively RBDSQ-screened subjects out of the 70 were confirmed as RBD.

The diagnosis of RBD was based on the presence of RWA and dream-enacting complex behaviour on v-PSG or patient history. On average, 7.53% of the REM epochs presented with RWA in the RBD positive group.Of the 29 RBD positive subjects, 12 manifested dream-enacting behaviour on v-PSG.

The LR for pPD was calculated for each subject. The iRBD group consisted of 22 (76%) subjects with an LR of probable pPD; two (7%) subjects met the criteria for possible pPD, and five were classified as negative for pPD. All 18 subjects in the RBD negative group – the control group — were classified as negative for pPD.

Table 1 presents a description of the demographic, v-PSG, and autonomic parameters of the two studied groups according to the presence of RBD. Significant statistical differences were found between the groups in terms of age, sleep efficiency, and periodic limb movements in sleep (PLMS) indices. IRBD subjects were older, had decreased sleep efficiency, and had more PLMS.

Relationship between HRV components and questionnaire-assessed autonomic parameters in iRBD patients

In iRBD subjects, we found significant inverse correlations of NMSS total to the natural logarithm of the LF and HF components of HRV during wakefulness: log LF: r = –0.59 (p = 0.001), log HF r = –0.54 (p = 0.003). Significant correlations were also observed between the urinary domain of autonomic function and log LF (r = –0.58; p = 0.001), as well as log HF (r = –0.54; p = 0.003) during wakefulness (Tab. 2). In the control group, we did not find any significant correlations. Also when considering the full cohort, there were no significant correlations.

By performing the ROC analysis, we obtained values of AUC for each of the HRV components. Only three HRV components had statistically significant AUC values. Of these three

Table 2. Correlations between HRV components and autonomic parameters in iRBD group

		Relaxed wakefulness				NREM				REM			
		LF (ms^2)	logLF	HF (ms^2)	logHF	LF/HF rat.	LF (ms^2)	logLF	HF (ms^2)	logHF	LF/HF rat.	LF (ms^2)	logLF	HF (ms^2)	logHF	LF/HF rat.
NMSS total	Pearson's r	–0.43*	**–0.59****	–0.35	**–0.54****	0.05	–0.18	–0.24	–0.18	–0.28	–0.06	–0.18	–0.45*	–0.16	–0.25	–0.14
	p-value	0.02	.001	0.06	0.003	0.814	0.346	0.22	0.353	0.146	0.759		0.014	0.405	0.198	
CVS	Pearson's r	–0.02	–0.17	0.06	–0.02	–0.16	0.03	0.01	0.12	0.07	–0.13	–0.09	–0.04	–0.06	0.02	–0.13
	p-value	0.921	0.375	0.76	0.907	0.415	0.874	0.976	0.543	0.733	0.51		0.836	0.77	0.907	
GIT	Pearson's r	–0.31	–0.27	–0.19	–0.11	–0.13	–0.19	–0.29	–0.03	–0.09	–0.19	0.02	0.01	0.09	0.03	–0.07
	p-value	0.099	0.15	0.32	0.559	0.519	0.326	0.125	0.879	0.645	0.337		0.975	0.634	0.895	
Urinary	Pearson's r	–0.41*	**–0.58****	–0.27	**–0.54****	0.05	–0.28	–0.24	–0.19	–0.32	–0.08	–0.17	–0.45*	–0.13	–0.22	–0.11
	p-value	0.026	0.001	0.153	0.003	0.813	0.137	0.213	0.315	0.096	0.671		0.015	0.511	0.245	
Sweating	Pearson's r	–0.09	–0.2	–0.3	–0.37*	0.23	0.22	0.1	–0.15	–0.11	0.23	–0.19	–0.41*	–0.29	–0.31	–0.07
	p-value	0.643	0.29	0.115	0.048	0.23	0.247	0.601	0.449	0.581	0.225		0.026	0.123	0.105	

*Correlation is significant at < 0.05 level (2-tailed). **Correlation is significant at < 0.01 level (2-tailed). In **bold** are marked correlations with a Pearson's correlation coefficient of either < –0.5 or > 0.5, considered significant correlations
CVS — cardiovascular system; GIT — gastrointestinal system; HF — high-frequency HRV component; HRV — heart rate variability; iRBD — idiopathic REM sleep behaviour disorder; LF — low-frequency HRV component; log — natural logarithm; ms^2 — absolute power of HRV component; NMSS — Non-Motor Symptoms Scale for Parkinson'sDisease; NMSS total — sum of scores of items in NMSS regarding autonomic function; Pearson's r — Pearson's correlation coefficient

HRV components, one of them had been described previously as also having a significant correlation to the total NMSS score in the correlation analysis: log LF during wakefulness; therefore, this HRV component was finally selected to be the HRV component that could more accurately predict significant dysautonomia. We further selected an optimal cut-off level for predicting significant dysautonomia, together with sensitivity and specificity values: log LF during wakefulness has an AUC of 0.74 and an optimal cut-off of 4.69 (sensitivity 91.7% and specificity 64.7%, p = 0.028) (Suppl. Material A).

Using binomial logistic regression, we described that the influence of age, gender and PSG variables is 44.1% (Nagelkerke r_2) on the prediction of significant dysautonomia in the group of iRBD subjects. The only variable that can significantly impact the prediction of significant dysautonomia was the AHI index, where an increase of 1 point in the AHI index decreases the chance of having significant dysautonomia by 19% (p = 0.017) (Suppl. Material B).

Differences in HRV between iRBD patients and controls

The subjects in the cohort did not show any statistically significant differences between the HRV components during wakefulness or NREM, and REM sleep, when comparing the iRBD group to the RBD negative group (Suppl. Material C).

A ROC curve was performed in the full cohort to predict iRBD based only on HRV values during wakefulness and sleep. No HRV component was able to independently predict the diagnosis of iRBD, which is reflected in the values of AUC without statistical significance (Suppl. Material D).

Using binomial logistic regression, we described that the influence of age, gender and PSG variables on the prediction of iRBD in the full cohort was 83%. The Nagelkerke r_2 indicated approximately 43% of the variance in the iRBD prediction was accounted for by independent factors. The only variable that could significantly impact the prediction of iRBD was gender: females were 88.1% less likely to have iRBD than males (p = 0.005) in the presented cohort.

Multiple regressions were used to predict how much of the variance of each HRV component in sleep and wake stages was accounted for by age, gender, AHI and PLMS indices, in the full cohort (Suppl. Material E). The HRV component which was most influenced by these variables was log LF in wakefulness (R^2 = 0.22).

Discussion

The presented study revealed that 50% of subjects after a questionnaire screening process were v-PSG proven as RBD--positive, which was lower than in a previous study [19]. Eighty--three per cent of the iRBD subjects in our cohort were at the time of diagnosis classified as possible or probable pPD, compared to zero subjects being positively screened in the control group, which was in accordance with previous observations [30, 31].

For the first time, changes in HRV were correlated with the questionnaire-assessed autonomic dysfunction. The study revealed correlations between NMSS questionnaire-assessed autonomic function scores and HRV indices in the iRBD group, especially with the low-frequency (LF) components of HRV in wakefulness, which mainly represent the sympathetic nervous system function.

In contrast, in the study we observed that although HRV is strongly correlated with general autonomic dysfunction in iRBD subjects (based on the total score for the questions regarding autonomic function in the NMSS), it is only weakly correlated with the separate domain of CVS function. The explanation for this could be that HRV is closely related to cardiac autonomic function, while the CVS domain in the NMSS questionnaire mostly concerns orthostasis, which more accurately represents peripheral vascular autonomic function, or it could be that the subjective nature of questionnaire--assessed dysautonomia in NMSS does not reflect all of the aspects of CVS function. However, Sumi et al. demonstrated that the decrease in HRV indices during the supine position can predict orthostatic hypotension, providing an alternative to the orthostatic challenge test [32]. While using the head-up tilt test, Rocchi et al. [33] described LF and LF/HF ratio as significantly higher in controls compared to iRBD, while we did not find statistically significant differences between both groups.

The other issue could be the reliability of subjective NMSS domains for orthostasis and objective head-up tilt test. Unfortunately, the presented study was set before the MDS updates for pPD evaluation, and such data was not available for the first patients included. A question that remains unanswered in the presented study is that while log LF was significantly correlated with autonomic questionnaires, the absolute power of LF was not. In practice, this finding means that it can only be a random statistical phenomenon, and not a relationship between quantities. Moreover, log LF in wakefulness was the HRV component which was the most affected by confounders. The assessment of HRV in the studied iRBD patients during any stage of sleep and wake is not able to identify the presence of subjectively reported dysautonomia.

In previous studies that only looked at HRV changes in patients with RBD, the findings were inconsistent as for the main impact on LF or HF component or distribution during sleep and wakefulness: Attenuated sympathetic nervous system activity has been observed in RBD patients (11 iRBD, 14 PD patients with RBD) when compared to controls, and being more pronounced in patients with PD [34]. Decreased HRV (both the sympathetic and parasympathetic components) in iRBD has been described when analysing 5-minute pre-sleep ECG segments [35]. Another study however reported reduced HF in RBD (47 individuals) compared to age- and gender-matched controls (26 individuals), along with reduced time-domain HRV components (RMSSD and SDRR). The latter study also observed that tonic activity in RWA was inversely correlated with LF and LF/HF ratio, and positively correlated with HF [36].

The other studies found reduced HRV during sleep in iRBD and RBD associated with neurodegenerative disorders [37]. Significant differences in HRV between iRBD and healthy control subjects were found in the very LF and LF components of HRV during wakefulness, independent of whether or not the iRBD subjects would eventually develop neurodegeneration [38]. The presented study failed to show significant changes in HRV between iRBD patients and controls in any sleep-wake stage.

It has been demonstrated that HRV can be easily influenced by other variables, such as age, gender, OSA, and PLMS [39–43]. There is a high interindividual variability in HRV, so there are no ranges of normative values for a given individual [44]. There were no significant differences between the study groups regarding comorbidities that may affect HRV evaluation (heart arrhythmia, diabetes mellitus type 2, arterial hypertension, thyroid disorder, neuropathy, myocardial infarction, and ischaemic heart disease) no regarding medication (antidepressants, beta-blockers, alpha-blockers, ACE inhibitors and sartans, calcium-channel blockers, diuretics, statins and antiaggregants). Lower HF, reflecting deficient vagal inhibition, has been correlated with stress, anxiety, and increased morbidity [45]. It was reported that LF power was lower in healthy individuals who developed type 2 diabetes mellitus over an average follow-up period of 8.3 years, with no differences in HF power [46].

Since, in the presented study, iRBD patients differed from controls in terms of age, gender and PSG variables, we considered that confounding factors were involved in HRV changes. We demonstrated that gender could have significantly influenced the prediction of iRBD using HRV. Despite the fact that there were men and women in a ratio of 1:1.2 in the entire cohort obtained by the questionnaire survey, the gender distribution in the iRBD (male 76%) group and the non-RBD group (male 22%) was clearly uneven. The higher representation of the male gender in the iRBD group is also in accordance with previous findings, which led to the expression of a 1.5-fold increased risk for pPD in males [27]. The high ratio of women in the iRBD-negative group could indicate that the questionnaire survey in women fails to differentiate the motor and dream activity in women associated with other sleep and mental disorders, especially the abuse of psychoactive substances. No other independent variable (age, AHI and PLMS indexes) had a significant effect on this prediction. In the group of iRBD subjects, we observed that AHI may be a significant confounder (even if patients with severe OSA were excluded from the study).

Limitations

This study has several limitations. Firstly, the limited number of the studied subjects, due to iRBD rarity, should be followed by studies on larger patient cohorts. The nature

of our study did not allow for having age- and gender-matched subjects. In addition, while our study evaluated autonomic symptoms based on subjective patient reports correlated to objective HRV components, other multimodal objective autonomic examinations, such as orthostatic and/or head-up tilt test, the quantitative sudomotor axon reflex test, thermoregulatory sweat test, urodynamic investigations, as well as emerging GIT autonomic tests [47], should be included in future studies.

Conclusions

Questionnaire screening for RBD positively predicted the disease in 50% of subjects. HRV changes failed to differentiate iRBD patients from controls, as HRV changes were affected by age, sex, and AHI. The presented study did not confirm the possibility of using HRV from v-PSG records of patients with iRBD to predict dysautonomia expressed by the NMSS questionnaire.

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