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CLINICAL REVIEW

Heart rate variability in insomnia patients: A critical review of the literature

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SUMMARY

Heart rate variability (HRV) is an objective marker that provides insight into autonomic nervous system dynamics. There is conflicting evidence regarding the presence of HRV impairment in insomnia patients. Web-based databases were used to systematically search the literature for all studies that compared the HRV of insomnia patients to controls or reported the HRV of insomnia patients before and after an intervention. 22 relevant papers were identified. Study characteristics were summarised, HRV measures were extracted and a risk of bias assessment for each study was performed. We were limited in our ability to synthesise outcome measures and perform meta-analyses due to considerable differences in patient (and control) selection, study protocols, measurement and processing techniques and outcome reporting. Risk of bias was deemed to be high in the majority of studies. As such, we cannot confirm that HRV is reliably impaired in insomnia patients nor determine the HRV response to interventions. Whilst HRV impairment in insomnia is a widely accepted concept, it is not supported by empirical evidence. Large longitudinal studies incorporating 24-hour recordings are required to elucidate the precise nature of HRV dynamics in insomnia patients.

Introduction

Heart rate variability (HRV) describes the variation in time between consecutive heart beats, which is commonly referred to as the RR (R wave to R wave) or NN (normal beat to normal beat) interval. Pacemaker cells located in the sinoatrial node of the heart possess autorhythmicity to maintain heart rate regularity. The heart rate (HR), however, is modulated by a number of physiological factors which alter autonomic nervous system control and increase variability at various frequencies. There are two prominent approaches for quantifying heart rate variation which use spectral or non-spectral techniques to generate HRV measures.

Non-spectral methods involve mathematical derivations of the NN interval. When taken from an electrocardiogram (ECG), this interval is determined by measuring the length in time between consecutive sinoatrial R wave peaks. As many non-spectral derivations report the HRV in time (milliseconds) or units, they are collectively referred to as time-domain measures. Four time-domain measures are recommended for use by the task force of the European society of cardiology and the North American society of pacing and electrophysiology when assessing HRV for estimation of short term (root mean square of successive differences of NN intervals (RMSSD)), long term (standard deviation of the averages of NN intervals in five minute segments of entire recording (SDANN)) and overall HRV (standard deviation of NN intervals (SDNN), HRV triangular index) [1]. A description of these HRV measures can be found in Table 1.

Spectral analysis of HRV enables the evaluation of frequency-domain measures. As parasympathetic-mediated changes to HR occur more quickly than sympathetic adjustments, the use of spectral analysis to determine frequency can provide insight into autonomic nervous system dynamics. It has been accepted previously that low frequency (LF) activity is a correlate of

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Abbreviations

ECG	electrocardiogram
EEG	electroencephalogram
HF	high frequency power
HFnorm	high frequency power (in normalised units)
HR	heart rate
HRV	heart rate variability
LF	low frequency power
LF/HF	low frequency to high frequency ratio
LFnorm	low frequency power (in normalised units)
NN interval	interval in time between successive normal beats (typically measured from the R wave of a QRS complex)
NREM	non rapid eye movement
pNN50	percent of NN intervals > 50 milliseconds different from previous
PSG	polysomnography
REM	rapid eye movement
RMSSD	root mean square of successive differences of NN intervals for period of interest
RR interval	interval in time between successive R waves (of a QRS complex)
SDANN	standard deviation of the averages of NN intervals in five minute segments of entire recording
SDNN	standard deviation of NN intervals for period of interest
TP	total power

parasympathetic and sympathetic activity whilst high frequency (HF) activity reflects parasympathetic activity only. As such the ratio between these (the LF/HF ratio) provides an estimate of sympathovagal balance which is the putative equilibrium of the sympathetic and parasympathetic systems. However, the physiological significance of the lower frequency bands (including LF and the LF/HF ratio) has been contested and caution is required when interpreting these measures [2–4]. This is further summarised in Table 1. For a more detailed explanation of the physiological correlates of HRV measures refer to the previous review of Stein and Pu [5].

Heart rate variability recordings are employed in a vast range of settings, popular due to the non-invasive methods used for data collection. The clinical utility of HRV was realised in the late 1980s when decreased HRV, defined by a reduction in 24-hour SDNN, was found to be a strong predictor of mortality post myocardial infarct [6]. HRV has since been used to investigate health and disease states for clinical and research purposes.

The incorporation of HRV analysis during sleep has been a logical extension as the ECG is a component of overnight polysomnography (PSG). This has acted as a catalyst for further examination on the bidirectional relationship between autonomic nervous system activity and sleep physiology [7]. It is not surprising that time and frequency-domain HRV measures, primarily from short recordings (i.e., less than 24 h), are increasingly being reported in the sleep literature.

HRV has circadian periodicity with significant alterations during the transition from wake to sleep and across sleep cycles [8,9]. Bonnemeier et al. [10] and Li et al. [11] have shown that vagal HRV measures follow a day-night pattern increasing during the night [12]. Importantly, these changes are correlated with age and sex [10,11]. There is also a shift in sympathovagal balance between non rapid eye movement (NREM) and rapid eye movement (REM) sleep [5,9,13]. Research has now progressed to investigating the associations between HRV, sleep disorders and their subsequent comorbidities and the incorporation of non-traditional HRV techniques [5,13,14].

Given the interplay between HRV and cardiac autonomic activity, the use of HRV in insomnia research may assist further investigation into the pathophysiology and potential health impacts of insomnia. With an estimated worldwide prevalence of 10%, insomnia is the most common sleep disorder [15–17]. Clinical diagnosis in accordance with the most recent diagnostic and

Table 1
Summary of common heart rate variability measures and their physiological correlates.

Measure	Description	Units	Autonomic inference
Time-domain measures			
HRV triangular index	Baseline width of the minimum square difference triangular interpolation of the highest peak of the histogram of all NN intervals, reflects total HRV	ms	–
NN interval	Time between two successive normal R wave peaks of a QRS complex	ms	–
pNN50	Percentage of number of adjacent NN interval pairs greater than 50 ms divided by the total number of NN intervals	%	Parasympathetic activity
RMSSD	Square root of the mean of the squared differences between successive NN intervals	ms	Parasympathetic activity
SDANN	Standard deviation of the average of NN intervals in all 5-minute segments of a 24 h recording, primarily reflects circadian HRV	ms	–
SDNN	Standard deviation of all NN intervals, typically from a 24 h recording, reflects total HRV	ms	–
Frequency-domain measures			
HF	High frequency power (0.15–0.4 Hz)	ms^2	Parasympathetic activity
HFnorm	Similar to HF but the high frequency power is normalised using total power	nu	Sympathovagal balance, with higher values representing increases in parasympathetic prevalence
LF	Low frequency power (0.04–0.15 Hz), significance is debated	ms^2	Purported to reflect both parasympathetic and sympathetic activity
LF/HF	Ratio of LF to HF, significance is debated	ratio	Purported to reflect sympathovagal balance
LFnorm	Similar to LF but the low frequency power is normalised using total power, significance is debated	nu	Sympathovagal balance, higher values may represent increases in sympathetic prevalence
Total power	Variance of all NN intervals, reflects total HRV	ms^2	–
VLF	Very low frequency power (0.003–0.04 Hz)	ms^2	Parasympathetic activity and the non-autonomic renin-angiotensin system effects

Abbreviations: HRV: heart rate variability; ms: milliseconds; nu: normalised units. Refs.: [1–5].