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Original article

Heart rate variability, sympathetic and vagal balance and EEG arousals in upper airway resistance and mild obstructive sleep apnea syndromes

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Abstract

Background and purpose: We questioned the role of respiratory events in obstructive sleep apnea syndrome (OSAS) and of upper airway resistance syndrome (UARS) on heart rate (HR) during sleep, paying specific attention to the termination of the abnormal breathing events and examining the presence of arousals or termination with only central nervous system (CNS) activation.

Patients and methods: Twenty patients, 10 with UARS and 10 with mild OSAS, were studied. A nocturnal polysomnogram was performed including measurement of respiratory variables and pulse transit time (PTT). According to the presence or absence of a PTT event indicative of autonomic nervous system (ANS) activation, 148 events were extracted after having been randomly chosen in each represented sleep stage, with or without an electroencephalogram (EEG) arousal >1.5 s. RR interval (RRI) in electrocardiogram (ECG) recordings, as well as heart rate variability, was calculated during 60 and 120 s, respectively. Period amplitude analysis (PAA) was applied for RR-interval analysis, and fast Fourier transformation (FFT) was applied to perform HR variability analysis.

Results: Visually scored EEG arousal was significantly associated with an increase in sympathetic index of heart rate, while PTT was associated with a drop in parasympathetic index, after the respiratory events. Patients with mild OSAS presented persistently shorter RRI when compared to patients with UARS. The latter also exhibited a significant decrease in parasympathetic index (High Frequency (HF)) at the termination of a respiratory event.

Conclusion: The HF component was only significantly decreased in patients with UARS, which indicates a predominant involvement of the parasympathetic tone in patients with UARS in comparison to those with OSAS.

Keywords: Heart rate variability; RR interval; Autonomic nervous system; Parasympathetic tone; Pulse transit time; Obstructive sleep apnea syndrome; Upper airway resistance syndrome

1. Introduction

The cardiovascular system is continuously modulated by the interaction between sympathetic and parasympathetic nerves. The activity of these two arms of the autonomic nervous system (ANS) is modified during normal sleep. The type and degree of the modulation is dependent on state [1–6]. During NREM sleep, compared to quiet supine wakefulness, a decrease in sympathetic activity is observed while parasympathetic activity is increased [5,7–10]. However, these overall ANS changes are modified by short lasting electroencephalogram (EEG) events, such as K-complexes or delta bursts [6,11]. The exact relationship between the observation of EEG discharges and changes in the effectors of the ANS, such as heart rate (HR), blood pressure (BP), and pulse transit time (PTT) is also unknown.

ANS changes have been described more frequently in REM sleep, where the tonic and phasic events have been dissociated [8,12], but this pattern may also be observed during slow wave sleep (SWS) [3]. Sleep disorders may disrupt this complex and state/stage-dependent interaction between parasympathetic and sympathetic tone. The disruption can be related to the intensity of abnormal peripheral stimuli [13,14]. ANS final response varies according to the degree of sensory recruitment triggered

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by any abnormal peripheral event that stimulates peripheral receptors, for instance.

One of the roles of the different subcortical relays in the ascending reticular system during sleep is to filter the ascending stimuli, to maintain sleep continuity, and to provide appropriate reflex response to peripheral challenges [15,16]. If subcortical reflexes cannot resolve the peripheral challenge, in case the intensity of the stimuli is too important, there will be a cortical involvement leading to an EEG arousal that will be the first step toward the possibility of providing an active and sometimes voluntary response to peripheral challenges [17–21]. ANS changes during sleep thus may be seen in association with different degrees of central nervous system (CNS) activation, including EEG arousal [22,11]. Peripheral changes during sleep interfere with ANS regulation, and it has been hypothesized that the disturbances of ANS regulation may increase the morbidity seen with sleep disorders [13,23–30]. The relationship between abnormal respiratory events during sleep and ANS changes is still little explored. We sought to evaluate the effects of sleep-disordered breathing on one indicator of ANS modulation, the heart rate during abnormal respiratory events, paying specific attention to presence/absence of EEG arousals or involvement of subcortical activation. To avoid important co-morbidity, we selected a patient population (a) with low frequency of obstructive sleep apnea (OSA) with minimum SaO2 drops, and (b) with upper airway resistance syndrome (UARS). We questioned (a) whether or not at the end of abnormal breathing events, UARS and mild OSAS patients presented similar changes in heart rate, an index of autonomic activation, (b) whether or not the presence of a visual EEG arousal made a difference on the observed heart rate change, and (c) whether or not we could dissociate the role of the sympathetic and parasympathetic components in the heart-rate response observed with the abnormal breathing events seen in these patients.

2. Methods

2.1. Subjects

Twenty patients, 10 with a low number of OSA events per hour of sleep and 10 with UARS, who fulfilled the inclusion and exclusion criteria described below were recruited from the sleep disorders clinic during a three-month period. All subjects signed an informed consent approved by the Institutional Review Board (IRB).

The inclusion criteria were as follows: men and women ranging in age from 18 to 50 years, clinically suspected of sleep-disordered breathing, without morbid obesity (defined as BMI $\geq$35 kg/m^2) with absence of drug or medication intake, absence of other sleep disorders and an Epworth Sleepiness Scale score $\geq$10 [31]. All subjects had a medical and sleep evaluation before entry. UARS was defined as absence of OSA at polysomnography, apnea–hypopnea index (AHI) $<$5 events/h, presence of flow limitation at nasal cannula/pressure transducer curve with flow decrease $<$30% of normal breath, SaO2 measured by pulse-oximetry always above 92%. Patients with UARS had a respiratory disturbance index (RDI) $\geq$5 events/h, and breathing events were not necessarily associated with a drop in SaO2 of 3% or more and/or an EEG arousal.

Table 1
Subject's demographic and sleep data (means$\pm$SD), N=20

	UARS (n=10)	OSAS (n=10)	
BMI	29.3$\pm$5.8	29.6$\pm$5.6	Ns
Age	39.7$\pm$8.6	46.5$\pm$10.0	Ns
TST (min)	340.9$\pm$53	321.0$\pm$70.0	Ns
Sleep efficiency %	76.4$\pm$12.8	76.9$\pm$10.3	Ns
AHI	2.7$\pm$2.1	15.3$\pm$8.1*	P=0.001
RDI	6.9$\pm$1.8	27.3$\pm$6.1*	P=0.001
Mean lowest SaO2	96.9$\pm$0.8	95.5$\pm$2.4	Ns
Stage 1%	15.1$\pm$8.7	15.2$\pm$3.7	Ns
Stage 2%	69.0$\pm$10.3	63.2$\pm$12.1	Ns
SWS %	3.9$\pm$8.3	6.5$\pm$11.4	Ns
REM sleep %	11.9$\pm$5.6	14.0$\pm$4.7	Ns
Sleep latency (min)	21.0$\pm$31.0	13.0$\pm$7.9	Ns
REM latency (min)	91.3$\pm$29.3	89.6$\pm$29.6	Ns
Total number of respiratory events	389	779	

Mann Whitney U-test, ns, non-significant; BMI, body mass index; TST, total sleep time; AHI, apnea–hypopnea index; RDI, respiratory disturbance index; SWS, slow wave sleep; REM, rapid eye movement.

The exclusion criteria were based on a review of the nocturnal polygraphic recording. Subjects with AHI $>$20 events/h, presence of other sleep disorders such as restless legs or periodic limb movement syndrome, baseline SaO2$\geq$93%, and episodes of SaO2 drops below 89%, were excluded from the study. Polysomnograms that presented frequent artifacts on EEG, electrocardiogram (ECG) or PTT signals, or with very long awakenings during sleep were also excluded. An individual not involved in the research analysis performed this exclusion. The final sample of 20 patients (Table 1) derived from an initial group of 53 successive recordings. Presence of a SaO2 drop below 89% during the recording was responsible for exclusion of 32 of the 33 subjects who did not meet criteria. This group of subjects has already been reported as they participated in a study on arousal and PTT [32].

2.2. Polygraphic recording

Patients arrived in the sleep clinic by 19:00 h but went to bed at their usual bedtime. A minimum of 7 h of PSG recording was obtained for all patients. The following sleep variables were collected and stored using amplifiers and pre-amplifiers Grass™ and a dedicated computerized