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Original Article

Heart rate variability and cardiorespiratory coupling in obstructive sleep apnea: elderly compared with young

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ABSTRACT

Introduction: Aging is known to be a major contributing factor to the increased risk of obstructive sleep apnea (OSA). With aging, breathing undergoes significant changes during sleep, increasing the prevalence of apnea events, which affects heart rate variability (HRV) and cardiorespiratory coupling (CRC).
Objectives: To compare HRV and CRC during wakefulness and sleep between young and elderly patients with and without OSA; and to determine whether the presence of OSA in young and elderly patients has a different impact on HRV and CRC during sleep.
Methods: One hundred subjects, 50 young (mean age, 27 ± 9; 20 normal and 30 OSA) and 50 elderly (mean age, 65 ± 7; 20 normal and 30 OSA), underwent polysomnography. Spectral, cross-spectrum, and HRV parameters were analyzed during wakefulness and sleep.
Results: The spectral analysis indicated that age affected HRV, with higher values of low frequency ($P < 0.05$) in elderly subjects during wakefulness and an interaction between the presence of OSA and age. OSA influenced HRV during sleep with lower LF/HF ratios during stage 2 (S2) and rapid eye movement (REM) sleep ($P < 0.05$), with an interaction between the presence of OSA and age in REM sleep. Elderly patients had significantly lower percent tachogram power coherent with respiration (%TPCR) during wakefulness ($P < 0.05$), and OSA led to lower %TPCR during S2.
Conclusions: Age and OSA have an unfavorable impact on HRV, with reduced autonomic modulation during wakefulness, S2, and REM sleep. Age affects CRC during wakefulness and the presence of OSA affects CRC during sleep.

1. Introduction

Obstructive sleep apnea (OSA) is a respiratory disorder characterized by recurrent airflow obstruction caused by total or partial collapse of the upper airways [1,2]. Aging is associated with increased apnea prevalence and is thus known to be a major factor contributing to the risk of OSA [3,4]. Moreover, elderly adults with OSA are at greater risk for cardiovascular disease (i.e. coronary artery disease, congestive heart failure, ischemic disease, and stroke) [5,6].

Cardiac autonomic function can be non-invasively assessed by analyzing the heart rate variability (HRV), which quantifies the changes in beat-to-beat intervals influenced by the combined effects of the sympathetic and parasympathetic nervous systems on the heart rate [7]. Clinical studies have consistently reported that decreased HRV is associated with sleep disorders [8–10]. During sleep, HRV is influenced by direct modulation of vagal efferent activity resulting from baroceptor responses to respiratory blood pressure fluctuations and from mechanical sinus node stretch determined by respiration-related changes in venous return [11].

Respiration undergoes important modifications during sleep and HRV is affected by sleep stage organization and by the presence of apnea events [12]. However, it is not known whether the effects of OSA on cardiac autonomic modulation in elderly subjects are different from those in young subjects, both during wakefulness and

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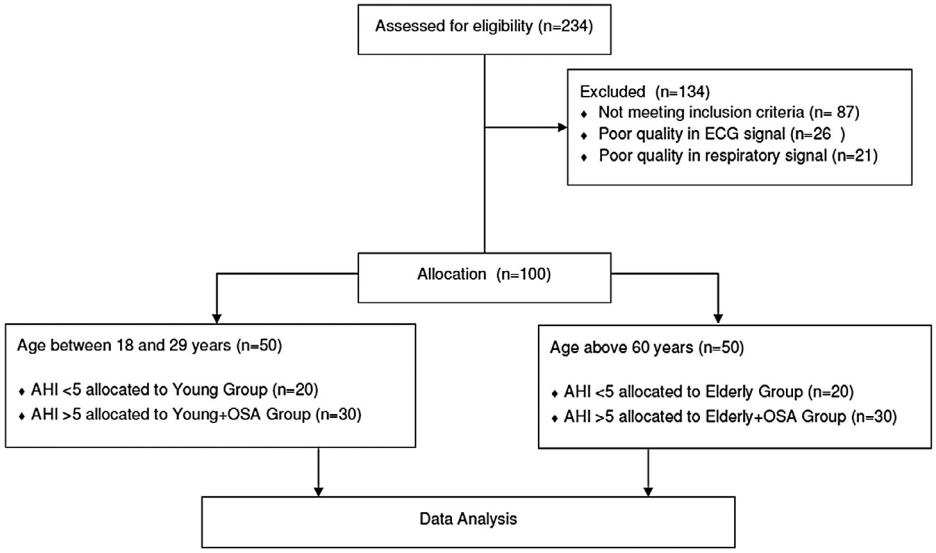

Fig. 1. Experimental protocol. ECG, electrocardiography.

sleep. It is not known whether different effects are likely to be observed during specific sleep stages. Since OSA as it relates to the senescence process is considered a risk factor for cardiac autonomic impairment, we hypothesized that HRV and cardiorespiratory coupling (CRC) would be worse in elderly subjects with OSA.

Therefore, the aim of the study was to contrast HRV and CRC during wakefulness and sleep in young and elderly subjects with OSA. Further, we aimed to determine whether the presence of OSA in young and elderly subjects has a different impact on HRV and CRC during different stages of sleep.

2. Methods

This was a cross-sectional study, by analysis of medical records involving young and elderly patients referred to our sleep medicine clinic between January 2011 and December 2012 for evaluation of excessive daytime somnolence, snoring, and suspected OSA. The study protocol was approved by the Ethics Committee of Federal University of São Carlos (N.401/2010 opinion) and was registered as a clinical trial (RBR-3jbm6d). All participants signed informed consent prior to the polysomnography. The present study was also conducted in full accordance with the Declaration of Helsinki.

2.1. Subjects

The patients completed a questionnaire concerning possible daily or nocturnal symptoms, substance abuse, medication, and medical history. The inclusion criteria in the elderly (aged >60 years) and young (aged 18–29 years) groups were normal electrocardiogram (ECG) during wakefulness and absence of cardiac and respiratory diseases. Exclusion criteria for selection of all subjects were: atrial fibrillation and other cardiac arrhythmias; history of myocardial ischemia, cardiomyopathy or myocardial infarction; cardiac pacemaker; sleep disorders such as periodic limb movement disorder; treatment with antiarrhythmic medications; diabetes and/or uncontrolled hypertension.

Clinically examined elderly patients with an apnea–hypopnea index (AHI) ≥ 5 events/h were assigned to the elderly + OSA group, whereas those with AHI < 5 were assigned to the elderly group. Clinically examined young patients with AHI ≥ 5 were assigned to the young + OSA group and young people with AHI < 5 were assigned to the young group (Fig. 1).

2.2. Signal processing

Nocturnal polysomnography (PSG) recordings were obtained from all subjects using an Icelera Fast-Poli 26i (Homed, São Paulo, Brazil) device and included the monitoring of electroencephalogram, electro-oculogram, oronasal flow by thermistor, transducer nasal pressure, thoracoabdominal movement, ECG, snoring, and body position [13]. A sleep specialist visually scored PSG recordings for sleep stages and apnea events. Total sleep time, number and duration of rapid eye movement (REM) periods, and number and duration of arousals were also measured [14].

Sleep stages, hypopneas, apneas, and arousals were scored using the standard recommended by the American Academy of Sleep Medicine [15,16].

The R peaks were detected on each ECG signal using the Pan–Tompkins algorithm [17]. The respirogram was extracted from each respiration signal by sampling it in correspondence with each R peak identified in the ECG signal [18].

2.3. HRV and CRC analysis

On both the tachogram and the respirogram, segments with 5-min-long portions of the first two complete non-REM (NREM)–REM sleep cycles were carefully checked to avoid arousals, ectopic beats, and artifacts. The more stable segments of sleep stages 2 and 3 and REM sleep were selected. For the wakefulness period, we analyzed a 5 min segment at beginning of the night that was free of ectopic beats and artifacts. Autoregressive (AR) analysis was performed on each tachogram and respiration portion to obtain an AR model to calculate the signal power spectral density, following a method previously described elsewhere [19–21].

In order to analyze the HRV in the frequency domain, spectral components were identified on the HRV signal spectrum in the low frequency (LF, 0.04–0.15 Hz) and in the high frequency (HF, 0.15–0.4 Hz) bands. LF power in normalized units [LF (nu)] and HF power in normalized units [HF (nu)] were also calculated.

The values of the power in the LF and the HF bands and the LF/HF ratio were calculated for each HRV signal portion, whereas only the HF component was considered for the respirogram. A bivariate analysis was conducted on the tachogram and the respirogram portions, in order to obtain the cross-spectrum between them. The coherence between the signals in the HF bands and the