Definition and Importance of Autonomic Arousal in Patients with Sleep Disordered Breathing

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KEYWORDS

• Arousal • Autonomic arousal • Cardiovascular risk • Blood pressure • Heart rate • Hypertension • Obstructive sleep apnea • Portapres

KEY POINTS

- Cardiovascular diseases are often found in patients with obstructive sleep apnea (OSA) because they share common risk factors such as age, gender, and metabolic disorders.
- In general, arousals indicate central nervous activation.
- In patients with sleep disordered breathing, nonphysiologic respiratory-induced arousals are predominant and cause most frequently changes in blood pressure.
- Polysomnography, including continuous blood pressure monitoring, allows insights into the cardiovascular regulation and thus allowing the qualitative and quantitative determination of autonomic arousals.

INTRODUCTION

Obstructive sleep apnea (OSA) is an increasingly common disorder that is strongly linked to cardiovascular diseases and increased mortality.[1–4] One of the most important parameters of the cardiovascular morbidity is the arterial hypertension. In a study by Peppard and colleagues,[5] OSA was a risk factor for hypertension and cardiovascular morbidity. It was reported that 40% of patients with OSA suffer from hypertension. A study on US drivers showed that 20% to 30% of patients with hypertension had OSA.[6] Hla and colleagues[7] found a significant relationship between increased blood pressure in patients with OSA and participants without OSA. The positive treatment effect of CPAP therapy on 24-hour blood pressure profiles of hypertensive patients with OSA proved the direct relation between both disorders.[8–11]

One reason that cardiovascular diseases are often found in patients with OSA is the sharing of common risk factors such as age, gender, and metabolic disorders. In addition, a causative relationship between OSA and cardiovascular diseases like hypertension and heart failure has been demonstrated.[12] Somers and associates[13,14] have argued that, among other factors, oxygen desaturation during an apnea event causes a

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high sympathetic activity when awake. This implies further increases in blood pressure and sympathetic activity during sleep.[13,14] Increased sympathetic activity and an elevated catecholamine level are seen day and night in patients with OSA.[15–17] Another influence exerted is the reduced baroreceptor sensitivity of patients with OSA during wakefulness and sleep.[18,19] Reduced baroreceptor sensitivity induces again an increased cardiovascular risk.[20,21] The arousal occurring after an obstructive apnea also seems to play an important role in blood pressure elevation.[22,23]

In general, arousals indicate a central nervous activation. According to the American Academy of Sleep Medicine recommendations from 2007, they are characterized by rapid electroencephalographic (EEG) frequency changes (alpha, theta) with a duration of 3 to 15 seconds,[24] but also lead to an activation of the autonomous nervous system with changes in heart rate and blood pressure. The terms used for that phenomenon are autonomic activation or autonomic arousal. During sleep, arousal could occur spontaneously as part of physiologic regulation processes, but they also could be induced by nonphysiologic stimuli like obstruction of the upper airways. Consequences of nonphysiologic arousals (>5/h) are fragmented sleep and sympathetic activation during the night as well as impairment of daytime functions. The aim of this study was to investigate the occurrence of autonomic arousal in a group of patients with sleep disordered breathing and to compare the results with a group of healthy volunteers. We wanted to establish the standardized term "autonomic arousal." With the help of visually scored arousal, we have provided a procedural definition of autonomic arousal.

MATERIALS AND METHODS

Subjects

The study protocol was approved by our ethics committee. All subjects gave informed consent. Twenty patients (10 male, 10 female; mean age, 54.4 $\pm$ 11.2 years) with OSA and 24 healthy volunteers (11 male, 13 female; mean age, 51.2 $\pm$ 8.6 years) without any kind of sleep disorders (controls) were studied in the sleep laboratory at the Charité University in Berlin. The controls were matched in age and gender to the patients. All subjects were Caucasian.

Subjects with a hypertonia in anamnesis were considered as hypertensive patients. Patients receiving antihypertensive medication had not tapered their treatment. The subjects with an Apnea/Hypopnea Index (AHI) of greater than 5 per hour were considered to have OSA, the so-called controls had an AHI of less than 5 per hour. Subjects were excluded if they were younger than18 years, had a body mass index (BMI) of greater than 40 kg/m^2, an alcohol or drug abuse disorder, thyroid disorder, chronic pain, neurologic or psychiatric disease, acute or severe chronic pulmonary, cardiac disease, or another severe medical disease. It was also important that the subjects did not travel across time zones or take part in another clinical study within 4 weeks before the start of our study. We excluded patients with OSA and a coexistent periodic limb movement disorder (Periodic Leg Movement Index >5 per hour).

To characterize the subjects we asked for data like body height and weight as well as medical history. Participants with a hypertension in anamnesis were considered hypertensive. A physical examination was performed.

Questionnaires

The standardized questionnaire Short Form (SF)-12, Pittsburgh Sleep Quality Index, Functional Outcomes of Sleep Questionnaire (FOSQ), and the Epworth Sleepiness Scale (ESS) were answered.

The SF-12 is the 1994 developed short version of the SF-36 (Medical Outcome Study Short Form), which detects health-related quality of life by self-assessment of physical and mental components of life quality. The Pittsburgh Sleep Quality Index is an internationally used test scrutinizing the severity of a sleep disorder. The FOSQ is a questionnaire testing the quality of life of patients with sleep disorders. The ESS is an international used method for subjective measurement of daytime sleepiness and consequent impairment.

Study Design

The subjects spent 2 subsequent nights in our sleep laboratory for recording a cardiorespiratory polysomnography (Embla Systems, Wessling, Germany) that included EEG: based on 10/20 system (C3, 01 against A2 and C4, 02 against A1), bilateral electrooculography, submental and tibialis anterior electromyography, electrocardiography, nasal airflow using nasal cannula, pulse oxyhemoglobin saturation (SpO_2) using a pulse oximeter and respiratory effort using chest and abdominal inductance belts. Especially for this study, continuous noninvasive nocturnal blood pressure measurement by Portapres system (Finapres Medical Systems BV by TNO Amsterdam, The Netherlands) was done (**Fig. 1**). Portapres is based on the arterial volume–clamp method and on the physical criteria for unloading the finger arteries.[25] For long-term monitoring of