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Prolonged partial obstruction during sleep is a NREM phenomenon

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ABSTRACT

Objective: Prolonged partial obstruction (PPO) is a common finding in sleep studies. Although not verified, it seems to emerge in deep sleep. We study the effect of PPO on sleep architecture or sleep electroencephalography (EEG) frequency.

Methods: Fifteen OSA patients, 15 PPO + OSA patients and 15 healthy subjects underwent a polysomnography. PPO was detected from Emfit mattress signal. Visual sleep parameters and median NREM sleep frequency of the EEG channels were evaluated.

Results: The amount of deep sleep (N3) did not differ between the PPO + OSA and control groups (medians 11.8% and 13.8%). PPO + OSA-patients' N3 consisted mostly of PPO. PPO + OSA patients had lighter sleep than healthy controls in three brain areas (Fp2-A1, C4-A1, O1-A2, p-values < 0.05).

Conclusion: PPO evolved in NREM sleep and especially in N3 indicating that upper airway obstruction does not always ameliorate in deep sleep but changes the type. Even if PPO + OSA-patients had N3, their NREM sleep was lighter in three EEG locations. This might reflect impaired recovery function of sleep.

1. Introduction

Phenotyping has opened up new ways of evaluating the pathophysiological processes behind sleep disordered breathing (SDB) and addressing the treatment options. Different methods to phenotype obstructive sleep apnoea (OSA) have been presented. For example, cluster analysis has revealed phenotypes associated with position and sleep stages (Joosten et al., 2012).

OSA, assessed using the apnoea-hypopnea index (AHI), is commonly more severe in supine position than in other postures (Cartwright, 1984; Pevernagie and Shepard, 1992; Cartwright et al., 1991). The pressure at which the pharynx collapses (P_{CRIT}) is found to be higher in supine than side position (Boudewyns et al., 2000; Isono et al., 2004; Ong et al., 2011; Penzel et al., 2001), and the higher AHI in supine position may be related to anatomical features (Isono et al., 2002; Ono et al., 2000; Saigusa et al., 2009), although the findings are not consistent (Jan et al., 1994; Walsh et al., 2008; Pevernagie et al., 1995; Martin et al., 1995).

In general, the AHI is higher in rapid eye movement (REM) sleep than in non-REM (NREM) sleep (Cartwright et al., 1991; Oksenberg et al., 2010). In addition, the AHI diminishes in deep sleep (Ratnavadivel et al., 2009). However, the usefulness of the AHI alone to quantify SDB has been criticised because long periods of prolonged partial obstruction without apnoea or hypopnea are common in SDB patients (Anttalainen et al., 2016; Tenhunen et al., 2013). Prolonged partial obstruction causes flow limitation in the nasal pressure signal (Hernandez et al., 2001) and can be assessed quantitatively by measuring oesophageal pressure (see Bao and Guilleminault, 2004). One feasible way to evaluate prolonged partial obstruction is the Emfit mattress sensor. The sleep mattress signal is usually scored into different breathing categories in 3-min epochs. Simply, the mattress signal is divided into three different breathing categories: non-obstructive breathing (NOB), periodic obstructive breathing (POB) that comprises periodic apnoea and hypopnea, and prolonged partial obstruction (PPO).

Based on our preliminary finding, it seems that PPO manifests during NREM sleep and also during deep NREM sleep (Rauhala et al., 2007). The aim of the present study is to clarify the appearance of PPO in the sleep stages. In addition, we evaluate whether PPO has an effect on the sleep architecture and frequency of NREM sleep

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electroencephalography (EEG). Furthermore, we evaluate the impact of sleeping position on PPO.

2. Methods

All patients were referred to the Sleep laboratory of Tampere University Hospital because of possible obstructive sleep apnoea (OSA). The control subjects were healthy volunteers recruited through advertisements. The volunteers received no payment for their participation in the study. Both patients and controls were first interviewed by telephone to make sure they met the eligibility criteria: aged between 20 and 65 years, no (other) sleep disorders, no clinically significant medical disorder (e.g., neurological illness, psychiatric disorder, hypo-/hyperthyroidism and no lung diseases other than currently asymptomatic asthma), no medication affecting the central nervous system and no substance or alcohol abuse. The patients' OSA diagnosis and the controls' healthiness were then confirmed by clinical interview and a diagnostic full-night polysomnography in a sleep laboratory. The OSA diagnosis was based on a clinical picture and subjective complaints of OSA and an AHI of > 10/h. The controls had to be asymptomatic and had an AHI of ≤5/h. The study was approved by the Ethical Committee of the Pirkanmaa Hospital District and all the subjects gave their written informed consent.

Sleep recordings were performed with the Embla N7000 device and Somnologica Studio software (Medcare®, Iceland). The recordings comprised six EEG derivations (Fp1-M2, Fp2-M1, C3-M2, C4-M1, O1-M2, O2-M1), two EOG channels, three electromyogram channels (chin and both legs), airflow measured with a thermistor and a nasal pressure transducer, thoracic and abdominal respiratory movements, pulse oximetry and position. In addition, an Emfit mattress (32 cm × 62 cm × 0.4 cm) was placed under a normal foam mattress below the thoracic area of the sleeping subject. The unfiltered Emfit signal was acquired directly as a separate trace in the Somnologica software. A sampling rate of 2 Hz was used for the pulse oximeter (SpO_2 and pulse rate), 10 Hz for respiratory movements and 200 Hz for all the other signals.

2.1. Visual analysis

Polysomnographies were classified into sleep stages according to standard criteria (Iber et al., 2007). The AHI was calculated as the number of obstructive apnoea and hypopnea per hour of sleep (Berry et al., 2012). In addition to total AHI, the AHI was calculated separately for supine and non-supine positions and for NREM sleep and REM sleep. Arousals were scored according to the criteria of the American Sleep Disorders Association (AASM, 1992).

The Emfit signal was visually scored in 3-min epochs into breathing categories as described in our previous work (Tenhunen et al., 2013). The mattress breathing categories used were non-obstructive breathing (NOB), obstructive periodic breathing (POB), and prolonged partial obstruction (PPO). PPO in Emfit signal is comprised of continuous respiratory-induced spikes, which are known to appear with increasing breathing effort (Fig. 1, Kirjavainen et al., 1996).The Emfit signal was scored visually from a lights off-event to the final awakening by two independent scorers with a scoring agreement of 87.8% (median, range 76.9% to 95.7%). The two independent scorers formed the consensus scoring used in the analyses. The percentage of time (referred to as TST) for NOB, POB and PPO were calculated. In addition, the number and the length of PPO-periods were calculated. Due to the epoch scoring, the minimum length of a PPO-period was 3 min.

In total, 45 OSA patients and 20 control subjects took part in the study. To evaluate the effect of prolonged partial obstruction (PPO) on sleep architecture, we formed three age-matched groups based on the AHI and amount of PPO-pattern. The OSA group had to have an AHI > 10, and time with PPO (as percentage of total sleep time) < 5%. The OSA + PPO group had to have an AHI > 10 and PPO > 15%. The subjects in the control group had to have an AHI < 5/h and PPO < 5%. Fifteen control subjects and 30 patients fulfilled the inclusion criteria, and each group comprised 15 male subjects.

2.2. Calculation of EEG median frequency

Mean frequency values were computed from each of the six EEG channels at 1-s time resolution by applying the method described in our previous work (Huupponen et al., 2009; Huupponen et al., 2011). This provided six overnight mean frequency curves with values ranging from 0.5 Hz to 30 Hz. The median of the mean frequency values during the NREM sleep time was extracted from each EEG channel.

2.3. Statistical analysis

Statistical analyses were performed with IBM® SPSS® Statistics version 22 (IBM corp.) with non-parametric tests because some of the parameters were not normally distributed and the sample sizes were small. The Friedman test and Kruskall-Wallis test were used to compare the multiple dependent and independent variables, respectively. The post hoc analyses were made by using the Wilcoxon and Mann-Whitney *U* tests and the comparisons were Bonferroni corrected. The probability level of 5% was considered to be significant in the statistical tests.

3. Results

The demographic data and sleep parameters of the subject groups are presented in Table 1. The groups did not differ by age, but the patients in the PPO + OSA group and in the OSA group than the control subjects. Both patient groups presented more daytime sleepiness than the controls as assessed by Epworth Sleepiness Scale (ESS).

There were no statistical differences between the groups in the sleep efficiency (SEI) or in the amount of N1 or REM sleep. The amount of deep sleep (N3) was diminished in the OSA group when compared with the other groups, and N2 sleep was more abundant in the OSA group than in the control group.

Median NREM EEG frequency (in Hz) was separately calculated for each EEG channel (Fig. 2). The EEG frequency was significantly higher in the OSA group than in the PPO + OSA group and the controls in all EEG-derivations. In addition, EEG frequency was higher in the PPO + OSA group than the controls frontopolarly and centrally in the right hemisphere (Fp2, C4) and occipitally in the left hemisphere (O1).

3.1. AHI, sleep stages and position

As expected, all the calculated AHIs as well as the desaturation index (ODI4) were lower in the control group than in the patient groups (Table 1). In the control group, the AHI in REM sleep (AHI REM) was higher when compared with the AHI in NREM sleep (AHI NREM, Table 1, p-value 0.005). The median AHI REM seems higher than the AHI NREM in the PPO + OSA group, whereas in the OSA group the median AHI NREM seems higher than the AHI REM. The AHI REM/AHI NREM comparisons within these groups did not, however, reach statistical significance.

In the PPO + OSA group, the AHI in supine position was higher compared with the AHI in non-supine position (p = 0.017). No significant differences were found in the OSA group or control group (p-values 0.128 and 0.363, respectively).

3.2. Mattress breathing categories with the effect of position

The control group had more non-obstructive breathing (NOB) than the two patient groups, whereas no statistical difference in NOB% was obtained between the PPO + OSA and OSA groups (Table 1). Both patient groups had more periodic obstructive breathing (POB) than the control group. Due to the inclusion criteria, the PPO + OSA group had