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Cardiovascular Regulation in Different Sleep Stages in the Obstructive Sleep Apnea Syndrome

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Introduction

Sleep is a complex phenomenon whose internal structure is currently described as a sequence of sleep stages. While this description is predominantly based on features of the electroencephalogram (EEG), other systems such as the cardiovascular one are clearly also affected by this structure.

Epidemiological studies confirm a causal relation between sleep disorders and a number of cardiovascular diseases [1]. An important of such disorders is the obstructive sleep apnea syndrome (OSAS), which means a patient has more than 15 respiratory events per hour, respectively an apnea hypopnea index (AHI) of > 15.

A powerful tool for the assessment of the resulting changes in autonomic control and cardiovascular state has been developed in the last 20 years with the analysis of heart rate variability (HRV) and blood pressure variability (BPV) [2, 3]. In this article the diagnostic relevance in parameters of HRV and BPV for detecting and evaluating pathological changes in cardiovascular regulation should be exemplarily demonstrated.

Materials and Methods

Data

This study investigates cardiovascular regulation in different sleep stages on data obtained through polysomnography of 38 subjects, 28 of which suffered from OSAS. These subjects where measured thrice: One diagnostic night (labeled DD) followed by a consecutive treatment night using continuous positive airway pressure (CPAP) and a follow-up night (labeled CPAP) after three month of treatment.

In order to assess the relationship to elevated blood pressure (BP), we seperatly consider the 18 normotensive (NT) and 10 hypertensive (HT) patients. Hypertension was defined by an office systolic BP (SBP) higher than $140\,\mathrm{mmHg}$ or diastolic BP (DBP) higher than $90\,\mathrm{mmHg}$. A group of 10 normotensive and sleep healthy persons were examined in a polysomnographic diagnostic night as controls (C).

Measures

To investigate the cardiovascular regulation non-invasively we use statistical time-domain and frequency-domain measures as proposed by the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology [2]. To allow statistical measures of variability that require stationary conditions in the underlying process, only the first 5 minutes of the largest undisturbed period of each sleep stage is considered for each subject.

The time domain parameters of HRV, BPV as well as baroreflex sensitivity (BRS) are used to characterize the autonomous regulation in different sleep stages and quantify the impacts of OSAS and associated hypertension on the vegetative control. Parameters in the frequency domain of HRV are used to distinguish sources of influence.

The BRS, which has proven to be an important marker for BP-HRV interaction, is defined as the reflectory change of beat-to-beat intervals (BBIs) related to increasing or decreasing SBP. The sequence method [4] provides an estimate of BRS.

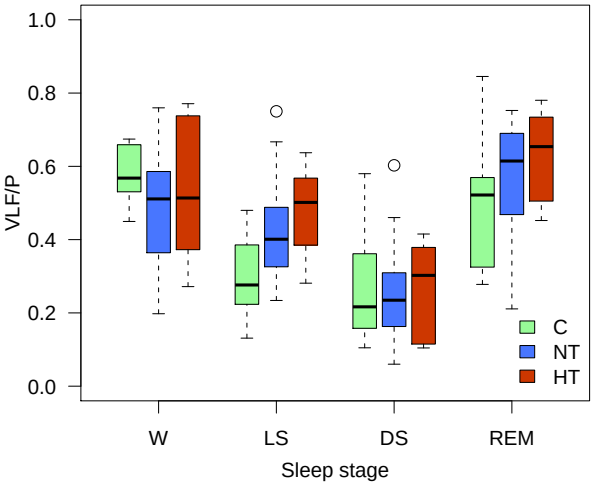
Statistical Analysis

Each parameter is seperately compared using a Kruskal-Wallis test for each group and sleep stage to detect sleep-stage-dependent changes in cardiovascular short term regulation. A Mann-Whitney test is applied to significant parameters to reveal the amount of contribution of the different sleep-stages. The influence of CPAP on parameters of HRV and BPV is evaluated by means of a Mann-Whitney test. The parameters are compared between the DD and CPAP nights for each sleep stage in groups NT and HT.

Results

Our study shows that several HRV and BPV parameters adequatly reflect complex sleep dynamics, demonstrating appreciable differences between sleep stages. Due to limits on available space and for reasons of comprehensibility only a limited set of the most significant parameters are presented here. Further results are available in [5].

Figure 1: Normalized power of the very low power spectral band (0.0033–0.04 Hz) for control subjects (C) as well als normotensive (NT) and hypertensive (NT) patients in all sleep stages during the diagnostic night. Kruskal-Wallis test for differences between the sleep stages is significant for each group (C and NT: $p < 0.001$, HT: $p < 0.01$).



Significant differences between the sleep stanges in all three goups are identifiable in the HRV parameter of the power in frequencies ≤ 0.04 Hz (VLF) normalized to the full spectral power (VLF/P) in BBI (C and NT: $p < 0.001$, HT: $p < 0.01$, cf. Figure 1). Mann-Whitney tests allow a more detailed comparison and reveal significantly changed values between: nocturnal epochs of awake stage (W) and light sleep (LS) (C: $p < 0.001$), W and deep sleep (DS) (C: $p < 0.01$, NT: $p < 0.01$, HT: $p < 0.05$), LS and DS (NT: $p < 0.01$, HT: $p < 0.05$), LS and rapid eye movement sleep (REM) (C: $p < 0.01$, NT: $p < 0.01$) as well as DS and REM (C: $p < 0.05$, NT: $p < 0.01$), HT: $p < 0.01$).

Evaluating the effects of CPAP on OSAS patients, BRS shows significant increases during non-REM sleep stages. Mann-Whitney tests reveal this improvement in LS (NT: 9.26 ± 2.6 vs. 12.6 ± 3.9 ms/mmHg, $p = 0.007$) and DS (NT: 7.67 ± 3.2 vs. 11.4 ± 3.8 ms/mmHg, $p = 0.007$; HT: 6.87 ± 1.7 vs. 10.7 ± 3.8 ms/mmHg, $p = 0.02$).

Discussion and Conclusions

The presented results demonstrate the importance of HRV and BPV analysis in the investigation of the autonomous nervous system. The difference in regulation in the different sleep stages are clearly shown. Additionally a positive effect of the three month CPAP therapy can be quantified using BRS.

The most pronounced changes in regulation during different sleep stages can be identified between DS and REM (cf. Figure 1). The substantial decrease in VLF/P of HRV apparent during non-REM sleep, particularly DS, may be presumed to arise through the depressed metabolic activity [6, 7]. This agrees with results of a study by Schumann et al. [8], which showed similar effects by means of detrended fluctuation analysis in that the long term correlations decrease in non-REM sleep in healthy subjects.

Both groups of OSAS patients (NT and HT) show a clear reduction of this effect where no differences between W and LS are visible. These changes are attributed to effects due to OSAS as they disappear in the follow-up measurement after CPAP treatment.

The increase of BRS, as a measure of the coupling between heart rate (HR) and BP, in all patients after three month of CPAP treatment towards those values found in controls, indicates a regression of a previous regulatory dysfunction. This finding confirms previous findings of CPAP-based improvement of BRS [9].

The small number of OSAS patients and controls as well as the non-ubiquity of undisturbed epochs for each sleep phase are a limitation of this study. No repeated measure tests could be applied as a result. To confirm our findings, prospective studies with larger patient and control groups are needed.

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