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SYNCHRONIZATION IN ELECTRICAL ACTIVITY SIGNALS OF THE BRAIN AND CARDIOVASCULAR SYSTEM DURING NOCTURNAL SLEEP IN OBSTRUCTIVE SLEEP APNEA

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Abstract

The changes in the synchronization based on wavelet bicoherence are studied in the case of real EEG and ECG signals recorded during nocturnal sleep in patients with obstructive apnea and healthy volunteers. The study involved 72 subjects. The study protocol was approved by the Ethics Committee of the Saratov State Medical University, Ministry of Health of the Russian Federation. The synchronization between the EEG and ECG signals in group of patients with obstructive sleep anoea demonstated a significant increase in the band $[0.7; 1.8]$ Hz against the background of relatively healthy participants. The maximum number of reliable differences between the groups under consideration was recorded in the deep N3 stage of sleep in the EEG channels F3, Fz, C3, P3, Pz, O1, T3. The report was presented at PhysCon 2024 "Features of ECG and EEG Signal Synchronization in Patients with Obstructive Sleep Apnea Syndrome during Nocturnal Sleep".

Key words

heart rate, numerical processing, ECG, EEG, wavelet bicoherence, synchronization, apnoe

1 Introduction

Synchronization of chaotic oscillations is a fundamental universal natural phenomenon observed in a wide class of technical and natural objects [Pikovsky et al., 2001]. Interest in this phenomenon is connected both with the theoretical importance of the research [Boccaletti et al., 2002; Elsakov et al., 2023; Smirnova et al., 2022], and a wide range of applied aspects [Andrievsky and Boikov, 2021; Sharma and Lather, 2024], for example, in neurophysiological problems [Zhuravlev et al., 2023; Plotnikov, 2021]. In this paper, the object of study is the activity of the body and its changes in obstructive sleep apnea. Obstructive sleep apnea is the most common breathing disorder during sleep, characterized by repeated episodes of cessation of breathing or a significant decrease in respiratory flow while maintaining respiratory efforts.

Intermittent hypoxemia accompanying apnea leads to activation of proinflammatory cytokines and endothelial dysfunction, and intrathoracic pressure fluctuations and sympathetic hyperactivation increase pressure load [Pinto et al., 2016]. Thus, the development of some cardiovascular diseases is directly associated with obstructive apnea, for example: arterial hypertension, heart rhythm disturbances, chronic heart failure [Muxfeldt et al., 2014].

Routine clinical studies typically use cardiorespiratory monitoring without EEG monitoring to measure obstructive sleep apnea (OSA). However, in neuroscience, changes in brain activity in OSA disorders are often considered [Selskii et al., 2023; Runnova et al., 2024]. A

recent study by *Rajeswari and Jagannath* showed that the right hemisphere of the study participants showed a strong positive association with sleep apnea [Rajeswari and Jagannath, 2024]. Early *Luo et al.* [Luo et al., 2015] found a significant trend towards right hemisphere changes in OSA, which was confirmed by other methods such as functional MRI and positron emission tomography. *Horovitz et al.* [Horovitz et al., 2008] observed disruption of connections for the prefrontal cortex in slow-wave sleep.

In this paper, we consider synchronization between electrophysiological signals of the brain and cardiovascular system, i. e. in electroencephalographic (EEG) and electrocardiological (ECG) signals recorded during the night sleep of OSA patients and practically healthy volunteers. These signals represent time series of complex oscillatory processes, the dynamics of which cannot be described, in general, by a phase-coherent attractor. In this regard, the phenomenon of synchronization between that could be considered based on the wavelet bicoherence approach, estimated complex numerical characteristics of a wide spectrum signals.

2 Materials and Methods

2.1 Materials

72 subjects participated in our work. The study protocol was approved by the Ethics Committee of the Saratov State Medical University of the Ministry of Health of Russia, and all experimental procedures were performed in accordance with the ethical standards laid down in the Declaration of Helsinki. All subjects were informed about the experimental procedures in details and have signed standard consent forms. Polysomnographic sleep studies were performed for each participant. The overnight sleep study included recording of a full "10–20" array EEG, electrocardiogram, photoplethysmogram, respiratory efforts of the chest and abdomen, an electromyogram of the lower jaw and lower limbs, and oculograms. Patients were divided into two groups depending on the apnea-hypopnea index (AHI), which determines the severity of OSA: AHI > 15 episodes per hour (ep/h) (main group, $n = 39$, including 28 men, median AHI 44.15, median age 47), $0 \leq$ AHI ≤ 15 ep/h (control group, $n = 33$, including 12 men, median AHI 2, median age 28).

Sleep recordings were divided into stages and phases in a standard manner, with a hypnogram constructed for each patient. Hypnograms, as well as electroencephalography and electrocardiography signals of the study participants, were used for further analysis.

2.2 Methods

We used the wavelet bicoherence to estimate the strength of the connectivity between EEG and ECG channels. The wavelet bicoherence has proved as a very powerful tool for the quantification of the interactions between biomedical signals on various oscillatory scales [Schiecke et al., 2015], including brain activity [Makarov et al., 2018; Le Van Quyen et al., 2001; Sakkalis, 2011].

The complex valued wavelet coefficients $W_i(f, t_0)$ for each EEG channel and ECG signal $x_i(t)$ was calculated as:

$$W_i(f,t_0) = \sqrt{f} \cdot \int_{t_0-4/f}^{t_0+4/f} x_i(t) \cdot \psi^* (f, t-t_0) \cdot dt, \quad (1)$$

where $i = 1, ..., 19$ was the number of considered EEG channel and $i = 20$ corresponded ECG recording, t_0 was specified the wavelet location on the time axis, "*" denoted the complex conjugate, and $\psi(f,t)$ was the mother wavelet function. We used the standard Morlet wavelet, which was often employed for processing of biological signals [Pavlov et al., 2012; Sitnikova et al., 2014]. To measure the degree of coherence between two signals, $x_{1...19}(t)$ and $x_{20}(t)$, we used the corresponding complex valued wavelet coefficients $W_{1...19}(f,t) = a_{1...19} + \imath b_{1...19}$ and $W_20(f,t) = a_{20} + \imath b_{20}$.

Wavelet bicoherence, $WB_{1...19,20}(f,t)$, was estimated based on the mutual wavelet spectrum $W_{i,j}(f,t)$ of the signals $x_{1...19}(t)$ and $x_{20}(t)$. Similarly to [Makarov et al., 2018; Bandrivskyy et al., 2004], the coefficients $Re[WB_{1...19,20}(f,t)]$ and $Im[WB_{1...19,20}(f,t)]$, presented as real and imaginary parts of mutual wavelet spectrum, were calculated as:

$$Re[WB_{1...19,20}(f,t)] = \frac{a_{1...19}(f,t) \cdot a_{20}(f,t) + b_{1...19}(f,t) \cdot b_{20}(f,t)}{\sqrt{a^2_{1...19}(f,t) + b^2_{1...19}(f,t)} \times \sqrt{a^2_{20}(f,t) + b^2_{20}(f,t)}}$$

and

$$Im[WB_{1...19,20}(f,t)] = \frac{b_{1...19}(f,t) \cdot a_{20}(f,t) - a_{1...19}(f,t) \cdot b_{20}(f,t)}{\sqrt{a^2_{1...19}(f,t) + b^2_{1...19}(f,t)} \times \sqrt{a^2_{20}(f,t) + b^2_{20}(f,t)}}$$

Thus, the synchronization value of each EEG and ECG channels, $x_{1...19}(t)$ and $x_20(t)$, at frequency f was calculated as follows:

$$WB_{1...19,20}(f,t) = \sqrt{(Re[WB_{1...19,20}(f,t)])^2 + (Im[WB_{1...19,20}(f,t)])^2}. \quad (2)$$

With wavelet bicoherence, $WB_{1...19,20}(f,t) = 1$, the signals $x_{1...19}(t)$ and $x_{20}(t)$ were completely synchronous for time t in frequency f. Conversely, in the case of zero bicoherence, $WB_{1...19,20}(f,t) = 0$, the signals exhibited a fully asynchronous mode. Accordingly, the value of $WB_{1...19,20}(f,t)$, changing within the given boundary values $[0; 1]$, provided complete information

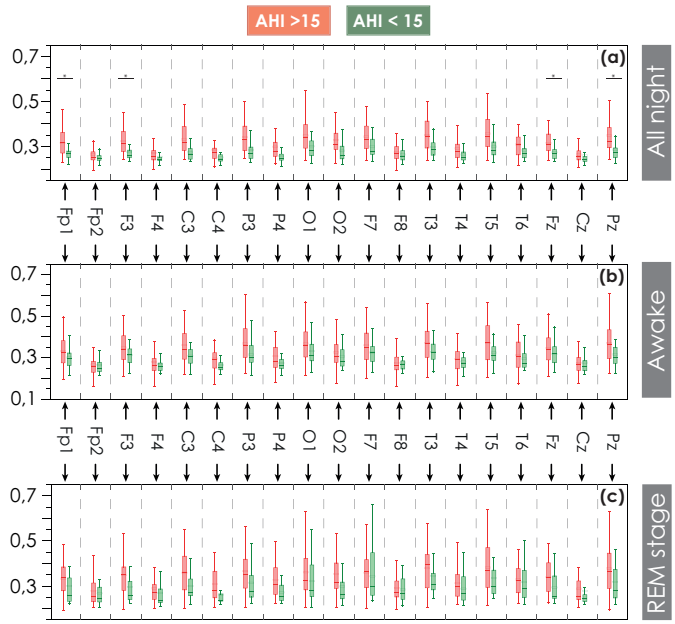

Figure 1. Distributions of connectivity strength $\langle WB \rangle_{I,II}$ between each EEG and ECG signals in groups practically healthy (green) and OSA – patients (red). (a), (b) and (c) – Estimations $\langle WB \rangle_{I,II}$ are made for the entire duration of the night, for the time intervals of awakenings and REM sleep, respectively. For each diagram, the names of the EEG channels are given in accordance with the standard arrangement of "10 – 20". The diagrams depict the following statistical characteristics of numerical indicators: the first and the third quartiles (25 – 75 %, inside the box); the median and the mean (transverse line and point inside the box, respectively); 1.5 interquartile ranges (shown by whiskers); and outliers represented by asterisks

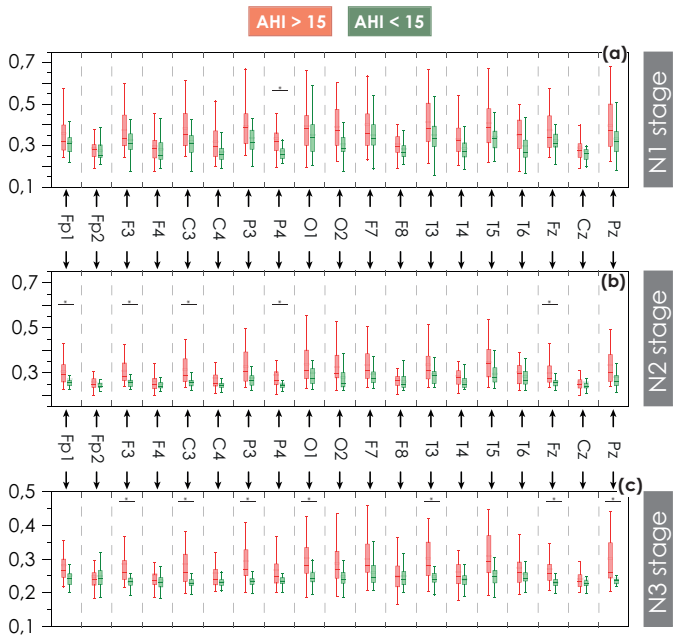

Figure 2. Distributions of connectivity strength $\langle WB \rangle_{I,II}$ between each EEG and ECG signals in groups practically healthy (green) and OSA – patients (red). (a), (b) and (c) – Estimations $\langle WB \rangle_{I,II}$ are made in N1, N2 and N3 stages, respectively. All designations are similar to Figure 1

about the connectivity of EEG and ECG signals on the time–frequency plane $(f; t)$.

We considered integral bicoherence, calculated between each EEG and ECG signals in frequency band, $\Delta f\,[0,7; 1,8]$, Hz, as:

$$WB^{\Delta f}_{1\ldots19,20}(f,t) = \frac{1}{1.1}\int_{0.7}^{1.8} WB_{1\ldots19,20}(f,t)\cdot df. \tag{3}$$

The band $[0,7; 1,8]$ was chosen due to the ECG dynamics, in which the main rhythm is observed near 1 Hz and is determined by the heart rate. In band Δf the time dependence of the value $WB^{\Delta f}_{1\ldots19,20}(f,t)$ was calculated for each EEG channel in every moment of the night recording.

Next, statistical processing of the wavelet bicoherence assessment results for polysomnographic recordings was performed. First of all, averaging was performed over the entire duration of the PSG recording and for each sleep stage or phase. Thus, each EEG channel of each participant in the study was characterized by 6 points – the WB synchronization measure averaged over the entire night recording (All night), over periods of night awakenings (Awake), over periods of rapid eye movement (REM), and for each stage of slow sleep (N1, N2, N3 stages). Secondly, the obtained results of $\langle WB \rangle_{I,II}$ assessment were averaged for two groups of study participants — practically healthy volunteers and patients with moderate and severe sleep apnea. As a result, diagrams were constructed, shown in Figures 1 and 2, demonstrating the main ranges of the considered values in each group, the median, and the spread of values. To compare quantitative data, the Mann-Whitney U test for independent samples was used. Results with p-values ≤ 0.005 were considered statistically significant. Statistical data processing was performed using STATISTICA version 10.0 for Windows (StatSoft Inc., Tulsa, Oklahoma, USA).

3 Results

The results of statistical evaluations of wavelet bicoherence $\langle WB \rangle_{I,II}$ in the groups of healthy study participants and OSA patients are shown in Figures 1 and 2. These results reflect the relationship between ECG and EEG in the band $[0.7; 1.8]$ Hz, describing the main dynamics of the heart rate. These characteristics were averaged both over the entire night (Fig. 1 (a)), and for various stages or phases, standardly identified on nocturnal sleep hypnograms.

Analysis of synchronization changes throughout the entire duration of the night, without dividing into differ-

ent stages and phases of sleep, demonstrates a general increase in the synchronization level for OSA patients (red diagrams in (Fig. 1 (a)). However, the differences become sufficiently reliable ($p < 0.005$) only when considering the assessments performed for the EEG recorded in the central occipital channel Pz and the frontal channels Fp1, Fz, F3.

Consideration of the patient's sleep, divided into stages and phases, makes the picture of synchronization more multifaceted. First of all, we note that the state of wakefulness and paradoxical sleep does not demonstrate significant or even pronounced differences in the assessments of synchronization of ECG – EEG signals in the band under consideration.

Further, the analysis of the stages of slow-wave sleep demonstrates a more interesting pattern of synchronization between the ECG and EEG in the frequency band under consideration. For the N1 sleep stage, significant differences between the synchronization measure in the practically healthy and OSA-patients groups are observed only for the EEG channel P4. With the deepening of sleep and the transition to stage N2, reliable differences are observed in the channels Fp1, F3, Fz, C3 and P4. When considering the slowest wave sleep, namely stage N3, reliable differences exist in the maximum number of EEG channels, namely F3, Fz, C3, P3, Pz, O1, T3.

4 Discussion

The considered pattern of synchronization between the channels of ECG and EEG activity at the fundamental heart rate demonstrates clear differences between patients with obstructive sleep apnea and healthy participants. In general, these differences are concentrated in the left hemisphere of the EEG, as well as the central channels. The only exception is the right channel P4, in which synchronization significantly increases in OSA patients during light sleep N1 and N2. The results of maximum changes in EEG/ECG synchronization, concentrated in the area of slow-wave sleep of patients, are in good agreement with the classical results of*Horovitz et al.* [Horovitz et al., 2008].

The differences in synchronization measures are greatest at the deepest stage of sleep, which may be associated with disturbances in normal recovery processes caused by the patients' underlying disease. As shown in [Fultz et al., 2019; Hablitz et al., 2019; Pavlov et al., 2020; Semyachkina-Glushkovskaya et al., 2018], changes in oscillatory characteristics of electroencephalography accompany the restorative processes of night sleep, correlated with variations in the permeability of the blood-brain barrier (BBB). In our work , higher changes in the degree of slow-wave synchronization between ECG and EEG signals are concentrated precisely in the area of slow-wave deep sleep, which is today associated with restorative processes, including those associated with the cleansing processes of the brain, expressed in an increase in the permeability of the BBB [Semyachkina-Glushkovskaya et al., 2017]. In addition, as shown in [Runnova et al., 2021], structural changes in the EEG during effects on the BBB permeability are most pronounced in the low-frequency region close to the band studied in this work. Thus, changes in the interaction of EEG and ECG activity during respiratory disorders may have a common underlying mechanism in changing the electrical activity of the brain during BBB disorders. In addition, there is some evidence that slow-wave activity modulates high-frequency gamma activity in the cerebral cortex, as shown for mathematical modeling of the FitzHugh-Nagumo network [Sevasteeva et al., 2021].

5 Conclusion

The paper considers changes in the synchronization measure estimated based on wavelet bicoherence for real EEG and ECG signals. EEG and ECG signals were recorded during night sleep of patients with apnea and healthy volunteers. Seventy two subjects participated in our work. The study protocol was approved by the Ethics Committee of the Saratov State Medical University of the Ministry of Health of Russia. The study results demonstrate statistically significant differences between the groups under consideration. The synchronization between the EEG and ECG signals in group of patients with obstructive sleep anoea demonstated a significant increase in the band $[0.7; 1.8]$ Hz against the background of relatively healthy participants. These differences are observed both in the assessments of the entire night recording and in the assessments of the N1, N2, N3 stages of slow sleep. For the REM sleep phase and states of awakening, the groups do not show reliable differences in the assessments of EEG/ECG synchronization. The maximum number of reliable differences between the groups under consideration was recorded during the deep N3 stage of sleep in the EEG channels F3, Fz, C3, P3, Pz, O1, T3.

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