Eur. Phys. J. Spec. Top. (2024) 233:457–462
https://doi.org/10.1140/epjs/s11734-024-01165-8

THE EUROPEAN PHYSICAL JOURNAL SPECIAL TOPICS

Editorial

Editorial on the special issue on neuro-sleep as a complex system

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Published online 23 April 2024

1 Introduction

Sleep is an integral part of our life. During sleep, we not only restore our energy spent during the day, but it is also the time for the formation of new synaptic contacts, cleansing brain tissue of toxins and metabolites, and active cell growth. Recent discoveries have established that sleep is an important informative platform for the development of new technologies for the treatment of brain diseases [1–6]. The study of sleep patterns has become a tool for creating new systemic markers of cerebral small vessel diseases, including Alzheimer's disease and brain pathologies associated with impaired permeability of the blood–brain barrier (BBB) [7]. In new scientific concept, neuro-sleep is considered as a complex system, which is studied with the help of interdisciplinary approaches [7, 8]. As a result of this revolutionary step, pioneering technologies for assessing BBB only by the EEG parameters and smart sleep portable gadgets for the stimulation of lymphatic removal of toxins from the brain are being created [9, 10].

This European Physical Journal Special Topics is a collection of papers highlighting new trends in the study of neuro-sleep as a complex system using multi-disciplinary methods, modeling, and machine learning approaches as well as innovative technologies for therapy of brain diseases during sleep.

(A) Methods for nonlinear signal analysis

Two papers by Guyo et al. [11] and by Pavlov and Semyachkina-Glushkovskaya [12] consider how detrended fluctuation analysis and its extensions provide new information about the current physiological state using electrocorticograms (EEG). Based on this information, analysis of physiological experiments can be performed more thoroughly than with a single diagnostic marker, such as the scaling exponent of the conventional approach dealing with fluctuations in the signal profile. Local fluctuations can vary significantly for nonstationarity data and their statistical analysis improves the detection of distinctions between physiological states. Several applications of extended fluctuation analysis to EEG signals are reported, namely in cases of anesthesia and sleep deprivation. It is shown that the method's performance is scale dependent, and the maximum differences between conditions quantified by conventional and extended fluctuation analysis can be associated with distinct scale ranges. Due to this, statistical analysis of local fluctuations in the signal profile becomes useful for the development of diagnostically significant markers of the system state.

The work by Drapkina et al. [13] analyzed the neural correlates of motor imagery at the level of brain functional networks using EEG. The authors explored the correlation between the latency of motor imagery and the characteristics of brain functional networks in the alpha and beta frequency ranges. The identified nodes hold promise as potential targets for non-invasive brain stimulation techniques such as transcranial magnetic stimulation or transcranial direct current stimulation. Stimulating these areas may enhance motor imagination ability

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and facilitate the rehabilitation process, especially for stroke patients with severe motor impairment. The study by Kurkin, Chepurova et al. [14] provided comparative assessment of source activity in both elderly and young adults across distinct laterality aspects of the motor task. It unearthed a noteworthy correlation between source power within the theta frequency range and the subjects' age, corroborating existing reference studies and thereby shedding newfound light upon the latent neural mechanisms at play. The study by Kurkin, Khorev et al. [15] investigated the distinct neural underpinnings of discriminative touch, affective touch (specifically the C tactile system), and knismesis. The authors examined the patterns of brain connectivity associated with fast, slow, and ultralight touches. The findings revealed significant differences in functional connectivity patterns between these touch conditions, with the majority of variations occurring in the theta frequency range. The obtained results shed light on the interplay between different touch submodalities and their distinctive processing in the brain, contributing to a comprehensive understanding of tactile perception. This research bridges a critical gap in our knowledge of the neural mechanisms underlying tactile perception and its role in shaping our perception of the world.

The articles of Zhuravlev et al. [16], Ulyanov et al. [17] and Runnova et al. [18, 19] are focused on the study of the EEG-changes associated with various pathological states using the nonlinear dynamics methods and complex systems analysis. Zhuravlev et al. [16] demonstrate the EEG markers of stress caused by orthodontic disease that was evaluated by a new method of frequency patterns for analysis, which revealed characteristic biomarkers in the electrical activity of the brain corresponding to the severity of orthodontic injuries. Ulyanov et al. [17] revealed the EEG-markers of attention in different age groups of patients with obstructive sleep apnea (OSA) using a modified method of recurrence analysis. Authors clearly identify the maximum differences between healthy volunteers and OSA patients in the area of high-frequency activity during the rapid eye moved (REM) sleep. Runnova et al. [18] propose the quantitative EEG characteristics of the patterns in OSA patients demonstrating different clusters in the density estimation space of the number and duration distributions of oscillatory patterns for high-frequency bands. In other article, Runnova et al. [19] clarify the EEG-patterns typical for microsleep that accompanies the monotonous solving of simple cognitive tasks. They estimate variabilities degree of different scenarios for controlling monotony in various population groups, differing in their social status, and/or characteristics of attention and other cognitive functions, can lead to interesting findings in the field of establishing different scenarios for controlling monotony.

(B) Mathematical models of brain electrical activity and neural networks

Kurbako et al. [20] and Ishbulatov [21] et al. present two models to investigate the human cardiovascular system and to test the algorithms for the analysis of real cardiovascular data. The models were designed using two very different approaches, and have different advantages. The first model does not consider the structure of the cardiovascular system, but provides quantitative simulation of the shape and spectral properties of real electrocardiogram and photoplethysmogram signals and was used to test and tune an algorithm for estimation of a promising health index, based on the phase dynamics analysis. The second model puts emphasis on simulation of the structure of the real cardiovascular system and respiratory system, both are physiologically linked and are affected by the central nervous system. The model can simulate various conditions, including sleep, and offers signals inaccessible in human studies, which can be analyzed to better understand the experimental results. Litvinenko et al. [22] present a model-theoretical study of the dynamics of sleep–wake switching with the participation of cortisol. The authors show that cortisol fluctuations can account for up to 15% of the total level of neural activity without critical deviation from the normal course of processes. These results are an important tool for the study of dynamic effects of humoral factors on sleep pattern and quality.

(C) Analysis of sleeping brain function

In a paper by Dorokhov et al. [23], the authors detect the EEG changes during performance of monotonous bimanual psychomotor test. They attempt that spontaneous awakenings from sleep stage 2 are accompanied by high-amplitude slow oscillations (SO) in the EEG, including K-complexes and other single slow waves. Their results shown that the hypnogram configuration, that SOs occur much more frequently just before awakenings (SO^1, 12 or less seconds before awakening) than within sleep episodes (SO^2). Some SOs were recorded after a behavioral awakening (SO^3), had never been shown before. These SO^1 were accompanied by sleepy spindles and alpha rhythm and differed in configuration from background SO^2 having a more simple pattern. A hypothesis is proposed that SO^1 occurred just before resuming performance are associated with the unconscious episodic memory that triggers awakening followed by recovery of conscious activity performed prior to falling asleep.

In the paper published by Cheremushkin et al. [24], the psychomotor test was used to study neural correlates of the efficiency of activity recovery during spontaneous awakening from the second stage of daytime sleep. It was found that the power of alpha, beta, and gamma EEG oscillations during preparation and initiation of psychomotor activity in the anterior and central brain regions is higher in the case when the subject starts pressing the button with his left (not leading) hand. The authors assume that his strategy for resuming the activity interrupted by short-term sleep is suboptimal and energy-consuming, requiring greater cognitive load during its implementation.

The paradigm of the bimanual psychomotor test proposed by Yakovenko et al. [25] can serve as a model for the transition of consciousness from related to wake–sleep transitions. One of the objective characteristics of the present functional state can be the amplitude–amplitude coupling of EEG rhythms. This indicator, presumably, may reflect both the activation of individual structural and functional brain systems and their conjugate activity. It was found that the total indicator of the EEG rhythms coupling shows great similarity in the work of the hemispheres. Regional characteristics, on the contrary, show interhemispheric differences over the same period of time. Probably, global bioelectric processes affecting the entire hemisphere have a different "origin" than spatially limited ones.

Studies of hemispheric asymmetry in humans during sleep and falling asleep give contradictory results—there is evidence of the dominance of both the right and left hemispheres when falling asleep. In a paper by Manaenkov et al. [26], the authors attempt to assess this asymmetry on a basis of short sleep episodes induced by an hour-long bimanual psychomotor test with mobile application on their smartphone. The authors demonstrate the absence of a strict hand dominance related to wake–sleep transitions—however, they argue that dynamic interhemispheric interactions are visible in behavioral patterns of participants.

A relatively simple model of a physical process enables to bridge the gaps in understanding of a more complex biological process and generating hypotheses about the mechanisms behind this biological process. In the paper published by Putilov et al. [27], a simple model was proposed to explain the work of mechanisms controlling 5 relatively stable sleep–wake stages and rapid transitions between them. The authors of this paper hypothesized that the competing interactions between three mutually inhibiting drives—for wake, the non-rapid eye moved (NREM) and REM sleep can work in a similar way as two-, two-, and one-way switch, respectively. Therefore, the electromechanical counterparts of five stages can be visualized as five variants of an electrical circuit connecting these three switches with three lamps. The authors also demonstrated that the estimates of stage-specific scores on the 1st and 2nd principal components of the electroencephalographic spectra can provide empirical evidence for plausibility of such linking on–off states of these switches to sleep–wake stages.

The paper published by Tkachenko et al. [28] evaluates psychophysiological predictors of the quality of monotonous activity during driver performance against the background of partial sleep deprivation. Four experiments that lasted 90 min with each subject were performed. Driving simulator data, EEG, ECG, videotape of the subject's face and questionnaires for drowsiness and general well-being were recorded. High-stress levels and chronic sleep deprivation were detected in the subjects. The values of physiological indices before errors indicate different causes of errors in experiments. Eye blinks and heart rate variability changed significantly before errors compared to the background state of each subject.

Aiming to answer the question of how the rest-activity cycle and subcutaneous temperature (SC) change with a decrease in ambient temperature, Kovalzon et al. [29] performed the experiments on predatory mammals living in spacious forested area. Body temperature as well as locomotor activity (LA) were recorded during 70 days using miniature data loggers in the autumn–winter period. The results show different responses to natural cold: (1) a circadian rise in SC which is not associated with an increase in LA (Amur cats); (2) a circadian rise in SC which correlates with an increase in LA (lynxes, domestic cats); (3) rises in SC which correlate with increases in LA, but are not circadian (sables, ferrets). The results demonstrate different strategies for adapting to natural cold in various predatory mammals in conditions of captivity.

D) Innovative Methods for Analysis of Sleeping Brain

Ilyukov et al. [30] present a modern technology for studying the electrical activity of the sleeping brain in freely moving rodents. In this work, a portable EEG platform was developed for the first time, combining an LED for phototherapy of brain diseases. The technology allows real-time simultaneous photo-exposure at the moment of EEG detection of NREM or wakefulness. The technology has no analogues in the world and is a pioneering step in the development of new non-invasive methods for treating sleep-related brain disease. Blockina et al. [31] demonstrate a unique method for studying the sleeping brain in real time will allow significant advances in the study of restorative mechanisms of sleep and will stimulate the development of promising smart-sleep technologies for therapy of brain diseases associated with sleep deficit or disturbance.

Blokhina et al. [31] demonstrate a unique method for optical monitoring of sleeping brain tissue in unanesthetized mice by training them to sleep under experimental conditions on a specially prepared mattress to which the mice become adapted over a long time. Successful execution of animal training allows the selection of mice that can sleep naturally under a head-mounted multiphoton microscope. The method is the golden key to progress in studying the scenario of the sleeping brain in rodents without the use of anesthesia, which significantly distorts the experimental data. The use of this method will significantly improve both the quality of the scientific results obtained and obtain fundamentally new data on the mechanisms of changes in the tissues of the sleeping brain. Terskov et al. [32] show the successful application of methods proposed by Ilyukov and Blokhina for photo-therapy of Alzheimer's disease during sleep in mice.

A review article by Shirokov et al. [33] highlights the use of new methods for studying the sleeping brain, such as portable EEG combined with phototherapy, for the treatment of brain tumors during sleep.

E) Methods for Study of Brain Pathology

The OSA is a multifactorial sleep disorder that is closely related to the disruption of sleep homeostasis. It is known that sleep spindles (SSs) supports sleep stability and may display a sleep protective function, but this sleep EEG pattern has not been well studied in patients with OSA. Madaeva et al. [34] investigated whether SS activity could be altered in middle-aged OSA patients with moderate degree of OSA compared with non-OSA subjects. The authors found that OSA leads to significant disruption of central SS density, reduction of their number and frequency in N2 sleep stages, but significantly increases SS amplitude. These findings can be evidence of the extinction of a brain protective mechanism against exciting stimuli during apnea episodes in OSA patients with a long duration of sleep disturbances.

Sleep is necessary to ensure the plasticity of the brain, growth and maturation, and development and improvement of mental abilities, particularly for children and adolescents. An advanced EEG monitoring can improve our understanding of the brain neuronal activity through studying the sleep patterns. In age-related neurophysiology, importance is attached to the formation and temporary changes in such EEG patterns such as slow-wave activity, SSs, vertex waves V-waves, K-complexes (KKs) and positive occipital sharp transients. However, one of the main sleep EEG phenomena which occur in N2 sleep stage, associated with a wide range of brain functions, such as memory and neuroplasticity, general intelligence and cognitive performance, and undergo changes throughout life, are SSs. The review of Berdina et al. [35] summarizes the modern literature on the formation of the main EEG sleep patterns in childhood and adolescence, especially SSs, and also identifies some studies conducted on age-related neurophysiology and EEG sleep characteristics and their associations with some diseases in adolescence.

Psychiatric disorders are often associated with the acute period of ischemic stroke that negatively affects the functional outcome of the patients, reduce their quality of life, and limits social reintegration. Tynterova et al. [36, 37] show that the post-stroke apathy and aggression is a most important for screening depressive and anxiety symptoms to model optimal patient therapy that can enhance rehabilitation options and predict the functional outcome of the stroke patient.

Nikelshparg et al. [38] studied an insect diapause using Raman spectroscopy. Diapause is a peculiar type of sleep in which the animal's motor activity completely ceases. This process is complex and remains poorly understood, therefore, new methods should be applied. Raman spectroscopy allowed authors to non-invasively estimate the molecular composition of diapausing insects and detect changes in distribution of carotenoids, lipids, and proteins.

2 Outlook

This issue highlights innovative multidisciplinary approaches to the study of neuro-sleep as a complex system, including the investigations of sleeping brain using the modern methods of nonlinear signal analysis, mathematical models of electrical brain activity and neural networks as well as the unique approaches for therapy of brain diseases during sleep. These new approaches are promising tools in better understanding the complex functions of the sleeping brain, allowing significant progress in the development of technologies for prognosis and preventing brain diseases.

We would like to thank all the authors of this issue for their contributions and many other scholars for rigorous and prompt peer reviews. We thank Sandrine Karpe for her great assistance in preparing this issue.

Data availability The data that support the findings of this study are available on request from the corresponding author.

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