Metabolism Of Brain Signals On Human Sleep: a review of mechanisms of action

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Systematic Review

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Abstract

Background

The global research shows that people suffer from a variety of sleep disorders and human actions are the result of neuronal function inside his brain, the feedback of this function can be received and processed as a signal emitted from the surface of the skull. EEG device can receive and record brain signals. Researchers have used a variety of methods to obtain and pre-process signals, extract and reduce the characteristics and types of classifiers in various studies. Research shows that there are three general states of wakefulness (stage 1 + REM sleep) and (stage 2 + deep sleep) separated by the EEG signal.

Methods

The study was performed in accordance with the PRISMA guidelines. A total of 740 articles were found from scientific literature databases (PubMed, Scopus, Web of Science and Wiley Online Library). After all exclusions, a final total of 64 articles were included in this review. The randomized controlled trials that have assessed at least one therapeutic outcome measured before and after intervention were included in the final analysis.

Results

A total of 64 studies were identified at the screening step. In the identification phase, total of 11 records were excluded from the further assessment and 53 records were entered into the screening phase in which Clinical Trial, Review, Books, Editorial were excluded from the review. In the eligibility stage, 49 records remained in the study where total of 34 studies were included for detailed review. Due to the heterogeneities in the available variables as well as the target aspects, the authors decided to review the studies comprehensively.

Conclusions

However, due to some concerns about its effectiveness, more targeted experiments are needed to identify more accurate targets and pathways responsible for the metabolism of its brain signals.

Background

Many people in the world today suffer from a variety of sleep disorders. To diagnose and treat these disorders, a number of biological signals are recorded in sleep laboratories, the most important of which are EMG, EEG and EOG. The state of sleep involves a combination of several physiological modulations, both at the level of central nervous system and peripheral tissues, taking place simultaneously and proceeding in concert. Even at the level of brain, the state is not uniform but consists of two main phases
(NREM and REM sleep) with division of NREM further to three sub-stages, and proceeding through the night following a tight choreography where the different phases proceed in predicted order. The present study focuses primarily on the metabolism of brain signal events during sleep, but it is important to understand that to fully understand sleep and brain signals, we must identify all the central and peripheral mechanisms involved in these modulations.

Sleep is defined through changes in cortical brain activity, which is reflected to typical waveforms in EEG-recordings, defining NREM 1-3 and REM sleep. Behavioral criteria for sleep state also include reduced responsiveness for external stimuli, decreased peripheral muscle tone and several behavioral signs (species-specific sleep posture, eye closure in many species etc.)7.

The deepest phase of NREM sleep, stage 3, is composed of large amplitude and low frequency (1-4Hz) waves, which are based on synchronized, slow frequency (about 1Hz) oscillations between UP and DOWN states of cortical neuronal networks8.

A fairly satisfactory explanation is provided by theories that connect this discontinuation of information flow from sensory organs with re-arrangement or consolidation of previously obtained information within the brain, predominantly in cortex, or in cortical/hippocampal connections. This brings the theories to the direction of neuronal plasticity, memory consolidation and learning. To summarize the core of these theories shortly, sleep favors neuronal plasticity either by enhancing newly formed, strong synapses or by removing (pruning) weak ones or doing both, while sleep deprivation is detrimental to many types of plasticity9,10,11,12.

I. ANATOMY OF SLEEP

The hypothalamus, a peanut-sized structure deep inside the brain, contains groups of nerve cells that act as control centers affecting sleep and arousal. Within the hypothalamus is the suprachiasmatic nucleus (SCN) – clusters of thousands of cells that receive information about light exposure directly from the eyes and control your behavioral rhythm. Some people with damage to the SCN sleep erratically throughout the day because they are not able to match their circadian rhythms with the light-dark cycle. Most blind people maintain some ability to sense light and are able to modify their sleep/wake cycle.

The brain stem, at the base of the brain, communicates with the hypothalamus to control the transitions between wake and sleep. (The brain stem includes structures called the pons, medulla, and midbrain.) Sleep-promoting cells within the hypothalamus and the brain stem produce a brain chemical called GABA, which acts to reduce the activity of arousal centers in the hypothalamus and the brain stem. The brain stem (especially the pons and medulla) also plays a special role in REM sleep; it sends signals to relax muscles essential for body posture and limb movements, so that we don’t act out our dreams.

The thalamus acts as a relay for information from the senses to the cerebral cortex (the covering of the brain that interprets and processes information from short- to long-term memory). During most stages of
sleep, the thalamus becomes quiet, letting you tune out the external world. But during REM sleep, the thalamus is active, sending the cortex images, sounds, and other sensations that fill our dreams.

The pineal gland, located within the brain's two hemispheres, receives signals from the SCN and increases production of the hormone *melatonin*, which helps put you to sleep once the lights go down. People who have lost their sight and cannot coordinate their natural wake-sleep cycle using natural light can stabilize their sleep patterns by taking small amounts of melatonin at the same time each day. Scientists believe that peaks and valleys of melatonin over time are important for matching the body's circadian rhythm to the external cycle of light and darkness.

The basal forebrain, near the front and bottom of the brain, also promotes sleep and wakefulness, while part of the midbrain acts as an arousal system. Release of adenosine (a chemical by-product of cellular energy consumption) from cells in the basal forebrain and probably other regions supports your sleep drive. Caffeine counteracts sleepiness by blocking the actions of adenosine. The amygdala, an almond-shaped structure involved in processing emotions, becomes increasingly active during REM sleep.

**II. MECHANISMES OF SLEEP**

Metabolism interactions and circadian rhythms at the neural, molecular, and cellular levels remain a major challenge in understanding the interaction between brain and peripheral clocks and determining how these interactions enhance energy homeostasis in the sleep-wake cycle. In this review, we evaluate the evaluation of brain signal metabolism on human sleep day and create new opportunities to understand and develop new therapies.

Circadian mechanisms involved in sleep regulation have been studied in great detail (for reviews see )⁴²,⁴³,⁴⁴. They involve the near-24-h cyclic suprachiasmatic nuclei (SCN) influence as driven by daily rhythms in clock gene expression. The mechanisms that underlie the homeostatic component of the two-process model are beginning to be understood at a biochemical level⁴⁵, and are affected by a wide range of variables such as food and water intake, gender, immune and stress status, activity levels, etc., many of which influence duration and intensity of sleep for several days. Several measures correlate with homeostatic sleep pressure, including sleep latency, electroencephalogram (EEG) slow-wave activity (SWA), brain metabolic levels, and cognitive task performance. SWA is measured by recording the amplitude of 0.5–4 Hz EEG oscillations (delta waves) and has been used as an index of non-rapid eye movement (non-REM) sleep intensity. Energy balance⁴⁶ and changes in synaptic strength⁴⁷ have also been linked to sleep homeostasis. However, none of these parameters provide a direct causal mechanism for the occurrence of sleep in the brain, although some biochemicals involved in sleep regulation promote sleep⁴⁵.

Not only has the sleep field lacked a full understanding of the basic sleep control mechanisms, it has also lacked a clear definition of what it is that sleeps. Prevailing theories about sleep homeostatic components rely on time-dependent or use-dependent processes such that the longer an animal remains awake or the more intense the activity, the more sleep it will need⁴⁸,⁴⁹.
Methods

The databases of the PubMed, Scopus, Web of Science and Wiley Online Library, using the set search terms. The study procedures were performed according to the guidelines of the PRISMA. The search terms were "Brain Signals" OR "Sleep". The date of the most recent search was 20 May 2019. Bibliographies of the retrieved records and review articles were manually reviewed to identify the records that may have been missed in the initial search. The titles, abstracts, and keywords of all retrieved records were reviewed and the eligible records were entered in the final review based on the inclusion and exclusion criteria. Only published, peer-reviewed studies on human subjects available in English were considered for this review. Studies examining brain signals on sleep in different protocols against dummy conditions were included in this study. Randomized and controlled trial studies were included.

The studies should have assessed at least one therapeutic outcome measured before and after an intervention. The studies that assessed only cognitive measures, studies on animal and healthy subjects were also excluded. Clinical trials without a randomized controlled design, conference abstracts, narrative reviews, and editorials were excluded from the review.

Result

A total of 64 studies were identified at the screening step. In the identification phase, total of 11 records were excluded from the further assessment and 53 records were entered into the screening phase in which Clinical Trial, Review, Books, Editorial were excluded from the review. In the eligibility stage, 49 records remained in the study where total of 34 studies were included for detailed review. Due to the heterogeneities in the available variables as well as the target aspects, the authors decided to review the studies comprehensively. This study focuses on advances in the use of brain signals in sleep and important factors in the results. In addition, the metabolism of brain signals on human sleep is discussed (Figure 1).

Discussion

The present study focuses primarily on the metabolism of brain signal events during sleep, but it is important to understand that to fully understand sleep and brain signals, we must identify all the central and peripheral mechanisms involved in these modulations. Although the human brain is 2% of the body’s weight, it accounts for 20% of its resting metabolism\textsuperscript{39,40,41}. This requirement for metabolic energy has important implications for the brain's evolution and function.

Sleep is an indispensable physiological process in people's daily life. Every day, most people spend about 30% of their time sleeping. After a day of study and work, the body and brain are in a state of fatigue. ability to respond to nerves and the functioning of organs slow down during sleep. Heartbeat, blood pressure, and metabolic rate decrease, and muscle tissue becomes loose. At this time, sleep is the best way to eliminate fatigue from the body\textsuperscript{19}.
Therefore, it is the best starting point to study sleep by studying the brain activity. EEG can accurately and quickly reflect the physiological changes of the human body; it belongs to an advanced biological signal.

It provides important analytical reference information for neurology, medicine, and other disciplines. It can accurately reflect the activity of the brain, and its application in sleep research is gradually becoming common. Each person has different characteristics and amplitudes of EEG signals in different sleep states, which reflects the different and complex functions of the brain at different stages. People's sleep cycle can be roughly divided into three periods, namely, rapid eye movement (REM), nonrapid eye movement (NREM), and wake (W).

In the 1820s, the German psychiatrist Berger discovered that the brain electrical activity of a person is different in the two states of waking and sleep. Since then, the study of sleep EEG has started. In the 1860s, Dumermuth et al. used fast Fourier transform to process EEG, which promoted its development in frequency domain analysis\(^20\).

The birth of EEG comes from the activity of neurons in the cerebral cortex. The amplitude, frequency, and phase of the waveform contained in the EEG have certain characteristics. The bandwidth of EEG is 0.5~100 Hz, and only 0.5~30 Hz part of spontaneous EEG is considered in clinical medicine.

According to frequency characteristics, it can be divided into four basic rhythm waves and nonbasic waves. During sleep, the rhythm waves appear regularly, and the irregular waves are nonfundamental waves.

In different sleep states, EEG signals are different. The characteristics of EEG in various states are as follows:

1. W Period
2. S1 Stage
3. S2 Period
4. S3 Stage

A local current is generated when neurons in the brain are activated during synaptic excitations of the dendrites, and is measured as EEG. Differences of electrical potentials are caused by summed postsynaptic graded potentials from pyramidal cells that create electrical dipoles between soma (body of neuron) and apical dendrites (neural branches)\(^21\). The highest influence on EEG comes from electrical activity of the cerebral cortex, due to its surface position\(^22,23\).

Later, in 1934, Adrian and Matthews published a paper verifying the concept of “human brain waves” and identified regular oscillations around 10e12 Hz, which they termed “alpha rhythm”\(^24\).
BRAIN WAVES

Brain waves are oscillating electrical voltages in the brain measuring just a few millionths of a volt. There are five widely recognized brain waves, and the main frequencies of human EEG waves are listed in Table 1.1 along with their characteristics.

<table>
<thead>
<tr>
<th>Frequency band</th>
<th>Frequency</th>
<th>Brain states</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gamma</td>
<td>&gt;35 Hz</td>
<td>Concentration</td>
</tr>
<tr>
<td>Beta</td>
<td>12-35 Hz</td>
<td>Anxiety dominant, active, external attention, relaxed</td>
</tr>
<tr>
<td>Alpha</td>
<td>8-12 Hz</td>
<td>Very relaxed, passive attention</td>
</tr>
<tr>
<td>Theta</td>
<td>4-8 Hz</td>
<td>Deeply relaxed, inward focused</td>
</tr>
<tr>
<td>Delta</td>
<td>0.5-4 Hz</td>
<td>Sleep</td>
</tr>
</tbody>
</table>

1.1 Characteristics of the Five Basic Brain Waves.

Indeed, by simultaneously capturing temporal, spectral, and spatial aspects of electrophysiological activity, modern EEG techniques (coupled with other neuroscience tools) hold great promise for understanding the complex organization and function of both non-rapid eye movement (NREM) and rapid eye movement (REM) sleep.

For example, aspects of NREM activity (most notably, slow oscillations (SOs)), sleep spindles, and their coupling, have been linked to aging and cognitive decline\(^27,28\), schizophrenia\(^29,30\), post-traumatic stress disorder\(^31,32\), autism\(^33,34\), as well as facets of cognitive, memory, and emotional functioning in healthy individuals (for reviews see\(^35,36,37\)). While increased interest in sleep EEG is to be welcomed, considerable theoretical and practical signal-processing expertise is needed to properly analyze sleep EEG and to assess the validity of published results.

Conclusion

The evidence previously examined clearly shows that several cases are different. There are mechanisms that signal the brain. Fifty years after Paul Greengard co-founded the field of signal transduction in neurons, tremendous progress has been made in the understanding of how different types of neurons react to their environment. But we still need low- and high-throughput analyses of the different genes and pathways at play in physiological and pathological processes in specific sets of neurons. However, due to some concerns about its effectiveness, more targeted experiments are needed to identify more accurate targets and pathways responsible for the metabolism of its brain signals.
Abbreviations

EEG: electroencephalogram; PRISMA: preferred reporting items for systematic reviews and meta-analyses; REM: rapid eye movement; NREM: non-rapid eye movement; SOs: slow oscillations

Declarations

Authors’ contributions

Conceptualization and design, AA and AA and SNI and HJ; Analysis and interpretation, AA and AA; Writing-Original draft preparation, AA and MA and HJ and NSM; Writing-Review & editing, AA and AA and SNI; Approval of manuscript, AA and SNI. All authors read and approved the final manuscript.

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Competing interests

There is no other competing interest declared by authors.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Consent to publish

Not applicable.

Ethics approval and consent to participate

Not applicable.

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References


Figures

Figure 1

The PRISMA flow chart of the study
Figure 2

2.1 Brain wave samples with dominant frequencies belonging to beta, alpha, theta, and delta bands and gamma waves.

- **Gamma Waves (30Hz-100Hz)**
  - Description: Motor Functions, higher mental
- **Beta Waves (12Hz-30Hz)**
  - Description: Normal waking state, concentration, focus, five physical sense, integrated
- **Alpha Waves (7.5Hz-12Hz)**
  - Description: Relaxed, light meditation, creative, super learning, conscious
- **Theta Waves (4Hz-7.5Hz)**
  - Description: Light sleep, deep meditation, creative, recall, fantasy
- **Delta Waves (0.1-4Hz)**
  - Description: Deep, dreamless sleep, non-REM sleep, unconscious