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MINIREVIEW

Functions of Sleep

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Summary

Sleep is essential component of life. Even though the research in this field develops constantly, there are still many aspects of this rather complex process that remains to be fully clarified. One of these aspects, reason why we actually sleep, is perhaps the most crucial. In this mini review we aim to address this question and discuss potential functions of sleep. Many recent scientific papers are currently available that covers similar topic. We tried to summarize these recent findings. There are certainly many ways how to approach this rather complex issue. Our article will specifically focus on role of sleep in neuronal development, synaptic plasticity, memory consolidation or mental health in general. Its role in immune system functioning will also be mentioned. Moreover, we will also consider more general functions of sleep, such as well-being of the organisms or securing survival of the individual. In conclusion, we will highlight possible main function of sleep.

Key words

Sleep • Functions • Nervous system • Mental health • Well-being

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Introduction

Sleep is an active state, with typical neuronal activity across particular sleep stages, which is an important part of life of probably every creature on Earth (Benington and Heller 1995, Savage and West 2007). Physiology of sleep has been thoroughly researched (Carley and Farabi 2016). However, the exact function of sleep seems to be still unclear. The aim of this review is to provide a list of possible functions of sleep, both affecting specifically central nervous system and having more general impacts.

Potential functions of sleep

Neurodevelopment

Particular sleep stages might play a role in neurodevelopment. This function has been speculated for rapid eye movement (REM) sleep. REM sleep might provide endogenous stimulation, especially during fetal development (Roffwarg *et al.* 1966). However, very little is known about electroencephalography (EEG) in human fetus from the developmental point of view (Anderson and Thomason 2013), hence clinical application of these findings lacks sufficient evidence.

REM sleep might be important for neurogenesis. Studies have shown that REM sleep deprivation in rats leads to impaired neurogenesis in the hippocampus and REM sleep was found to facilitate the proliferation of progenitor cells into neurons (Guzman-Marin *et al.* 2008). However, the study was conducted in rats and in fact no causal effect was proven. Authors themselves speculate that there is no evidence that having more REM sleep leads to facilitation of progenitor cell production. Furthermore, suppressed growth of progenitor cells observed after REM sleep deprivation could be the result of many other factors, resulting from sleep deprivation itself, such as worsening of metabolite clearance (Xie *et al.* 2013). Based on the evidence above, there is not

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sufficient evidence to argue role of REM sleep in neurodevelopment and neurogenesis with high degree of certainty.

Synaptic plasticity

Sleep might also play a role in synaptic plasticity. It is argued that during sleep, the overall depression of brain electric activity in rats leads to synaptic downscaling and overall balance of synaptic strength (Vyazovskiy *et al.* 2008). However, synaptic plasticity is also speculated to be affected by circadian rhythm as a circadian oscillation in synaptic plasticity was found (Frank and Cantera 2014). Thus, not only sleep but also other factors, such as circadian rhythms might contribute to the final level of synaptic plasticity.

Mental health

REM sleep is also claimed to play a role in coping with external epigenetic stimulation (Jouvet 1998). Sleep disturbances might also contribute to development of some psychiatric conditions, such as anxiety or depression (Peigneux and Leproult 2014). Many studies describe positive effect of sleep disturbances treatment on mental health (Wiebe *et al.* 2012, Anderson and Bradley 2013, Macera *et al.* 2013). Although the nature of this relationship remains to be uncovered, it seems obvious that sleep plays role also in psychological well-being.

Memory consolidation

Very extensive research is now focusing on memory consolidation and role of sleep in this process. One example could be its effect on declarative memory (Sheth *et al.* 2009). This study found that there was a positive effect on the immediate face recognition, however it did not help for long term memory consolidation. The positive effect was only observed in acute state, which could correlate with a better performance that is achieved after a good night sleep (Krueger *et al.* 2016) which in the study of Sheth *et al.* was on average almost 8 hours. Other researchers argue that sleep does not enhance remembering skills, specifically motor sequences, although it might prevent forgetting them (Rickard *et al.* 2008). As authors themselves acknowledged, there were many potential confounders (such as not controlling for a phase of the day or potential preceding sleep deprivation). The immediate improvement in remembering motor sequence tasks was not observed at all. However, this study did not properly control for confounders, such as sleep deprivation before testing which could reduce the performance at the first place. Hence, the effect of sleep on memory seems to be inconclusive. As many different aspects of memory were tested, the outcomes vary significantly (face recognition differs greatly from remembering motor sequences). Thus, the effect of sleep on memory might be heterogenous and could differ between particular types of memory. It might be highly confounded by preceding consequences, which could alter the performance of studied subjects. Furthermore, it seems that the effect of sleep on memory is most prominent in healthy young adults (Ficca *et al.* 2000, Peigneux and Leproult 2014) and the exact role of sleep in aging and memory impairment related to aging and neurodegeneration remains to be elucidated.

Metabolic functions

A number of specific functions of sleep are thought to be crucial in altering metabolic functions. Lowering metabolic rate and body temperature during sleep might help to restore energy loss that occurs during wakefulness (Ramm and Frost 1986), probably by promoting non rapid eye movement (NREM) sleep in which slow waves eventually reduce the glucose demand (Wisor 2013, Krueger *et al.* 2016). However, at least in CNS this might be secondary to the hyper-polarization, which generally leads to reduction of action potential transmission and to slow wave occurrence (Krueger *et al.* 2016). The reduction of energy demand might not be only brain specific (Benington and Heller 1995) but might be also important within the whole body (Jung *et al.* 2011). In general, reduced energy need might be a result of gross muscle hypotonia or atonia in sleep, as active muscles consume a large amount of energy (Lindstedt *et al.* 2001). Maintaining sleep could be necessary for maintaining this low demand state and thus allowing the energy to be restored and metabolism to work properly in the wake. Wakefulness is also connected with high amount of external stimuli that need to be filtered permanently and thus, reduction of CNS metabolism during sleep and subsequent energy restorative processes might be partly caused by higher threshold towards these external stimuli (Achermann *et al.* 1993, Brown *et al.* 2012). Moreover, many genes in CNS change their transcription during sleep and their products are involved in synthesis of complex macromolecules which leads among others to restoration of neurotransmitters that were used during wakefulness (Mignot 2008). Thus, role of sleep in energy metabolism is crucial.

Immune system

Potential relationship between sleep and immune system has long been investigated (Imeri and Opp 2009, Besedovsky *et al.* 2012). Cytokines and other factors, such as Tumor necrosis factor are involved in regulation of NREM sleep (Imeri and Opp 2009). Sleep also has a positive effect on antibody titers after immunization (Lange *et al.* 2011). The connection between sleep and immune system seems to be profound.

General well-being

Sleep might also contribute to the general well-being. Thousands of genes in CNS seem to alter their expression after sleep deprivation, most of which are responsible for enzymes of cholesterol synthesis and lipids transport proteins (Mackiewicz *et al.* 2007). Thus, loss of sleep might also lead to structural changes in CNS. On the enzymatic level, sleep deprivation was found to decrease the activity of superoxide-dismutase in rat brain (Ramanathan *et al.* 2002). On the contrary, on the gross level of CNS, no fatal changes of CNS tissue have been observed in rats even when sleep deprivation was carried out towards lethal extreme (Cirelli *et al.* 1999, Frank and Cantera 2014). However, in this experiment animals died eventually. Thus, it could be argued that some effect of sleep absence, perhaps occurring firstly in tissues other than CNS must have occurred, causing the death of the animals. Furthermore, sleep deprivation affects various organ systems also in humans. Lack of sleep is associated with obesity (Hasler *et al.* 2004, Rácz *et al.* 2018), diabetes, glucose intolerance (Gottlieb *et al.* 2005) or cardiovascular diseases (Ayas *et al.* 2003). On the other hand, it does not mean that increased amount of sleep than normal sleep would assure better house-keeping functions. Still, it could be claimed that sleep might support general well-being by having house-keeping functions, not only on the level of CNS but also in the whole body by various mechanisms. Evolutionary role of sleep is also speculated, as sleep seems to be in some way important for the majority of species (Peigneux and Leproult 2014). However, given the heterogeneity of sleep patterns across species, this role might be more complex rather that promoting one particular mechanism (Peigneux and Leproult 2014).

Securing sufficient performance for survival

Achieving sufficient level of activity in an appropriate timing is another and perhaps a key function of sleep. Along with evolutionary need of success in the competition with others, restoration of performance might be a crucial capacity to survive. This capacity worsens after sleep deprivation (Van Dongen *et al.* 2003, Krueger *et al.* 2016). Another theory claims, that sleep is an adaptive function, resembling the dormant state, which leads to the optimal behavioral timing (Siegel 2009). Siegel *et al.* (2009) describe animals which sleep during winter when the sources of food are limited or animals sleeping in particularly long cycles in order to be active at specific time when the food availability is maximal and predator risk minimal (Siegel 2009). Obviously, the diversity of sleep patterns in wild life is huge and the speculation about its role remains to be studied more in depth.

Even if the function of sleep was "only" adaptive, it could be hypothesized as being the most important function of all as it allows the individual and species to survive in the environment. Keeping the body working, preventing it from risk of wasting the energy stores inappropriately and ensuring the sufficient performance in order to overcome all potential challenges in life could be vital for the life on Earth.

What is the main function of sleep?

Sleep seems to be fundamental for survival, but sleep alone would not be sufficient enough to improve evolutionary chances of species. It is also not really possible to separate sleep from wakefulness and all the necessary processes that happen during wakefulness and might later be vital for achieving good sleep, such as energy intake (Reilly and Waterhouse 2007, Yamaguchi *et al.* 2013). As sleep appears to be a fundamental property of neurons, even grown i*n vitro* (Jewett *et al.* 2015), sleep and wake seem to be strongly interconnected, so a specific function of wakefulness should be also determined to clarify sleep functions. If the function of being awake is to maintain energy, produce offspring and survive as a species (Schmidt 2014), then sleep only has a similar general function of maintaining ideal condition for organisms to survive.

Conclusion

There are several aspects of sleep, which could be called as functions of sleep. The results of sleep deprivation mentioned above further illustrate the importance of it. As they all have rather similar endpoint

in house-keeping functions, such as keeping general well-being, assuring the sufficient energy stores to achieve sufficient performance, obtaining enough food without being at risk of predators or being able to produce progeny, it could be hypothesized that the main function of sleep is to survive – both as an individual and species. This function could be eventually a function closely connected to wakefulness and thus an inseparable aspect of life.

Conflict of Interest

There is no conflict of interest.

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