Functions of Sleep

Authors: Miletínová, E [1,2]; Bušková, J [1,2]

[1] National Institute of Mental Health, Topolová 748, Klecany, 25057, Czech Republic

[2] Third Faculty of Medicine, Charles University in Prague, Ruská 87, Prague, 100 00, Czech Republic

Corresponding Author: Eva Miletínová, email: eva.miletinova@nudz.cz; National Institute of Mental Health, Topolová 748, Klecany, 25067, Czech Republic

Summary

In this short communication the potential functions of sleep will be discussed. Specifically, role of sleep in neuronal development, synaptic plasticity, mental health, memory consolidation or immune system functioning will be discussed, along with more general functions of sleep, such as well being of the organisms or securing survival of the individual. In conclusion, the main function of sleep will be speculated.

1. 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.

2. Potential Functions of Sleep

2.1. 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 thal REM sleep deprivation in rats leads to impaíred neurogenesis in the híppocampus and REM sleep was found to facilitate the proltferation 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 sufficient evidence to argue role of REM sleep in neurodevelopment and neurogenesis with high degree of certainty.

2.2. 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.

2.3. 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.

2.4. 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.

2.5. 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.

2.6. 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.

2.7. 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 occured, 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).

2.8. 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.

3. 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.

4. 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.

5. Conflict of Interest

The authors declare no conflict of interest.

6. Acknowledgements

This project was supported by Charles University under grant Progres Q35 and 260533/SVV/2021.

7. References

ACHERMANN, P, DIJK, DJ, BRUNNER, DP & BORBELY, AA: A model of human sleep homeostasis based on EEG slow-wave activity: quantitative comparison of data and simulations. Brain Res Bull 31: 97-113, 1993.

ANDERSON, AL & THOMASON, ME: Functional plasticity before the cradle: a review of neural functional imaging in the human fetus. Neurosci Biobehav Rev 37: 2220-32, 2013.

ANDERSON, KN & BRADLEY, AJ: Sleep disturbance in mental health problems and neurodegenerative disease. Nat Sci Sleep 5: 61-75, 2013.

AYAS, NT, WHITE, DP, MANSON, JE, STAMPFER, MJ, SPEIZER, FE, MALHOTRA, A & HU, FB: A prospective study of sleep duration and coronary heart disease in women. Arch Intern Med 163: 205-9, 2003.

BENINGTON, JH & HELLER, HC: Restoration of brain energy metabolism as the function of sleep. Prog Neurobiol 45: 347-60, 1995.

BESEDOVSKY, L, LANGE, T & BORN, J: Sleep and immune function. Pflugers Arch 463: 121-37, 2012.

BROWN, RE, BASHEER, R, MCKENNA, JT, STRECKER, RE & MCCARLEY, RW: Control of sleep and wakefulness. Physiol Rev 92: 1087-187, 2012.

CARLEY, DW & FARABI, SS: Physiology of Sleep. Diabetes Spectr 29: 5-9, 2016.

CIRELLI, C, SHAW, PJ, RECHTSCHAFFEN, A & TONONI, G: No evidence of brain cell degeneration after long-term sleep deprivation in rats. Brain Res 840: 184-93, 1999.

FICCA, G, LOMBARDO, P, ROSSI, L & SALZARULO, P: Morning recall of verbal material depends on prior sleep organization. Behav Brain Res 112: 159-63, 2000.

FRANK, MG & CANTERA, R: Sleep, clocks, and synaptic plasticity. Trends Neurosci 37: 491-501, 2014.

GOTTLIEB, DJ, PUNJABI, NM, NEWMAN, AB, RESNICK, HE, REDLINE, S, BALDWIN, CM & NIETO, FJ: Association of sleep time with diabetes mellitus and impaired glucose tolerance. Arch Intern Med 165: 863-7, 2005.

GUZMAN-MARIN, R, SUNTSOVA, N, BASHIR, T, NIENHUIS, R, SZYMUSIAK, R & MCGINTY, D: Rapid eye movement sleep deprivation contributes to reduction of neurogenesis in the hippocampal dentate gyrus of the adult rat. Sleep 31: 167-75, 2008.

HASLER, G, BUYSSE, DJ, KLAGHOFER, R, GAMMA, A, AJDACIC, V, EICH, D, ROSSLER, W & ANGST, J: The association between short sleep duration and obesity in young adults: a 13-year prospective study. Sleep 27: 661-6, 2004.

IMERI, L & OPP, MR: How (and why) the immune system makes us sleep. Nat Rev Neurosci 10: 199-210, 2009.

JEWETT, KA, TAISHI, P, SENGUPTA, P, ROY, S, DAVIS, CJ & KRUEGER, JM: Tumor necrosis factor enhances the sleep-like state and electrical stimulation induces a wake-like state in co-cultures of neurons and glia. Eur J Neurosci 42: 2078-90, 2015.

JOUVET, M: Paradoxical sleep as a programming system. J Sleep Res 7 Suppl 1: 1-5, 1998.

JUNG, CM, MELANSON, EL, FRYDENDALL, EJ, PERREAULT, L, ECKEL, RH & WRIGHT, KP: Energy expenditure during sleep, sleep deprivation and sleep following sleep deprivation in adult humans. J Physiol 589: 235-44, 2011.

KRUEGER, JM, FRANK, MG, WISOR, JP & ROY, S: Sleep function: Toward elucidating an enigma. Sleep Med Rev 28: 46-54, 2016.

LANGE, T, DIMITROV, S, BOLLINGER, T, DIEKELMANN, S & BORN, J: Sleep after vaccination boosts immunological memory. J Immunol 187: 283-90, 2011.

LINDSTEDT, SL, LASTAYO, PC & REICH, TE: When active muscles lengthen: properties and consequences of eccentric contractions. News Physiol Sci 16: 256-61, 2001.

MACERA, CA, ARALIS, HJ, RAUH, MJ & MACGREGOR, AJ: Do sleep problems mediate the relationship between traumatic brain injury and development of mental health symptoms after deployment? Sleep 36: 83-90, 2013.

MACKIEWICZ, M, SHOCKLEY, KR, ROMER, MA, GALANTE, RJ, ZIMMERMAN, JE, NAIDOO, N, BALDWIN, DA, JENSEN, ST, CHURCHILL, GA & PACK, AI: Macromolecule biosynthesis: a key function of sleep. Physiol Genomics 31: 441-57, 2007.

MIGNOT, E: Why We Sleep: The Temporal Organization of Recovery. PLOS Biology 6: 0661-0669, 2008.
PEIGNEUX, P & LEPROULT, R: Theories on the functions of sleep. In: Sleep Medicine Textbook. BASSETTI, C, DOGAS, Z & PEIGNEUX, P (eds). European Sleep Research Society (ESRS), Regensburg, 2014.
RÁCZ, B, DUŠKOVÁ, M, STÁRKA, L, HAINER, V & KUNEŠOVÁ, M: Links Between the Circadian Rhythm, Obesity and the Microbiome. Physiol Res 67: S409-S420, 2018.
RAMANATHAN, L, GULYANI, S, NIENHUIS, R & SIEGEL, JM: Sleep deprivation decreases superoxide dismutase activity in rat hippocampus and brainstem. Neuroreport 13: 1387-90, 2002.
RAMM, P & FROST, BJ: Cerebral and local cerebral metabolism in the cat during slow wave and REM sleep. Brain Res 365: 112-24, 1986.
REILLY, T & WATERHOUSE, J: Altered sleep-wake cycles and food intake: the Ramadan model. Physiol Behav 90: 219-28, 2007.
RICKARD, TC, CAI, DJ, RIETH, CA, JONES, J & ARD, MC: Sleep does not enhance motor sequence learning. J Exp Psychol Learn Mem Cogn 34: 834-42, 2008.
ROFFWARG, HP, MUZIO, JN & DEMENT, WC: Ontogenetic development of the human sleep-dream cycle. Science 152: 604-19, 1966.
SAVAGE, VM & WEST, GB: A quantitative, theoretical framework for understanding mammalian sleep. Proc Natl Acad Sci U S A 104: 1051-6, 2007.
SHETH, BR, NGUYEN, N & JANVELYAN, D: Does sleep really influence face recognition memory? PLoS One 4: e5496, 2009.
SCHMIDT, MH: The energy allocation function of sleep: a unifying theory of sleep, torpor, and continuous wakefulness. Neurosci Biobehav Rev 47: 122-53, 2014.
SIEGEL, JM: Sleep viewed as a state of adaptive inactivity. Nat Rev Neurosci 10: 747-53, 2009.
VAN DONGEN, HP, MAISLIN, G, MULLINGTON, JM & DINGES, DF: The cumulative cost of additional wakefulness: dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. Sleep 26: 117-26, 2003.
VYAZOVSKIY, VV, CIRELLI, C, PFISTER-GENSKOW, M, FARAGUNA, U & TONONI, G: Molecular and electrophysiological evidence for net synaptic potentiation in wake and depression in sleep. Nat Neurosci 11: 200-8, 2008.
WIEBE, ST, CASSOFF, J & GRUBER, R: Sleep patterns and the risk for unipolar depression: a review. Nat Sci Sleep 4: 63-71, 2012.
WISOR, JP: The sleep-deprived hippocampus: a loss in translation. Physiol Genomics 45: 26-7, 2013.
XIE, L, KANG, H, XU, Q, CHEN, MJ, LIAO, Y, THIYAGARAJAN, M, O'DONNELL, J, CHRISTENSEN, DJ, NICHOLSON, C, ILIFF, JJ, TAKANO, T, DEANE, R & NEDERGAARD, M: Sleep drives metabolite clearance from the adult brain. Science 342: 373-7, 2013.
YAMAGUCHI, M, UEMURA, H, KATSUURA-KAMANO, S, NAKAMOTO, M, HIYOSHI, M, TAKAMI, H, SAWACHIKA, F, JUTA, T & ARISAWA, K: Relationship of dietary factors and habits with sleep-wake regularity. Asia Pac J Clin Nutr 22: 457-65, 2013.