THE IMPORTANCE OF SLEEP IN THE VARIOUS PHASES OF LIFE: A REVIEW OF THE LITERATURE

Lucas Augusto Niess Soares Fonseca,[1] Danilo José Martins de Souza,[1] Ruan Teixeira Lessa,[1] Tayná Beato Ferreira,[1] Luiz Henrique Salamoni Abad,[2] Nathália Barbosa do Espírito Santo Mendes,[3]

ABSTRACT

Objective. Expand and disseminate research data from the literature since 2000 on sleep and its correlated physiological implications, innovating by organizing the text chronologically, according to the phases of life, and by expanding the discussions about sleep worldwide. Methodology. The bibliographic researches that supported this work were carried out in the main indexes of the medical area, such as Google Scholar, SciELO and PUBMED, and filtered only original review articles, original articles, theses, books, guidelines and recommendations of official scientific bodies published between 2000 and 2019. Results. Sleep is substantial for cognitive development, memory storage, hormonal homeostasis, among many other physiological mechanisms, and has a wide relationship with the appearance of various diseases in case of poor quality or deprivation. Several studies have correlated both deprivation and excess of sleep with the manifestation of systemic diseases, such as cardiovascular diseases, diabetes, immunosuppression and obesity. Conclusion. The efficiency of sleep can be associated with the everyday habits of an individual. At the same time, it should be as valued as physical activity and healthy diet in contemporary society. However, efforts should still be promoted in order to disseminate the importance of sleep in the various phases of life.

Keywords: Sleep-Wake Disorders; Sleep Deprivation; Sleep Stages; Sleep Slow-Wave; Sleep REM.

A IMPORTÂNCIA DO SONO NAS DIVERSAS FASES DA VIDA: UMA REVISÃO DA LITERATURA

RESUMO

Objetivo. Ampliar e divulgar dados de pesquisas constantes da literatura desde o ano 2000 sobre o sono e suas implicações fisiológicas correlacionadas, inovando ao organizar cronologicamente de acordo com as fases da vida e ao expandir as discussões sobre o sono mundialmente. Metodologia. As pesquisas bibliográficas que embasaram este trabalho foram executadas nos principais indexadores da área médica, como Google Scholar, SciELO e PUBMED, sendo filtrados apenas artigos de revisão, artigos originais, teses, livros, diretrizes e recomendações de órgãos científicos oficiais publicados no período de 2000 a 2019. Resultados. O sono é substancial para o desenvolvimento cognitivo, salvamento de memórias, homeostase hormonal, dentre diversos outros mecanismos fisiológicos e possui vasta relação com o aparecimento de várias enfermidades em caso de sua má qualidade ou privação. Vários estudos correlacionaram tanto a privação quanto o excesso de sono à manifestação de doenças sistêmicas, como as cardiovasculares, a diabetes, a imunossupressão e a obesidade. Conclusão. A eficiência do sono pode ser associada aos hábitos corriqueiros do indivíduo. Paralelamente, ele deveria ser tão valorizado quanto a atividade física e a dieta saudável na sociedade contemporânea. Contudo, esforços ainda devem ser promovidos no sentido de disseminar a importância do sono nas diversas fases da vida.

Palavras-chave: Transtornos do Sono-Vigília; Privação do Sono; Fases do Sono; Sono de Ondas Lentas; Sono REM.

[1] Acadêmicos do Curso de Medicina do Centro Universitário Presidente Antônio Carlos – UNIPAC-JF

[2] Docente da Disciplina de Neuroanatomia do Curso de Medicina do Centro Universitário Presidente Antônio Carlos – UNIPAC-JF. Médico Especialista em Neurocirurgia pelo Hospital Municipal Miguel Couto – RJ. Membro Titular da Sociedade Brasileira de Neurocirurgia.

[3]Docente da Disciplina de Metodologia Científica do Curso de Medicina do Centro Universitário Presidente Antônio Carlos – UNIPAC-JF. Mestre em Ciências Biológicas pela Universidade Federal de Juiz de Fora – UFJF.

Autor para correspondência: Lucas Augusto Niess Soares Fonseca. E-mail: lucas.niess@gmail.com

INTRODUCTION

Sleep is one of the most complex and refined physiological processes that the human body has to perform the maintenance of various mechanisms inherent to its homeostasis, especially in the nervous system[1]. Examples are the synthesis of new neuronal synapses (neuronal plasticity), which strengthen the memories[2], and the renewal of the immune system every night, making the individual more resistant to several diseases[3].

In addition, dreams also seem to be essential markers for quality sleep. Its importance is related to the development of creativity and problem solving, which are peculiarities restricted to the human species. During dreams, neuronal synapses look for distant and infrequent connections, making information that was never previously associated to make sense together[4].

Amongst sleep-inducing elements, there are melatonin and adenosine. The first is secreted by the pineal gland and acts as a signal for light presence in the environment, meaning its levels in the central nervous system (CNS) are very low around noon, but very high around midnight[5]. Adenosine on the other hand, a neuromodulator that reduces the need for energy by nerve cells, can be considered a kind of sleep "pressure". This substance is almost completely removed from the CNS during sleep periods, but its concentration gradually increases as we stay awake[6].

Another important sleep inducer is the circadian cycle. Its meaning derives from the Latin "circa diem", which means "about a day". This cycle is managed by the suprachiasmatic nucleus, a small and diffuse conglomerate of neuronal cells in the anterior hypothalamus, and functions as an endogenous biological clock of about 24 hours that regulates various physiological processes, including sleep, organizing them chronologically during the day[7].

It is important to note that all of the above-mentioned sleep inducers operate independently of each other, that is, the physiological or pathological disturbance of one of these signals does not interfere in itself with the daily sleep-wake rhythm, since other mechanisms will be in operation to guarantee the correct harmonization of sleep periods[7].

Structurally, sleep is known to have two major subdivisions: REM (rapid eye movement) and NREM (non-rapid eye movement). Moreover, these different moments of sleep occur sequentially and cyclically on the same night of rest. However, its duration varies according to the evolution of the hours, and there is usually more NREM in the first hours of sleep and more REM in the last hours of the early morning[8].

Moreover, each of these sleep subdivisions has distinct functions for the body. NREM sleep promotes CNS restoration every night, conserves body energy, cools the brain and body as a whole, and invigorates the immune system. REM sleep, on the other hand, promotes adaptation to emotional events through dreams, consolidates memory, strengthens the CNS through endogenous stimulation and stimulates creativity[3]. Other peculiarities of these types of sleep can be observed in **Chart 1**.

Chart 1 - The structural and functional characteristics of REM and NREM sleep

	Structure	Functions
REM sleep	Asynchronous waves from the occipital to the frontal lobe, disordered, with total blockage of somatic efferent pathways	Neuronal interconnections, reasoning, creativity, self-control (emotional IQ)
NREM sleep	Slow and synchronized waves from frontal to the occipital lobe, well defined and with thalamic block (somatic afferent pathways)	Memory rescue, long to medium term memorization, communication between distant encephalon regions, hormonal release and modulation, physiological recovery

Source: Walker (adapted).

In contrast to all these benefits of a 7-9-hour night sleep for adults[9], contemporary society is increasingly restricting itself from this restorative mechanism, whether by rigid routines or even by demerits of sleep in the social imaginary.

Therefore, this article's aim is to clarify, through a review of the state of the art, the indispensable functions of sleep during the different phases of life, from the fetal period to old age.

METHODS

This review article was developed from the data survey found in the literature. The related bibliographic researches were made from February to May 2019 in indexers and scientific databases such as SciELO (Scientific Electronic Library Online), PUBMED (National Library of Medicine of the National Institute of Health), BVS-Bireme (Biblioteca Virtual em Saúde[F4]) and Science Direct.

The keywords used in the research were: “sleep structure”, “sleep neurophysiology”, “sleep functions”, “REM sleep”, “NREM sleep”, “fetus sleep”, “pregnant woman sleep”, “sleep in the childhood”, “sleep in adolescence”, “sleep in adulthood”, “sleep in older ages”, “sleep and autism”, “sleep and immune system”, “sleep and cardiovascular system”, “sleep and obesity”, “sleep and diabetes”, “sleep and metabolism”, “sleep and reproductive system”, “sleep and genetics” and “sleep disorders”. Their respective correspondents in Portuguese and Spanish were also consulted. Only the works considered more significant, that is, in line with the approach cutout of this systematic review, were analyzed in order to guarantee the adequate theoretical basis for the evolution and discussion of the theme.

In this way, review articles, original articles, theses, books, guidelines and recommendations from official scientific bodies published from 2000 to 2019 were included. From this chronological filtering a total of 150 texts were analyzed and read. Of these, 51 sources were duly cited as references, which present original scientific properties that are more relevant to the approach of this work, in order to carry out the development and structuring of this article.

RESULTS AND DISCUSSION

SLEEP IN THE GESTATIONAL PERIOD

Sleep is responsible for modulating multiple physiological processes and a quality night's sleep is able to optimize vast functions throughout the human body[10].This fact extends itself not only to the comfort of the pregnant woman, but also to the correct development of the fetus.

As for mothers, the physiological and biochemical changes of pregnancy make women more susceptible to developing specific sleep disorders, such as obstructive sleep apnea and restless legs syndrome. These discomforts during pregnancy, especially in the last

[F4] Virtual Health Library.

trimester, may influence drug misuse, either to generate comfort or induce sleep. Many of these medications even lead to teratogenies and anomalous fetal development[11].

In addition, snoring is an important marker of poor sleep quality and is present in large portions of pregnant women. In a study by Tsai et al[12], their direct relationship with pre-labor blood pressure was analyzed. In various analyzes, snoring remained a significant predictor of higher diastolic blood pressure. Clinical evaluation and screening for snoring are of utmost importance in obstetric practice to prevent adverse cardiovascular consequences in the period prior to the birth of the baby.

Still in this bias, maternal sleep disorders, specifically sleep apnea and daytime sleepiness, influence negatively the expression of fetal leukocyte telomeres. These, in their turn, are responsible for protecting the genes and their deficiency and promote an early aging of the immune system of the fetus in question[13].

Fetal sleep has distinctive features of normal adult sleep and these peculiarities are mainly related to the immaturity of the fetal prosencephalon and the initial steps of brainstem maturation. Because of that, newborns do not demonstrate slow-wave brain sleep activity (SWS), which appears only between the second and sixth months of life[14]. Moreover, there are indications that maternal biological markers, such as the circadian cycle, coordinate the physiological process of still immature fetal sleep[15].

Thus, the main distinguishing feature of a fetus or newborn's sleep is in the REM stage, which begins immediately after falling asleep, unlike adults, who do not have significant amounts of this sleep phase in the early minutes. It is also interesting to note that the ratio of REM to NREM sleep in the fetus is 50% to 50%, while the pattern presented in adults is 20% to 80%, respectively. In addition, late fetuses and newborns initially have sleep cycles of only 50 to 60 minutes, although the total sleep time is longer than in adults. Only from the age of three does the mature sleep pattern appear, culminating in a deep sleep stage approximately every 90 minutes[14].

It is also essential for the mother to be healthy and undergoing prenatal care with a qualified health professional during her pregnancy. In addition to the already known harm caused by maternal consumption of alcohol, nicotine, amphetamines and other drugs on the growth and weight gain of the baby, including generating withdrawal syndrome in more fragile newborns[16], recent studies have correlated substance abuse with sleep-related abnormalities. Examples of that are the worsening sleep quality and efficiency[17] and even the preponderance of children with autistic spectrum[18], who have 30 to 50% less time spent in REM sleep than children considered healthy.

SLEEP IN CHILDHOOD

Childhood is the interval between birth and 12 years old, period in which most brain connections are established[19]. During this period, the maturation of high-level brain circuits is sensitive. Theses circuits process sophisticated aspects of the world, such as communication, interpretation of facial expressions and language learning, among other complex functions[20].

Studies conducted by Klein et al[21] have shown that sleep disorders are frequent complaints of children and affect about 19% of the child population. As suggested by Walker[8], sleep is responsible for strengthening neural connections, that is, improving brain plasticity. Therefore, sleep deficiencies lead to deficiencies in complete cognitive formation.

In this sense, poor sleep quality affects considerably neural functions by worsening the children's cognitive and behavioral performance, as well as their attention, memory, concentration, temperament and academic performance[22]. Sleepiness has also been shown to have the strongest relationship with school performance[23] and in children and adolescents sleep deprivation manifests itself in the difficulty of waking up to go to school and also in sleeping during classes, which are contributing factors for poor school performance[24].

According to Dewald et al[23], the effects of sleep disorders were greater for younger people, which may be explained by incisive changes in the prefrontal cortex during this younger age. Moreover, it was observed that, during the first 10 months of life, more restlessness during sleep and a more fragmented sleep pattern were moderately associated with lower scores on the mental development index[25].

Sleep quality can also be used as a previous marker of Attention Deficit Hyperactivity Disorder (ADHD). Comparing the sleep stability of children affected and not affected by ADHD, results confirmed the hypothesis that sleep-wake system instability is an intrinsic feature of children with ADHD[26].

SLEEP IN ADOLESCENCE

Adolescence is a critical stage of development accompanied by multiple changes that affect various physiological and psychological functions, dreaming being one of them[27]. Concomitantly, the parameters related to sleep quality and cognitive function of adolescents are altered[28].

At this stage, there are changes in the operation of the hypothalamus-pituitary axis and gonads, directly related to hormonal release, appearance of secondary sexual characteristics, physical and behavioral changes, and cognitive factors of adolescence[29]. Pre-

adolescence and adolescence are periods in which these factors converge when producing changes in sleep and alertness cycles[28].

Due to pubertal hormonal influences, there is a delay of approximately two hours in the early night of sleeping and awakening time[30], which correlates with delayed melatonin secretion times[31,32]. Related to this, studying in the morning period may negatively reflect on the efficiency and sleep quality of adolescents while studying in the afternoon period suggests a better quality of sleep, which induces a favorable cognitive performance[27].

Sleep proves to be a strong long-term memory stabilizer, especially between codification and restudy, so recall of items in mass is most impaired in adolescents exposed to sleep restriction. In contrast, spaced learning provides strong protection against the effects of sleep deprivation on memory performance, while adolescents who have insufficient sleep are more likely to forget items studied at short time intervals[33].

The National Sleep Foundation recommends from 8 to 10 hours of sleep per night for teens between the ages 13 and 17[34]. However, when sleep is sacrificed for other nighttime activities, test results and performance on the following day's tasks usually decline[27,33]. Therefore, a more effective strategy for long-term learning would be regular study, in other words, daily and coordinated in order to address different disciplines without overload with sufficient sleep episodes[33].

There is also an association between decreased REM sleep and the proportionality's increase of NREM, quantitatively improving post-synaptogenesis synaptic pruning in childhood and adolescence[35], which eradicates unused synapses and is generally considered a beneficial process[36]. With that said, deep NREM sleep, which inspects and refines the brain during adolescence, enhances brain maturation mechanisms[35].

In addition, magnetic resonance imaging (MRI) studies have revealed that myelogenesis continues, and the neurocircuit remains structurally and functionally vulnerable to significant increases in sexual hormones (estrogen, progesterone and testosterone) during puberty, interfering with learning[37,38]. In parallel, there is the development of the prefrontal cortex, which is very important for the rational behavioral performance of adolescents[35,36].

Therefore, adolescence, at the biological level, is characterized by a transition between childhood and adulthood. In its turn, it predefines physical and neuronal transformations[28,31] due to the important changes in sleep cycles[28], which influence long-term learning and memory[33].

SLEEP IN ADULT AGE

About 5 sleep cycles of 90 minutes each occur in adult individuals. At each cycle, all stages of sleep manifest (REM, NREM1, NREM2, NREM3, and NREM4), despite their different proportions. In the first half of the night, for example, REM sleep is almost nonexistent, while being predominant in the second half. At the same time, deep NREM sleep is abundant early in the sleep period, but quite scarce at the beginning of the next morning[8].

Regarding the functional benefits of a sufficient night's sleep, several studies have already correlated lack and excess sleep with various illnesses. In the following, we will cite several of these studies and their respective results for different systemic components of the human organism.

In the cardiovascular system, people who sleep 5 hours or less daily have been associated with a 39% increased risk of coronary heart disease compared with individuals who have 8 hours of sleep daily[39]. These effects are mainly due to the dysregulated functioning of the autonomous sympathetic nervous system due to the lack of suspension of adrenaline, the neurotransmitter of this system, which should occur every night during a satisfactory sleep time[8].

Another study, this time associating lack of sleep with the adult immune system, proved the immunosuppressive effect of prolonged alertness. Only a modest amount of sleep deprivation impacted immune cells count and altered nocturnal secretion of pro-inflammatory cytokines such as interleukin-6[40].

As for the metabolic pathways of the human body, both lack and excess sleep proved to be harmful. In these situations, a number of regulatory substances are decompensated and even the brain's demand for glucose is lowered and the ingested glucose intolerance is increased. In the study done by Gangwisch et al[41], individuals who slept 5 hours or less per day were 47% more likely to develop diabetes over the next 10 years compared with a control group. In addition, those who slept 9 hours or more were 52% more likely to get diabetes under the same conditions.

In relation to obesity, the meta-analysis study conducted by Wu, Zhai and Zhang[42], involving 197,906 individuals, revealed that short sleep duration is strongly related to future obesity. However, the opposite, that is, the long duration of sleep, is not related in the same way.

In the reproductive system, the effects of sleep deprivation led to a 25% reduction in total sperm count in men with severe disorders and consequent chronic sleep deprivation in a

sample of 953 healthy young Danes[43]. In women, poor sleep can cause infertility and problems in conception due to the mismatch of female reproductive hormones [44].

Finally, the study conducted by Möller-Levet et al[45] demonstrated that an individual's quality of sleep alters the expression of their gene structures. From blood transcriptome samples, the researchers concluded that 711 genes were hypo or hyper-stimulated by insufficient sleep in a sample of 26 people, including genes related to circadian rhythm, sleep homeostasis, oxidative stress, and metabolism in general.

SLEEP IN OLD AGE

Old age is constantly associated with sleep problems, as poor quality of sleep is considered a possible inevitable consequence of aging. Such quantitative and qualitative changes in post-sixties age can be explained and emphasized by numerous social, physiological and pathological factors.

Restorative sleep is of undoubted importance for physical and emotional well-being in any age group and especially in old age. Despite the consensus on sleep quality decline being a consequence of advanced age, this decline is much more related to factors that are combined to age. Examples are the use of illicit drugs at an earlier age, ingestion of alcohol, caffeine and nicotine[46].

The poor quality of sleep in the elderly related to socioeconomic factors is discussed by Santos. This study revealed that in the city of Paranaíba, with lower HDI, there is a greater number of complaints mainly related to problems such as: non-restorative sleep, early awakening and difficulty maintaining and initiating sleep[47].

Still significantly associated with socioeconomic and health-related factors it is possible to highlight some frequent problems in the elderly, such as sleeping less than four hours a night, daytime sleepiness and nocturnal awakenings often caused by urinary incontinence and use of sleeping drugs[48].

Another eminent factor in the decreasing quality of sleep in the elderly is related to biological sex. According to the research conducted by Moreno (2019)[49], the number of older women with sleep disorders is generally higher than in men in the same age group. This is due to sleep-related illnesses that are very common in older women, such as urinary incontinence and nocturia.

Such weakened bladder-related problems can be an aggravating factor for sleep fragmentation, leading to a reduction in sleep efficiency – the percentage of time you fall

asleep while you are in bed. The more efficiency is reduced, the greater the risk of mortality and the decline in the quality of their physical and mental health[35].

According to Pereira[50], symptoms such as insomnia, falls and daytime naps, very common in old age, may be also related to sleep quality. Still in this study, falls are associated with females above 80 years old, daytime naps and depressive symptoms. In addition, falls can also be related to the problem of fragmented sleep, mainly related to nocturnal bathroom visits[35].

These visits may be a potential risk of falls on account of factors such as cognitive stunning when waking up and the environment being naturally dark. It may also be related to the possible deficient blood pressure, showing that the changing position when standing up can cause dizziness and instability[35].

RELATIONSHIP BETWEEN AGE AND SLEEP CHARACTERISTICS

According to National Sleep Foundation[34,35], it is possible to categorize each age group according to their sleep peculiarities, as shown in **Chart 2**.

Chart 2 - Comparative synthesis between sleep characteristics in the different life periods

	Age range	Recommended sleep time	Sleep Pattern (REM and NREM)	Specifics and importances
Fetal period	Period before birth	It varies with the gestation weeks, an average of 11 to 17 hours per day.	Sleep predominates over wakefulness. At 6 months of age, the relationship between REM and NREM sleep is 50% to 50%.	Intense synaptogenesis and direct entry into REM sleep after falling asleep
Childhood	From 1 month to 12 years old	From 10 to 13 hours a day	At 5 years old, the proportion is 30% REM and 70% NREM.	Cognitive motor development and growth (GH hormone)
Adolescence	From 13 to 17 years old	From 8 to 10 hours a day	20% REM and 80% NREM. Sleep consolidation with adult characteristics	Cognitive maturation
Adult age	From 18 to 64 years old	From 7 to 9 hours a day	5 cycles of sleep with 90 minutes each	Prevention of systemic diseases and maintenance of mental health
Old age	65 years old and older	From 7 to 8 hours a day	Time spent on REM sleep may decline and sleep efficiency drops from 70% to 80%.	Sleep segmentation and quality deterioration due to comorbidities

Source: National Sleep Foundation, Walker (adapted).

CONCLUSION

Sleep is the second most characteristic behavior of human existence. Thus, it is impracticable for an individual to spend several days without sleep. It is also known that through it there is the physiological and functional renewal of our body. Therefore, our systems are invigorated after each night of sleep and can achieve proper homeostasis.

Along those lines, it is essential to maintain an ideal daily sleep constancy according to each age group, since sleep has a wide relationship with the appearance of various diseases. Several studies have correlated both deprivation and excess sleep with the manifestation of systemic diseases such as cardiovascular disease, diabetes, immunosuppression and obesity.

With that being said, sleep efficiency can be associated with an individual's ordinary habits. At the same time, it should be as valorized as physical activity and healthy diet in contemporary society. Thus, sleep efficiency can be associated with an individual's ordinary habits. At the same time, it should be as valued as physical activity and healthy diet in contemporary society. However, as this premise is not yet a reality, efforts should be promoted both in the medical and academic fields to disseminate the importance of sleep in various stages of life. With this literature review article, it is hoped that this information can be accessed by a larger number of people and, consequently, contribute to more quality sleep.

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