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SLEEP QUALITY AND MEMORY: AN INTEGRATIVE REVIEW

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ABSTRACT

Introduction: Sleep deprivation modifies the lives of millions of people everyday and has a deep impact in brain molecular biology. These effects begin with a neuron working change, by DNA and RNA level and it results at modifications in neuronal plasticity and in absence's regulation of cognitive functions, including learning and memory. A quality sleep contributes directly for the correct performance from activities by a biological cycle correspondent to a 24h period, besides, it is essential in consolidation memory process, which ones modifies depending about the circadian schedule that occurs. **Aim:** Review available research in literature that investigates changes in sleep quality and the relationship with human adult's memory. **Methods**: Articles from this review was selected by means of two revisers (M.T) and (B.W) through search questions and structured according to adult's human dates, except of exposure to light or prolonged sleep period, sleep disorders associate with memory alterations. **Results:** Circadian rhythm changes are directly associated with sleep performance and often interfere in memory execution in everyday life. **Conclusion:** About the exposed, verified that appropriate sleep is essential to the physiological system homeostasis as all; in this way, seems that individuals with sleep private make own adaptations in their physiological system trying to figure out everyday life situations and after that to perpetuate species; however how much physiological systems are affected regarding cardiovascular and neurodegenerative diseases still are not correctly understood.

KEYWORDS: Chronobiology, sleep disorders, memory, circadian rhythm, humans.

INTRODUCTION

Biological functions including endogenous hormone secretion, central body temperature and the wakeful sleep cycle are controlled by different physiological systems, which are influenced by circadian rhythms.[1] In the Central Nervous System (CNS) the control of these biological rhythms is performed by the Supraquiasmatic Nucleus (NQS), located in the anterior hypothalamus, and responsible for the internal circadian pacemaker. The synchrony between internal and external rhythms occurs according to the time of day through external time oscillators known as Zeitgebers, as well as by light, which regulates the endogenous synthesis of melatonin.[1,2] Finally, sleep is also considered an integral part of circadian rhythms, acting directly in the regeneration of bodily functions during the waking period.[3]

Chronobiology is the science that allows the investigation and quantification of biological phenomena and mechanisms associated with the temporal structure, including the rhythmic manifestations of life. The term derives from: *chronos* (time), *bios* (life) and logos (studies, or treatises).[4] Considering that chronobiology is the natural existence of a biological rhythm, Franz Halberg in 1959 coined the Latin term circadian: circa = approximately; dies = day, in order to refer to the rhythms created daily in a period of approximately 24 hours that fluctuates independently of any environment.[5]

The moment in which the sleep-wake cycle has been

studied, mainly with the purpose of visualizing the importance of homeostatic factors, including circadian rhythms, in addition to predicting or recognizing clinical abnormalities. Although, even knowing that these factors can influence human sleep, it is difficult to measure the importance of physiological conditions, without imposing sleep deprivation, due to the interdependence between these factors.[6]

However, it is known that periods of sleep deprivation are capable of modifying the standard of living of millions of people daily and having a profound impact on brain functionality. These effects begin as changes in the functioning of a neuron's metabolism, at the level of DNA and RNA, and result in changes in neuronal plasticity and dysregulation of cognitive functions, including learning and memory.[7]

Circadian sleep disorders occur when endogenous factors are out of sync from the light and dark environmental phases. Given that the CNS participates in the control and maintenance of sleep in certain areas of the brain, it can be said that there is a relationship between circadian changes and human performance, whether in daytime functions, cognition and / or physical performance.[5] Sleep quality is important for the proper performance of activities in a biological cycle, being fundamental in the process of memory consolidation, which is modified, depending on the circadian time in which it occurs.[2]

The first indicators of memory consolidation can be measured during immediate rest after coding the periods experienced in a biological cycle.[8] It is during total sleep deprivation that changes in the functioning of neurobiological processes can be perceived, such as the cognitive pattern.[9] In general, restorative sleep adjusts cognitive function during the subsequent waking phase; therefore, memory consolidation is dependent on the quality of sleep.[10,11] Thus, the aim of this study is to review research available in the literature that investigates the relationship between changes in sleep quality and efficiency in the memory of adult humans.

METHODS

This research was carried out through an integrative literature review according to a predefined protocol in which the articles were strategically selected through research questions and structured according to the PICO acronym data: adult humans, overexposure to light or period prolonged sleep, sleep disorders associated with changes in memory.

Eligibility criteria

The included studies were complete and published original articles, without limitation of the year of publication, being series of cases and clinical trials, which used as means of evaluation the following resources: sleep protocol accompanied with the use of actimeter, neuropsychological tests, questionnaires of sleep quality. The language of the studies was not chosen, which presented a control group or not. Articles made on humans and adults were selected.

Ineligibility criteria

The excluded studies were those that used animal models or pharmacological means to treat changes in sleep and / or memory. Information sources and search strategy. Two researchers (T.M./W.B.) Conducted the integrated search separately in relevant electronic databases for this subject: MEDLINE / PUBMED and SCIENCE DIRECT. The survey was conducted from February to June 2018 using a combination of the following MESH terms: “memory disorders, circadian rhythm”, “disorders sleep, human” (MEDLINE / PUBMED) and the keywords “Chronobiology, memory”, “human sleep” (SCIENCE DIRECT).

Selection of studies

Two reviewers (T.M./W.B.) Independently selected the studies by reading the titles and abstracts following the eligibility criteria. The selected studies were then carefully read and subjected to a first calibration. In cases where there was some disagreement on any of the selected articles after reading them in full, the results were discussed, until there was agreement. In the first calibration performed by the simple agreement index using a rule of three, the value was 85%. After the final selection of articles, there was a second calibration between the two reviewers (T.M./ W.B.), in which the agreement rate was 100%.

Data collection procedure

The data collected in the studies included author / year, population / age, type of study, objective, method / time of intervention, evaluation techniques, results obtained.

RESULTS

Selection of studies

After searching for articles in the databases, a total of 451 articles were found by the reviewers, 258 from the MEDLINE / PUBMED database with the descriptors MESH: (Memory Disorders AND Circardian Rhythm AND Disorders Sleep AND Human) and 193 articles from the database SCIENCE DIRECT with the keywords (chronobiology AND memory AND human sleep), these refined by original articles.

After applying the article selection strategy in accordance with the adopted eligibility and ineligibility criteria, ten articles were finally selected to be analyzed, see Figure 1.

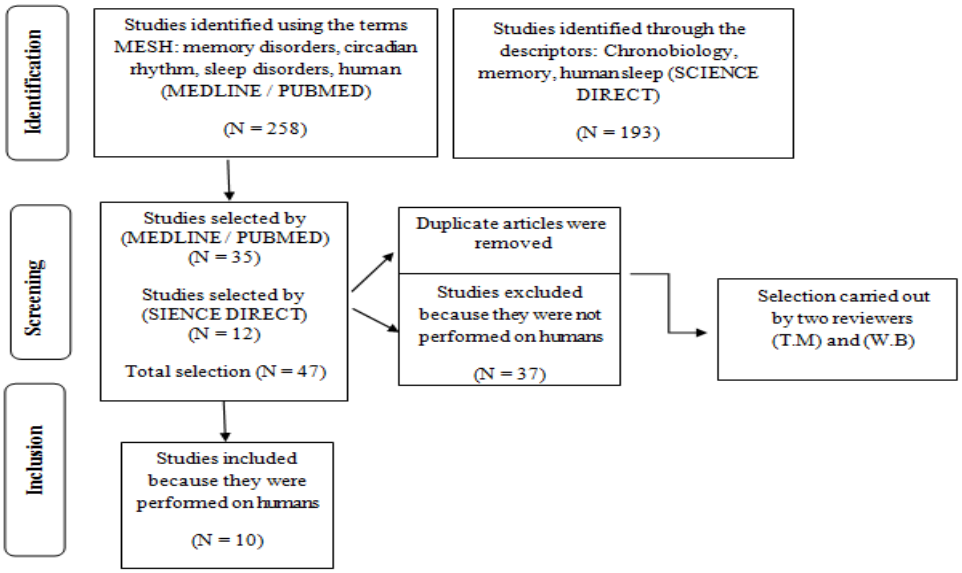

Figure 1: Flowchart of the selection of studies included in the literature review.

Study characteristics

Among the main findings of this review, it was found that between the years 2007, 2009, 2012, 2014, 2016 and 2017 were found studies that deal with the topic of changes in sleep and memory in the investigated databases. Among the ten studies included in this review, seven used the actimeter as a technique for monitoring daily motor activity. Sleep quality questionnaires, neuropsychological and cognitive tests were carried out in three studies.As for the results obtained by using the actimeter, five studies suggest that changes in circadian rhythm influence the performance of cognitive function, such as memory and other functions such as mood, attention span and reaction time.

Regarding the statistical analysis, of the ten articles evaluated, more than 4,000 humans participated, since in only one of the studies 3,237 samples were used through a randomized study. Five studies specified the tests they used in decisions regarding memory changes.In view of the analyzes carried out in this review, it was observed that changes in circadian rhythm are directly associated with sleep performance, as it is during this phase that external stimuli become less relevant and short-term memories are consolidated into permanent patterns,[12] the changes considered as variations in memory, differentiation in sleep and neuropsychological changes can be briefly described, see table 1.

Table 1: Studies selected by the integrative literature review.

AUTHOR, YEAR	POPULATION / AGE	TYPE OF STUDY	OBJECTIVE	INTERVENTION METHOD / TIME	TECHNIQUES USED	RESULTS
(13)	N = 31 (18 Female) Age: 19-56 years	Longitudinal study	Investigate the effects of white light sources on cognitive, visual, mood and cardiac output	The study consisted of three night laboratory visits under different white light conditions, separated by an intervention period of 1 week. Volunteers avoided alcoholic beverages, exposure to the sun, daytime naps and intense physical activity on the days of the laboratory visit.	*PVT MDBF WM FM CCT* Volunteers avoided alcoholic beverages, exposure to the sun, daytime naps, and intense physical activity on the days of the laboratory visit.	Changes in MDBF in the state of "tired-awake" and "nervous - calm" ↑ on FM under light condition N / S in other tests performed

(14)	N = 26 adults Age = or ↑ 55 years	Longitudinal study	Measure the activity of circadian rhythms in a group of healthy people	The actmetry device was used continuously on the participants' non-dominant wrist for one week (except prolonged bathing or swimming). Recordings for six full days were used to analyze sleep and activity levels.	*MMSE NART WechslerMemoryScale: Logical Memory I and II (LM I, LM II)* *VPA I and II VR I e VR II MEQ* Sleep diaries using Actmetria	Minimal differences between sleep and circadian activity ↓ Memory performance in WMS tests: Logical Memory I and II
(15)	N = 58 participants Age: = 50 years or ↑	Case series	Determine whether mild cognitive impairment (CCL) is related to changes in sleep.	Participants used an actimetry clock and sleep diaries for 2 weeks, in addition to undergoing sleep assessments during the night.	Sleep diaries using Actmetria *MMSE HSO DLMO PSG*	↑ in waking time in patients with MCI ↓ of memory performance in patients with MCI
(16)	N = 44 young people Age: between 12 and 30 years.	Case series	Categorize whether circadian disorders occur by "Participants used an actimetry clock and sleep diaries for 2 weeks, in addition to undergoing sleep assessments during the night. above).	Participants completed diaries and / or actigraphy for 7 days and continuous nights before of a circadian assessment	*HDRS HSO DLMO* Actmetria Diaries Circadian assessment	N / S in relation to disease stages ↓ melatonin levels in patients with established sleep disorders
(17)	N = 3237 (VISAT volunteers randomly drawn from 3 regions in the south of France) Age: 32 ≤ 62 years	Cross-sectional study	Assess the influence of night work on cognitive performance verbal memory	Standardized medical intervention protocol for data collection Data collected during the annual medical examination by an occupational physician	VISAT 2 self-administered questionnaires on working conditions validated by the doctor 1 health questionnaire completed by the doctor Cognitive Tests	↓neuropsychological performance with increased night work rhythm Cognition tends to be impaired with night work
(18)	N = 16 healthy participants (7 women and 9 men) Age: 28.4 years ± 8.9	Case series	Assess whether sleep at night facilitates memory consolidation	Participants completed test sessions in 4 conditions: night sleep; watch of the day; night watch; daytime sleep Participants went to a designated room at the Center for Clinical investigations at	Normal sleep schedule Inverted sleep schedule *MST*	Sleep benefits both the acquisition and consolidation of memory and the benefits are independent of the shift. There was an improvement in motor

				Brigham and Women's Hospital for 2 8-day visits.		performance in patients with biological sleep.
(19)	N = 6 healthy adults (one woman) Age: 26.8 ± 5.2 years	Case series	Assess whether circadian rhythms influence memory performance	28h forced circadian dragging protocol Programmed wake in low light 9.33h of sleep programmed in the dark 73 days of studies at the Clinical Research Center in Brigham and Women's Hospital	Voice recorder as night watch time recorder Pulse actimeter	The modulation of circadian rhythms influence memory performance and other changes such as mood, attention, and reaction time.
20)	N = 152 Women between 16 and 30 years old	Case series	To characterize sleep profiles and circadian disorders in young people with affective disorder for early intervention of mental health problems in young people	Participants filled out a sleep diary and used pulse actmetry on the non- dominant arm for approximately 14 days	*HDRS SOFAS* Actmetria Comprehensive battery of neuropsychological tests	No differences were found in neuropsychological tests Changes in Actmetria data suggested circadian changes.
(21)	N = 50 young people with depression or bipolar disorder Age: 13-33 years	Case series	Investigate associations between sleep, mood changes and cognitive functions	Pulse actmetry for approximately 2 weeks A psychologist conducted an initial assessment of psychiatric symptoms and neuropsychological functions within 100 days after the start of monitoring	Monitoring by Actmetria Neuropsychological assessment	N / S neuropsychological evaluation regarding sleep in patients with depression and bipolar disorder
(22)	N = 372 university students Age: 18 - 20 years	Cross-sectional study	Investigate the direct effects of the sleep chronotype, its symptoms and influences.	Participants filled out psychological instruments applied by 2 individuals in the classroom for 2 weeks.	*MEQ DES ISI ESS*	Daytime sleepiness can cause pathologies Chronobiological characteristics influence sleep quality

Legenda: **PVT=** Psychomotor Vigilance Task; **MDBF=** Multidimensional Mood Questionaire; **WM=** Visual Memory Test; **FM=** Farnsworth–Munsell 100 hue test; **CCT=** Character Comparison Test; **N/S=** Não sgnificante; **MMSE=** The Mini Mental State Exam; **NART=** The National Adult Reading Test; **VPA=** Verbal Paired Associates I and II; **VR=** Visual Reproduction I and II; **MEQ=** The Morningness-Eveningness Questionnaire; **MMSE=** Mini Mental State Examination Score; **HSO=** Habitual Sleep Onset; **DLMO=** Dim Light Melatonin Onset; **PSG=** Polysomnographic; **VISAT=** Aging, Health and Work; **DES=** Dissociative Experiences Scale; **ISI=** Insomnia Severity Index; **ESS=** Epworth Sleepiness Scale; **HDRS=** Hamilton Depression Rating Scale; **MST**= Motor Sequence Task; **HDRS=** Hamilton Depression Rating Scale; **SOFAS=** Social and Occupational Functioning Assessment Scale.

Researchers studied the effects of white light sources on cognitive, visual performance and cardiac output correlating to the time of day. Through a sample of healthy humans submitted to an 8-hour sleep protocol for seven days, exposed to the impact of three light spectra with varying portions of wavelength ("low", "moderate" and "high"), identify that after the intervention period in a room with light spectra during sleep, changes in mood can be noticed.[13]

In another study carried out in humans, it was determined through a group of participants exposed to a circadian sleep protocol that mild cognitive impairment (CCL) is related to changes in sleep, considering that during the period of use of the actimeter and the performance neuropsychological tests, there was an increase in waking time and at the same time a decrease in memory performance in patients with MCI.[15]

In this same perspective, it was identified in a cross-sectional study carried out with a sample of 3,237 humans that sleep is so interconnected with circadian rhythms that night workers can present greater declines in terms of memory and other cognitive aspects. Workers who spend about fifty nights a year awake show changes in neuropsychological tests suggestive of cognitive deficits, which show a gradual tendency of memory loss associated with increased exposure time to night work.[17]

Another study carried out with a sample of 6 humans observed that after 73 days of using the actimeter and inducing a sleep protocol in the laboratory, the modulation of circadian sleep rhythms influences memory performance and other functions such as mood, attention and the reaction time,[19] Still in order to demonstrate the relationship between sleep and memory, a study carried out in 16 humans submitted to a laboratory protocol for night and day sleep obtained as a result that sleep benefits both the acquisition and consolidation of memory and that these benefits independent of the shift in which the circadian rhythm of sleep occurs.[18]

DISCUSSION

Through this review, the existence of integration between the internal timing mechanisms known as "biological clocks", behavioral and interaction functions with the environment was verified, and there is a regulation of the sleep-wake cycle, with light being one of the greatest influences for the control of this rhythmicity.[4] Studies have shown how the development of a harmony of the sleep-wake cycle is relevant among the biological cycles, and that sleep works with a restorative purpose as well as being fundamental in the consolidation of memory.[23]

Regarding sleep time, a study was carried out in 67 healthy young adults during a night period with prolonged stimulation of bright light in night shifts and wearing dark glasses during sun exposure followed by a daytime sleep episode in the dark for 5 days. These authors verified the need for a circadian readjustment of sleep where the night time is the time capable of producing substantial benefits to neuro-behavioral measures. For this finding, a salivary collection of melatonin was performed in addition to neuro-behavioral tests, which identified that daytime sleep alone is not enough to produce neuro-behavioral benefits.[24]

In contrast, other researchers verified by means of a laboratory protocol associated with a day-night sleep schedule and a sequence of repeated motor acquisition in laboratory visits, that regardless of the biological time in which sleep occurs, it positively influences the consolidation of sleep. Memory,[18] Other authors, on the other hand, carried out a study with the objective of verifying whether age is responsible for affecting memory performance and executive functions, such as the waking sleep rhythms. Analyzes performed through actmetrics and standardized cognitive tests showed that there is a relationship between circadian rhythm and cognitive domains; this association was independent of the main effects of age, suggesting changes in resting activity and cognitive performance in elderly people.[25]

Starting from the same principle of age, other authors used self-administered questionnaires and cognitive tests in an annual clinical evaluation and identified that night work in adulthood influences verbal memory and cognitive performance in old age (ROUCH et. Al, 2007). In another more recent study, authors realized that poor sleep quality can negatively influence the functioning of biological rhythms. Through a cross-sectional study applied in classrooms of young university students, it can be noted that daytime sleepiness can facilitate the emergence of pathologies such as changes in memory (such as temporary amnesia), slowness of movements and behavioral changes.[22]

According to this perspective, studies have shown that neuro-behavioral deficits accumulate according to the days of partial sleep loss at levels equivalent to 1 or 3 nights with total sleep loss. Authors revealed that after days of chronic sleep restriction (less than 7 hours a night), a significant daytime cognitive impairment can already be perceived.[26]

Other researchers investigated partial sleep deprivation in 12 handball athletes. They identified daytime variations in activity time (reaction time - RT) performed in the field with partial sleep deprivation administered over 6 days with a recovery period of 72 hours. During each sleep condition, the subjects performed selective and constant tasks in the morning and afternoon, which showed an increase in RT and a decrease in the level of attention and cognitive performance; therefore, partial sleep deprivation affects the diurnal variation in cognitive performance and increases RT, reducing the ability to pay attention in the afternoon (JARRAYA et.

al, 2012).

In another study, the researchers also focused on assessing the impact of sleep deprivation on the particular component of cognitive performance, such as the ability to access and use declarative knowledge. For this purpose, 8 healthy young male adults spent 10 days in the laboratory and before the established sleep deprivation time (3 nights of total sleep deprivation). The authors showed that prolonged awake time leads to a significant decrease in memory performance verified by performing tasks of a task of adding / subtracting single digit numbers, given to patients every 2h of the 3 days of total sleep deprivation, changes in impact and fatigue in the recovery of knowledge were relevant even in simple tasks that do not depend on acquired knowledge (GUNZELMANN et. al, 2012).

Even the relationship between night work and sleep has been better demonstrated in other studies. Authors, through a differentiated intervention, examined the melatonin levels and the cognitive function capacity of crew members of a simulated space mission for a period of 105 days, assuming that the success of long- term space missions depends on the ability to alertness and high levels of cognitive function in the operational complex of the specialists present. Even with the provision of measures to promote awakening, such as supplementary light promoting higher levels of melatonin and permitted use of caffeine, impairments were also observed in cognitive function and in the performance of work shift activities through assessments, such as: test mathematical, cognitive tests, Stroop test (evaluates colors and words) and the Visual Analogue Scale (EVA) test, thus indicating that long-term night work suggests the need for alternative solutions to be carried out successfully (BARGER et, al. 2014).

According to the memory disorders associated with poor sleep quality and its consequences, there are studies that suggest treatment measures for memory disorders. In a survey, authors described a brief morning treatment in elderly people with memory impairment and their respective caregivers (dyads). These 54 dyads were exposed to phototherapy (bright white or dark red light) for 30 minutes for 14 consecutive days associated with sleep hygiene therapy. The data demonstrated that there was a positive relationship between and sleep efficiency, improvement in the symptom of insomnia and depressive symptoms.[27]

CONCLUSION

Given what was presented in this review article, it can be said that adequate sleep is essential for the homeostasis of physiological systems as a whole. The DOHaD (Developmental Origin of Health and Disease) theory seems to be a way to explain the biological adaptations made by individuals deprived of sleep over time. Thus, it seems that individuals deprived of sleep make adaptations in their physiological systems, seeking to adapt to day-to-day situations to maintain themselves and then perpetuate the species; however, how much the physiological systems will be harmed in the future, including the appearance of diseases such as cardiovascular diseases, including systemic arterial hypertension, stroke, acute myocardial infarction, as well as neurodegenerative diseases such as Alzheimer's disease and parkinson's it is certainly not understood.

Epigenetic aspects should be further investigated as they play a critical role in the regulation of gene expression in the context of memory storage. There is evidence to suggest that sleep loss affects the epigenome and these epigenetic changes can mediate the changes in cognition seen after sleep interruption. The relationship between sleep and the epigenome is just beginning to be elucidated, but there is evidence that epigenetic changes occur after sleep deprivation. In the future, these changes in the epigenome could be used as therapeutic targets for sleep-related disorders.

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