REVIEW ARTICLE

Sleep and cognition

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Abstract

Inadequate sleep is a burning issue in today's modern world. Sleep and cognition are closely interrelated. Sleep deprivation negatively affects various aspects of cognition including working, short-term and long-term memories, attention, reaction time, visuomotor performance, reasoning ability, and judgment. Disorders with cognitive abnormalities also have negative impact on sleep. This review studies the clinical aspects of interplay between sleep and cognition. We have also focused on the assessment of sleep and cognition. Researchers are required in the field of sleep and cognition. Sleep has potential to become future diagnostic and therapeutic marker in cognitive disorders.

Keywords: Sleep, Sleep deprivation, Cognition.

Introduction

Sleep is a state of perceptual or conscious nonresponsiveness, reduced movement of the skeletal muscles, and decelerated metabolism.[1]Sleep appears to restore energy and well-being and bolster immune function, thermoregulation, tissue recovery, and consolidation of memory.[1]

"Sleep to remember" as sleep has an integral role in memory. Sleep-dependent memory processing leads to stabilization, augmentation, and consolidation of explicit (declarative) and implicit (nondeclarative) memories.

Cognition stands for Latin verb *cognosco* ("with" + "know"), which broadly means "to conceptualize" or "to recognize." Cognition is acquisition of knowledge and includes attending, remembering, and reasoning. Learning is acquisition of the information, and memory is retention and storage of learned information. Memory can be classified in a time-dependent manner into short-term and long-term memories. Long-term memory is declarative or nondeclarative (procedural) memory. There are multiple factors that affect memory and cognition, i.e., personal factors, psychological factors, environmental factors, nutrition, genetics, and physiological factors. The most important physiological factor affecting cognition is sleep. Absent, insufficient, or fragmented sleep impairs memory. In this review, we will discuss the role of sleep in cognition, cognition in sleep disorders, and sleep in cognitive disorders.

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Role of Sleep in Cognition

Encoding and retrieval of memory occurs during wake time, whereas consolidation takes place during sleep. Consolidation is a process that transforms new labile memories that were encoded in the wake state to a more stable representation, which later incorporates into the network of other existing long-term memories.[2]Consolidation occurs most efficiently offline, i.e., in sleep, as the process of encoding and consolidation may not interfere among each other, leading to hallucinations.[3]Researches are undergoing on the mechanism through

which sleep supports memory consolidation and into different types of consolidation, i.e., synaptic consolidation and system consolidation. In SWS, slow oscillations, ripples and spindles re-activate and redistribute hippocampus-dependent memories to neocortical sites at minimum cholinergic activity, whereas in REM sleep, in plasticity related gene activity promote synaptic consolidation of memories in the cortex at high cholinergic and theta activity.[2]

Recent evidence supports differential role of slow wave sleep (SWS) and rapid eye movement (REM) sleep for different types of memory consolidation. The latest dual process hypothesis proposes that SWS specially benefits declarative memory, while REM sleep preferentially affects nondeclarative memories (Figure 1)[2,8]

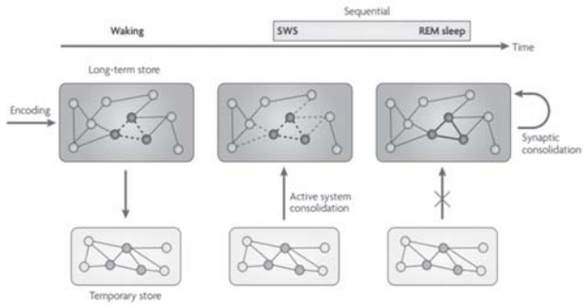

Figure 1: Sequential contributions of slow wave sleep (SWS) and REM sleep to memory consolidation in a two-stage memory system: During waking, memory traces are encoded in both fast learning (temporary store) and slow learning (long-term store). System consolidation: During subsequent SWS, newly encoded memories are reactivated (dotted lines) promoting their reorganization and integration into preexisting long-term memories network. Synaptic consolidation: During ensuing REM sleep, long-term and temporary memory stores disentangles, which promotes encapsulation of system consolidated memories (thicker lines).[2,8]

Assessment of the Effects of Sleep on Cognition

Sleep affects many aspects of cognition, and, hence, different functions such as attention, memory, decision-making, reaction time, and executive functioning must be evaluated separately. Clinical history remains the critical in assessment of sleep-related problems. Patient's history should be supplemented by information by bed partner or family member who may have different view of patient's mood, behavior, and cognitive functioning. The 3P framework in insomnia history comprising of predisposing, precipitating, and perpetuating factors must always be remembered.[9] Nocturnal polysomnography remains the gold standard laboratory test for sleep disorders (Figure 2 and Table 1).[9]

Newer developments into cognitive neuropsychology have helped sleep researchers to conduct more precise tests on cognition. These researches have helped us understand the real-world tasks that are affected from sleep deprivation (SD).[10]

Table 1: Assessment of sleep and cognition

Assessment of sleep	Assessment of cognition
• History • Sleep dairy • Subjective - Epworth Sleepiness Scale (ESS) - Stanford Sleepiness Scale (SSS) - The Pittsburgh Sleep Quality Index (PSQI) - Patient-Reported Outcomes Measurement Information System (PROMIS) • Objective - Multiple Sleep Latency Test (MSLT) - Maintenance of Wakefulness Test (MWT) - Polysomnography (PSG) • Actigraphy	• Attention – Psychomotor vigilance task (PVT) – Serial addition and/or subtraction task – Simple reaction time • Working memory – N-back/digit recall/digit span • Long-term memory – Word memory test paired word learning • Visuomotor performance – Letter cancelation task – Trail-making task • Verbal functions • Response inhibition – Go–No–Go (response inhibition) – Stoop (color-word, emotional, specific)

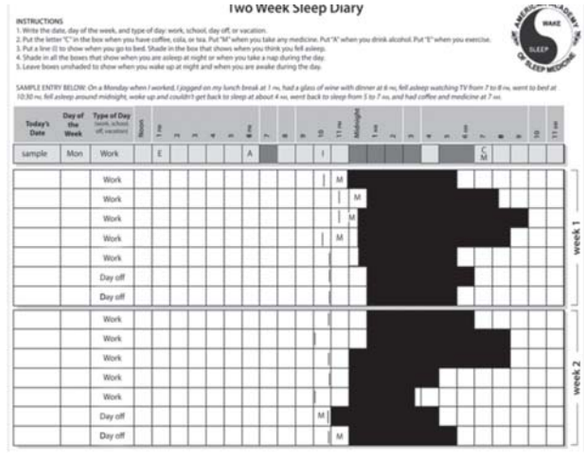

Figure 2: Example of sleep diary[9]

Impact of Sleep Deprivation on Cognition

SD can be caused by poor sleep quality or insufficient sleep quantity. Sleep deprivation is a growing issue with the present "24/7" society. Greater than one-third people sleep less than 7 h in night on weekdays.[11]

Sustained wakefulness of 17 h decreases performance similar to blood alcohol level of 0.05%.[12]

In a recent survey, around 17% people felt asleep at the wheel in past 2 years.[13] Prevalence of sleep-related accidents owing to increased reaction time was 7.0% (13.2% needed hospital care, and 3.6% experienced fatalities).[13] The most common reasons for falling asleep while driving was poor sleep in previous night (42.5%) and poor sleeping habits (34.1%)[13]

SD can be either acute total SD (acute continuously awake for 24–72 h) or chronic partial SD, and both induce adverse changes in cognitive performance. SD in general affects alertness and attention in the form of attention lapses: microsleeps characterized by very short periods of sleep-like EEG activity (>3 s), slowing of cognitive processing, wake-state instability, and so on (Table 2)[14]

Total SD chiefly impairs working memory and attention with effect on decision-making and long-term memory (free recall is more affected than recognition).[14]Other cognitive functions affected are visuomotor performance, reasoning ability, rigid thinking, perseveration errors, and difficulty in utilizing new information in complex tasks, which require innovative decision-making. There are lack of studies accessing effects of cognition with chronic partial SD, but attention, especially vigilance, is affected.[14]

Table 2: Impact of sleep deprivation

Impact of sleep deprivation	
Systemic	Cognition
High blood pressure	Lack of concentration
Risk of heart disease increase heart rate variability attack	Attention deficits
Risk of obesity	Distractibility
Risk of type 2 diabetes	Increased reaction time
Impaired immune system	Reduced vigilance
Growth suppression	Impaired judgment
Lack of energy	Increased errors
Fatigue	Forgetfulness
	Memory lapses or loss
	Hallucinations
	Anxiety
	Depression

Brain adapts to chronic sleep restriction. In a study involving 66 normal volunteers, 7 days of sleep restriction degraded psychomotor vigilance performance in a sleep-dose-dependent manner. In mild to moderate sleep restriction, brain adaptation was sufficient to stabilize performance, although at a reduced level.[15]

In a study comparing effects of acute versus chronic partial SD, acute sleep restriction induced a high increase in sleep propensity in middle-aged study participants, but adaptation to chronic sleep restriction occurred beyond day 3 of restriction.[16]

One recovery night restored daytime sleepiness and cognitive performance deficits induced by acute or chronic sleep deprivation.[16]

Killgore et al.[19] concluded in their study on 26 healthy volunteers that sleep loss leads to temporary changes in cognition, emotion, and behavior consistent with mild prefrontal lobe dysfunction.

Impact of Sleep in Disorders of Cognitive Impairment

Aging affects various aspects of sleep. Total sleep time, sleep efficiency, percentage of REM sleep, and SWS showed a significant age-related decrease ($P< 0.05$) in a population-based study with 1024 individuals (20–80 years). Night-time spent awake after sleep onset (WASO), arousal index, sleep latency, REM sleep latency, and the percentage of stages 1 and 2 showed a significant age-related increase ($P< 0.05$)[18]; 45% of Alzheimer's disease (AD) patients have sleep disturbances.[19]

Sleep and AD pathology have a bidirectional relationship.[20]

Sleep abnormalities are similar but more severe in AD patients than in elderly people. There are microalterations in sleep architecture, sleep fragmentation, reduced nocturnal sleep duration, and inversion of sleep–wake cycle.[19]

Aggregation of β-amyloid (Aβ) in the brain begins

years before the clinical symptoms of AD occur. A study on APPswe/PS1δE9 mouse model suggest that Aβ aggregation markedly deteriorated the sleep–wake cycle and virtual elimination of Aβ deposits in the mouse brain by active immunization with Aβ(42) normalized the sleep–wake cycle again.[21]

In a cross-sectional study of 145 cognitively normal individuals, amyloid deposition was associated with worse sleep quality but without reduced sleep quantity in preclinical AD subjects.[22]

Sleep phenotypes can be reliable translational biomarkers for research in AD.[23]

The prevalence of obstructive sleep apnea (OSA) increases with aging but seems higher in patients with AD. A randomized-controlled study on 39 AD with sleep-disordered breathing patients showed that a positive impact of continuous positive airway pressure (CPAP) treatment have on cognitive function in such patients.[24] Acetyl cholinesterase inhibitors seem to have beneficial effects on both sleep pattern and memory.[19]

No evidence that melatonin/ramelteon are beneficial to AD patients with sleep problems.[25]

There is some evidence to support the use of a low dose (50 mg) of trazodone, although larger trial is needed to allow a more definitive conclusion.[25]

Cognition in Sleep Disorders

Besides decline in alertness level with respect to healthy subjects, chronic sleep disorders such as primary insomnia (PI), OSA, and narcolepsy are also associated with poor memory performance.

Reduced amount of SWS and increased amounts of stage 1 sleep in patients with PI impairs sleep-dependent memory consolidation, especially for declarative information.[26]

In a recent meta-analysis by Fortier-Brochu et al.,[29] they analyzed 24 studies of 639 insomnia patients and 558 normal sleepers. Significant impairments ($P< 0.05$) for tasks assessing episodic memory, problem solving, manipulation in working memory, and retention in working memory were found in insomnia patients.[27]

But, no significant group differences were observed for tasks assessing general cognitive function, perceptual and psychomotor processes, procedural learning, verbal functions, different dimensions of attention (alertness, complex reaction time, speed of information processing, selective attention, and sustained attention/vigilance), and some aspects of executive functioning (verbal fluency and cognitive flexibility).[27]

Adult OSA is associated with cognitive dysfunction. Sleep fragmentation and reduced SWS in OSA impairs sleep-dependent consolidation for verbal declarative information and correlates with number of completed non-REM–REM sleep cycles overnight.[26]

The obstructive events lead to reduction in blood oxygen saturation (hypoxemia) with increase in blood carbon dioxide (hypercapnia) and sympathetic activity. Resolution of airway obstruction occurs with arousal from sleep. Bucks et al. did a meta review on neurocognitive function in OSA. Patients with OSA showed deficits in attention/vigilance, delayed long-term visual and verbal memory, visuospatial/constructional abilities, and executive function. Language ability and psychomotor function remained unaffected by OSA. There were equivocal effects on working memory, short-term memory, and global cognitive functioning. Attention/vigilance dysfunction correlated with sleeps fragmentation and decline in global cognitive function correlated with hypoxemia. CPAP for OSA improved executive dysfunction and delayed long-term verbal and visual memory, attention/vigilance, and global cognitive functioning.[28]

Sleep fragmentation, frequent REM sleep episode at sleep onset, and excessive daytime sleepiness in narcolepsy with cataplexy patients impairs sleep-dependent component for procedural visual skills.[26] In two studies by Naumann et al.[31] on narcolepsy patients showed impairments in attention and executive function tasks, which involved higher demands on inhibition or task management abilities, whereas relatively routine memory and attention tasks were largely unaffected or only mildly impaired in narcolepsy.[29]

Cognitive deficits seen in restless legs syndrome (RLS) may also result from ineffective sleep, but only a few studies support this. Recent study explores the prevalence and symptoms associated with RLS in an older French population (318 subjects: 219 women and 99 men, aged 68.6 ± 0.8 years). Patients with RLS showed lower cognitive performances at Stroop and verbal fluency tests than non-RLS participants ($P< 0.05$ and $P = 0.002$, respectively).[30]

Conclusion

It is correctly said-sleep to remember and remember to sleep as consolidation of memory occurs in sleep. Sleep and cognition seems to have bidirectional relationship.

Sleep-related disorders affect cognition. All patients with impaired cognition must be accessed for sleep sufficiency and efficiency. Improvement in sleep quality and quantity positively influences cognition. Similarly, disorders of cognitive impairment such as AD reveal associated sleep loss. Sleep studies are potential candidate as biomarkers for early AD. Improvement in sleep quality in such patients provides better quality of life.

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