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The consequences of acute sleep deprivation on hippocampus-dependent memories

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ABSTRACT

While the exact functions of sleep are not completely understood, it is a crucial part of daily life and comprises series of events that follows a consistent nightly cycle, enabling the human body to function at its best. More than 30% of adults suffer from sleep deprivation (SD). SD can lead to negative effects on cognitive performance including learning and memories. Here we review the consequences of acute SD on hippocampus- dependent memories, and activity and connectivity of different brain regions involved in the memory processing by focusing on neuroimaging studies.

Keywords: sleep deprivation, memory, hippocampus, brain networks, functional connectivity, neuroimaging.

Abbreviation list

SD: sleep deprivation; NREM: non-rapid eye movement; REM: rapid eye movement; WM: Working memory; DLPFC: dorsolateral prefrontal cortex; DMN: default mode network; LTP: long-term potentiation; TMS: transcranial magnetic stimulation

INTRODUCTION

Sleep is a vital physiological process that plays an essential role in maintaining both physical and mental health [1]. It is marked by a significant reduction in consciousness and responsiveness to sensory stimuli, both of which can be rapidly reversible [2]. Sleep affects almost every bodily and mental function and causes intricate alterations in the physiology of numerous systems [3]. The body performs the necessary processes to support brain function and general health while you sleep [3]. At various stages of sleep, important processes like neurogenesis and synaptogenesis take place. Sleep is also essential for removing toxins that build up around brain cells while we are awake. Cerebrospinal fluid production and circulation rise significantly while you sleep, aiding in the removal of toxins like beta-amyloid from brain tissues. Sleep is also essential for preserving mental balance and controlling emotions. Getting enough sleep is essential for all cognitive processes, including learning, memory consolidation, attention, language, reasoning, creativity, and decision-making.

Brain activity undergoes significant changes during both non-rapid eye movement (NREM) [4] and rapid eye movement (REM) [5] sleep stages. Sleep is therefore anticipated to be essential for brain function [6]. Older adults usually need 8 to 9 h of sleep per night, while healthy adults need 7 to 9 h [1]. The most prevalent sleep-related complaint, sleep deprivation (SD), can result from losing even one hour of sleep [7]. A reduction in the typical length or quality of sleep is a hallmark of SD [7]. If SD lasts for one or two days, it is

classified as acute SD, while prolonged deprivation is referred to as chronic SD [8]. The severity of SD can differ among individuals. Acute SD affects more than 30% of the population, and chronic SD is estimated to affect 6-10% globally [8].

Significant life stress, disease, physical or psychological harm, and environmental factors like light, noise, and extremely high or low temperatures are some of the factors that can lead to SD [9]. Cognitive function is compromised in people with SD, and they frequently perform worse on tasks requiring logical and analytical reasoning. They usually struggle with tasks that require sustained attention and take longer to react to environmental stimuli [6]. People with SD are more vulnerable when engaging in activities that demand heightened attention, like driving, because it impairs executive functions and raises sleep pressure [10]. The neurological changes associated with the consequences of SD are the focus of considerable research. Various studies have sought to explore the alterations in activity or connectivity within the relevant neuronal networks. Here, we review neuroimaging studies that examine how memory-related brain networks are impacted by acute SD in humans.

Effect of acute SD on working memory

Working memory (WM) - the ability to maintain information over very brief periods of time - is traditionally thought to rely heavily on frontoparietal attention networks, but recently has been shown that it can also rely on the hippocampus [10, 11]. Higher order cognitive processes like reasoning, learning, and comprehension are supported by it [12]. Due to its importance in complex cognitive processes, WM's composition and structure have been the subject of extensive research [12]. Three components make up Baddeley's (2007) model of the WM system: the central executive, which is the main component, two subordinate systems, the phonological loop, which actively recalls verbal information and passively stores it, and the visuospatial sketchpad, which maintains and manipulates visual and spatial information [13]. Baddeley (2012) later introduced another subsystem, the episodic buffer, which temporarily integrates diverse information from multiple coding systems [14]. Besides Baddeley's multi-component model, there are alternative WM models, such as Cowan's embedded-processes model and Oberauer's concentric model, but the multi-component model created by Baddeley remains the most widely accepted [15–17].

SD also affects WM, which has anatomical similarities to the attention system. Studies have demonstrated a correlation between reduced activity in the dorsolateral prefrontal cortex (DLPFC) and posterior parietal regions and deficiencies in WM and attention tasks [18–22]. Similar to attention tasks, variations in thalamic activity [20–22] and inappropriate persistence of default mode network (DMN) activity occur during WM tasks in sleep-deprived conditions [19–21]. Furthermore, the extent of abnormal DMN activity while engaged in tasks is a predictor of the severity of WM deficits in individuals who are sleep-deprived [20, 21, 19]. Consequently, the inappropriate regulation of on-task versus off-task network control may represent a shared mechanism behind the impairments in both attention and WM that result from SD [23].

Because the thalamus plays a critical role in cortical arousal, changes in thalamic activity and connectivity can predict WM performance deficits under SD conditions, much like changes observed during attention tasks [23]. For example, in people who are sleep- deprived, increased feelings of drowsiness and worse WM performance are associated with increased connectivity between the hippocampus, thalamus, and DMN [24, 25]. On the other hand, improved WM performance recovery under SD conditions is linked to increased thalamic-precuneal connectivity as opposed to a well-rested state [23]. This finding lends credence to the theory that during SD, the brain undergoes compensatory neural activity, which could help some behaviors partially recover [26].

People who are sleep deprived exhibit reduced signals in extrastriate (visual) cortical areas during visual WM tasks in addition to decreases in activity in frontoparietal regions [19, 22]. According to recent research, performance impairments may be caused by this regional decrease in task-related activation. In particular, it has been demonstrated that applying transcranial

magnetic stimulation (TMS) to the extrastriate cortex of people who are sleep-deprived improves visual WM performance and restores it to baseline levels [27, 28]. Notably, WM performance has been maintained for up to 3 days without sleep when TMS is applied to these extrastriate areas every 6 h for 18 h [27]. The reproducibility of these findings is unclear, though, because the effects of TMS interventions in the context of SD are not always dependable [29]. Significant practical ramifications could result from the development of a trustworthy intervention technique, especially in industries like aviation or military operations where prolonged focus is necessary and SD is common [23].

Effect of acute SD on hippocampal memory

The benefits of sleep on the offline consolidation of hippocampus-dependent memories after learning have been shown in numerous studies [30]. The majority of neuroimaging studies have focused on how SD impacts the initial encoding of hippocampus-dependent memories, whereas there has been little research on the detrimental effects of SD on this process [30].

The ability of the hippocampus to produce long-term potentiation (LTP), an electrical measure of neuroplasticity, is markedly compromised in animals with SD [31]. The increase of LTP tends to fade more rapidly, even when it is successfully induced [31]. Moreover, SD impairs neurogenesis in the hippocampus and inhibits the synthesis of proteins associated with neuroplasticity [32].

Neural plasticity is impacted by the buildup of the metabolic waste adenosine outside of cells during extended periods of awake. Increased adenosine levels decrease the signaling of AMPA and NMDA receptors in the hippocampus, which are both necessary for sustaining sustained LTP, and interfere with intracellular cAMP signaling in rodents [30]. The impacts on plasticity may result from two overlapping factors: excessively extended wakefulness or inadequate sleep, as adenosine is removed from the brain during sleep [23].

Building on these findings, early behavioral and neuroimaging research in humans has shown that a single night of SD reduces activity related to learning and encoding in the medial temporal lobe, particularly the hippocampus [33]. Furthermore, auditory stimulation that maintains total sleep duration through selective deprivation of NREM slow-wave sleep also decreases hippocampal encoding-related activity and related learning [26]. A causal role for slow-wave sleep in encoding hippocampal memory is further supported by the fact that increasing the strength of NREM slow-wave activity through transcranial stimulation improves hippocampal learning ability after sleep [34].

Additionally, SD has an impact on learning-related hippocampus connections. When storing visual episodic memories under SD conditions, the hippocampus's functional connection with the perceptual regions of the occipital (visual) cortex and nearby areas in the medial temporal lobe is reduced [26]. On the other hand, SD is also associated with heightened hippocampal connection with subcortical arousal areas, including as the thalamus and brainstem [26]. Although it is insufficient to enhance behavioral performance, this increase has been regarded as a compensatory mechanism meant to activate basic arousal networks [26].

According to a recent study, an individual's vulnerability to the effects of SD on memory encoding can be predicted by the structural morphology of the human hippocampus, specifically the volume of the CA3-dentate gyrus subfield [35]. Furthermore, it was discovered that the same measurement was associated with the amplitude of NREM slow-wave oscillations during recovery sleep, which in turn affected how well memory encoding skills recovered when reassessed following recovery sleep [23]. Thus, a new trait-like feature and possible biomarker for comprehending how memory processing is impacted by and recovers from the disruptive effects of SD may be found in the morphology of the hippocampus subfields [23].

During memory encoding, the hippocampus is a component of a wider network of anatomically and functionally related cortical regions rather than operating independently [23]. While some of these regions, like the DLPFC and posterior parietal regions, play supportive roles by facilitating directed attention, others, like sensory perceptual areas, are believed to directly contribute to the encoding of memory

representations [19]. This theory is supported by human neuroimaging research, which has demonstrated that SD is associated with deficits in the hippocampus's function in encoding new memories as well as impairments across broader networks [36]. For example, during visual episodic-memory tasks, a 24-h SD decreases activity in areas of the posterior parietal cortex and DLPFC that are critical for goal-directed attention. More unclear are SD's effects on the scene-selective fusiform cortex, which could point to a breakdown in frontoparietal networks' top-down attentional control or a disturbance in the visual cortex's capacity to process visual scenes [37]. Nevertheless, the degree of memory impairment brought on by SD and the intensity of attentional lapses during tasks are correlated with the degree of activity changes in all three cortical regions (frontal, parietal, and occipital) [23].

Significant differences in DMN activity within cortical regions have been noted during episodic memory encoding after SD, which is similar to tasks involving WM and selective attention [38]. In particular, there was a 93% sensitivity and a 92% specificity in separating participants who were sleep-deprived from those who were well-rested based on the degree of decreases and increases in activity of the anterior cingulate and precuneus, two important DMN nodes [38]. Therefore, in people who are sleep-deprived, unstable control of the DMN may be a common neural trait associated with deficiencies in a variety of cognitive tasks, such as attention, WM, and episodic memory [23].

The neurochemical underpinnings of memory-encoding deficits linked to SD have only been examined in one study, which found that giving an acetylcholinesterase inhibitor, which amplifies the central synaptic effects of acetylcholine, partially restored activity in the frontoparietal and fusiform regions of participants who were sleep-deprived to levels similar to those of people who were well-rested [36]. Notably, the most significant improvements from this treatment were seen in participants who exhibited the largest reductions in brain activity during a semantic judgment task and had the poorest performance in word recognition when sleep-deprived [23]. In other words, those who were most affected by sleep loss on these tasks showed the greatest recovery of function after receiving the drug.

Acetylcholinesterase inhibitors have a direct effect on sensory processing and are known to improve attentional processes that support episodic memory [39]. Cholinergic effects on arousal may contribute to this effect. Hippocampal networks may become more involved in sensory and attentional processing in the cortex as a result of these inhibitors' promotion of hippocampus plasticity mechanisms [23]. As a result, research has demonstrated that when compared to a placebo, acetylcholinesterase inhibitors improve task performance by increasing activation in the visual and parietal cortices during visual short-term memory tasks in sleep-deprived individuals [40].

For many diseases and conditions that affect both sleep and memory functions, the hippocampus's incapacity to correctly encode memories following SD is important on a translational level [23]. Dementia and aging are two prominent instances. Significant NREM sleep deficits are seen in older adults in cognitively healthy conditions, and these problems are exacerbated in Alzheimer's disease patients [41]. Reduced encoding-related activity in the hippocampus the next day, which correlates with the severity of learning difficulties, is predicted by disruptions in NREM sleep, as well as decreased slow-wave activity and sleep spindles in older adults, particularly in Alzheimer's patients [42, 34]. As people age, sleep disruption may have an impact on cognitive decline, especially on hippocampus-dependent memory processing. In order to combat age-related declines in hippocampus-dependent memory, this evidence points to sleep restoration as a potentially effective therapeutic approach and a preventative measure during midlife [41].

CONCLUSION

The detrimental impacts of SD are evident in both general behavior and cognitive function. Reduced mental function and slower reaction times result from sluggish neurological pathways. In order to cope until the brain can be reactivated, the body's systems go into a sort of survival mode. Uneven brain stimulation can cause erratic reactions to SD. This can be caused by differences in thalamic

activity, synaptic renormalization, the function of the lymphatic system, activity in the DMN, as well as in the amygdala and hippocampus. As a result, this may affect memory consolidation and WM. A person's brain benefits from enhanced cognitive function and quicker reaction times after they receive the recommended amount of sleep. To confirm the precise mechanisms and effects of SD, more research is required.

DECLARATIONS

The author declares no conflicts of interest.

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