



## While You Were Sleeping: Memory Consolidation and REM Sleep

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### Abstract

As researchers have tried to determine the “purpose” of sleep, they have discovered its ability to improve memory consolidation by either stabilization or enhancement. Neuroscientists have demonstrated that different stages of sleep perform distinct functions in memory consolidation. This paper examines the memory function of REM sleep. Through reviewing diverse experiments and considering alternate hypotheses, data is synthesized to create a cohesive perspective on the memory function of REM sleep and demonstrate that the future of the field rests upon researchers’ ability to successfully integrate behavioral and molecular levels of analysis.

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### Introduction

While ancient philosophers considered sleep an outlet for prophecy and enlightenment, sleep’s phenomenology and function continues to baffle neuroscientists, psychologists and philosophers alike (Siegel, 2001). However, it was Sigmund Freud’s *Interpretation of Dreams* that finally offered a “theoretical framework” for a comprehensive examination of human behavior and compelled scientists to delve into the darkness of sleep to illuminate mental processes (Freud, 1913; Cartwright, 2004). With Freud’s insight and the advent of modern-day neuroscience techniques, researchers have begun to understand the phenomenology and function of sleep. In this pursuit, scientists have unearthed the memory function of sleep and demonstrated its ability to improve memory consolidation by either stabilization or enhancement. As research has continued and specialization has intensified, neuroscientists have acknowledged that different stages of sleep, i.e. rapid eye movement (REM) and non-REM, execute distinct functions in memory consolidation. Continuing in the pioneering tradition of Freud, I will investigate memory consolidation and its relation to REM sleep in hopes that yesterday’s darkness will produce today’s enlightenment.

One of the greatest challenges in studying the role of sleep in memory processing is its heterogeneity. Sleep is not a single unified process, but rather is constituted by the cyclic episodes of REM and non-REM sleep, which includes slow wave sleep (SWS) and sleep stages 1 and 2 (Diekelmann & Born, 2010). Furthermore, this cycle changes throughout the night, with SWS dominating the early part of the night and REM sleep prevailing in the later half. These sleep stages differ in their respective patterns of electrical field potential oscillations: SWS is distinguished by slow oscillations, sharp wave-ripples and slow spindles, while REM sleep is characterized by ponto-geniculo-occipital (PGO) waves and theta activity. PGO waves are phasic electrical bursts of synchronized neural activity that originate in the pontine brainstem and project to the lateral geniculate nucleus and visual cortex. Theta activity refers to the 4-8 Hz oscillations that predominate in the hippocampus. Furthermore, these sleep stages differ in neuromodulator activity: SWS is typified by low levels of acetylcholine (ACh) and cortisol and REM sleep is characterized by high levels of ACh and cortisol and low levels of norepinephrine (Diekelmann & Born, 2010). With these many distinguishing factors, it is no surprise that neuroscientists believe that SWS and REM sleep execute discrete functions in the memory processing that occurs during sleep.

### Behavioral Studies

In light of the fact that sleep both facilitates and optimizes long-term encoding and recall, behavioral studies have investigated the relationship between REM sleep and learning processes (Siegel, 2001). In order to demonstrate REM sleep's role in memory consolidation, researchers have conducted behavioral studies that have indicated that REM sleep duration increases with learning. According to Carlyle Smith (1995), a leading researcher in the field, elevated levels of REM sleep follow both aversive and appetitive learning tasks in rats. These REM sleep increases appear at varying times ranging from three hours to thirty-six hours. In order to investigate the relationship between REM sleep duration and learning in human subjects, Smith and Lapp (1991) examined REM sleep levels in senior college students during an examination period. Although REM sleep duration may have remained constant, they showed an increase in the intensity of REM sleep, as measured by the density of rapid eye movements. However, while these studies have demonstrated the correlation between REM sleep and learning, they have also inspired debate and criticism. To begin, researchers have struggled to devise an effective method of quantifying learning. For example, while researchers often define learning as confined to a specific task in a controlled situation, the data could be misleading if other forms of learning continued to occur outside of the laboratory procedure (Siegel, 2001). Furthermore, since stress has been shown to increase REM sleep, researchers must eliminate this confounding variable by comparing the experimental group to a control group with equivalent stress levels. While empirical criticism is not unfounded and these behavioral studies are not without flaw, it must be emphasized that when taken as a whole, these studies provide a compelling argument for a correlation between learning and REM sleep.

Other behavioral researchers who investigate this relationship have employed an effective method to assess the necessity of REM sleep to memory. Using the traditional platform deprivation technique, researchers deprive rats of REM sleep by placing them on platform in water. When rats assume a maximally relaxed REM-induced posture on this platform, they will fall into the water (Siegel, 2001). Researchers utilizing this direct method of eliminating REM sleep without disrupting SWS, researchers have found mixed results. Whereas REM deprivation effectively blocked consolidation in some studies, other studies found no effect or even improved consolidation, leading many researchers to argue that REM sleep has no role in memory consolidation (Siegel, 2001). As Horne (1984) warns in his cautionary review, the "confinement [and] frustration" experienced by the rat elicits a heightened state of arousal that potentially disrupts memory retrieval. Indeed, when an alternate technique was used to disrupt REM sleep in a less stressful manner, no such learning deficits were observed (Hulzen & Coenen, 1982). This suggests that stress is the underlying variable for memory deficits in REM deprivation studies.

Further REM deprivation studies in humans have demonstrated the idea that REM sleep may not be as important in memory consolidation as many believe. As REM sleep is associated with low levels of serotonergic and norepinephrinergic activity, selective re-uptake inhibitors of serotonin (SSRI) and norepinephrine (SNRI) effectively suppress REM sleep by increasing the levels of these neurotransmitters at the synapse (McCarley, 2007). Therefore, these widely used anti-depressant drugs offer an invaluable opportunity to study REM deprivation in human subjects (Smith, 1995). Clinical studies have challenged the REM sleep hypothesis by demonstrating that depressed patients on long-term SSRI or SNRI treatments did not suffer detriments in procedural memory consolidation (Amado-Boccaro, Gougoulis, Litré, Galinowski & Lôo, 1995). Furthermore, in a recent study examining the effects of REM sleep deprivation by SSRI or SNRI administration, researchers found that pharmacological suppression of REM sleep did not impair procedural memory consolidation (Rasch, Pommer, Diekelmann & Born, 2009).

While criticism of the REM sleep hypothesis must be considered in full, other research has helped to explain the mixed results of REM sleep deprivation studies. For example, the discovery that post-training memory consolidation only occurs in specific time windows during REM sleep, led to the realization that deprivation was only effective during specific REM sleep windows (Smith, 1995). Further, as these "windows" occur at varying times, it is highly probable that the mixed results in REM sleep deprivation studies derive from researchers failing to uniformly deprive REM sleep in the proper windows. When considering studies demonstrating preserved procedural memory function despite pharmacological suppression of REM sleep, it is apparent that certain "unidentified processes ... [such as] high cholinergic activity and the expression of plasticity-related early genes that are critical to memory consolidation and normally associated with REM sleep...may persist during REM sleep suppression after SSRI or SNRI administration" (Rasch et al., 2009). While researchers continue to argue about the conclusions one may draw from these inconsistent REM sleep deprivation studies, the ultimate path to a single, clear conclusion will be in the development of a more controlled REM sleep deprivation experiment.

## **Theories of Sleep: The Dual Process and Sequential Hypothesis**

Researchers, in an effort to organize increased information in the field into concise theories on memory consolidation, have formulated a dual process and sequential hypothesis. Continued research that examines the different stages of sleep and their respective relation to consolidation has led many sleep scholars to formulate and adopt a dual process hypothesis for memory processing. Accounting for the considerable differences between SWS and REM sleep in both electrical field potential oscillations and neurochemical release, the dual process hypothesis distinguishes the memory consolidation functions that arise from different stages of sleep (Maquet, 2001). By conducting experiments comparing SWS to REM sleep, researchers have reliably demonstrated that SWS facilitates declarative memory consolidation whereas REM sleep benefits non-declarative types of memory such as procedural and emotional memory (Diekelmann & Born, 2010). One such study, conducted by sleep researchers Werner and Born (1999), compares the retention rate of two different memory tasks following sleep periods of equal length with varying proportions of SWS and REM sleep. In accordance with the dual process hypothesis, the spatial rotation task (declarative memory) produced greatest recall when it followed early SWS-rich sleep whereas enhancements on the word-stem priming task (procedural memory) were greatest following late REM-rich sleep. In its assumption of a simplistic approach, the dual process hypothesis maintains that SWS promotes declarative, hippocampus-dependent memory and REM sleep benefits non-declarative hippocampus-independent memory (Diekelmann & Born, 2010). However, while simplicity benefits our understanding of sleep processing, researchers must be wary and critical of its convenient divisions.

While considerable sleep research aligns with the dual process hypothesis, this highly simplistic model loses credibility with the advent of further research that examines the differential functions of SWS and REM sleep. The apparently clear line between SWS and REM sleep begins to blur when one considers evidence linking REM sleep to facilitated declarative memory consolidation and SWS to improved procedural skill memories (Diekelmann & Born, 2010). A recent study examining the learning-dependent changes in sleep effectively demonstrates that memory consolidation during sleep is not a “unitary process” but rather a dynamic, flexible procedure whereby different types of procedural memories can elicit dissociable effects on sleep stages (Fogel, Smith & Cote, 2007). By measuring sleepers’ levels of neurophysiology activity (spindles, rapid eye movements, K-complexes and EEG spectral power) before and after various types of learning tasks, researchers could determine whether changes in activity were indicators of plasticity or mechanisms for memory processing. While REM sleep is traditionally implicated in non-declarative memory, the researchers found a marked increase in theta activity (4-7 Hz brain wave) from baseline after training on the paired associates test, thereby providing “the first evidence to indicate that REM sleep theta is involved in the consolidation of declarative memory.” (Fogel et al., 2007). Furthermore, by demonstrating that “different types of learning affect different sleep states in different EEG frequency bands in dissociable brain regions and have unique phasic markers,” the authors suggest that researchers must abandon the simplistic nature of the dual process hypothesis in order to account for the complex variability of memory processing during sleep. In response to this, researchers have proposed the sequential hypothesis, a model for memory processing which argues that in order for optimal consolidation of both procedural and declarative memories to occur, SWS and REM sleep must take place in succession. By challenging the practice of ascribing specific sleep stages to particular aspects of memory consolidation, the sequential hypothesis offers a more holistic view to the study of sleep and memory. However, while both the dual process and sequential model offer important insights into the nature of sleep, they also highlight the dynamic, ever-changing nature of sleep research and thus urge for a flexible, multilevel approach for the study of memory processing in sleep.

### **Molecular Studies**

For a comprehensive investigation of the memory processing that occurs in REM sleep, one must examine learning and memory on a molecular scale. With the publication of *The Organization of Behavior* in 1948, Donald Hebb provided the framework within which neuroscientists have conceptualized consolidation processes for the past sixty years. Stemming from Hebb’s theory that “the persistence or repetition of a reverberatory activity (or ‘trace’) tends to induce lasting cellular changes that add to its stability,” neuroscientists currently hold that consolidation occurs during sleep after encoding and relies upon the reactivation of the “trace” involved in the encoding of the information (Hebb, 1949; Diekelmann & Born, 2010). This “reverberating activity” promotes system consolidation by instigating the redistribution of newly encoded memories into long-term storage, and facilitates synaptic consolidation by inducing enduring synaptic changes necessary to stabilize memories (Diekelmann & Born, 2010).

In its investigation of synaptic consolidation, research has focused primarily on SWS, based on the hypothesis that SWS plays a preferential role in the reactivation of memory traces. Support for this belief derives in part from research that manipulated memory reactivation during sleep by presenting odor cues that

were previously presented during a visuospatial learning task (Rasch, Buchel, Gais & Born, 2007). By altering the sleep stage during which the odor cue was re-presented, the researchers demonstrated that presentation of an odor cue during SWS significantly enhanced performance in comparison to trials in which the cue was presented in REM sleep (Rasch et al., 2007). Therefore, while reactivations induced by odor re-presentation during SWS facilitated memory consolidation, those elicited in REM sleep produced no such enhancement, thereby suggesting a preferential role of SWS in reactivation processes. However, while the reactivation of memory traces have been shown to preferentially occur in SWS, reverberating activity has also been observed in REM sleep (Diekelmann & Born, 2010). One study demonstrating neuronal reactivation in REM sleep arose from the work of neuroscientists Kenway Louie and Matthew A. Wilson (2001). While recording from place cells in the CA1 region of the hippocampus, Louie and Wilson trained rats to run around a circular track. Following acquisition of this behavioral task, electrophysiological activity was monitored during task performance and sleep immediately before and after behavior. Since task performance elicits distinct hippocampal firing patterns, Louie and Wilson (2001) inspected REM sleep for similar patterns of electrophysiological activity. In accordance with their hypothesis, the results confirmed that the temporally sequenced neuronal ensemble firing patterns observed during behavioral experience are reactivated at an equivalent timescale during REM sleep. While this study is but one of many showing neuronal replay in REM sleep, it effectively demonstrates the potential neuronal mechanisms behind memory consolidation in REM sleep. Indeed, it is possible that this reverberation functions as a method of transferring encoded memories into a long-term store, thus re-organizing and stabilizing the information (Diekelmann & Born, 2010). When considering REM sleep's role in system consolidation, it thus seems that the sixty-year-old Hebbian theory that neurons that fire together wire together still holds.

Although REM sleep contributes to system consolidation, it plays a more substantial role in synaptic consolidation. Evidence suggests that REM sleep mechanistically implements the synaptic strengthening of memory representations through long-term potentiation (LTP) (Diekelmann & Born, 2010). Illustrating LTP's essential role in memory consolidation, sleep-dependent plasticity has been shown to rely upon the activation of "the postsynaptic machinery crucial for induction and maintenance of LTP," specifically glutamatergic receptors (Marcos, 2006). Since the reactivations of glutamatergic circuits occur preferentially in REM sleep and support LTP, they provide valuable insight into the potential mechanisms of synaptic consolidation (Diekelmann & Born, 2010). In order to enrich our understanding of memory processing in REM sleep, researchers have also examined the anatomical changes underlying synaptic strengthening. Following Hebb's theory that long-term memory consolidation involves anatomical changes at the synaptic level, REM sleep has been shown to mediate the expression of plasticity-related immediate early genes (IEGs) through hippocampal LTP. For example, researchers have argued that one such IEG, *zif-268*, plays a critical role in synaptic consolidation in REM sleep (Ribeiro, Goyal, Mello & Pavlides, 1999). In order to support this claim, researchers have linked *zif-268* levels to LTP induction in the hippocampus, neuronal morphological changes after exposure to a novel environment and other plasticity-related phenomena (Ribeiro et al., 1999). Furthermore, *zif-268* expression seems to preferentially occur in REM sleep over SWS and waking conditions. While the examination of *zif-268* certainly elucidates the expression of IEGs in REM sleep, it also offers insight into the selective, flexible nature of memory consolidation. As *zif-268* represents only one of the many IEGs, it is probable that different types of learning alter the expression of various subsets of IEGs, thus allowing for a flexible, selective method for long-term memory consolidation in REM sleep. Based on the abundance of literature surrounding gene expression in REM sleep, researchers are confident that REM sleep is particularly suited for synaptic consolidation.

Drawing from the research indicating that each sleep stage is preferentially suited for specific memory processing, the active consolidation hypothesis offers a comprehensive theory on memory consolidation. This increasingly popular hypothesis argues that the selective reactivation of memory traces during sleep initiates an active consolidation process whereby SWS and REM sleep each perform discrete and necessary functions (Diekelmann & Born, 2010). Initiating the sequence of events leading to consolidation, memory traces during waking are encoded both in a fast-learning, temporary storage as well as a slow-learning long-term storage. In subsequent SWS, traces of recently encoded memories are repeatedly reactivated causing a strengthening of connections within the neocortex that thereby incorporates the newly encoded memories into long-term storage (Diekelmann & Born, 2010). Due to substantial research demonstrating SWS preferential role in reactivation, this reactivation-dependent enhancement and reorganization has focused primarily on SWS. However, it should be noted that these critical effects could also be attributed to REM sleep, which, demonstrated by Louie and Wilson's study (2001), can facilitate the reactivation of place cells. Whereas SWS most effectively and broadly contributes to this reactivation process, REM sleep acts primarily to strengthen memory traces and stabilize the underlying synaptic connections in the long-term memory storage (Diekelmann & Born, 2010).

This claim is firmly supported by evidence correlating REM sleep with plasticity-related IEG activity. While the active consolidation hypothesis offers a convenient framework that clearly defines each sleep stage's respective processes and function, its simplistic approach must be considered critically. Indeed, when one considers the incredible complexity and depth of sleep research, it seems very improbable that the lines separating the various stages' respective functions are as clear as the hypothesis suggests.

### **The Electrophysiology of Sleep**

While current hypotheses fail to encompass sleep's many complexities, a richer conceptualization of REM sleep's role can be gained by considering the field potential oscillations that characterize REM sleep. As each sleep stage is characterized by specific electrical field potential rhythms, it stands to reason that the sleep architecture itself underlies, or at least elucidates memory processing. In this pursuit, researchers have linked REM sleep's distinctive PGO waves and theta activity to the sleep memory consolidation processes that occur in REM sleep (Diekelmann & Born, 2010).

Research has indicated that the density of PGO waves directly correlates with the degree of consolidation. By investigating the molecular underpinnings behind this relationship, a recent study illuminated PGO waves potential role in consolidation in rats. Not only did the researchers demonstrate a robust increase in REM sleep PGO-wave density after training on an avoidance task, they also showed that this increase correlated with improvement in post-sleep task performance (Datta, Li & Auerbach, 2008). Furthermore, PGO waves were associated with enhanced activity of plasticity-related IEGs and brain-derived neurotrophic factor in the dorsal hippocampus and amygdala, i.e. the very genes that contribute to memory processing and brain development. Taken together, these findings provide substantial evidence that activation of the PGO-wave generator initiates a cascade of molecular and cellular events that facilitate memory consolidation (Datta et al., 2008).

Just as PGO waves support REM sleep-dependent consolidation processes, so do theta waves. Research has suggested that theta waves serve as a means by which REM sleep modulates the fate of memories. For example, by examining the firing patterns of hippocampal CA1 place cells during REM sleep following familiar or novel experiences in rats, researchers found that the firing-phase determined which synapses were strengthened or weakened (Poe, Nitz, McNaughton & Barnes, 2000). Exposure to a novel track induced neuronal firing on the positive phase of the hippocampal theta rhythm and thus led to long-term potentiation (LTP). In contrast, experience with a familiar stimulus provoked neuronal discharge on the negative phase and thereby led to long-term depression (LTD). As the authors suggest, the experience-dependent theta phase shift supports the hypothesis that circuits may be modified during REM sleep by selectively strengthening recently acquired memories and weakening older ones. However, the mechanism by which this decisive phase reversal occurs remains unknown.

### **Dreaming**

With evidence from both behavioral and molecular studies, researchers have successfully spanned multiple levels to demonstrate REM sleep's important role in memory consolidation. However, this investigation would be incomplete if it did not consider the very facet of REM sleep that triggered its initial fame and epitomizes its mystery. I am referring, of course, to dreaming. While Freud lacked the tools of modern neuroscience, he asserted that dreams "do not originate in another world" but rather reflect a "senseful physiological structure" that offers insight into waking behavior (Freud, 1913). This sentiment echoed again in the late 20<sup>th</sup> century with Jonathan Winson's notion that sleep provides a powerful lens into the issues that motivate and impede our ability to both learn and alter behavior (Winson, 1985). Unfortunately, despite the innovative speculation of these great thinkers, science still fails to adequately explain "why we dream or what we dream about" (Payne & Nadel, 2004).

However, current researchers believe that by examining *what* we dream about, we will in turn elucidate *why* we dream in the first place. Specifically, researchers have revisited Freud's examination of dream content by investigating how the "sequence of dreams reveals the way new experience is being related to older memories," thus highlighting the processes of consolidation (Cartwright, 2004). Indeed, in examining dream stories, scientists have confirmed the commonsense view that dream narratives are not mere reflections of waking thoughts but rather a synthesis of both recent and long-term memory traces. To support their idea that dream content reflects the memory consolidation that occurs across sleep stages, researchers. Payne and Nadel (2004) demonstrated that variations in cortisol levels across sleep affects the communication between the hippocampus and neocortex, which thereby impacts both the memory consolidation processes that occur during sleep as well as the phenomenology of dreams. For instance, while cortisol levels are low early in nocturnal sleep they begin to rise during the middle of the sleep period, eventually peaking right before waking

hours. These rising cortisol levels instigate both rapid and delayed changes in neural functions, ultimately altering or disrupting communication between the hippocampus and the neocortex. As these high cortisol levels coincide with late-night REM sleep, they can account for both the memory processing and dream content that occurs in this REM sleep. By impeding hippocampal-neocortical communication, elevated cortisol levels disrupt the consolidation of declarative memories and promote the consolidation of procedural memories (Payne & Nadel, 2004). Due to the “specificity and discrete nature” of procedural memories, the consolidation of these memories optimally benefits from the REM sleep-associated synaptic consolidation in localized brain circuits (Diekelmann & Born, 2010). In contrast, the consolidation of declarative memories relies upon “the integration of features from different memories in different memory systems and corresponding information transfer between brain areas, that is SWS-dependent consolidation” (Diekelmann & Born, 2010). Furthermore, cortisol impacts dream narrative as dreams occurring in REM sleep exhibit a non-episodic, fragmented, bizarre nature indicative of exclusive neocortical activation (Payne & Nadel, 2004). Thus, while Payne and Nadel’s (2004) research illustrates the correlation between cortisol levels and off-line memory consolidation, it is not without holes. However, despite these holes, their research signifies a critical shift in neuroscience’s treatment of dream content, from their dismissal as inconsequential, random emanations from the “unthinking pons” to their reverence as a lens through which to view off-line memory consolidation (Cartwright, 2004). Indeed, with this application, dream content could not only reveal *what* we dream, but perhaps also *why*.

### Future Directions

Ensuring a steady foundation of thought upon which sleep researchers continue to build are the works of Freud and Hebb. Freud provides a theoretical framework that encourages scientists to dive into the plunging depths of sleep to uncover truths about behavior while Hebb offers a valuable conceptualization of memory formation as a process in which reverberating activity drives the consolidation processes (Cartwright, 2004). Building on this, some researchers have worked from the top down with behavioral studies such as those examining the effect of REM sleep deprivation on consolidation processes. Others have chosen to build from the bottom up, designing molecular studies investigating phenomena including the mechanisms of LTP and phase shifts of theta waves. However, researchers must ultimately recognize that neither behavioral nor molecular analyses are complete on their own, and that the future of the field rests upon their ability to successfully synthesize these perspectives.

Future behavioral studies must evolve from convoluted platform techniques and pharmacological studies by distinguishing the individual features of REM sleep (i.e. theta waves, PGO spikes, neuromodulator activity, gene expression) that facilitate various types of memory consolidation. For instance, by blocking gene expression with an mRNA cap analog in rats during REM sleep, researchers could determine whether the expression of plasticity-related IEGs is necessary for various types of memory consolidation. And if plasticity-related IEG expression is proven essential for memory consolidation, they may ask whether such expression still persists in pharmacological studies despite the apparent deprivation of REM sleep. In a similar vein, researchers could administer drugs that alter brain waves in rats so as to determine the specific functions of theta waves. Future studies must examine neuromodulators as well, not only to ascertain whether cortisol’s effect can be generalized, but also to verify that Payne and Nadel’s (2004) experimental results can be attributed to cortisol alone. The study of sleep promises to illuminate crucial aspects of behavior such as learning and memory and poses potential to elucidate human functioning.

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### References

- Amado-Boccaro, I., Gougoulis, N., Poirier-Littre, M. F., Galinowski, A., & Loo, H. (1995). Effects of antidepressants on cognitive functions: A review. *Neuroscience & Biobehavioral Reviews*, 19(3), 479-493. doi: 10.1016/0149-7634(94)00068-C.
- Cartwright, R. D. (2004). The role of sleep in changing our minds: A psychologist’s discussion of papers on

- memory reactivation and consolidation in sleep. *Learning & Memory*, 11, 660-663. doi: 10.1101/lm.75104.
- Datta, S., Guangmu L. & Sanford, A. (2008). Activation of phasic pontine-wave generator in the rat: a mechanism for expression of plasticity-related gene and proteins in the dorsal hippocampus and amygdala. *European Journal of Neuroscience*, 27, 1876-1892. doi: 10.1111/j.1460-9568.2008.06166.x.
- Diekelmann, S. & Born, J. (2010). The memory function of sleep. *Sleep*, 11, 114-126. doi: 10.1038.nrn2762.
- Fogel, S.M., Smith, C.T. and Cote, K.A (2007). Dissociable learning-dependent changes in REM and non-REM sleep in declarative and procedural memory systems. *Behavioral Brain Research*, 180, 48-61. doi: 10.1016/j.bbr.2007.02.037.
- Freud, S. (1913). *The Interpretation of Dreams* (AA. Brill, Trans.). New York: The Macmillan Company (Original work published 1900).
- Hebb, D. O. (1949). *The organization of behavior: A neuropsychological theory*. New York: Wiley
- Horne, J.A. (1984) The consolidation hypothesis for REM sleep function: stress and other confounding factors: A Review. *Biological Psychology*, 18, 165-84. doi:10.1016/0301-0511(84)90001-2.
- Hulzen, Z.J. & Coenen, A.M. (1982). Effects of paradoxical sleep deprivation on two-way avoidance acquisition. *Physiological Behavior*, 29, 581-587. doi: 10.1016/0031-9384(82)90223-2.
- Marcos, F.G. (2006). Blockade of postsynaptic activity in sleep inhibits developmental plasticity in visual cortex. *Neurocortex*, 17, 1459-1463. doi: 10.1097/01.wnr.0000233100.05408.e4.
- Kenway, L. & Wilson, W.A. (2001). Temporally structured replay of awake hippocampal ensemble activity during rapid eye movement sleep. *Neuron*, 29,145-56.
- Maquet, P. (2001). The role of sleep in learning and memory. *Science*, 294, 1048-1052. doi: 10.1126/science.1062856.
- McCarley, R.W (2007). Neurobiology of REM and NREM sleep. *Sleep Medicine*, 8, 302-330. doi: 10.1016/j.sleep.2007.03.005.
- Payne, J. & Nadel, L.N. (2004). Sleep, dreams and memory consolidation: The role of the stress hormone cortisol. *Learning and Memory*, 11, 671-678. doi: 10.1101/lm.77104.
- Pilhal, W. & Born, J. (1999). Effects of early and late nocturnal sleep on priming and spatial memory. *Psychophysiology*, 36, 571-582. doi: 10.1111/1469-8986.3650571.
- Poe, G. R., Nitz, D.A., McNaughton, B.L., and Barnes, C.A. (2000). Partial hippocampal inactivation: effects on spatial memory performance in aged and young rats. *Behavioral Neuroscience*, 114(5), 940-9.
- Rasch, B., Pommer, J. Diekelmann, S. and Born, J. (2009). Pharmacological REM sleep suppression paradoxically improves rather than impairs skill memory. *Nature Neuroscience*, 12, 396 397, doi: 10.1038/nn.2206.
- Rasch, B., Buchel, C., Gais, S. & Born, J. (2007). Odor cues during slow-wave sleep prompt declarative memory consolidation. *Science*, 315, 1426-1429. doi: 10.1126/science.1138581.
- Ribeiro, S., Goyal, V., Mello, C.V. & Pavlides, C. (1999). Brain gene expression during REM sleep depends on prior waking experience. *Learning and Memory*, 6, 500-508. doi: 10.1101/lm.6.5.500.
- Siegel, J.M. (2001). The REM sleep-memory consolidation hypothesis. *Science*, 294, 1058-1063. doi: 10.1126/science.1063049.
- Smith, C. (1995). Sleep states, memory processes and synaptic plasticity. *Behavioral Brain Research*, 78, 49-56. doi:10.1016/0166-4328(95)00218-9.
- Smith, C. & Lapp L. (1991). Increases in numbers of REMS and REM density in humans following an intensive learning period. *Sleep*, 4, 325-330.
- Winson, J. (1978). Loss of hippocampal theta rhythm in spatial memory deficit in the rat. *Science*, 201, 160-163. doi: 10.1126/science.663646.