



Memory Consolidation Is Similar in Waking and Sleep

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Abstract

Purpose of Review I review the current status of the hypothesis that sleep is critically involved in memory consolidation and conclude that there are major methodological problems with the studies used to support this hypothesis.

Recent Findings Memory consolidation is similar in quiet waking and sleep (Humiston GB, Tucker MA, Summer T, Wamsley EJ. *Sci Rep* 18;9(1):19345, 2019), and suppression of REM sleep for long periods is compatible with learning and highly adaptive behavior (Lyamin OI, Korneva SM, Obukhova ED, Mukhametov LM, Siegel JM. *Dokl Biol Sci* 463:211-4, 2015; Lyamin OI, Kosenko PO, Korneva SM, Vyssotski AL, Mukhametov LM, Siegel JM. *Current Biology* 28(12):2000-5, 2018); despite their considerable abilities to navigate and remember, African elephants have very small amount of sleep, and learning interference effects have not been adequately controlled for in studies purporting to show sleep-dependent memory consolidation (Sosic-Vasic Z, Hille K, Kroner J, Spitzer M, Kornmeier J. *Frontiers in psychology* 9:82, 2018; Yonelinas AP, Ranganath C, Ekstrom AD, Wiltgen BJ. *Nat Rev Neurosci* 20(6):364-75, 2019).

Summary Memory consolidation clearly occurs in both sleep and waking. Whether, and the extent to which, consolidation might differ in these two states has not been conclusively determined.

Keywords Memory · Consolidation · Learning · Sleep · REM sleep · Waking

Introduction

We learn continuously when we are awake. We all have the daily experience of remembering information learned in the morning, 16 h later, after many distractions with no intervening sleep. Similarly, we all have the experience of taking in information at night before sleep onset and remembering that information in the morning. Clearly, some level of memory consolidation occurs in both waking and sleep. Therefore, the concept of sleep having a critical role in memory consolidation rests on the hypothesis that much better long-term memory consolidation occurs during sleep than waking.

To critically evaluate this hypothesis, we must take “interference” effects into account. If you learn something before or after the experimenter induced learning that is being measured in the typical sleep-memory study, it degrades recall of the tested information. For example if you tell a subject that the capital of Australia is Canberra and then allow the subject to have a normal night’s sleep, there is a high probability that the subject will remember this upon awakening. If on the other hand you tell the subject that the capital of Australia is Canberra, the capital of Brazil is Brasilia, the capital of Canada is Ottawa, the capital of Iceland is Reykjavik, the capital of Libya is Tripoli, the capital of Pakistan is Islamabad, etc., it is much less likely the subject will remember the capital of Australia. The effect of proactive and retroactive interference is dependent on the temporal juxtaposition, complexity, and similarity of the encountered material to the associations being tested. Interference is a well-established concept in the learning literature [1–6]. Under interference conditions, such as exist during sleep deprivation, subjects, by staying awake, necessarily interacting with the experimenter keeping them awake and experiencing the laboratory environment, will remember more than just the items that are presented. But they may be less able to recall the particular items the experimenter is measuring. This can lead to the mistaken

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conclusion that sleep is required for memory consolidation [7].

Recent work has, for the first time, dealt with this issue. It was shown that a quiet waking period or a meditative waking state in which the environment is being ignored, produces a gain in recall similar to that seen in sleep, relative to an active waking state or a sleep-deprived state [8–16].

A second issue in sleep-learning studies is the effect of sleep deprivation procedure itself. In humans, the subject either has to be awakened frequently, or has to engage in alternative activities that disrupt the individuals' normal sleep pattern, depriving them of hours of sleep. Although various forms of automated sleep deprivation [17, 18] and “gentle handling” have been used in animal studies, it is very difficult to control for the psychological and physiological stress produced by awakening/sleep deprivation. In human studies, sleepiness after a pattern of disrupted sleep is as great as that resulting from complete sleep deprivation, even though total sleep time is not greatly reduced [19]. However, this pattern of disrupted sleep is routinely used in animal studies of the role of sleep in memory consolidation. Stress combined with sleepiness is likely to disrupt recall in addition to the effects of waking interference. Human sleep deprivation studies to detect an effect of sleep on memory consolidation have generally been carried out over one to three days. A single night of sleep manipulation is typically followed by testing one or two days later after recovery sleep, i.e., these studies are not testing, or claiming, effects of sleep loss on recall weeks later.

REM sleep has been hypothesized to have a key role in memory consolidation [20]. But it has been reported that near total REM sleep deprivation for a period of 14 to 40 days by administration of the monoamine oxidase inhibitor phenelzine has no apparent effect on cognitive function in humans [21]. A systematic study using serotonin or norepinephrine re-uptake inhibitors to suppress REM sleep in humans had no deleterious effects on a variety of learning tasks [22, 23]. Humans rarely survive the damage to the pontine region which when discretely lesioned in animals greatly reduces or eliminates REM sleep [20, 23–25]. However, one such subject with pontine damage that severely reduced REM sleep has been thoroughly studied. The studies show normal or above normal cognitive performance and no deficit in memory formation or recall [26•]. It has been claimed that learning results in greater total amounts of sleep, or greater amounts of REM sleep [27], or greater amounts of sleep spindles, or slow wave activity. However, a systematic test of this hypothesis in 929 human subjects with night-long EEG recording found no such correlation with retention [28•].

An alternate approach to studying the correlates of sleep is to compare the sleep of humans and other mammals, to test the idea that animals with larger brains or more complex social and cognitive structures have more total sleep or more REM sleep. Human sleep amounts and “intensity” is neither greater

than nor less than that of other mammals with smaller brains and brain/body ratios and less apparent cognitive capability [29]. The animal with the most REM sleep is the platypus [20, 30] and the related monotreme the echidna [20, 31]. Figure 1 from Siegel (2005) compares animals with high and low amounts of REM sleep. No correlation with cognitive capability is apparent.

A recent addition to phylogeny studies is a study we did of African elephants in the wild. Continuous actigraphic recording over 35-day periods revealed an average sleep duration of 2.1 h a day, half of what has been reported in zoo elephants and the lowest daily sleep duration in any animal yet studied. In the wild, elephants frequently go more than 36 h without sleep—an elephant all-nighter [32•]. Elephants have earned a reputation for having complex social interactions and a prodigious memory, which allows them to navigate over distances of as much as 35 miles a day and keep track of the location of vegetation that is available for consumption—to say nothing of the elephant's reputation as an animal that “never forgets.”

We have previously reported that cetaceans, the order that includes whales and dolphins, do not have REM sleep, despite being capable of complex learning and having brains that are larger than human brains [33–38]. Unlike terrestrial mammals, newborn cetacean calves go without any sleep for a period of nearly at least a month after birth, a period in which they are learning vital skills, with their mothers showing a similar period of continuous activity. NonREM slow wave EEG activity occurs only unihemispherically in cetaceans [39].

To follow up on this finding, we recently studied sleep in the fur seal (*Callorhinus ursinus*). This otariid pinniped has bilaterally symmetrical slow wave EEG and REM sleep amounts similar in quantity and duration to that seen in humans and dogs when on land. However, when in water, where they spend about 7 months of the year, they have unihemispheric slow waves, just like dolphins. Moreover, they have a near total suppression of REM sleep. When they return to land there is no “rebound” of REM sleep, with REM amounts returning to baseline levels [40•]. It is difficult to reconcile the extended absence of REM sleep and the hypothesis that REM sleep is required for memory consolidation, with the virtually complete absence of REM sleep during the most challenging portion of the fur seal's life span, in which they hunt, learn to locate and track predators and raise their young.

Manipulation of or stimulation within waking or sleep states and interventions dependent on circadian phase can differentially affect retention. But the methodological issues, including interference and cortisol release linked to awakening as well as the phylogenetic data mentioned above, are not consistent with memory consolidation being tightly linked to the duration of nonREM or REM sleep, whether spontaneous or experimenter manipulated [41–46]. Effective memory consolidation clearly occurs in both waking and sleep states in humans and across mammalian species.

Conclusion

Although sleep deprivation has major effects on performance, memory consolidation occurs in both sleep and waking and purported differences between sleep and waking consolidation may be due to interference effects. Despite the complex cognitive capacity of humans, human REM and nonREM sleep does not differ from that of animals with much lesser cognitive ability.

References

Papers of particular interest, published recently, have been highlighted as:

- Of importance
1. Susic-Vasic Z, Hille K, Kroner J, Spitzer M, Kornmeier J. When learning disturbs memory-temporal profile of retroactive interference of learning on memory formation. *Front Psychol*. 2018;9:82.
 2. Underwood BJ. Interference and forgetting. *Psychol Rev*. 1957;64(1):49–60.
 3. Krakauer JW, Ghez C, Ghilardi MF. Adaptation to visuomotor transformations: consolidation, interference, and forgetting. *J Neurosci*. 2005;25(2):473–8.
 4. Underwood BJ, Postman L. Extraexperimental sources of interference in forgetting. *Psychol Rev*. 1960;67(2):73–95.
 5. Nee DE, Jonides J, Berman MG. Neural mechanisms of proactive interference-resolution. *NeuroImage* 2007 Dec;2007/08/23(4): 740–51.
 6. Solesio E, Lorenzo-Lopez L, Campo P, Lopez-Frutos JM, Ruiz-Vargas JM, Maestu F. Retroactive interference in normal aging: a magnetoencephalography study. *Neurosci Lett*. 2009;456(2):85–8.
 7. Yonelinas AP, Ranganath C, Ekstrom AD, Wiltgen BJ. A contextual binding theory of episodic memory: systems consolidation reconsidered. *Nat Rev Neurosci*. 2019 Jun;20(6):364–75.
 8. • Humiston GB, Tucker MA, Summer T, Wamsley EJ. Resting states and memory consolidation: a preregistered replication and meta-analysis. *Sci Rep* 2019;9(1):19345. **Shows memory consolidation in waking states.**
 9. Bailes C, Caldwell M, Wamsley EJ, Tucker MA. Does sleep protect memories against interference? A failure to replicate. *PLoS One*. 2020 Feb 13;15(2).
 10. Brokaw K, Tishler W, Manceor S, Hamilton K, Gaulden A, Parr E, et al. Resting state EEG correlates of memory consolidation. *Neurobiol Learn Mem* 2016 Apr;130:17–25. doi: <https://doi.org/10.1016/j.nlm.2016.01.008>. Epub@2016 Jan 21.:17–25.
 11. • Humiston GB, Wamsley EJ. A brief period of eyes-closed rest enhances motor skill consolidation. *Neurobiol Learn Mem* 2018 Nov;155:1–6. doi: <https://doi.org/10.1016/j.nlm.2018.06.002>. Epub@2018 Jun 5.:1–6. **Shows motor skill consolidation during quiet waking periods.**
 12. Murphy M, Stickgold R, Parr ME, Callahan C, Wamsley EJ. Recurrence of task-related electroencephalographic activity during post-training quiet rest and sleep. *Sci Rep*. 2018 Mar 29;8(1):5398–23590.
 13. Tucker MA, Humiston GB, Summer T, Wamsley E. Comparing the effects of sleep and rest on memory consolidation. *Nat Sci Sleep*. 2020 Feb 3;12:79–91. <https://doi.org/10.2147/NSS.S223917.79-91>.
 14. • Wamsley EJ, Hamilton K, Graveline Y, Manceor S, Parr E. Test expectation enhances memory consolidation across both sleep and wake. *PLoS ONE* 2016 Oct;11(10):e0165141. **Demonstrates comparable memory consolidation during sleep and waking.**
 15. Scullin MK. Sleep, memory, and aging: the link between slow-wave sleep and episodic memory changes from younger to older adults. *Psychol Aging*. 2013;28(1):105–14.
 16. Cordi MJ, Br R. How robust are sleep-mediated memory benefits? *Curr Opin Neurobiol*. 2021;67:1–7.
 17. Rechtschaffen A, Gilliland MA, Bergmann BM, Winter JB. Physiological correlates of prolonged sleep deprivation in rats. *Science*. 1983;221:182–4.
 18. Bergmann BM, Kushida CA, Everson CA, Gilliland MA, Obermeyer W, Rechtschaffen A. Sleep deprivation in the rat: II. *Methodol Sleep*. 1989;12:5–12.
 19. Bonnet MH, Arand DL. Clinical effects of sleep fragmentation versus sleep deprivation. *Sleep Med Rev*. 2003 Aug;7(4):297–310.
 20. Siegel JM. Rapid eye movement sleep. In: Kryger MK, Roth T, Dement WC, editors. *Principles and practice of sleep medicine*. 6 ed. Elsevier; 2017. p. 78–95.
 21. Wyatt RJ, Fram DH, Kupfer DJ, Snyder F. Total prolonged drug-induced REM sleep suppression in anxious-depressed patients. *Arch Gen Psychiatry*. 1971 Feb;24:145–55.
 22. Rasch B, Pommer J, Diekelmann S, Born J. Pharmacological REM sleep suppression paradoxically improves rather than impairs skill memory. *Nat Neurosci*. 2009 Apr;12(4):396–7.
 23. Siegel JM, Nienhuis R, Tomaszewski KS. REM sleep signs rostral to chronic transections at the pontomedullary junction. *Neurosci Lett*. 1984;45:241–6.
 24. Siegel JM, Tomaszewski KS, Nienhuis R. Behavioral states in the chronic medullary and mid-pontine cat. *Electroencephalogr Clin Neurophysiol*. 1986;63:274–88.
 25. Shan L, Dauvilliers Y, Siegel JM. Interactions of the histamine and hypocretin systems in CNS disorders. *Nat Rev Neurol*. 2015 Jul;11(7):401–13.
 26. • Magidov E, Hayat H, Sharon O, Andelman F, Katzav S, Lavie P, et al. Near-total absence of REM sleep co-occurring with normal cognition: an update of the 1984 paper. *Sleep Med* 2018;52:134–7. **A case report on a human with very high level of cognition despite brain damage that greatly reduced REM sleep.**
 27. Smith C, Rose GM. Posttraining paradoxical sleep in rats is increased after spatial learning in the Morris water maze. *Behav Neurosci*. 1997 Dec;111:1197–204.
 28. • Ackermann S, Hartmann F, Papassotiropoulos A, de Quervain DJ, Rasch B. No associations between interindividual differences in sleep parameters and episodic memory consolidation. *Sleep* 2014 Oct 17;38(6):951–9. **A study of memory consolidation with more than 900 human subjects and all-night EEG recording, showing no changes in sleep correlated with learning, despite prior, smaller studies' claims to have seen such effects.**
 29. Siegel JM. Clues to the functions of mammalian sleep. *Nat*. 2005 Oct 27;437(7063):1264–71.
 30. Siegel JM, Manger PR, Nienhuis R, Fahringer HM, Shalita T, Pettigrew JD. Sleep in the platypus. *Neuroscience*. 1999 Jun;91(1):391–400.
 31. Siegel JM, Manger P, Nienhuis R, Fahringer HM, Pettigrew J. The echidna *Tachyglossus aculeatus* combines REM and nonREM aspects in a single sleep state: implications for the evolution of sleep. *J Neurosci*. 1996;16:3500–6.
 32. • Gravett N, Bhagwandin A, Sutcliffe R, Landen K, Chase MJ, Lyamin OI, et al. Inactivity/sleep in two wild free-roaming African elephant matriarchs - does large body size make elephants the shortest mammalian sleepers? *PLoS ONE* 2017 Mar 1;12(3): e0171903. **A study of wild African elephants showing average sleep time of only 2.1 hours/day despite their complex social structure, navigation of up to 40 km/day, and ability to learn**

- complex tasks. This is the lowest daily sleep amount reported in any mammal.**
33. Lyamin O, Pryaslova J, Lance V, behaviour SJA. continuous activity in cetaceans after birth. *Nat.* 2005;435(7046):1177.
 34. Lyamin OI, Manger PR, Ridgway SH, Mukhametov LM, Siegel JM. Cetacean sleep: An unusual form of mammalian sleep. *Neurosci Biobehav Rev.* 2008 Oct;32(8):1451–84.
 35. Branstetter BK, Finneran JJ, Fletcher EA, Weisman BC, Ridgway SH. Dolphins can maintain vigilant behavior through echolocation for 15 days without interruption or cognitive impairment. *PLoS One.* 2012;7(10):e47478.
 36. Ridgway S, Keogh M, Carder D, Finneran J, Kamolnick T, Todd M, et al. Dolphins maintain cognitive performance during 72 to 120 hours of continuous auditory vigilance. *J Exp Biol.* 2009 May 15;212(10):1519–27.
 37. Oelschlager HHA. The dolphin brain—a challenge for synthetic neurobiology. *Brain Res Bull.* 2008 Mar 18;75(2–4):450–9.
 38. Reiss D, Marino L. Mirror self-recognition in the bottlenose dolphin: a case of cognitive convergence. *Proc Natl Acad Sci U S A.* 2001 May 8;98:5937–42.
 39. Lyamin OI, Mukhametov LM, Siegel JM. Relationship between sleep and eye state in Cetaceans and Pinnipeds. *Arch Ital Biol.* 2004 Jul;142(4):557–68.
 40. • Lyamin OI, Kosenko PO, Korneva SM, Vyssotski AL, Mukhametov LM, Siegel JM. Fur seals suppress REM sleep for very long periods without subsequent rebound. *Current Biol* 2018 Jun 18;28(12):2000–5. **Shows that fur seals suppress REM sleep for long periods of time, weeks or longer, during which they engage in complex social behavior, learn, and track the location of food, predators, and conspecifics.**
 41. Siegel JM. Mechanisms of sleep control. *J Clin Neurophysiol.* 1990;7:49–65.
 42. Siegel JM. Sleep viewed as a state of adaptive inactivity. *Nat Rev Neurosci.* 2009 Oct;10(10):747–53.
 43. Vertes RP, Eastman KE. The case against memory consolidation in REM sleep. *Behav Brain Sci.* 2000;23:867–76.
 44. • Vertes RP, Linley SB. No cognitive processing in the unconscious, anesthetic-like, state of sleep. *J Comp Neurol* (in press) 2020. **Critically examines the sleep-memory consolidation hypothesis from the standpoint of cortical activity as indexed by the electroencephalogram.**
 45. McGregor R, Wu M-F, Barber G, Ramanathan L, Siegel JM. Highly specific role of hypocretin (orexin) neurons: differential activation as a function of diurnal phase, operant reinforcement vs. operant avoidance and light level. *J Neurosci.* 2011;31(43):15455–67.
 46. • Lyamin OI, Korneva SM, Obukhova ED, Mukhametov LM, Siegel JM. Evaluation of the ability of northern fur seals to perceive and visually discriminate images under the conditions of sleep loss. *Dokl Biol Sci* 2015;463:211–4. doi: <https://doi.org/10.1134/S0012496615040080>. Epub@2015 Sep 3.:211–4. **Shows a lack of effect of sleep deprivation on learning visual discrimination.**

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