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Declarative Memory: Sleep Protects New Memories from Interference

Interference is one of the most fundamental phenomena in memory research: acquiring new memories causes forgetting of other, related memories. A new study shows that sleep, interposed between learning episodes, can mitigate the extent to which new (post-sleep) learning interferes with recall of previously acquired knowledge.

Kenneth A. Norman

How does the brain protect existing memories from being destroyed or distorted by new learning? This puzzle, labeled the stability-plasticity dilemma by [1], has been at the forefront of memory research for several decades. In the 1970s and 1980s, when researchers started to build explicit computer models of how the brain stores memories, they found that these neural network models of memory tend to show catastrophic levels of memory interference [2,3]: implanting new memories in the network causes distressingly fast forgetting of previously stored memories. This problem occurs because memories are stored in an overlapping fashion in these models, as they are in the brain. A given synapse might participate in storing multiple related memories (for example, memory for your breakfast today versus yesterday), so adjusting the strength of that synapse to strengthen one memory might distort another memory that relies on that synapse. While numerous psychological studies have demonstrated that new learning does, in fact, interfere with recall of existing memories [4–6], it is also clear that the interference effects observed in behavioral studies are much smaller than those predicted by the simple neural network models mentioned above.

This discrepancy has led researchers to puzzle over what kinds of mechanisms (not present in these simple models) the brain might use to protect stored memories. Computational neuroscientists have come up with several different ideas about how the brain avoids catastrophic interference (for example, see [1,7,8]). One of the most intriguing of these ideas is that sleep might play a role in reinforcing and protecting existing knowledge. The gist of the idea is that sleep provides an opportunity for the brain to 'think about what it already knows', strengthening and potentially also refining existing memories so they are less likely to be disrupted by new learning. Some researchers [8] also have argued that learning during sleep can serve to repair damage to existing memories; just as a building with a crumbling infrastructure can be repaired (if it is accessed before it collapses), a damaged memory can be repaired so long as the memory is still coherent enough to be accessed during sleep.

A new study by Ellenbogen et al. [9], published recently in Current Biology, directly explores the role of sleep in protecting new memories from interference. To accomplish this goal, the authors used the AB–AC word pair learning paradigm [10]. In this paradigm, subjects learn a set of word pairs, such as shoe–banana; call this the A–B set. Next, subjects learn a new set of word pairs, the A–C set, where the 'A' words from before are paired with new words, for example shoe–stapler. Later, subjects are given the 'A' words, such as shoe, and asked to recall both words that were paired with each 'A' word. Previous studies using this paradigm have found that learning the A–C items impairs subsequent recall of the A–B items [4,10].

To address the role of sleep in mitigating interference, Ellenbogen et al. [9] set up their study such that one group of subjects slept between learning the A–B pairs and learning the A–C pairs, and another group of subjects did not sleep during that interval; subjects were tested on A–B and A–C pairs after learning the A–C pairs. The experiment also included 'no interference' control conditions that were identical to the aforementioned conditions, except subjects did not learn any A–C items. The authors found that the negative effect of A–C learning on A–B recall was much smaller in the sleep condition than in the no-sleep condition. Thus, it appears that something happens during sleep — when interposed between A–B and A–C learning — that makes the A–B trace less vulnerable to interference.

What mechanisms could be responsible for this sleep benefit? The least interesting possibility is that waking experience, interposed between A–B and A–C learning, causes degradation of memories, and that sleep benefits memory simply by minimizing this incidental interference. However, Ellenbogen *et al.* [9] demonstrated that this is not a viable explanation of their data, by showing that a 24 hour retention interval, including sleep, results in less interference than a 12 hour wake-only retention interval, despite the fact that subjects actually spent more total time awake in the 24 hour condition.

Another possibility is that sleep-learning effects are caused by the hippocampus 're-playing' new memories to cortex during sleep (for example, see [11,12]; for a theoretical discussion see [7]). This hippocampal re-play mechanism, over time, will result in strengthening of the cortical trace of the A–B pair, and it can also lead to strengthening of the hippocampal trace itself. These strengthening effects should result in an across-the-board increase in recall, even when no interference is present. In keeping with this view, Ellenbogen *et al.* [9] found a small but significant benefit of sleep on A–B recall even when no A–C pairs were learned (for similar findings, see [13,14]). But the fact that the sleep benefit was so much larger in the interference condition versus the no-interference condition suggests that, in addition to some amount of basic strengthening, sleep might act more specifically to mitigate interference.

One interesting possibility is that rehearsing memories during sleep serves to differentiate these memories. According to this view, sleep-learning 'tunes' memory traces so they are more likely to be retrieved in response to the original stimulus, and less likely to be retrieved in response to other stimuli [15,16] (see [17] for neural data showing sharpening of sensory receptive fields with experience). Relating this to the Ellenbogen *et al.* [9] study: if A–B memories undergo differentiation during sleep, this will reduce the extent to which A–B memory traces are activated during A–C learning,

which, in turn, will reduce the extent to which A–B memories are overwritten or otherwise distorted during A–C learning.

Other explanations of the sleep benefit are also possible. For example, if sleep helps subjects clear out their 'mental context', so that they are in a very different overall mindset pre-sleep and post-sleep, this might help subjects to form distinct, non-interfering memory traces for A–B and A–C items (for discussion of contextual shift effects and AB–AC interference, see [4]).

Much more theoretical work needs to be done to flesh out these explanations — for example, how are memories selected for rehearsal during sleep; how might sleep-learning lead to differentiation of stored memories — and more empirical work is needed to tease these explanations apart. One promising approach would be to merge the interference design used by Ellenbogen *et al.* [9] with sophisticated neural-recording methods that have been used in animal studies to track the re-emergence of memories during sleep (for example [18,19]). For example, to test the idea that sleep-rehearsal differentiates A–B from A–C memories, one could measure how often A–B patterns are rehearsed during sleep, and see if increased rehearsal is associated with a decrease in the similarity of the neural patterns that are present during A–B versus A–C learning.

In summary: The role of sleep in memory protection has been the subject of extensive theoretical speculation. By showing that it is possible to empirically investigate the relationship between sleep and interference, the Ellenbogen *et al.* [9] study opens the door to an exciting dialogue between theory and experimentation — one that should lead to a much richer understanding of how the brain reconciles old and new knowledge.

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