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Is There a Role for Pattern Separation during Sleep?

Jia-Hou Poh and James Nicholas Cousins

Centre for Cognitive Neuroscience, Duke-NUS Medical School, Singapore 169857

Review of Hanert et al.

Sleep plays an important role in supporting long-term memory formation (Diekelmann and Born, 2010). Beyond preserving specific details from different events, sleep can facilitate the abstraction of generalities across events (Ellenbogen et al., 2007; Lewis and Durrant, 2011). Although these two processes are seemingly incompatible, the complementary learning systems (CLS) model proposes that this can be achieved through the interaction of two separate memory systems (McClelland et al., 1995). The CLS posits that the hippocampal system serves as a rapid learning system that allows the preservation of event details through sparse coding, in which each event or stimulus is coded only by a small proportion of hippocampal neurons. In addition, the model posits that during periods of sleep, the hippocampus initiates replay of encoded memories, providing gradual training for the slow-learning neocortical system (McClelland et al., 1995).

Support for this process of systems consolidation comes from observations of a coordinated hippocampo–cortical dialogue during sleep oscillations, alongside neuronal replay of waking experience in the hippocampus and neocortex, as well as demonstration that both of these phenomena are causally linked to memory consolidation (Bendor and Wilson, 2012; Maingret et al., 2016). Neural replay is thought to facilitate the integration and generalization of learned information through recruiting overlapping representations in the neocortical system (McClelland et al., 1995). A role for replay in strengthening memories for specific details within the hippocampus is not often discussed, but Hanert et al. (2017) recently posited that neural replay during sleep facilitates pattern separation, resulting in more distinct memory representations for previously encoded information.

Pattern separation is thought to occur during encoding, where the activation of a small proportion of hippocampal neurons minimizes representational overlaps between distinct events (Hunsaker and Kesner, 2013). Functionally, pattern separation reduces competitive interference between related memoranda and thus facilitates more accurate retrieval. Sleep before learning appears to be essential for effective pattern separation, because sleep deprivation can impair the ability to discriminate between similar items during encoding (Saletin et al., 2016). However, it is less certain whether periods of sleep following learning continue to facilitate pattern separation of learned information.

A recent study by Hanert et al. (2017) sought to address this with a widely used behavioral paradigm for examining pattern separation in humans (Stark et al., 2013). Participants encoded several objects that were tested immediately and tested again after a 10 h retention interval that consisted of daytime wakefulness (wake group) or a night of sleep (sleep group). During the recognition test, participants were shown items that were previously seen (Targets), items that were similar to those previously seen (Lures), and items that were new (Foils). They were required to indicate whether each item was "Old", "Similar", or "New", and pattern separation performance was determined based on the successful identification of Lure items as being Similar.

Comparing behavioral performance on the immediate and the delayed test, the authors demonstrated that pattern separation performance declined over a period of intervening wakefulness, but was preserved across sleep. In addition, slow oscillation density and spindle density, both of which have been associated with the occurrence of neural replay, were correlated with subsequent pattern separation performance in the sleep group. Based on these observations, the authors suggest that sleep stabilizes pattern separation in the hippocampus, and speculate that this relates to neural replay during sleep.

Although Hanert et al. (2017) used a well validated behavioral pattern separation task, it is not clear that the observed sleep-related benefit can truly be attributed to stabilization of pattern separation. When pattern separation is weakened across a delay, we expect both a reduction

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Correspondence should be addressed to Dr. Jia-Hou Poh, Centre for Cognitive Neuroscience, Duke-NUS Medical School, 8 College Road, Singapore 169857. E-mail: jiahou.poh@u.nus.edu.sg.

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in Similar responses, and an increase in Old responses to Lure items. Although Hanert et al. (2017) observed the former in the wake group, there was no evidence of an increase in false recognition (Old responses to Lure items were 30.62% and 32.08%, respectively). Additionally, whereas impaired pattern separation should more strongly affect lures of greater similarity, the Wake group exhibited the reverse pattern, with the decrement being larger for lures with lower similarity. The authors' conclusion that sleep stabilizes pattern separation is based on this relative deterioration of performance across wakefulness, but these inconsistent findings may point toward an alternative explanation.

There are several clues to suggest that the reduced scores on pattern separation might be driven by greater forgetting in the Wake group. The clearest indication comes from the recognition memory score (i.e., correctly identifying target images as Old), where the Wake group showed greater forgetting compared with the Sleep group. This is consistent with the expected mnemonic benefits of sleep (Diekelmann and Born, 2010). Moreover, the decrement in pattern separation performance was driven by a larger increase in the proportion of New responses to Lure items made by the Wake group (6.85–29.54%), which is also indicative of general forgetting. Together, greater general forgetting of the wake group appears to be a more parsimonious account for the observed results.

Although the results reported by Hanert et al. (2017) may not be attributable primarily to better pattern separation following sleep, the premise that offline replay can support pattern separation in the hippocampus is one that deserves greater attention, because it may provide a mechanistic account for several observations regarding sleep-dependent memory consolidation. As stated above, pattern separation during encoding minimizes representational overlaps, and can reduce the interference between related memoranda. Furthermore, recent work has shown that competitive interference during learning can drive the demand for pattern separation in the hippocampus, and the successful differentiation of competing representations is related to reduced interference (Hulbert and Norman, 2015; Chanales et al., 2017). Sleep has been shown to reduce both proactive and retroactive interference (Abel and Bäuml, 2014), but this has primarily been attributed to systems consolidation, where memory representations in long-term neocortical stores are gradually strengthened, rendering them less susceptible to disruption (Diekelmann and Born, 2010). Pattern separation constitutes another plausible mechanism to explain how interference can be reduced following sleep.

At the neural level, pattern separation within the hippocampus during periods of sleep could be supported via a combination of synaptic potentiation during memory replay (Wilson and McNaughton, 1994) and synaptic depression during the downscaling of memory networks (Tononi and Cirelli, 2014). In the same manner that representational overlaps are minimized across repeated encoding events (Chanales et al., 2017), neural replay provides an opportunity for such differentiation to occur. This process could be further complemented by the downscaling of synapses, which has been proposed as a means of preventing synaptic saturation in memory networks. Synaptic downscaling could eliminate weak/unstable synapses associated with newly learned information and enable the "sharpening" of hippocampal representations. Such a mechanism within the hippocampal network could account for several observations linking reactivation of hippocampal-dependent memories during sleep with more accurate recall and plasticity (Rasch et al., 2007).

This combination of potentiation and depression during sleep was proposed to account for the formation of cognitive schemata during systems consolidation (Lewis and Durrant, 2011). Neurons that code shared elements of memories were suggested to be more strongly activated across repeated replays and would therefore survive the downscaling process, leading to the abstraction of commonalities or "gist" and a loss of specific details within cortical representations (Lewis and Durrant, 2011). Here we propose that similar mechanisms of targeted synaptic potentiation and depression occurring within the hippocampus could emphasize the differences between sparsely coded memoranda, rather than extract commonalities, resulting in enhanced pattern separation.

A lasting role for hippocampal pattern separation in memory is seemingly at odds with the well established decline of retrieval-related hippocampal activity over time (Takashima et al., 2006). However, it has been suggested that the hippocampus continues to be necessary for retrieving detailed autobiographical memories (Nadel and Moscovitch, 1997), and several imaging studies have observed continued hippocampal involvement in retrieval after a night of sleep (Ritchey et al., 2015) and also after longer delays (Bonnici et al., 2012). It is therefore plausible that pattern separation after initial encoding might continue to contribute to the evolution of memories over time.

Despite the intuitive appeal, further experimentation is required to examine whether sleep does indeed support pattern separation in the hippocampus. The work of Hanert et al. (2017) suggests that this may be the case, but also highlights the problems inherent in determining the underlying mechanisms for the mnemonic benefits of sleep, particularly when inferring from behavioral data alone. Future work would benefit from examining how sleep and neural replay changes memory representations for competing information. Imaging techniques that examine patterns of activity associated with individual memories, such as multivoxel pattern analysis, will likely prove invaluable to determine whether pattern separation plays a role during sleep.

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