changes in spatial and temporal context (absent any retrieval driving context reinstatement). But replay seems to be more persistent and adaptive than this, as it can occur as frequently for a remote spatial context as for the current environment[2]; has been observed 10 hours after exposure to a novel environment, with stronger activity during sleep than wake periods[3]; and, critically, can occur more for infrequently experienced[4], gradually learned[5] and weakly encoded[6] information. These findings may not be strictly inconsistent with CB, but they are not motivated by it; additional mechanisms would be needed to explain why context is more strongly reinstated in these situations, especially during sleep.

We think there is strong evidence that sleep benefits memory beyond the reduction of contextual interference, and that this active process drives systems consolidation (as defined above). If sleep primarily benefits hippocampus-dependent memory by reducing interference or through local consolidation processes, specific active cortical events and hippocampal–cortical interactions during sleep should not be robustly and causally related to later memory. However, cortical replay coincides with hippocampal replay[7] and high-frequency replay-associated bursts called ripples[8], and this coupling is associated with later memory[9]. Hippocampal and neocortical ripples coincide and their coupling increases with learning[10], and disrupting the coupling between hippocampal ripples and cortical sleep spindles impairs memory retention[11]. In addition, optimal replay relies on the potential for spindles to occur[12], and artificially boosting individual slow oscillations increases spindle power and improves memory[13]. These processes seem to promote systems consolidation: timing optogenetic stimulations of the neocortex precisely to hippocampal ripples enhances endogenous hippocampal–neocortical coupling and alters neocortical neuronal spiking patterns that support behaviour[14].

Yonelinas et al. argue that replay primarily reflects prior memory formation rather than driving subsequent memory transformation. However, they acknowledge that post-encoding hippocampal activity may cause local cellular consolidation or re-encoding that could sometimes "lead to the formation of strong neocortical semantic representations that could support decontextualized memory for remote events". This latter mechanism fits well into our conceptualization of systems consolidation; we contend that this is a feature, rather than a side effect, of replay. Although more work is needed for full confidence in this contention — such as experiments that carefully track and manipulate the influence of the hippocampus on cortical representations[15] — we think the evidence already points to replay having a critical and active role in driving consolidation across memory systems.

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Competing interests
The authors declare no competing interests.

Reply to 'Active and effective replay: systems consolidation reconsidered again'

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In their Correspondence article (Active and effective replay: systems consolidation reconsidered again. *Nat. Rev. Neurosci.* https://doi.org/10.1038/s41583-019-0191-8 (2019))[1], Antony and Schapiro agree that the concept of contextual binding (CB) described in our Opinion article (A contextual binding theory of episodic memory: systems consolidation reconsidered. *Nat. Rev. Neurosci.* **20**, 364–375 (2019))[2] is crucial for explaining episodic memory, and that many aspects of standard systems consolidation theory are probably incorrect. They also point to some recent sleep and replay studies that might be taken as evidence for a form of systems consolidation that maintains that the hippocampus rapidly trains the cortex during offline periods of sleep or rest. Although we agree that these findings are compatible with a modified form of systems consolidation, we contend that the studies summarized by Antony and Schapiro do not necessitate such an account.

For example, demonstrations that replay correlates with subsequent memory, or that sharp wave–ripple (SWR) activity in the hippocampus correlates (in some instances) with activity in the cortex[3], are consistent with other theoretical accounts such as CB. That is, because episodic memory involves hippocampal binding of item information and context information that is in the cortex, residual or potentiated encoding activity across the hippocampus and cortex should be observed after the nominal encoding event is over, even if the hippocampus is not actively training the cortex at the time. Furthermore, although experimental manipulations of SWRs in the hippocampus and/or neocortex can affect subsequent memory[4], the studies performed to date do not show whether those manipulations prevented the hypothesized transfer of information from the hippocampus to the cortex, or whether they affected the hippocampal or cortical representations themselves. For instance, it would be reasonable to infer that interfering with hippocampal function during an SWR could disrupt a hippocampal (or cortico-hippocampal) memory trace, or that

reactivating hippocampal memory traces during a delay could affect subsequent memory performance, even if the hippocampus is not active in training the cortex.

Although the present evidence does not compel a systems consolidation account, future studies could provide more definitive evidence. For example, studies show that as little as 60 minutes of sleep leads to considerable reductions in forgetting. If these rapid effects of sleep reflect systems consolidation, hippocampal lesions should produce accelerated rates of forgetting over delays that include sleep. Studies reviewed in our paper do not support this prediction[5], but perhaps future studies will show otherwise.

Another important question for future research will be to determine whether replay observed in rodents is related to putative replay reported in humans. Rodent research on replay and its potential role in systems consolidation has focused largely, if not entirely, on reactivation of place cell sequences during sleep and quiet wakefulness, and have focused on examining activity observed in well-learned spatial environments. It would be important to know whether one can observe this type of replay in tests of memory in humans that are more analogous to those described in theories of systems consolidation. Regardless of whether future studies of post-encoding activity are ultimately found to provide stronger support for context models or systems consolidation models, we agree with Antony and Schapiro that such studies will continue to have an important impact on the field.

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Competing interests
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