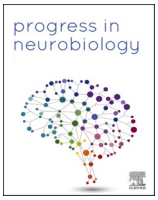
Progress in Neurobiology 250 (2025) 102778

Contents lists available at ScienceDirect

Progress in Neurobiology

journal homepage: www.elsevier.com/locate/pneurobio



Awake reactivation of cortical memory traces predicts subsequent memory retrieval

Wei Duan [a,b,1], Pingping Lu [a,b,1], Zhansheng Xu [c,d], Jing Wang [e], Yue Lu [a,f], Mengyang Wang [e], Ken A. Paller [g], Nikolai Axmacher [h], Liang Wang [a,b,*]

[a] State Key Laboratory of Cognitive Science and Mental Health, Institute of Psychology, Chinese Academy of Sciences, Beijing, China
[b] Department of Psychology, University of Chinese Academy of Sciences, Beijing, China
[c] Faculty of Psychology, Tianjin Normal University, Tianjin, China
[d] Key Research Base of Humanities and Social Sciences of the Ministry of Education, Academy of Psychology and Behavior, Tianjin Normal University, Tianjin, China
[e] Department of Neurology, Sanbo Brain Hospital, Capital Medical University, Beijing, China
[f] Sino-Danish College (SDC), University of Chinese Academy of Sciences, Beijing, China
[g] Department of Psychology and Cognitive Neuroscience Program, Northwestern University, Evanston, USA
[h] Department of Neuropsychology, Institute of Cognitive Neuroscience, Faculty of Psychology, Ruhr University Bochum, Bochum, Germany

ARTICLE INFO

Keywords:
Awake reactivation
Cortical memory trace
Memory consolidation
Ripple
Hippocampal-cortical dialogue

ABSTRACT

Brief periods of rest after learning facilitate consolidation of new memories. Memory reactivation and hippocampal-cortical dialogue have been proposed as candidate mechanisms supporting consolidation. However, the study of these mechanisms has mostly concerned sleep-based consolidation. Whether and how awake reactivation can selectively consolidate cortical memory traces to guide subsequent behavior requires more human electrophysiological evidence. This study addressed these issues by utilizing intracranial electroencephalography (iEEG) recordings from 11 patients with drug-resistant epilepsy, who learned a set of object-location associations. Using representational similarity analysis, we found that, among the multiple cortical memory traces of object-location associations for the same object generated through several rounds of learning, the association corresponding to memory traces with stronger cortical activation during wakeful rest was more likely to be retrieved later. Awake reactivation of cortical memory trace was accompanied by increased hippocampal ripple rates and enhanced theta-band hippocampal-cortical communication, with hippocampal interactions with cortical regions within the default mode network preceding cortical reactivation. Together, these results suggest that awake reactivation of cortical memory trace during post-learning rest supports memory consolidation, predicting subsequent recall.

1. Introduction

Memory is a dynamic process that can be separated into two distinct cognitive states: an online encoding/retrieval state and an offline consolidation state (Nadel et al., 2012; Schreiner and Staudigl, 2020; Wamsley, 2019). The offline memory consolidation state minimizes the processing of new information, thereby reducing interference with existing memory traces, stabilizing them, and potentially facilitating their transformation and reorganization in the brain (Nadel et al., 2012; Schreiner and Staudigl, 2020; Tambini and Davachi, 2019; Wamsley, 2019; Xue, 2022). Reactivation, the re-expression of neural activity patterns (i.e., memory traces) encoding previous experiences commonly occur offline (e.g., during sleep). Offline reactivation across hippocampal–cortical networks and hippocampal-cortical interaction are posited as key candidate mechanisms in mediating memory consolidation (Denis and Cairney, 2023; Favila et al., 2020; Klinzing et al., 2019; Schreiner and Staudigl, 2020; Tambini and Davachi, 2019). Evidence from sleep-related studies indicates that the strength of reactivation correlates with subsequent memory performance (Dupret et al., 2010; Van De Ven et al., 2016), whereas interruption of reactivation can impair later memory performance (Gridchyn et al., 2020). Although sleep has often been emphasized in extensive studies of memory consolidation, evidence demonstrates that post-learning wakeful rest can also facilitate the consolidation and prolonged retention of memory

* Corresponding author at: State Key Laboratory of Cognitive Science and Mental Health, Institute of Psychology, Chinese Academy of Sciences, Beijing, China.
E-mail address: lwang@psych.ac.cn (L. Wang).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.pneurobio.2025.102778
Received 22 January 2025; Received in revised form 30 March 2025; Accepted 14 May 2025
Available online 15 May 2025

traces (Axmacher et al., 2009; Craig et al., 2015; Dewar et al., 2012). In addition, reactivation has been observed during wakeful rest in both rodents and humans (Carr et al., 2011; Chang et al., 2023; Deuker et al., 2013; Diba and Buzsáki, 2007; Foster and Wilson, 2006; King et al., 2022; Staresina et al., 2013; Tambini and D'Esposito, 2020). Furthermore, fMRI studies in humans have shown that the strength of reactivation during wakeful rest is associated with subsequent memory performance (Staresina et al., 2013). Together, these lines of evidence suggest that memory consolidation is not restricted to sleep but can also occur during wakeful rest.

Associative memories are typically learned across multiple repetitions via retrieval practice. This leads to the question whether each of these retrieval and re-learning rounds induces a separate, transformed version of a memory trace whose fate can be tracked through its reactivation during subsequent consolidation and retrieval stages. Indeed, multiple trace theory suggests that several consecutive retrieval attempts to induce multiple hippocampal traces of the same event (Nadel et al., 2000; Nadel and Moscovitch, 1997). Memory traces are underpinned by engram cells, which are not confined to the hippocampus but are distributed across multiple cortical regions(Tonegawa et al., 2018). Moreover, the notion of a whole-brain engram complex, comprising functionally connected engram ensembles across diverse brain regions, has been proposed(Josselyn and Tonegawa, 2020). Selectively reactivating cortical engram neurons during memory consolidation or retrieval can increase subsequent memory strength and facilitate memory retrieval, respectively(Guskjolen and Cembrowski, 2023). Research on competing memories has shown that successfully retrieved target memories exhibit higher item-specific reactivation during retrieval, while reactivation of competing memories is suppressed (Wimber et al., 2015). Moreover, weaker reactivation of target memories increased the likelihood of retrieving competing memories (Kuhl et al., 2011, 2012). Research using the method of targeted memory reactivation (TMR) can selectively manipulate reactivation during sleep to study mechanisms of improved later memory performance (Lewis and Bendor, 2019). This evidence offers insights into selective consolidation during wakeful rest for competitive memory traces and inspired us to speculate that selective reactivation of memory traces during wakeful rest may predict subsequent memory retrieval.

It has been proposed that wakeful rest serves as an offline state and shares neurobiological features of consolidation with sleep, influencing memory through offline reactivation (Wamsley, 2019). An animal study indicated that awake hippocampal replay (i.e., sequential reactivation) was more inclined towards storing and updating memories, proposing that the replay provides a common neural mechanism for preserving experiences and promoting consolidation during both wakefulness and sleep (Gillespie et al., 2021). Reactivation during sleep often co-occurs with hippocampal ripples (Dupret et al., 2010; Ego-Stengel and Wilson, 2010; Ji and Wilson, 2007; Peyrache et al., 2009; Rothschild et al., 2017; Zhang et al., 2018). Similar observations have been reported in rodent studies during wakeful rest (Chang et al., 2023; Nguyen et al., 2024; Sugden et al., 2020). However, a human intracranial EEG study found that although reactivation was observed in both offline brain states, reactivation and ripples co-occurred during sleep but not during wakeful rest, and only ripple-triggered reactivation during sleep supports memory retention (Zhang et al., 2018). Additionally, memory consolidation is inseparable from the hippocampal-cortical dialogue. Evidence has shown that interfering with hippocampal-cortical interaction during sleep or wakeful rest reduces the efficiency of memory consolidation (Novitskaya et al., 2016; Tambini et al., 2010; Xia et al., 2017). These findings suggest that the neural mechanisms through which reactivation, hippocampal ripple, and hippocampus-cortical dialogue jointly support human memory consolidation during wakeful rest require further investigation. Moreover, the temporal hierarchical structure among these processes remains to be elucidated.

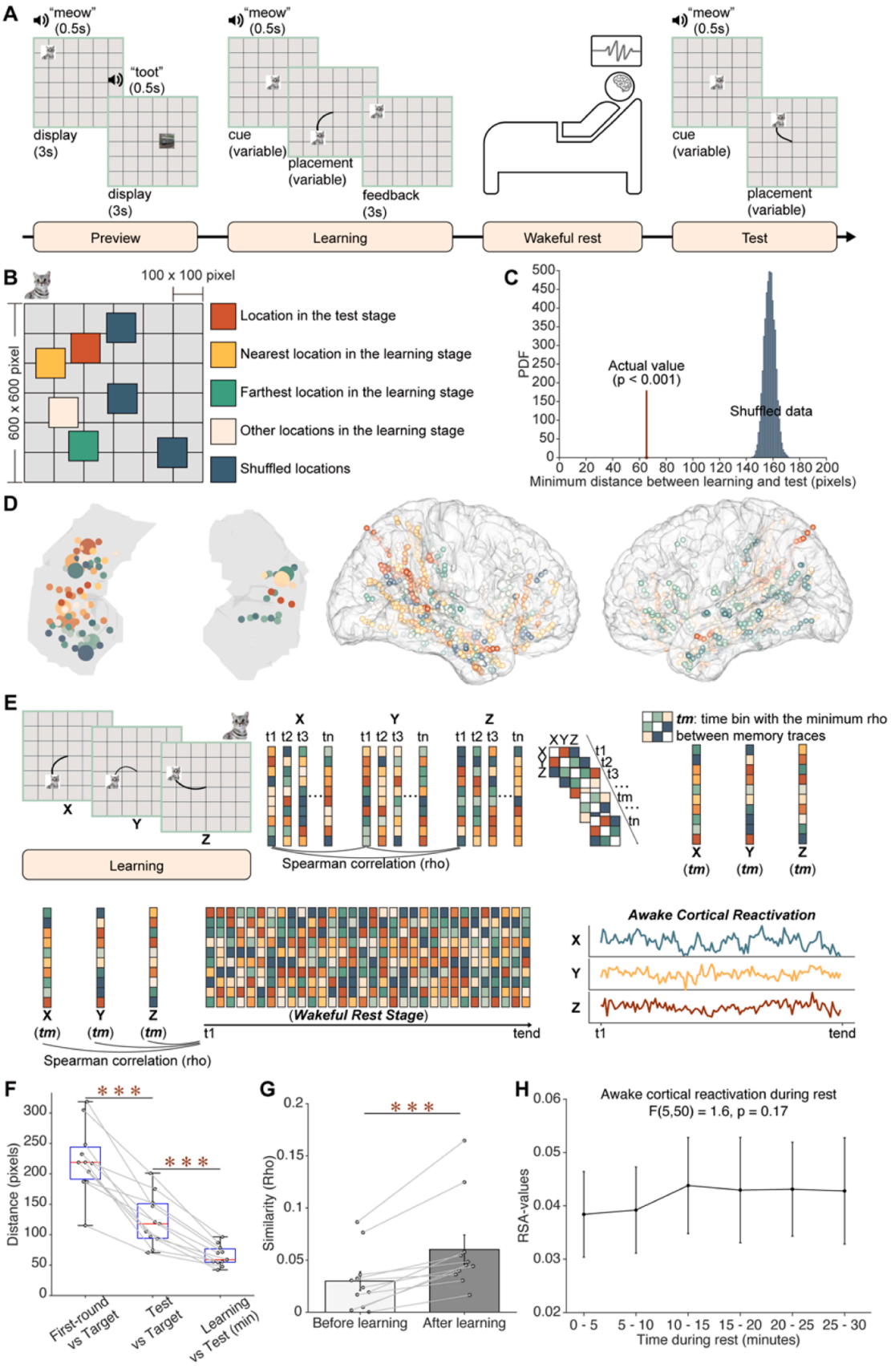
This study aims to explore how awake reactivation of cortical representational patterns supports the selective consolidation of multiple cortical memory traces sharing the same experience. To elucidate this question, we leveraged intracranial electroencephalography (iEEG) recordings to precisely measure hippocampal and cortical signals from patients with drug-resistant epilepsy who performed an object-location association task followed by a period of wakeful rest (Fig. 1**A**). The high spatialtemporal resolution of iEEG provides a unique opportunity to elucidate the neural mechanisms underlying offline memory consolidation supported by awake reactivation (Schreiner and Staudigl, 2020), offering insights into the temporal hierarchical relationship among reactivation, hippocampal ripple, and hippocampal-cortical interaction. Representational similarity analysis (RSA) was adopted as a metric of memory reactivation to examine the functional role of awake reactivation of cortical memory trace (abbreviated as 'awake cortical reactivation') in selective consolidation and its relation with memory benefits during subsequent retrieval.

2. Results

2.1. Retrieved spatial location biased towards the drop location during learning

An object-location association task was performed by 11 epilepsy patients, and iEEG data were recorded synchronously (Fig. 1**A,** Fig. 1**D** and Table S1, see Methods for details). In short, the task required participants to grasp the correspondence between objects and locations on the screen. Participants were provided with 50 objects in total. In the learning stage, participants needed to learn to place each object at its target location on two consecutive times. Thus, several rounds of learning generated multiple cortical memory traces in participants' brain about the object locations (Locations in the learning stage, Los-Learn). In the test stage (i.e., retrieval stage), participants were required to place the object at its target location. To ensure that the patients were engaged in the test stage, we calculated the patients' drop errors before and after learning, which were defined as the Euclidean distance between the response location and target location. The results showed that the patients' drop errors were significantly reduced in the test phase compared to the first round of the learning phase ($t(10) = -7.08$, $p < 0.001$, Fig. 1**F**). It should be noted that the behavioral metric was not concerned with the behavioral performance of object-location memory, but with the relationship between the actual location (Location in the test stage, Lo-Test) of one object and its multiple drop locations (Los-Learn) in the learning stage. Specifically, we speculated that the participants' Lo-Test would be biased toward one of the Los-Learn. In other words, instead of randomly placing the object on the grid during the retrieval stage, the participant may choose one from previous response locations (i.e., Los-Learn) to drop. To verify this hypothesis, we first calculated the distance between Lo-Test and each Lo-Learn for each object and extracted the minimum one. The minimum distance between Lo-Test and Los-Learn was averaged across objects and participants and compared to a null distribution. The null distribution was obtained by repeating the above procedure 1000 times, where the minimum distances were instead calculated between Lo-Test and an equal number of randomly generated positions (Fig. 1**B** and Fig. 1**C,** see Methods for details). The result showed that the minimum distance was smaller than the 99.9th percentile of the distribution sorted in a descending order (Fig. 1**C**). Moreover, we observed that the minimum distance between Lo-Test and Los-Learn was significantly smaller than the distance between Lo-Test and the target location ($t(10) = -6.90$, $p < 0.001$, Fig. 1**F**).

A series of control analyses were conducted to validate the robustness of our observations. We first repeated the analysis for each participant to demonstrate the stability of this drop location-biased retrieval effect at the individual level, and a consistent effect was observed in 10 of the 11 participants (Figure S1). In addition, the location of the last learning round was closer to the target location in the spatial domain and closer to the test stage in the time domain, which could lead to a stronger cortical memory trace being more likely to be retrieved.



(caption on next page)

Fig. 1. Experimental Protocol, Behavioral Results and Analysis Strategy. (A) Experimental Protocol. The object-location association task consisted of four stages: preview, learning, rest and test. In the preview stage, 50 different objects accompanied by object-specific sounds were presented one by one at different locations. In the learning stage, a object was presented in the center of the screen in each trial, and participants were required to place the object to its correct location. Then the correct location was presented as the feedback. The test stage was identical with learning except for the absence of the feedback. (B) Schematic depiction of different drop locations of the same object. The distance between target location and each drop location was used to group the drop locations into the nearest, the farthest and other locations (3 other locations on average) in the learning stage. By randomly selecting equal number of locations from all the placement locations of this participant, the shuffled locations were generated. (C) Minimum distance between learning and test stages, which was averaged across objects and participants. The null distance distribution was generated by calculating the distance between random sampling locations and the drop location in the test stage. The red bar was the average over participants and denoted the actual minimum distance between the nearest Lo-Learn in the learning stage and the location in the test stage. (D) Depiction of electrode contact locations, with left panel for the hippocampus and both middle and right panel for the cortex. Electrode contacts from different participants are denoted in different colors. One hippocampal contact was selected to identify ripples (marked by large spheres). (E) Schematic depiction of the pipeline for the RSA between neural patterns of cortical memory traces in the learning stage and neural patterns in the whole rest stage. The time-resolved LRS profile was obtained by repeating the calculation of spearman correlation between one neural vector in the learning stage and each of multiple neural vectors in the wakeful rest stage. (F) Drop error (Euclidean distance in pixels) decreased significantly in the test phase compared to the first round of the learning phase (Second boxchart versus First boxchart); The minimum (min) distance between Lo-Test and Los-Learn was significantly smaller than the distance between Lo-Test and the target location (Third boxchart versus Second boxchart). (G) Reactivation strength of cortical memory traces during wakeful rest periods before and after learning. (H) No significant differences in cortical reactivation during wakefulness among different time courses. $^{*}p < 0.05$, $^{***}p < 0.001$. All error bars in this study indicate SEM.

Therefore, we repeated the analysis after excluding the last learning round, and the effect was remained (Figure S2).

2.2. Awake cortical reactivation predicts subsequently retrieved location

Next, we aimed to investigate whether the cortical reactivation of different memory traces sharing the same object could predict subsequent retrieval preference for these traces. The initial step was to estimate the neural patterns specific to cortical memory traces, a critical prerequisite for identifying their reactivation (Schreiner and Staudigl, 2020). The frequency-resolved RSA was implemented between cortical memory traces of the same object-location associations during the learning stage to generate a time-resolved cortical memory trace similarity (learning-learning similarity) (Fig. 1**E** and Figure S3D). Since different memory traces are associated with the same object, time points exhibiting high similarity are more likely to reflect object-level shared or overlapping representations rather than the distinct representations of specific traces. Additionally, previous studies have demonstrated that maintaining relatively distinct and low-similarity memory representations can mitigate interference between overlapping memories, thereby enhancing subsequent learning and performance (Favila et al., 2016; Hulbert and Norman, 2015). Hence, the time bin with the lowest cortical memory trace similarity was used to obtain cortical memory trace-specific pattern (i.e., 0.7 s before placement in the current study, Fig. 1**E** and Figure S3D). To directly determine whether awake cortical reactivation reflected task relevant information rather than inherent properties of the memory system, we compared the cortical reactivation strength of encoding-related cortical memory traces during wakeful rest periods before and after learning. The results revealed that awake reactivation strength after encoding was significantly higher than that before encoding (After learning versus Before learning: $t(10) = 4.79$, $p < 0.001$, Fig. 1**G**), indicating that awake cortical reactivation indeed reflected the learning-induced cortical memory traces. Additionally, repeated-measure ANOVA showed that there was no significant difference in cortical reactivation among different time courses of the wakeful rest period after learning ($F_{(5,50)} = 1.64$, $p = 0.17$, Fig. 1**H**), indicating that awake cortical reactivation did not prefer a specific time window.

Previous studies have shown that the successful memory retrieval benefited from spontaneous offline reactivation, and demonstrate that the degree of reactivation can predict subsequent memory performance (Deuker et al., 2013; King et al., 2022; Schreiner et al., 2021; Staresina et al., 2013; Van De Ven et al., 2016). We hypothesized that a similar mechanism may exist in competitive cortical memory traces sharing a common target, whereby the memory trace that was successfully extracted during subsequent test experienced a higher cortical reactivation during the wakeful rest period after learning, leading to a selective consolidation of that cortical memory trace. A serial analysis method was employed to test our hypothesis. First, we extracted cortical memory trace with the highest reactivation for each object, along with its corresponding encoding location. We reasoned that the distance between this encoding location and the retrieval location of the object during subsequent test should be the shortest, and assessed the significance level of the guess accuracy. The results showed that the accuracy was significantly higher than 97 % of random guesses (Fig. 2**A**, permutation test, see Methods for details). Next, we correlated the distance between the Los-Learn and the Lo-Test with the reactivation strength of the cortical memory trace of the Los-Learn during the wakeful rest stage. This calculation was performed independently for each subject, and the resultant correlation coefficient was averaged and compared with a null distribution. The results showed that the reactivation strength was significantly negatively correlated with the distance between the Los-Learn and the Lo-Test (Fig. 2**B**, permutation test, see Methods for details). Furthermore, we directly extracted the nearest Lo-Learn and the farthest Lo-Learn from the Lo-Test, and compared the reactivation intensity between the cortical memory traces of them. The results show that the cortical memory trace of the nearest Lo-Learn showed a significantly stronger reactivation intensity than the cortical memory trace of the farthest Lo-Learn ($t(10) = 2.83$, $p = 0.018$, Fig. 2**C**). A control analysis was performed to further illustrate the relationship between the competitive strength of the cortical memory trace which was scaled by the distance between the nearest Lo-Learn (minimum competitive strength) and the farthest Lo-Learn (maximum competitive strength) and the difference in the intensity of reactivation of the two cortical memory traces. The results indicated that the farther the distance between the two Los-Learn was (i.e., the larger competitive strength), the greater the difference in awake cortical reactivation strength of the two cortical memory traces ($r = 0.83$, $p < 0.001$, Fig. 2**D**).

When directly comparing the time-resolved reactivation intensity of the nearest Lo-Learn with that of the farthest Lo-Learn during test (learning-test similarity), a reasonable result was observed that the cortical memory trace of the nearest Lo-Learn displayed a higher reactivation level and thus won the competition (cluster-based permutation test, see Methods for details, Figure S3C). These results suggest that the target cortical memory trace was reactivated more strongly during the retrieval stage while the competing cortical memory trace was relatively weaker, and thus the reactivation strength of cortical memory trace during retrieval would predict subsequent behavior.

Finally, we assessed the validity of the time bin used to obtain cortical memory trace-specific pattern. Accordingly, we calculated the similarity between the pattern of the nearest Lo-Learn cortical memory trace at a single time point during the learning stage and the pattern during the rest period and averaged the values to obtain the Learning-rest similarity (LRS) at that time point. This calculation was repeated for each time period of 1 s before placement to obtain a time-resolved LRS signal of the nearest (and farthest) Lo-Learn cortical memory

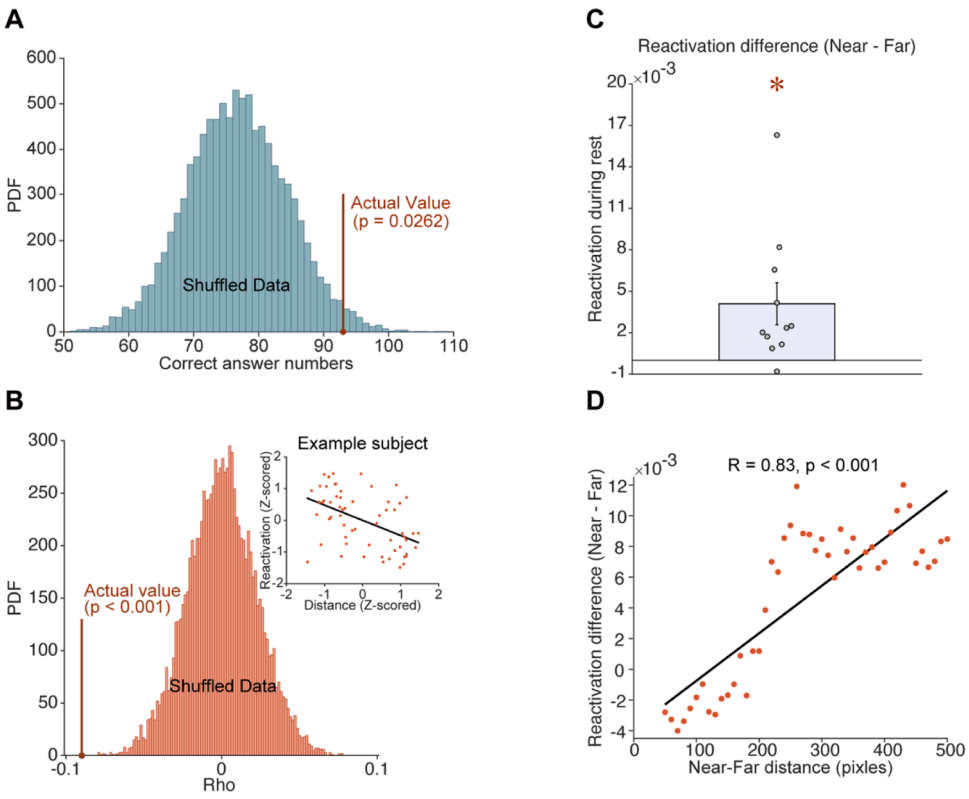


Fig. 2. Awake cortical reactivation predicts subsequent retrieval location. (A) The correct number of guesses based on LRS. It was assumed that the location in the learning stage, whose cortical memory trace had the highest similarity with the neural pattern in the whole rest stage, could be the closest to the drop location in the test stage. According to this assumption, the correct number of the above guesses for all objects from all participants was calculated and marked in a red vertical bar. The null distribution of correct number of guesses was generated by shuffling the label of cortical memory trace in learning stage and recalculating the correct number. (B) Significant correlation between the LRS strength and the normalized distance to the retrieval location in the test stage. The null distribution of correlation coefficient was generated by shuffling the correspondence between the distance and LRS strength of cortical memory trace and recalculating the correlation coefficient. Inset: an example subject. (C) The differences of LRS strength of the cortical memory traces (nearest location versus farthest location). (D) The correlation between the differences of LRS strength of the cortical memory traces (nearest location versus farthest location) and the distance between the locations (nearest location versus farthest location). * $p < 0.05$.

trace during the learning stage. A comparison of the time-resolved LRS of the nearest and the farthest Lo-Learn cortical memory trace showed a significant difference, with significant temporal clustering distributed around 0.7 s before placement (cluster-based permutation test, see Methods for details, Figure S3E), which was consistant with the time bin (i.e., 0.7 s before placement) used for the cortical memory trace-specific representation. This result demonstrated that multiple cortical memory traces may retain separate and unique representations during the learning stage. Additionally, we employed an alternative approach to validate the selection of the time bin by examining the relationship between LLS (Figure S3D) and LRS (Figure S3E) at the time-bin level. Specifically, for each time bin preceding object placement during the learning phase (time window: −1000 ms to −100 ms, in 20 ms intervals, yielding in 46 time points), we computed the representational similarity between cortical activity patterns of different memory traces associated with the same object (Figure S3F, X-axis, LLS). We then assessed the awake reactivation strength of these cortical activity patterns separately for near and far memory traces and calculated the differential reactivation strength (Near - Far) between them (Figure S3F, Y-axis, LRS). Our analysis revealed a significant negative correlation between pattern similarity during the learning stage and the differential reactivation strength during the rest stage ($r = -0.66$, $p < 0.001$). This finding suggests that selecting time points with lower representational similarity during learning for subsequent reactivation analysis more effectively captures the competitive dynamics between memory traces, with near memory traces exhibiting a greater advantage in reactivation during wakeful rest.

2.3. Electrophysiological signatures of awake cortical reactivation

Evidence from human electrophysiological recording suggests that hippocampal ripples play a critical role in reactivation and sleep offline memory consolidation (Norman et al., 2019; Zhang et al., 2018). Therefore, we further analyzed the contribution of hippocampal ripples to awake cortical reactivation. To evaluate this, the cortical LRS peaks were identified for each cortical memory trace using 2.5 standard deviations as thresholds (Fig. 3**A**, top pannel). Based on this criterion, we calculated the rate of cortical reactivation peaks during the wakeful rest period before and after learning for each patient. The results showed that the awake cortical reactivation peak rate increased in all patients after learning ($t(10) = -8.77$, $p < 0.001$, Fig. 3**A**, bottom pannel). After ripple detection, a significantly higher hippocampal ripple rate time-locked to the cortical LRS peaks was observed (Fig. 3**C** and Fig. 3**D**, cluster-based permutation test, see Methods for details). Furthermore, we examined the consistency of this effect across participants, and observed that 8 out of 11 participants showed ripple-reactivation co-occurance (Figure S5). We also noted that some studies employed different ripple detection methods (Kunz et al., 2024; Schreiner et al., 2024; Staresina et al., 2015). To verify that the results were not driven by variations in detection criterions or the specific hippocampal contacts, we incorporated all hippocampal electrodes, applied a different ripple detection criterion (filtering in 80–120 Hz and at least 3 cycles) and recalculated the ripple rate around the reactivation peak. The effect remained (Figure S4D).

The next aim was to assess whether cortical memory trace-specific

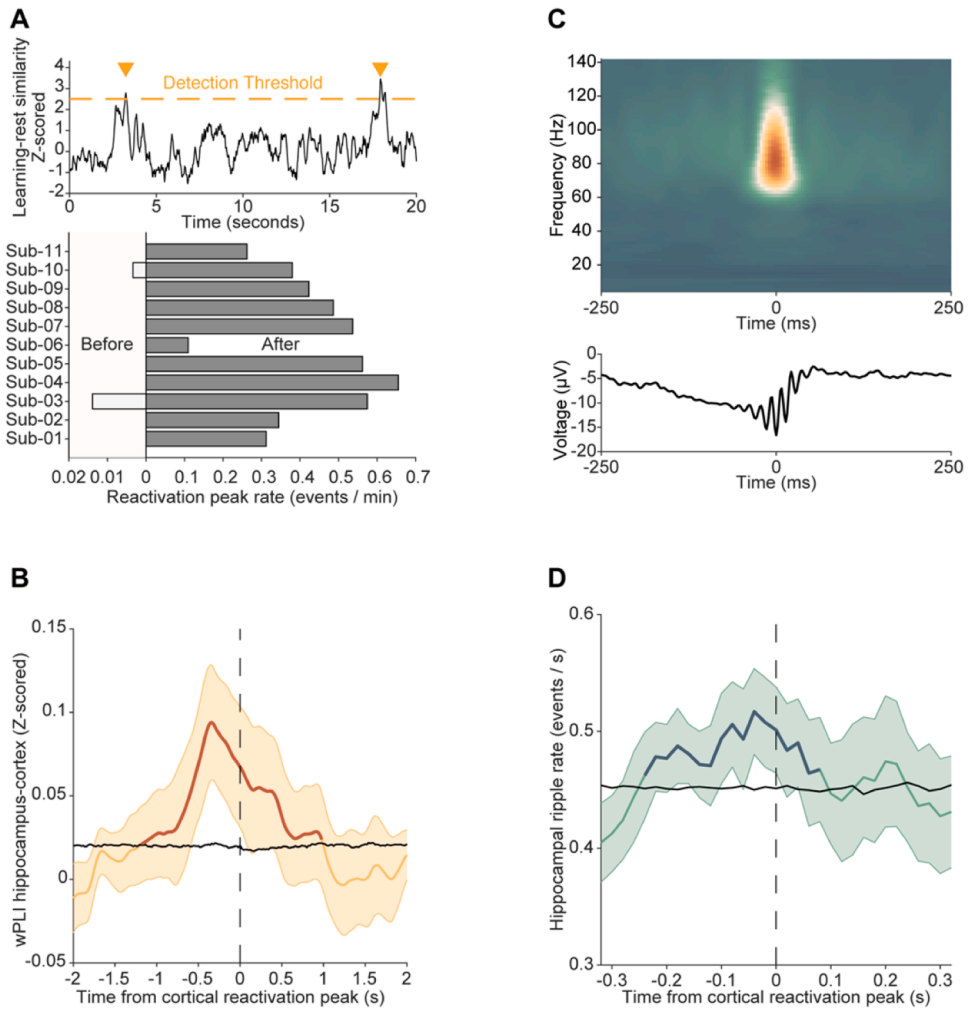


Fig. 3. Electrophysiological signatures of awake cortical reactivation. (A) Awake cortical reactivation peak. Top: cortical LRS values exceeding 2.5 SD were identified as reactivation peaks. Bottom: the rate of reactivation peaks detected during wakeful rest before and after learning (events / min). (B) Increased theta-band (4–8 Hz) wPLI between hippocampus and cortex around awake cortical reactivation peak. The line in bold represents the significant cluster in wPLI (-1180–980 ms around reactivation peak; $p < 0.001$). The black line is the threshold value of $p < 0.01$ with 1000 shuffles. (C) Peri-ripple spectrogram (top) and re-referenced field potential (bottom) of one hippocampal contact. (D) Hippocampal ripple rate around awake cortical reactivation peak. The line in bold represents time cluster with significantly increased hippocampal ripple rate (-240–80 ms around reactivation peak, $p < 0.001$). The black line is the threshold value of $p < 0.01$ with 1000 shuffles.

awake reactivation was accompanied by hippocampal-cortical interaction, which was traditionally observed during sleep-related consolidation (Schreiner and Staudigl, 2020). The hippocampal-cortical interaction was then directly examined with phase-locking values (PLV) and weighted phase lag index (wPLI) as metrics of communication between hippocampus and cortex. Theta oscillations can orchestrate the synchronous activities across remote neuron assembles and play a critical role in both inter-regional communication and episodic memory (Herweg et al., 2020). We inferred that theta-band (4–8 Hz) hippocampal-cortical interaction may be increased around the cortical LRS peaks. Consistently, significant theta-band hippocampal-cortical PLV clusters were obtained when aligned to the cortical LRS peaks (Figure S4C, cluster-based permutation test, see Methods for details). A control analysis was performed to detect hippocampal and cortical theta oscillations, and the results showed that cortical reactivation was accompanied by an increase in theta activity in the hippocampal-cortical network (Figure S4A **and B**). To validate the robustness of inter-regional communication finding, we also calculated the weighted phase lag index (wPLI) and still observed a significant theta-band hippocampal-cortical wPLI cluster around the reactivation peak (Fig. 3**B**). Additionally, the individual-level analysis suggested that 7 out of 11 exhibited strong connectivity-reactivation coupling (wPLI, Figure S7; 7 out of 11 for PLV, Figure S6). Together, our result revealed that cortical reactivation was associated with increased hippocampal ripple rate and enhanced hippocampal-cortical interaction during wakeful rest.

2.4. Temporal dynamics of reactivation, hippocampal ripple, and hippocampal-cortical interaction

The interplay between reactivation, hippocampal ripple, and hippocampal-cortical interaction is a crucial yet challenging question, particularly in understanding their temporal hierarchy. To address this, we first examined the temporal relationship between hippocampal ripple and cortical reactivation by identifying the peak time points of cortical reactivation and quantifying the time intervals between ripple occurrences and these peaks. Our results showed no significant temporal precedence between hippocampal ripple and cortical reactivation ($t(10) = 0.91$, $p = 0.385$, Fig. 4A). An additional analysis detecting the proportion of trials in which ripple event occurred before the cortical reactivation peak yielded consistent results ($t(10) = 0.39$, $p = 0.703$, Fig. 4B).

Similarly, we analyzed the temporal dynamic between cortical-

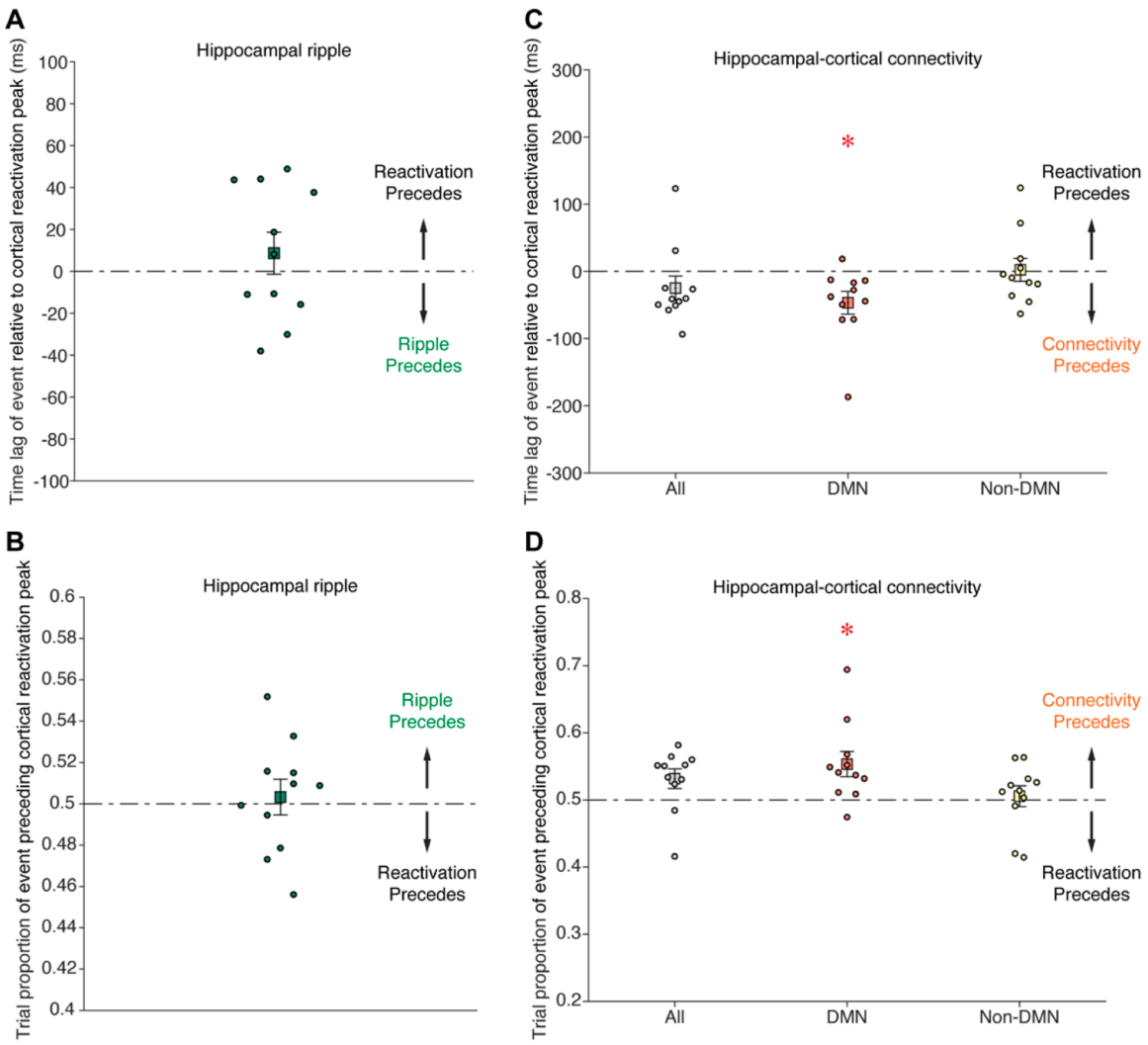


Fig. 4. Temporal dynamics of reactivation, hippocampal ripple, and hippocampal-cortical interaction. (A) Time lag of ripple relative to awake cortical reactivation peak. (B) Trial proportion of ripple preceding awake cortical reactivation peak. (C) Time lag of hippocampal-cortical connectivity peak relative to awake cortical reactivation peak. (D) Trial proportion of hippocampal-cortical connectivity peak preceding awake cortical reactivation peak. * $p < 0.05$.

hippocampal connectivity peaks and cortical reactivation peaks, again finding no significant lead-lag effect ($t(10) = -1.44$, $p = 0.181$, p_fdr $= 0.271$, Fig. 4C, first bar). However, given that different cortical regions may contribute differently to cortical-hippocampal connectivity, especially considering prior work highlighting the role of the default mode network (DMN) in ripple/reactivation related memory processing (Higgins et al., 2021; Huang et al., 2024; Kaefer et al., 2022; Kaplan et al., 2016; Norman et al., 2021; Nour et al., 2023), we specifically extracted electrode contacts within the DMN and re-examined their connectivity with the hippocampus. Interestingly, we found that the peak connectivity between the DMN and hippocampus significantly preceded cortical reactivation ($t(10) = -2.89$, $p = 0.016$, p_fdr $= 0.048$, Fig. 4C, second bar), whereas this effect was absent for non-DMN electrode contacts ($t(10) = 0.15$, $p = 0.887$, p_fdr $= 0.887$, Fig. 4C, third bar). To further validate this effect, we conducted an alternative analysis by quantifying the proportion of trials in which connectivity peak occurred before reactivation peak. The results remained consistent ($t(10) = 2.27$, $p = 0.046$, p_fdr $= 0.069$, first bar; $t(10) = 2.97$, $p = 0.014$, p_fdr $= 0.042$, second bar; $t(10) = 0.37$, $p = 0.719$, p_fdr $= 0.719$, third bar; Fig. 4D), demonstrating a significant temporal precedence of DMN-hippocampal connectivity over cortical reactivation, which was not observed in other brain network (Figure S8A-B). Furthermore, 7 out of 11 participants exhibited a consistenst effect, indicating inter-participant robustness (Figure S8C). Overall, our results suggest that there is no significant temporal relationship between awake cortical reactivation and hippocampal ripple, but hippocampal-DMN connectivity consistently precedes cortical reactivation during wakeful rest.

3. Discussion

This study utilized iEEG recordings to reveal memory reactivation during wakeful rest based on multiple cortical memory traces derived from several learning trials prior to the rest period. These reactivation measures were associated with subsequent retrieval and also used to identify electrophysiological signatures of offline memory consolidation. Specifically, the extent to which memory traces showed enhanced cortical reactivation during wakeful rest predicted location of later retrieval. Furthermore, an increase in hippocampal ripple rate and hippocampal-cortical interaction was observed at the peak of awake cortical reactivation, with hippocampal-DMN interaction preceding the peak of awake cortical reactivation.

3.1. Different roles of online and offline awake reactivation in memory process

Awake reactivation, occurring both online and offline, influences memory differently across brain states. Electrophysiological studies in rats revealed that interrupting hippocampal ripples during learning disrupted hippocampal replay and impaired learning performance (Jadhav et al., 2012). The coordinated hippocampal-prefrontal reactivation was observed during learning, emphasing the role of awake cortical reactivation in memory processes (Jadhav et al., 2016). Moreover, awake reactivation during learning is stronger and more structured compared to sleep, playing a critical role in initial spatial learning (Tang et al., 2017). Overall, awake reactivation could support memory-guided behavior by providing a high-fidelity representation of behavioral experiences.

Single-neuron recordings in humans have shown selective reactivation of specific neurons in various regions before free recall, suggesting that reactivation underlies spontaneous recollection (Gelbard-Sagiv et al., 2008; Khuvis et al., 2021). Additionally, ripple-coupled reactivation in higher-order visual areas linked ripple activity to the recall process (Norman et al., 2019). Further evidence supports that successful retrieval is associated with enhanced cortical reactivation, increased ripple coupling between cortex and medial temporal lobe (MTL), and ripple-related replay of cortical spiking sequences (Vaz et al., 2019, 2020). Consistent with these findings, we observed increased hippocampal ripple rate aournd cortical reactivation, and showed that cortical memory traces closest to the retrieval location were more strongly reactivated. Collectively, these studies indicate that ripple-related reactivation may serve as a candidate mechanism supporting successful memory retrieval.

Although both wakeful rest and sleep states can support memory consolidation, it remains unclear whether the two offline states perform distinct functions in consolidation. A well-designed study demonstrated that while cued memory reactivation during both wakefulness and sleep prevented the forgetting of low-value associations, reactivation during the waking state primarily enhanced the specific target association, whereas reactivation during sleep benefited the entire set of low-value associations (Oudiette et al., 2013). This finding suggests that consolidation during waking state strengthens specific, salient memories, whereas sleep consolidates and integrates all related memories. It is important to note that participants in that study were watching a movie during the wakeful period, rather than engaging in “pure” wakeful rest, which may influence the interpretation of these findings. A recent review elaborates a similar perspective, arguing that wakefulness reliably enhances memory traces and supports online task-related behavior, while sleep fosters the formation of integrative and schematic representations and facilitates memory generalization (Tambini and Davachi, 2019). Consistent with prior research (Deuker et al., 2013; King et al., 2022; Staresina et al., 2013; Tambini and D’Esposito, 2020), our results indicate that reactivation during wakeful rest can predict subsequent performance. Specifically, cortical memory traces with higher reactivation intensity are more likely to be successfully retrieved. While our study provides evidence for the role of awake reactivation in memory consolidation, it does not allow for a direct comparison of the fidelity of reactivation between the wakeful resting state and sleep. Future studies should address this gap to further elucidate these mechanisms.

3.2. Electrophysiological mechanism of cortical reactivation supporting memory consolidation during wakeful rest

Memory consolidation in offline brain states strengthens previously encoded experiences by reducing external attention and fostering an internally focused state (Tambini and Davachi, 2019; Wamsley, 2019). Repeated offline reactivation of neural patterns that occurred during experiences constitutes an attractive mechanism for memory consolidation, and is observed both during sleep and wakeful rest (Schreiner and Staudigl, 2020; Tambini and Davachi, 2019; Wamsley, 2019). Our results confirmed that cortical neural patterns associated with multiple cortical memory traces during learning were selectively reactivated during wakeful rest, with the extent of reactivation predicting the retrieval probability of those cortical memory traces. These findings provide direct electrophysiological evidence that awake cortical reactivation supports consolidation, consistent with the framework that reactivation is a general mechanism for memory updating, storage, and consolidation (Gillespie et al., 2021). This raises the question of whether wakeful rest and sleep share common neurophysiological mechanisms of reactivation favoring memory consolidation.

Evidence from human studies demonstrated that hippocampal-cortical interaction also occur during wakeful rest and can lead to memory benefits (Tambini et al., 2010; Tambini and D’Esposito, 2020). Consistent with this observation, enhanced theta-based hippocampal-cortical connectivity reported in our data support an active hippocampal-cortical dialogue during wakeful rest. Additionally, ripples detected during wakeful rest were associated with BOLD signals in various brain regions, further supporting hippocampal-cortical interactions (Logothetis et al., 2012). In line with numerous studies (Carr et al., 2011; Diba and Buzsáki, 2007; Foster and Wilson, 2006; Nour et al., 2021; Zhang et al., 2018), our data also revealed the presence of hippocampal ripples during wakeful state. Substantial evidence, including our own data, indicate that hippocampal ripple-coupled cortical reactivation, similar to that observed during sleep state, also occurs during wakeful state (Chang et al., 2023; Nguyen et al., 2024; Sugden et al., 2020).

Overall, our findings support the hypothesis that reactivation plays a consistent role in preserving experiences during wakeful rest, as in sleep, suggesting that memory consolidation is characterized by hippocampal ripple-coupled reactivation and hippocampal-cortical dialogue in both brain states (Gillespie et al., 2021; Tambini and Davachi, 2019; Tang and Jadhav, 2019). However, the neural implementation of the hippocampal-cortical dialogue differs in the two different brain states. The active systems consolidation framework emphasizes the hippocampal-neocortical dialogue during sleep which is mediated by a triple coupling of slow oscillations (SO), spindles, and ripples (Brodt et al., 2023; Denis and Cairney, 2023; Klinzing et al., 2019; Schreiner and Staudigl, 2020; Staresina, 2024; Watson and Buzsáki, 2015). It has been proposed that reactivation during sleep may favor global network connectivity through this triple coupling, whereas awake reactivation is more local due to the absence of sleep-specific SO and spindles, with this shift from local to global reactivation potentially explaining the differences in consolidation properties between the two offline brain states (Genzel and Robertson, 2015). Furthermore, data from human resting-state scalp EEG indicated that memory improvements were associated with increased SO activity, indicating that SO activity during wakeful rest may facilitate hippocampal-cortical communication and promote memory consolidation (Brokaw et al., 2016). Further studies are needed to elucidate the neural oscillatory signatures of awake reactivation that underlie hippocampal-cortical dialogue related to memory consolidation.

3.3. Temporal hierarchy of reactivation, hippocampal ripple and hippocampal-cortical connectivity

Investigating the temporal dynamics of cortical reactivation, hippocampal ripple, and hippocampal-cortical interaction can deepen our understanding of the candidate mechanisms by which awake reactivation supports memory consolidation. Electrophysiological data during sleep in rodents support the view that ripple-related reactivation originates in the hippocampus and subsequently spreads to the cortex (Ji and Wilson, 2007; Klinzing et al., 2019; Peyrache et al., 2009). In addition, similar temporal relation has been found in iEEG recordings during memory retrieval in humans (Vaz et al., 2019, 2020). However, our data suggest that cortical reactivation and hippocampal ripple

co-occur during wakeful rest, with no clear temporal hierarchy between them. Therefore, future studies with more extensive human electrophysiological recordings are needed to investigate whether the temporal relationship that hippocampal ripple precede cortical reactivation remains stable during sleep, wakeful rest, and active retrieval.

The brain regions comprising the DMN increase their activity during quiet rest, or offline states (Menon, 2023; Raichle, 2015). Many studies have reported ripple/reactivation-related enhanced activity in the DMN (Higgins et al., 2021; Kaplan et al., 2016; Norman et al., 2021; Nour et al., 2023), supporting the view that these two spontaneous brain dynamics—offline reactivation and intrinsic DMN activity—work together to support memory consolidation (Kaefer et al., 2022). In addition, recent study has shown that increased reactivation probability enhances the connectivity between the hippocampus and the DMN (Huang et al., 2024). Inspired by these findings, our focus on the temporal structure between cortical reactivation and hippocampal-cortical interaction revealed an interesting result: only hippocampal-DMN connectivity consistently preceded cortical reactivation. Our results support a synergistic role for these two intrinsic brain dynamics, suggesting that they may work together to support memory consolidation during wakeful rest. Furthermore, we believe the observed temporal structure between reactivation and hippocampal-cortical interaction aligns well with the "call-up" framework, which posits that during the transfer of information, reader can establish inter-regional connectivity through low-frequency synchronization, followed by high-frequency oscillations from the sender region transmitting specific information. For instance, cortical SOs and spindles precede hippocampal ripple activity to facilitate memory transfer during sleep-dependent memory consolidation (Buzsáki, 2010, 2019). Our results suggest that a comparable process may occur during wakeful rest, where the DMN first establishes connectivity with the hippocampus via theta-band coupling, followed by hippocampal ripple and cortical reactivation.

4. Conclusion

In conclusion, our study demonstrates that awake reactivation of multiple cortical memory traces derived from learning experiences can bias subsequent memory retrieval, potentially determining what will be remembered later. Furthermore, our data suggest that awake cortical reactivation is associated with enhanced hippocampal-cortical communication and an increase in hippocampal ripple rate, with hippocampal-DMN interaction preceding awake cortical reactivation. These findings provide empirical evidence for the role of awake cortical reactivation in memory consolidation and shed light on the underlying electrophysiological mechanisms.

5. Methods and materials

5.1. Participants

Eleven patients (2 females and 9 males; mean age ± standard deviation (SD): 23.9 ± 5.4 years) with medically refractory temporal lobe epilepsy were recruited in the current study at Beijing Sanbo brain hospital. They underwent stereotactic implantation of depth electrodes to pinpoint epileptogenic zones. Demographic information for each patient is detailed in Supplementary Table 1. All participants reported normal or corrected-to-normal visual acuity and normal color vision. Informed consent was obtained from all participants, and the study protocols were approved by the Ethics Committee of Beijing Sanbo Brain Hospital.

5.2. Experimental protocol

Participants learned to associate each of 50 unique objects (small squares, 2.3 cm per side) with one specific location on a grid displayed on a 13.6 cm (600 pixels) square monitor. Concurrently, each object was paired with a distinctive sound (e.g., goblet with a breaking sound). This object-location association task has been used in previous target memory reactivation studies (Berkers et al., 2018; Rudoy et al., 2009; Van Dongen et al., 2012). The original object-location association task consisted of six stages: preview, learning, rest, test, sleep, and post-sleep test. Since the sleep stages and post-sleep testing stages were not related to this study, the data from the two stages were not used here and the procedures for the sleep phase and post-sleep testing phase are not described here. During the preview stage, subjects familiarized themselves with the experimental instructions and the unique locations of each object. In the learning stage, participants placed each object at its correct location, with trials being self-paced and terminated by a button press confirming object placement. Correct placements were displayed for 3000 ms as feedback. Participants repeated learning rounds with objects in random order until all were placed within 3.4 cm (150 pixels) of their correct location for two consecutive rounds. Objects correctly placed in two consecutive rounds were omitted from subsequent rounds. Each object has an average of 5 rounds of learning. After completing the learning, the subjects rested for about 30–40 minutes. During the rest period, the subjects were asked not to do things that consume cognitive resources (such as reading books, playing games, etc.) and not to sleep. Afterwards, the test stage assessed the memory performance of all 50 objects without feedback. The average time spent by participants was 29.9 ± 9.4 minutes in the learning stage, and 5.9 ± 0.6 minutes in the test stage.

5.3. Minimum distance between locations in learning and test stage

We wanted to investigate whether the location of the object placed during the test was associated with previous cortical reactivation. We thus hypothesed that the recalled position during the test would be close to one of the placed positions during the learning stage for the same object. To test it, we calculated the Euclidean distance between the recalled position during the test stage and the locations placed during the learning stage for each object. Since each object had multiple trials during learning, we took the minimum distance as the closest one for this object. Afterwards, we randomly selected several positions from all the placement locations of this participant as surrogate learning positions (the same number as the actual learning round) and recalculated the closest distance between the real testing positions and these surrogate positions. We repeated the above steps 5000 times and generated a distribution to test our hypothesis.

5.4. Electrophysiological recordings

The surgical implantation of electrodes was conducted based solely on clinical requirements. Intracerebral multiple-contact electrodes (8–16 contacts; dimensions: length 2 mm, diameter 0.8 mm, spacing 1.5 mm; Huake-Hengsheng Medical Technology Co. Ltd., Beijing, China) were implanted using a robot-assisted stereotactic surgery system. Intracranial EEG recordings were acquired using a Nicolet system (128 channels, sampling rate: 512 Hz; Thermo Nicolet Corporation).

5.5. Electrode reconstruction and localizations

To accurately determine the anatomical placement of the electrodes, post-implantation CT images were co-registered with pre-operative T1-weighted MR images using FreeSurfer (v6.0.0, http://surfer.nmr.mgh.harvard.edu/). The localization of the implanted electrodes was achieved using established software (Qin et al., 2017), and the accuracy of electrode contact localization was visually verified. Subsequently, all electrode coordinates were normalized onto the Montreal Neurological Institute (MNI) standard space.The precise locations of the electrode contacts in the hippocampus were anatomically identified for each patient using FreeSurfer's parcellation algorithm (Desikan et al., 2006) and confirmed through visual inspection.

5.6. Preprocessing and data analysis

Data analysis was performed in MATLAB (MathWorks Inc., Natick, MA) using EEGLAB (Delorme and Makeig, 2004), Fieldtrip (Oostenveld et al., 2011), analysis scripts published in previous studies (Janca et al., 2015; Norman et al., 2019) as well as custom-developed scripts in this study. Following methods similar to a previous study (Zhang et al., 2018), we re-referenced all intracranial EEG (iEEG) data, excluding hippocampal contacts, by computing the average activity across all contacts. This approach aimed to enhance the specificity of representational patterns at individual contacts. For each hippocampal contact, we subtracted a reference signal from a nearby white-matter contact to mitigate common noise, as described by Norman et al. (2019). Power-line interference noises (50 Hz and its harmonics) were removed using a notch filter (implemented as a Hamming windowed FIR filter, applied via EEGLAB's pop_eegfiltnew function). Detection of epileptiform spikes in each hippocampal contact was performed using the ISARG (Intracranial Signal Analysis Research Group) method with default settings (Janca et al., 2015), available at http://isarg.fel.cvut.cz (version 16). The number of IEDs detected for each subject is provided in Table S1. Additionally, the mean peri-IED field potential and spectrogram are shown in Figure S4E-**F**. To prevent artifact-ripple detections, ripples occurring within 100 ms of each epileptiform spike were excluded from analysis.

5.7. Time-frequency analysis

Spectral decomposition of LFP data (learning and rest stage) for all cortical and hippocampal contacts was done using Morlet wavelets (seven cycles, frequency bin: 2 Hz, step bin: 20 ms) implemented in Fieldtrip. Then we normalized the iEEG power using Z-score across all time bins at each frequency bin.

5.8. Representational similarity analysis

RSA was performed by correlating the spectral power across frequencies (2–140 Hz, with 2-Hz steps from 2 to 10 Hz and a 10-Hz step from 20 to 140 Hz) and across all cortical channels, separately for each time bin, using Spearman's correlation (Liu et al., 2021).

Learning-rest similarity (LRS): first, we calculated the cortical neural activity similarity of the same object across multiple trials during the learning period (A time window of −1000 ms to placement was used to maximize the number of included trials. Figure S3A showed that all trials in the learning stage had a reaction time greater than 1 second), and the resulting similarity was averaged across objects and participants. Considering the competition across multiple cortical memory traces and the need for different cortical memory traces to be stored separately, the time bin with the lowest cortical memory trace-cortical memory trace similarity was used to obtain cortical memory trace-specific pattern. Therefore, we correlated the cortical memory trace-specific pattern with the activity pattern across the entire wakeful rest period (30 minutes). For each cortical memory trace, this analysis yielded the time series of learning-rest similarity.

Learning-test similarity (LTS): As each object had multiple trials during the learning period, and only one during the testing period, we correlated the pattern of each learning trial with the pattern of testing trial for same object (separately for each time bin, from −1000 ms to the placement, Figure S3B showed that 98.4 % of the trials in the test stage had a reaction time greater than 1 second).

5.9. Offline cortical reactivation detection

Previous studies have found that cortical reactivation is accompanied by hippocampal ripples and interaction between hippocampus and cortex during both sleep and wakeful rest (see reviews: (Brodt et al., 2023; Denis and Cairney, 2023; Klinzing et al., 2019; Schreiner and Staudigl, 2020; Staresina, 2024; Tambini and Davachi, 2019; Tang and Jadhav, 2019; Watson and Buzsáki, 2015)). In this study, we further tested the relation between cortical reactivation and hippocampal ripples during wakeful rest. Therefore, we needed to find time periods of pronounced cortical reactivation. First, we smoothed the time series of LRS (with a 200 ms sliding window) for each cortical memory trace. Reactivation events were identified from the smoothed signal when they exceeded 2.5 standard deviations (SD) above the average value. The reactivation peak was the maximum within each event. Adjacent events with less than 2000 ms separation (peak-to-peak) were deleted. In total, 90.5 % of the cortical memory traces contained one or more reactivation events, with an occurrence rate 0.42 ± 0.16 per minute. We also used the same threshold to calculate the occurrence rate of reactivation during the pre-learning resting state as a baseline, which was 0.0016 ± 0.0042 per minute.

5.10. Behavioral prediction

We wanted to investigate whether the reactivation during rest is related to behavioral performance during subsequent testing, that is, whether the cortical memory trace with the highest reactivation intensity during rest is closest to the recalled position during test. Among multiple cortical memory traces of each object (i.e., the objects with at least three trials, 73 % of the total objects), we took the average LRS across time to obtain the resting reactivation score for each cortical memory trace and then inferred that the cortical memory trace with the highest resting reactivation score would be closest to the recalled position in the subsequent test. If correct, we marked this object as 1, otherwise 0. In the control conditions, we shuffled the resting reactivation scores within each object and repeated the above analysis 10,000 times to generate a null distribution.

On the other hand, we calculated the correlation between the resting reactivation score and the distance between the recall position. Among multiple cortical memory traces of each object, we normalized the resting reactivation score and the placement distance (Euclidean distance between the position during learning and the position during testing), respectively. Then we calculated the correlation between resting reactivation score (Z-scored) and distance (Z-scored) for each participant. Afterwards, we shuffled the labels and repeated the above steps 10,000 times to generate a null distribution of control condition.

5.11. Offline hippocampal ripple detection

For each participant, the hippocampal contact located in the hippocampus was utilized for ripple detection. We employed established ripple detection scripts (Norman et al., 2019) to identify ripple events during rest stages.

The re-referenced local field potentials (LFPs) recorded in the hippocampal contact were filtered within the frequency range of 70–180 Hz using a Hamming windowed sinc finite impulse response (FIR) filter. We calculated the analytic amplitude of the LFPs using a Hilbert transform, followed by clipping extreme values (using Least-Median-Squares and clipped to 4 SD above the mean value). The clipped signal was then squared and smoothed using a FIR low-pass filter with a 40 Hz cutoff frequency. Ripple events were identified from the original signal (squared but unclipped) when they exceeded 4 standard deviations (SD) above the clipped signal. Event duration was extended until the ripple power fell below 2 SD. Events shorter than 20 ms or longer than 200 ms were excluded from further analysis. Adjacent ripples with less than 30 ms separation (peak-to-peak) were merged. To avoid including potential pathological events, any ripple events occurring within 100 ms of inter-ictal epileptic discharges (IEDs) were removed from analysis.

5.12. Connectivity analysis

To evaluate the connectivity between the hippocampus and cortex

during rest, we calculated the phase-locking value (PLV) and the weighted phase lag index (wPLI). PLV quantifies the consistency of phase differences between a pair of electrodes and is expressed as:

$$\mathrm{PLV(f)} = \frac{1}{N}\left|\sum_{n=1}^{N} e^{\varnothing_{xy[n]}}\right|$$

Where N denotes total time points and $\varnothing_{xy[n]}$ indicates the phase difference between the two time courses x and y.

The wPLI quantifies the consistency of phase differences weighted according to their distance from the real aixs and is expressed as:

$$wPLI = \frac{N^{-1}\sum_{n=1}^{N}|Im(S_{xy[n]})|Sgn(Im(S_{xy[n]}))}{N^{-1}\sum_{n=1}^{N}|Im(S_{xy[n]})|}$$

Where N denotes total time points and $Im(S_{xy[n]})$ indicates the imaginary part of the cross_spectral density at time point. *Sgn* indicates the sign (+1/-1 for positive/negative values, and 0 for zero values).

In this study, we performed band-pass filtering on the preprocessed data using *eegfilt.m* from EEGLAB (4–8 Hz). The complex signal at each contact was extracted using a Hilbert transform. Then we calculated the PLV/wPLI of each hippocampal-cortical contact pair using a sliding window (window size: 1000 ms, step size: 20 ms). Finally, the PLV/wPLI values were averaged across contact pairs to yield a time series, which was then Z-scored over time to indicate the connectivity strength between the hippocampus and cortex.

5.13. Temporal hierarchy analysis

We calculated the occurrence times of hippocampal ripples within a 1-second window centered around the peak of each reactivation event and recorded their time intervals relative to the reactivation peak. These intervals were then averaged across trials for each subject to obtain the mean time delay per subject. A *t*-test was performed at the subject level to determine whether the mean time delay significantly deviated from zero. Additionally, we computed the proportion of trials in which the time delay was negative (i.e., ripples preceded the reactivation peak) for each subject and compared this proportion to 50 % using *t*-test.

Using a similar approach, we identified the peak times of cortical-hippocampal connectivity (measured by wPLI, to mitigate volume conduction effects) within a 1-second window around each reactivation peak. Only connectivity peaks exceeding two standard deviations above the mean were considered. We then assessed the significance of the time delays relative to zero and the proportion of trials with negative delays compared to 50 %.

5.14. Statistical analysis

For cluster-based permutation tests of comparisons between conditions, we first performed paired t-tests and then identified clusters based on a threshold ($p < 0.05$) and summed the t-values within the clusters. We then shuffled condition labels, repeated the above operation 1000 times, and extracted the largest cluster in each permutation. Finally, we determined the significance of an original cluster's t-value according to its order among the 1000 permutations.

For cluster-based tests of single conditions (ripple rate, PLV/wPLI and theta power during cortical reactivation peak), we compared it with the null distribution formed by a shuffling procedure. We randomly chose some time points (same number as the actual situation) as surrogate reactivation peaks during the rest period, and then calculated those metrics (ripple rate, PLV/wPLI and theta power) for each participant using these surrogate reactivation peaks. After repeating the above operation 1000 times, we obtained a null distribution that allowed us to determine which time points in the original data were significant ($p < 0.01$). Afterwards, we identified consecutive significant time periods as clusters and summed the metrics within the cluster to get the original cluster size. With the same approach, we also found clusters in every shuffled data and extracted the largest cluster. Finally, we determined the significance of an original cluster according to its order among the distribution of shuffled clusters.

CRediT authorship contribution statement

Wei Duan: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Pingping Lu**: Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation. **Zhansheng Xu**: Writing – original draft, Investigation, Data curation. **Jing Wang**: Writing – original draft, Data curation. **Yue Lu**: Visualization, Writing – review & editing. **Mengyang Wang**: Writing – original draft, Data curation. **Ken A. Paller**: Writing – review & editing, Writing – original draft, Investigation. **Nikolai Axmacher**: Writing – review & editing, Writing – original draft, Investigation. **Liang Wang**: Writing – review & editing, Writing – original draft, Supervision, Investigation, Funding acquisition, Conceptualization.

Declaration of Competing Interest

The authors declare no competing interests.

Acknowledgments

This study was supported by the National Natural Science Foundation of China (32020103009, 32471110), the STI2030-Major Projects (2022ZD0205000), the Ministry Key Project (GW0890006), the Scientific Foundation of the Institute of Psychology, Chinese Academy of Sciences (E2CX4215CX), and the ERC grant agreement (864164) (ERC-CoG "GridRepresentations"). We also thanks for the support from the Core Facilities of Institute of Psychology, CAS.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.pneurobio.2025.102778.

Data Availability

The data and code presented in the figures of this study can be accessed via: https://doi.org/10.5281/zenodo.15093274. The raw iEEG data acquired from the patients can be provided by contacting the corresponding author.

References

Axmacher, N., Draguhn, A., Elger, C.E., Fell, J., 2009. Memory processes during sleep: beyond the standard consolidation theory. Cell. Mol. Life Sci. 66 (14), 2285–2297. https://doi.org/10.1007/s00018-009-0019-1.

Berkers, R.M.W.J., Ekman, M., Van Dongen, Eelco V., Takashima, A., Barth, M., Paller, Ken A., Fernández, G., 2018. Cued reactivation during slow-wave sleep induces brain connectivity changes related to memory stabilization. Sci. Rep. 8 (1), 16958. https://doi.org/10.1038/s41598-018-35287-6.

Brodt, S., Inostroza, M., Niethard, N., Born, J., 2023. Sleep—a brain-state serving systems memory consolidation. Neuron 111 (7), 1050–1075. https://doi.org/10.1016/j.neuron.2023.03.005.

Brokaw, K., Tishler, W., Manceor, S., Hamilton, K., Gaulden, A., Parr, E., Wamsley, E.J., 2016. Resting state EEG correlates of memory consolidation. Neurobiol. Learn. Mem. 130, 17–25. https://doi.org/10.1016/j.nlm.2016.01.008.

Buzsáki, G., 2010. Neural Syntax: cell assemblies, synapsembles, and readers. Neuron 68 (3), 362–385. https://doi.org/10.1016/j.neuron.2010.09.023.

Buzsáki, G., 2019. The Brain from Inside Out. Oxford University Press. https://doi.org/10.1093/oso/9780190905385.001.0001.

Carr, M.F., Jadhav, S.P., Frank, L.M., 2011. Hippocampal replay in the awake state: a potential substrate for memory consolidation and retrieval. Nat. Neurosci. 14 (2), 147–153. https://doi.org/10.1038/nn.2732.

Chang, H., Esteves, I.M., Neumann, A.R., Mohajerani, M.H., McNaughton, B.L., 2023. Cortical reactivation of spatial and non-spatial features coordinates with

hippocampus to form a memory dialogue. Nat. Commun. 14 (1), 7748. https://doi.org/10.1038/s41467-023-43254-7.
Craig, M., Dewar, M., Della Sala, S., Wolbers, T., 2015. Rest boosts the long-term retention of spatial associative and temporal order information: Rest Boosts Spatial Associative and Temporal Order Memories. Hippocampus 25 (9), 1017–1027. https://doi.org/10.1002/hipo.22424.
Delorme, A., Makeig, S., 2004. EEGLAB: An open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. J. Neurosci. Methods 134 (1), 9–21. https://doi.org/10.1016/j.jneumeth.2003.10.009.
Denis, D., Cairney, S.A., 2023. Neural reactivation during human sleep. Emerg. Top. Life Sci. 7 (5), 487–498. https://doi.org/10.1042/ETLS20230109.
Desikan, R.S., Ségonne, F., Fischl, B., Quinn, B.T., Dickerson, B.C., Blacker, D., Buckner, R.L., Dale, A.M., Maguire, R.P., Hyman, B.T., Albert, M.S., Killiany, R.J., 2006. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. NeuroImage 31 (3), 968–980. https://doi.org/10.1016/j.neuroimage.2006.01.021.
Deuker, L., Olligs, J., Fell, J., Kranz, T.A., Mormann, F., Montag, C., Reuter, M., Elger, C. E., Axmacher, N., 2013. Memory consolidation by replay of stimulus-specific neural activity. J. Neurosci. 33 (49), 19373–19383. https://doi.org/10.1523/JNEUROSCI.0414-13.2013.
Dewar, M., Alber, J., Butler, C., Cowan, N., Della Sala, S., 2012. Brief wakeful resting boosts new memories over the long term. Psychol. Sci. 23 (9), 955–960. https://doi.org/10.1177/0956797612441220.
Diba, K., Buzsáki, G., 2007. Forward and reverse hippocampal place-cell sequences during ripples. Nat. Neurosci. 10 (10), 1241–1242. https://doi.org/10.1038/nn1961.
Dupret, D., O'Neill, J., Pleydell-Bouverie, B., Csicsvari, J., 2010. The reorganization and reactivation of hippocampal maps predict spatial memory performance. Nat. Neurosci. 13 (8), 995–1002. https://doi.org/10.1038/nn.2599.
Ego-Stengel, V., Wilson, M.A., 2010. Disruption of ripple-associated hippocampal activity during rest impairs spatial learning in the rat. Hippocampus 20 (1), 1–10. https://doi.org/10.1002/hipo.20707.
Favila, S.E., Chanales, A.J.H., Kuhl, B.A., 2016. Experience-dependent hippocampal pattern differentiation prevents interference during subsequent learning. Nat. Commun. 7 (1), 11066. https://doi.org/10.1038/ncomms11066.
Favila, S.E., Lee, H., Kuhl, B.A., 2020. Transforming the concept of memory reactivation. Trends Neurosci. 43 (12), 939–950. https://doi.org/10.1016/j.tins.2020.09.006.
Foster, D.J., Wilson, M.A., 2006. Reverse replay of behavioural sequences in hippocampal place cells during the awake state. Nature 440 (7084), 680–683. https://doi.org/10.1038/nature04587.
Gelbard-Sagiv, H., Mukamel, R., Harel, M., Malach, R., Fried, I., 2008. Internally generated reactivation of single neurons in human hippocampus during free recall. Science 322 (5898), 96–101. https://doi.org/10.1126/science.1164685.
Genzel, L., Robertson, E.M., 2015. To replay, perchance to consolidate. PLoS Biol. 13 (10), e1002285. https://doi.org/10.1371/journal.pbio.1002285.
Gillespie, A.K., Astudillo Maya, D.A., Denovellis, E.L., Liu, D.F., Kastner, D.B., Coulter, M. E., Roumis, D.K., Eden, U.T., Frank, L.M., 2021. Hippocampal replay reflects specific past experiences rather than a plan for subsequent choice. Neuron 109 (19), 3149–3163.e6. https://doi.org/10.1016/j.neuron.2021.07.029.
Gridchyn, I., Schoenenberger, P., O'Neill, J., Csicsvari, J., 2020. Assembly-specific disruption of hippocampal replay leads to selective memory deficit. .e6 Neuron 106 (2), 291–300. https://doi.org/10.1016/j.neuron.2020.01.021.
Guskjolen, A., Cembrowski, M.S., 2023. Engram neurons: encoding, consolidation, retrieval, and forgetting of memory. Mol. Psychiatry 28 (8), 3207–3219. https://doi.org/10.1038/s41380-023-02137-5.
Herweg, N.A., Solomon, E.A., Kahana, M.J., 2020. Theta Oscillations in human memory. Trends Cogn. Sci. 24 (3), 208–227. https://doi.org/10.1016/j.tics.2019.12.006.
Higgins, C., Liu, Y., Vidaurre, D., Kurth-Nelson, Z., Dolan, R., Behrens, T., Woolrich, M., 2021. Replay bursts in humans coincide with activation of the default mode and parietal alpha networks. e7 Neuron 109 (5), 882–893. https://doi.org/10.1016/j.neuron.2020.12.007.
Huang, Q., Xiao, Z., Yu, Q., Luo, Y., Xu, J., Qu, Y., Dolan, R., Behrens, T., Liu, Y., 2024. Replay-triggered brain-wide activation in humans. Nat. Commun. 15 (1), 7185. https://doi.org/10.1038/s41467-024-51582-5.
Hulbert, J.C., Norman, K.A., 2015. Neural differentiation tracks improved recall of competing memories following interleaved study and retrieval practice. Cereb. Cortex 25 (10), 3994–4008. https://doi.org/10.1093/cercor/bhu284.
Jadhav, S.P., Kemere, C., German, P.W., Frank, L.M., 2012. Awake Hippocampal sharp-wave ripples support spatial memory. Science 336 (6087), 1454–1458. https://doi.org/10.1126/science.1217230.
Jadhav, S.P., Rothschild, G., Roumis, D.K., Frank, L.M., 2016. Coordinated excitation and inhibition of prefrontal ensembles during Awake Hippocampal sharp-wave ripple events. Neuron 90 (1), 113–127. https://doi.org/10.1016/j.neuron.2016.02.010.
Janca, R., Jezdik, P., Cmejla, R., Tomasek, M., Worrell, G.A., Stead, M., Wagenaar, J., Jefferys, J.G.R., Krsek, P., Komarek, V., Jiruska, P., Marusic, P., 2015. Detection of interictal epileptiform discharges using signal envelope distribution modelling: application to Epileptic and non-epileptic intracranial recordings. Brain Topogr. 28 (1), 172–183. https://doi.org/10.1007/s10548-014-0379-1.
Ji, D., Wilson, M.A., 2007. Coordinated memory replay in the visual cortex and hippocampus during sleep. Nat. Neurosci. 10 (1), 100–107. https://doi.org/10.1038/nn1825.
Josselyn, S.A., Tonegawa, S., 2020. Memory engrams: recalling the past and imagining the future. Science 367 (6473), eaaw4325. https://doi.org/10.1126/science.aaw4325.
Kaefer, K., Stella, F., McNaughton, B.L., Battaglia, F.P., 2022. Replay, the default mode network and the cascaded memory systems model. Nat. Rev. Neurosci. 23 (10), 628–640. https://doi.org/10.1038/s41583-022-00620-6.
Kaplan, R., Adhikari, M.H., Hindriks, R., Mantini, D., Murayama, Y., Logothetis, N.K., Deco, G., 2016. Hippocampal sharp-wave ripples influence selective activation of the default mode network. Curr. Biol. 26 (5), 686–691. https://doi.org/10.1016/j.cub.2016.01.017.
Khuvis, S., Yeagle, E.M., Norman, Y., Grossman, S., Malach, R., Mehta, A.D., 2021. Face-selective units in human ventral temporal cortex reactivate during free recall. J. Neurosci. 41 (15), 3386–3399. https://doi.org/10.1523/JNEUROSCI.2918-19.2020.
King, B.R., Gann, M.A., Mantini, D., Doyon, J., Albouy, G., 2022. Persistence of hippocampal and striatal multivoxel patterns during awake rest after motor sequence learning. iScience 25 (12), 105498. https://doi.org/10.1016/j.isci.2022.105498.
Klinzing, J.G., Niethard, N., Born, J., 2019. Mechanisms of systems memory consolidation during sleep. Nat. Neurosci. 22 (10), 1598–1610. https://doi.org/10.1038/s41593-019-0467-3.
Kuhl, B.A., Rissman, J., Chun, M.M., Wagner, A.D., 2011. Fidelity of neural reactivation reveals competition between memories. Proc. Natl. Acad. Sci. 108 (14), 5903–5908. https://doi.org/10.1073/pnas.1016939108.
Kuhl, B.A., Bainbridge, W.A., Chun, M.M., 2012. Neural reactivation reveals mechanisms for updating memory. J. Neurosci. 32 (10), 3453–3461. https://doi.org/10.1523/JNEUROSCI.5846-11.2012.
Kunz, L., Staresina, B.P., Reinacher, P.C., Brandt, A., Guth, T.A., Schulze-Bonhage, A., Jacobs, J., 2024. Ripple-locked coactivity of stimulus-specific neurons and human associative memory. Nat. Neurosci. 27 (3), 587–599. https://doi.org/10.1038/s41593-023-01550-x.
Lewis, P.A., Bendor, D., 2019. How targeted memory reactivation promotes the selective strengthening of memories in sleep. Curr. Biol. 29 (18), R906–R912. https://doi.org/10.1016/j.cub.2019.08.019.
Liu, J., Zhang, H., Yu, T., Ren, L., Ni, D., Yang, Q., Lu, B., Zhang, L., Axmacher, N., Xue, G., 2021. Transformative neural representations support long-term episodic memory. Sci. Adv. 7 (41), eabg9715. https://doi.org/10.1126/sciadv.abg9715.
Logothetis, N.K., Eschenko, O., Murayama, Y., Augath, M., Steudel, T., Evrard, H.C., Besserve, M., Oeltermann, A., 2012. Hippocampal–cortical interaction during periods of subcortical silence. Nature 491 (7425), 547–553. https://doi.org/10.1038/nature11618.
Menon, V., 2023. 20 years of the default mode network: a review and synthesis. Neuron 111 (16), 2469–2487. https://doi.org/10.1016/j.neuron.2023.04.023.
Nadel, L., Moscovitch, M., 1997. Memory consolidation, retrograde amnesia and the hippocampal complex. Curr. Opin. Neurobiol. 7 (2), 217–227. https://doi.org/10.1016/S0959-4388(97)80010-4.
Nadel, L., Samsonovich, A., Ryan, L., Moscovitch, M., 2000. Multiple trace theory of human memory: Computational, neuroimaging, and neuropsychological results. Hippocampus 10 (4), 352–368. https://doi.org/10.1002/1098-1063(2000)10:4< 352::AID-HIPO2> 3.0.CO;2-D.
Nadel, L., Hupbach, A., Gomez, R., Newman-Smith, K., 2012. Memory formation, consolidation and transformation. Neurosci. Biobehav. Rev. 36 (7), 1640–1645. https://doi.org/10.1016/j.neubiorev.2012.03.001.
Nguyen, N.D., Lutas, A., Amsalem, O., Fernando, J., Ahn, A.Y.-E., Hakim, R., Vergara, J., McMahon, J., Dimidschstein, J., Sabatini, B.L., Andermann, M.L., 2024. Cortical reactivations predict future sensory responses. Nature 625 (7993), 110–118. https://doi.org/10.1038/s41586-023-06810-1.
Norman, Y., Yeagle, E.M., Khuvis, S., Harel, M., Mehta, A.D., Malach, R., 2019. Hippocampal sharp-wave ripples linked to visual episodic recollection in humans. Science 365 (6454), eaax1030. https://doi.org/10.1126/science.aax1030.
Norman, Y., Raccah, O., Liu, S., Parvizi, J., Malach, R., 2021. Hippocampal ripples and their coordinated dialogue with the default mode network during recent and remote recollection. Neuron 109 (17), 2767–2780.e5. https://doi.org/10.1016/j.neuron.2021.06.020.
Nour, M.M., Liu, Y., Arumuham, A., Kurth-Nelson, Z., Dolan, R.J., 2021. Impaired neural replay of inferred relationships in schizophrenia. Cell 184 (16), 4315–4328.e17. https://doi.org/10.1016/j.cell.2021.06.012.
Nour, M.M., Liu, Y., Higgins, C., Woolrich, M.W., Dolan, R.J., 2023. Reduced coupling between offline neural replay events and default mode network activation in schizophrenia. Brain Commun. 5 (2), fcad056. https://doi.org/10.1093/braincomms/fcad056.
Novitskaya, Y., Sara, S.J., Logothetis, N.K., Eschenko, O., 2016. Ripple-triggered stimulation of the locus coeruleus during post-learning sleep disrupts ripple/spindle coupling and impairs memory consolidation. Learn. Mem. 23 (5), 238–248. https://doi.org/10.1101/lm.040923.115.
Oostenveld, R., Fries, P., Maris, E., Schoffelen, J.-M., 2011. FieldTrip: open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data. Comput. Intell. Neurosci. 2011, 1–9. https://doi.org/10.1155/2011/156869.
Oudiette, D., Antony, J.W., Creery, J.D., Paller, K.A., 2013. The role of memory reactivation during wakefulness and sleep in determining which memories endure. J. Neurosci. 33 (15), 6672–6678. https://doi.org/10.1523/JNEUROSCI.5497-12.2013.
Peyrache, A., Khamassi, M., Benchenane, K., Wiener, S.I., Battaglia, F.P., 2009. Replay of rule-learning related neural patterns in the prefrontal cortex during sleep. Nat. Neurosci. 12 (7), 919–926. https://doi.org/10.1038/nn.2337.
Qin, C., Tan, Z., Pan, Y., Li, Y., Wang, L., Ren, L., Zhou, W., Wang, L., 2017. Automatic and precise localization and cortical labeling of subdural and depth intracranial electrodes, 10–10 Front. Neuroinformatics 11. https://doi.org/10.3389/fninf.2017.00010.

Raichle, M.E., 2015. The brain's default mode network. Annu. Rev. Neurosci. 38 (1), 433–447. https://doi.org/10.1146/annurev-neuro-071013-014030.
Rothschild, G., Eban, E., Frank, L.M., 2017. A cortical–hippocampal–cortical loop of information processing during memory consolidation. Nat. Neurosci. 20 (2), 251–259. https://doi.org/10.1038/nn.4457.
Rudoy, J.D., Voss, J.L., Westerberg, C.E., Paller, K.A., 2009. Strengthening individual memories by reactivating them during sleep, 1079–1079 Science 326 (5956). https://doi.org/10.1126/science.1179013.
Schreiner, T., Staudigl, T., 2020. Electrophysiological signatures of memory reactivation in humans. Philos. Trans. R. Soc. B: Biol. Sci. 375 (1799), 20190293. https://doi.org/10.1098/rstb.2019.0293.
Schreiner, T., Petzka, M., Staudigl, T., Staresina, B.P., 2021. Endogenous memory reactivation during sleep in humans is clocked by slow oscillation-spindle complexes. Nat. Commun. 12 (1), 3112. https://doi.org/10.1038/s41467-021-23520-2.
Schreiner, T., Griffiths, B.J., Kutlu, M., Vollmar, C., Kaufmann, E., Quach, S., Remi, J., Noachtar, S., Staudigl, T., 2024. Spindle-locked ripples mediate memory reactivation during human NREM sleep. Nat. Commun. 15 (1), 5249. https://doi.org/10.1038/s41467-024-49572-8.
Staresina, B.P., 2024. Coupled sleep rhythms for memory consolidation. Trends Cogn. Sci. 28 (4), 339–351. https://doi.org/10.1016/j.tics.2024.02.002.
Staresina, B.P., Alink, A., Kriegeskorte, N., Henson, R.N., 2013. Awake reactivation predicts memory in humans. Proc. Natl. Acad. Sci. 110 (52), 21159–21164. https://doi.org/10.1073/pnas.1311989110.
Staresina, B.P., Bergmann, T.O., Bonnefond, M., Van Der Meij, R., Jensen, O., Deuker, L., Elger, C.E., Axmacher, N., Fell, J., 2015. Hierarchical nesting of slow oscillations, spindles and ripples in the human hippocampus during sleep. Nat. Neurosci. 18 (11), 1679–1686. https://doi.org/10.1038/nn.4119.
Sugden, A.U., Zaremba, J.D., Sugden, L.A., McGuire, K.L., Lutas, A., Ramesh, R.N., Alturkistani, O., Lensjø, K.K., Burgess, C.R., Andermann, M.L., 2020. Cortical reactivations of recent sensory experiences predict bidirectional network changes during learning. Nat. Neurosci. 23 (8), 981–991. https://doi.org/10.1038/s41593-020-0651-5.
Tambini, A., D'Esposito, M., 2020. Causal contribution of awake post-encoding processes to episodic memory consolidation. Curr. Biol. 30 (18), 3533–3543.e7. https://doi.org/10.1016/j.cub.2020.06.063.
Tambini, A., Davachi, L., 2019. Awake reactivation of prior experiences consolidates memories and biases cognition. Trends Cogn. Sci. 23 (10), 876–890. https://doi.org/10.1016/j.tics.2019.07.008.
Tambini, A., Ketz, N., Davachi, L., 2010. Enhanced brain correlations during rest are related to memory for recent experiences. Neuron 65 (2), 280–290. https://doi.org/10.1016/j.neuron.2010.01.001.
Tang, W., Jadhav, S.P., 2019. Sharp-wave ripples as a signature of hippocampal-prefrontal reactivation for memory during sleep and waking states. Neurobiol. Learn. Mem. 160, 11–20. https://doi.org/10.1016/j.nlm.2018.01.002.
Tang, W., Shin, J.D., Frank, L.M., Jadhav, S.P., 2017. Hippocampal-prefrontal reactivation during learning is stronger in awake compared with sleep states. J. Neurosci. 37 (49), 11789–11805. https://doi.org/10.1523/JNEUROSCI.2291-17.2017.
Tonegawa, S., Morrissey, M.D., Kitamura, T., 2018. The role of engram cells in the systems consolidation of memory. Nat. Rev. Neurosci. 19 (8), 485–498. https://doi.org/10.1038/s41583-018-0031-2.
Van De Ven, G.M., Trouche, S., McNamara, C.G., Allen, K., Dupret, D., 2016. Hippocampal offline reactivation consolidates recently formed cell assembly patterns during sharp wave-ripples. Neuron 92 (5), 968–974. https://doi.org/10.1016/j.neuron.2016.10.020.
Van Dongen, E.V., Takashima, A., Barth, M., Zapp, J., Schad, L.R., Paller, K.A., Fernández, G., 2012. Memory stabilization with targeted reactivation during human slow-wave sleep. Proc. Natl. Acad. Sci. 109 (26), 10575–10580. https://doi.org/10.1073/pnas.1201072109.
Vaz, A.P., Inati, S.K., Brunel, N., Zaghloul, K.A., 2019. Coupled ripple oscillations between the medial temporal lobe and neocortex retrieve human memory. Science 363 (6430), 975–978. https://doi.org/10.1126/science.aau8956.
Vaz, A.P., Wittig, J.H., Inati, S.K., Zaghloul, K.A., 2020. Replay of cortical spiking sequences during human memory retrieval. Science 367 (6482), 1131–1134. https://doi.org/10.1126/science.aba0672.
Wamsley, E.J., 2019. Memory consolidation during waking rest. Trends Cogn. Sci. 23 (3), 171–173. https://doi.org/10.1016/j.tics.2018.12.007.
Watson, B.O., Buzsáki, G., 2015. Sleep, memory & brain rhythms. Daedalus 144 (1), 67–82. https://doi.org/10.1162/DAED_a_00318.
Wimber, M., Alink, A., Charest, I., Kriegeskorte, N., Anderson, M.C., 2015. Retrieval induces adaptive forgetting of competing memories via cortical pattern suppression. Nat. Neurosci. 18 (4), 582–589. https://doi.org/10.1038/nn.3973.
Xia, F., Richards, B.A., Tran, M.M., Josselyn, S.A., Takehara-Nishiuchi, K., Frankland, P. W., 2017. Parvalbumin-positive interneurons mediate neocortical-hippocampal interactions that are necessary for memory consolidation. eLife 6, e27868. https://doi.org/10.7554/eLife.27868.
Xue, G., 2022. From remembering to reconstruction: the transformative neural representation of episodic memory. Prog. Neurobiol. 219, 102351. https://doi.org/10.1016/j.pneurobio.2022.102351.
Zhang, H., Fell, J., Axmacher, N., 2018. Electrophysiological mechanisms of human memory consolidation. Nat. Commun. 9 (1), 4103. https://doi.org/10.1038/s41467-018-06553-y.