

Multiple memory systems for efficient temporal order memory

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Abstract

We report distinct contributions of multiple memory systems to the retrieval of the temporal order of events. The neural dynamics related to the retrieval of movie scenes revealed that recalling the temporal order of close events elevates hippocampal theta power, like that observed for recalling close spatial relationships. In contrast, recalling far events increases beta power in the orbitofrontal cortex, reflecting recall based on the overall movie structure.

KEYWORDS

hippocampus, human, iEEG, orbitofrontal cortex, temporal memory

Remembering the order of event occurrence is fundamental to episodic memory. Converging evidence suggests that at least two copies of events are encoded in parallel in distinct brain regions during memory formation (Nadel et al., 2000; Sutherland et al., 2020; Tse et al., 2011). One system retains events with high fidelity and is hippocampal-dependent. The other system encodes schematic information and engages the prefrontal cortex. At recall, memories are reconstructed when we combine our understanding of the unfolding of events in time with episodic information (Bartlett, 1932). Episodic memory, especially recalling the temporal order of events, requires the hippocampal network, evident from the behavior of patients with hippocampal lesions who have impairments in recalling past events in the same order as they were encountered (Dede et al., 2016; Downes et al., 2002). Functional MRI and lesion studies suggest that in addition to the hippocampus (HPC), the orbitofrontal cortex (OFC) is also involved in successful temporal order recall (Duarte et al., 2009; Johnson et al., 2022). However, the neural mechanisms by which the HPC and the OFC support temporal order memory are unclear.

Temporal memory, shaped by the relatedness of the sequence of events, can be studied as the absolute time relative to salient event

boundaries (Montchal et al., 2019) or as the recency of events relative to each other (DuBrow & Davachi, 2016; Jafarpour et al., 2022). At encoding, both the OFC and HPC track the temporal relatedness of events (Jafarpour et al., 2019), and the left HPC is known to represent the temporal approximation of events (Ezzyat & Davachi, 2014). Temporal order recall is easier for events with distinct contexts occurring far apart in time (DuBrow & Davachi, 2016). This suggests that the temporal context of far events enables temporal order judgment without the need to recall the episodic details of an event's recency. Recalling memories with high precision engages the HPC (Eldridge et al., 2000), however, tracking the temporal order of long sequences of events with high fidelity would require substantial HPC resources. Accordingly, we hypothesized that memory systems utilize OFC for recalling the temporal order of far events, while HPC retrieves the episodic details necessary for recalling the temporal order of close events.

We investigated the neural dynamics within the HPC and the medial OFC in the left hemisphere that support recognition of the temporal order of events from long-term memory. Epileptic patients undergoing seizure monitoring ($n = 8$, 3 female, Table S1) watched a

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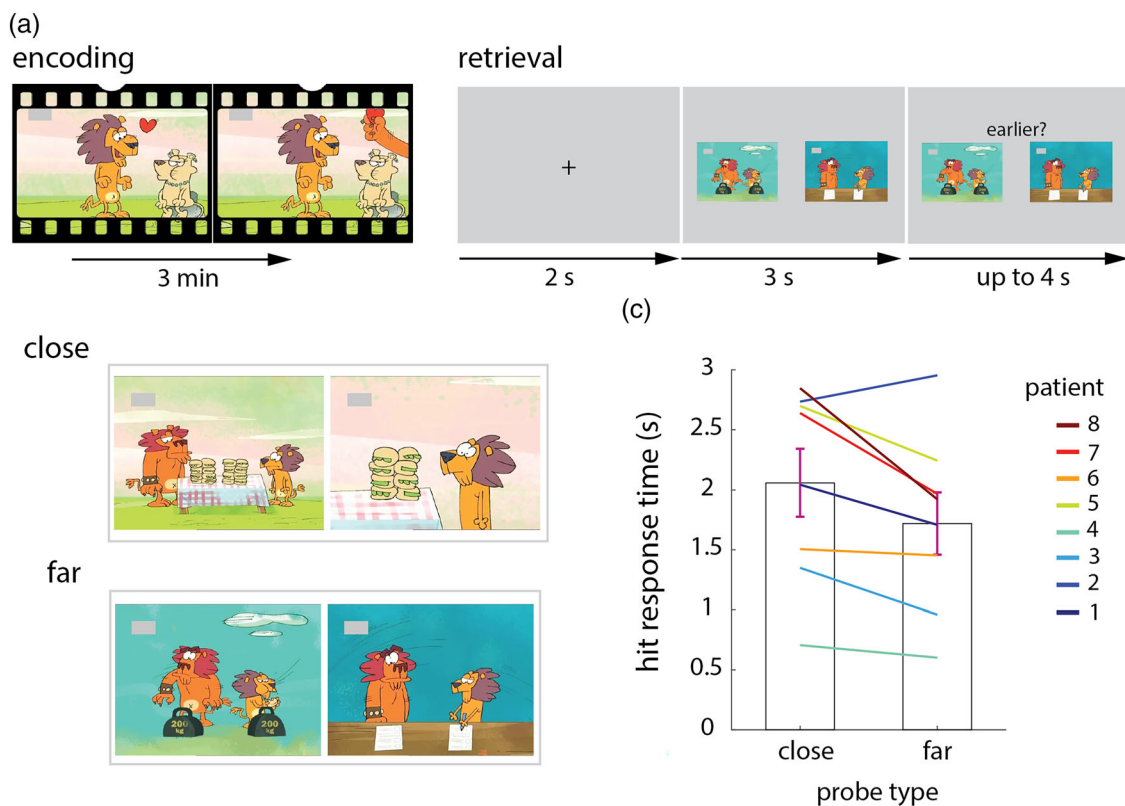


FIGURE 1 Experimental design and behavior. (a) At encoding, participants watched a novel animation (3 min long) and were informed that memory would be assessed. At retrieval, participants performed a temporal order recognition task. Each temporal order retrieval trial started with a fixation point to draw attention to the middle of the screen. Then, two frames of the movie were shown side by side. After 3 s, an instruction appeared asking about the order of the probes. Pseudo-randomly, the instruction was split to ask for the selection of the earlier or later frame. This design allowed us to study the neural mechanism of memory recall that is separate from preparing for the response. (b) An example of the *close* (top) and *far* (bottom) prompts. The close probes were neighboring movie frames that were visually distinct, while the far probes were between 12 and 60 s apart and were more contextually distinct than the close events (see Supporting Information). (c) It took longer to correctly recall the temporal order of close events than far events. Patients' responses are color-coded and numbered according to (Table S1). The error bars show SEM.

novel animated movie and, after brief delay including a 2-min rest period, determined the order of movie frames that were presented in pairs (Figure 1a,b). Subjects performed equally well in recalling close and far events (paired *t*-test $t(7) = 1.7$, $p = .86$). However, response times were longer for close events compared to far events (paired *t*-test $t(7) = 2.64$, $p = 0.03$; Figure 1c), indicating that temporal order judgment was more demanding for the close events.

We compared the power spectral density (PSD) for correct temporal judgment of close and far events during the 2 s after the probe onset (i.e., prior to the cue for response selection). At a group-level analysis, we compared the coefficients of the contrast between close and far correct temporal judgments against zero (for no differences) in a mixed effect model due to the unequal number of regional contacts across the patients. The results showed that theta power was higher for recalling the order of close events than for far events in the HPC ($n = 7$; 4–8 Hz, peaking at 6.5 Hz, $p < .001$). This effect was also observed in two additional peaks in a narrow band at 32–42 Hz and a broader high-frequency band of 100–170 Hz ($p < .001$). By contrast, beta power in the left OFC was higher for recalling the order

of far compared to close events ($n = 6$; 20–25 Hz, peaking at 22.5 Hz, $p = .012$, with no differences observed in frequencies above 30 Hz; Figure 2).

Although we observed significant group differences across conditions and contacts, within-contact contrasts differences were not statistically significant. A power calculation based on these data recommends at least 50 trials for detecting within-contact differences with 0.9 power, which was more than was feasible in the time available with each participant. An advantage of the adopted group-level experimental design is that, despite a low number of trials, the experimental effects can be evaluated across participants. A limitation of the study is that we are not able to evaluate single trial and single contact responses. The overall results suggest enhanced theta/alpha-band, low gamma-band, and high frequency power in the HPC is associated with successful retrieval of episodic information in temporal order recall, whereas enhanced beta-band power in the OFC supports the temporal order recall of far events.

The HPC is connected to the medial OFC both directly and indirectly through the entorhinal cortex and para-hippocampus gyrus

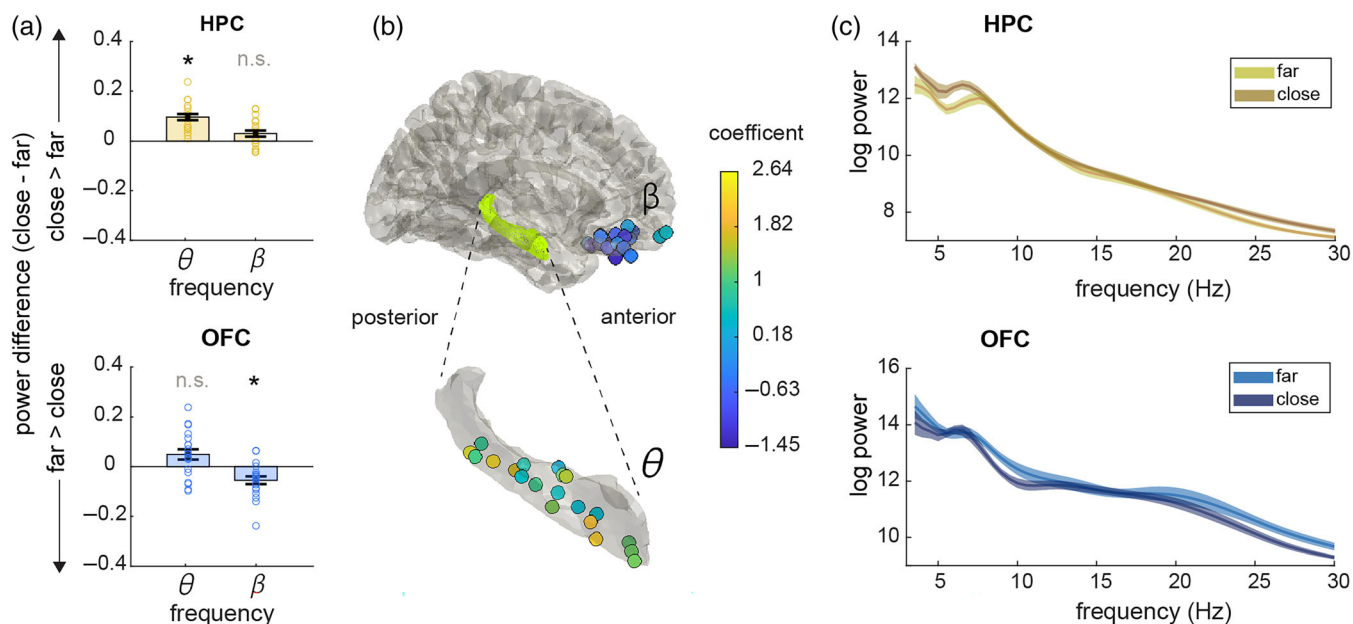


FIGURE 2 Hippocampal and OFC power differences between close and far events. (a) HPC theta-band (4–8 Hz) power was higher for close compared to far temporal memory recall (top). This effect was reversed for beta-band power in the OFC (20–25 Hz; bottom). * $p < .005$ and n.s. for $p > .05$. Error bars indicate SEM. (b) The coefficient for the comparison between recalling close and far events shown in the HPC (in theta-band) and in the OFC (in beta-band). A positive coefficient supports higher power in recalling close compared to far events; whereas a negative coefficient supports higher power in recalling far compared to close events. (c) Example of the PSD in one contact in the OFC (top) and one contact in the HPC (bottom). The shaded area shows SEM.

(Aggleton, 2012). The entorhinal cortex—specifically the lateral entorhinal cortex along with the neighboring perirhinal cortex—has been implicated in the precision of recalling the time of an event relative to the task onset (a salient event boundary) (Montchal et al., 2019) and these cortical regions have direct connections to both HPC and the OFC (Aggleton, 2012). Far events are more likely to have an intervening salient event boundary during encoding, raising the possibility that the order of far events can be inferred relative to the event boundaries and the gist of the movie structure without the need for hippocampal input. However, HPC is essential for temporal order memory of close events that are not anchored to the boundaries of a sequence (Heuer & Bachevalier, 2013). In the spatial domain, the absence of fine-resolution para-hippocampal representation disturbs the resolution of hippocampal spatial representation for places that are away from the salient boundaries (Mallory et al., 2018). Similarly, we hypothesize that, in parallel to the spatial neural mechanism, input from the entorhinal cortex to HPC may support recalling the temporal order of close events in fine detail. The present study did not include eye-tracking data but, given the known relationship between saccadic eye-movements and hippocampal activity (Jutras et al., 2013; Jutras & Buffalo, 2010), an interesting area of future study would be to examine hippocampal theta-band oscillations and eye movements during the recall of close versus far events.

The OFC represents the gist structure of the flow of events that strengthens with consolidation (Kitamura et al., 2017), such as learning a reward value that follows an event (Rich & Wallis, 2017). In

contrast, HPC activity corresponds to the detailed order of events that closely follow each other (Karlsson & Frank, 2009; Kornysheva et al., 2019). We propose that at retrieval, HPC provides a signal of the temporal order of close events following the top-down signal from the OFC, congruent with reports from rodents (Place et al., 2016). Given the known role of hippocampal-cortical interaction in support of memory consolidation, an interesting area for future study would be to examine changes in these temporal memory signals with longer retrieval delays, such as after a night of sleep. Converging evidence suggests that the existence of multiple traces of memory benefits long-term memory consolidation (Nadel et al., 2000; Sutherland et al., 2020; Tse et al., 2011). Here, we show that, in a short time after encoding, multiple memory traces in HPC and OFC support efficient temporal order memory, enabling recall of far events with the support of the OFC and close events with hippocampal activity.

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DATA AVAILABILITY STATEMENT

The movie and the data that support the findings of this study are openly available in OSF.IO at DOI [10.17605/OSF.IO/932A5](https://doi.org/10.17605/OSF.IO/932A5).

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SUPPORTING INFORMATION

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