

Reviewed Preprint

v1 • January 16, 2026

Not revised

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Competing interests: No competing interests declared

Reviewing editor: Caleb Kemere, Rice University, United States

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Distinct goal location beta frequency dynamics in hippocampus and prefrontal cortex across learning

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eLife Assessment

This paper represents a **valuable** contribution to our understanding of how LFP oscillations and beta band coordination between the hippocampus and prefrontal cortex of rats may relate to learning. Enthusiasm for the reported results was moderated by the concern that some key analyses need to be done, and highly relevant details about task, data, and statistics were missing. Consequently, the reviewers considered the evidence to be **incomplete** in this version of the manuscript.

<https://doi.org/10.7554/eLife.108623.1.sa4>

Abstract

Neural activity at goal locations contributes to learning by providing feedback on the success of preceding actions. This period engages neocortical and hippocampal networks, which serve distinct functions in processing reward and forming associations with experience that lead to reward. A neocortical network signature for reward feedback processing is beta oscillations (15–30 Hz). Beta oscillations are thought to coordinate distributed neural processes across brain regions. However, it is unknown whether beta oscillations coordinate hippocampal-neocortical networks during the goal period, or how their dynamics relate to learning. Here, we show that beta oscillations occur in both hippocampal CA1 and the prefrontal cortex (PFC) when rats reach goal locations in spatial navigation tasks. Despite the presence of beta oscillations in both regions after goal entry, beta activity in each region differed in spectral and temporal properties. These differences suggest that the hippocampus and PFC are not strongly coupled at the beta frequency. We found the strengths of PFC and CA1 beta oscillations across learning were inversely related: PFC beta activity increasing in strength and CA1 beta activity decreasing in strength. Beta burst properties in PFC also had an inverse relationship to those of hippocampal sharp wave-ripples (SWRs), a prominent hippocampal process required for learning. We found a subset of PFC neurons modulated by both beta and hippocampal SWRs, which had distinct task-related firing patterns. Our results suggest that during outcome processing at goal locations, the neocortex and hippocampus are independently modulated by beta oscillations before becoming coordinated for memory-related processes during SWRs.

Introduction

Learning leads to changes in distributed neural networks across the brain. During learning, diverse neural processes across brain networks need to be coordinated, which is hypothesized to rely on neural oscillations that rhythmically couple activity in connected brain regions. This coupling between groups of brain regions is thought to be dynamic, creating functionally interacting subnetworks to support specific neural processes when required. A neural oscillation that is hypothesized to support these functions is beta (15–30 Hz) (Bibbig et al., 2002 [↗](#); Gourévitch

et al., 2010 [\[1\]](#); Igarashi et al., 2014 [\[2\]](#); Jayachandran et al., 2023 [\[3\]](#); Kopell et al., 2011 [\[4\]](#); Lundqvist et al., 2024 [\[5\]](#); Miles et al., 2023 [\[6\]](#); Spitzer & Haegens, 2017 [\[7\]](#); Symanski et al., 2022 [\[8\]](#)). Beta oscillations occur in many brain regions, including sensory (Gervais et al., 2007 [\[9\]](#); Kay et al., 1996 [\[10\]](#); Martin et al., 2004 [\[11\]](#)), neocortical (Baker et al., 1997 [\[12\]](#); Buschman et al., 2012 [\[13\]](#); Cohen et al., 2007 [\[14\]](#); Cohen et al., 2015 [\[15\]](#); Dubey et al., 2023 [\[16\]](#); HajiHosseini & Holroyd, 2015 [\[17\]](#); HajiHosseini et al., 2020 [\[18\]](#); Iturra-Mena et al., 2023 [\[19\]](#); Kawasaki & Yamaguchi, 2013 [\[20\]](#); Koloski, Hulyalkar, et al., 2024; MacKay & Mendonça, 1995 [\[21\]](#); Pesaran et al., 2008 [\[22\]](#); Voloh et al., 2020 [\[23\]](#); Walsh et al., 2025 [\[24\]](#); Xiao et al., 2024 [\[25\]](#)), subcortical (DeCoteau et al., 2007 [\[26\]](#); Feingold et al., 2015 [\[27\]](#); Howe et al., 2011 [\[28\]](#); Lansink et al., 2009 [\[29\]](#); Leventhal et al., 2012 [\[30\]](#); Quinn et al., 2010 [\[31\]](#); Sturman & Moghaddam, 2012 [\[32\]](#)) and limbic regions (Amaya et al., 2024 [\[33\]](#); Berke et al., 2008 [\[34\]](#); Fourcaud-Trocmé et al., 2019 [\[35\]](#); França et al., 2014 [\[36\]](#); França et al., 2021 [\[37\]](#); Igarashi et al., 2014 [\[38\]](#); Jackson et al., 2024 [\[39\]](#); Jayachandran et al., 2023 [\[40\]](#); Kay & Freeman, 1998 [\[41\]](#); Rangel et al., 2015 [\[42\]](#); Rangel et al., 2016 [\[43\]](#); Samson et al., 2017 [\[44\]](#); Symanski et al., 2022 [\[45\]](#)). Beta oscillations are associated with a wide range of cognitive functions, including sensory perception (Kay, 2014 [\[46\]](#)), reward processing (Cohen et al., 2007 [\[47\]](#)), top-down control (Engel & Fries, 2010 [\[48\]](#)) and novelty detection (Marco-Pallarés et al., 2015 [\[49\]](#)). Despite their widespread occurrence and association with diverse cognitive functions, a less-understood aspect of beta oscillations is their contribution to modulating or coordinating brain networks during learning, when rules are not fully understood and performance is improving. Most studies investigating beta dynamics across the brain have primarily focused on performance after initial learning, but three lines of work in sensory-limbic, striatal, and amygdala networks point to beta playing a role in supporting learning. Sensory-association learning studies suggest that beta activity coordinates sensory-limbic networks to enable the formation of associations between the sensory cue and its behavioral relevance (Fourcaud-Trocmé et al., 2019 [\[35\]](#); Martin et al., 2007 [\[50\]](#); Martin et al., 2004 [\[11\]](#)), beta oscillations dynamics in the ventral striatum change as habits are formed (Howe et al., 2011 [\[28\]](#)), and beta oscillations in the basolateral amygdala can drive reward reference (Amaya et al., 2024 [\[33\]](#)). However, the patterns of learning-related changes in beta oscillations across brain networks remain unclear, since the dynamics of beta during learning outside of olfactory and striatal networks are not known. Here, we ask how beta dynamics contribute to spatial learning in hippocampal-neocortical networks, which are brain regions known to play central roles in supporting memory processing and guiding behavior.

To understand how beta oscillations in hippocampal-neocortical networks change with learning, we focus on an important period for driving learning: when the reward outcome is revealed. We refer to this period as the “goal” phase of a task. Beta oscillations have been observed during equivalent task periods in both human and non-human animal studies. Neocortical beta oscillations during this period have been associated with processing outcomes, where feedback from the presence or absence of the reward can inform future actions and drive learning (Cohen et al., 2011 [\[51\]](#)). Goal-related beta oscillations have been observed in frontal cortical regions (Cohen et al., 2007 [\[14\]](#); Kawasaki & Yamaguchi, 2013 [\[20\]](#)), including the anterior cingulate cortex (ACC) (Iturra-Mena et al., 2023 [\[19\]](#); Xiao et al., 2024 [\[25\]](#)), the prefrontal cortex (PFC) (HajiHosseini & Holroyd, 2015 [\[17\]](#); HajiHosseini et al., 2020 [\[18\]](#); Voloh et al., 2020 [\[23\]](#)) and the orbitofrontal cortex (OFC) (Koloski, Hulyalkar, et al., 2024; Koloski, O’Hearn, et al., 2024), in primate and rodent species. Beta oscillations in these frontal cortical regions have been hypothesized to provide top-down cortical control of connected networks (Babapoor-Farrokhran et al., 2017 [\[52\]](#); Benchenane et al., 2011 [\[53\]](#); Bressler & Richter, 2015 [\[54\]](#); Brovelli et al., 2004 [\[55\]](#); Buschman et al., 2012 [\[13\]](#); Dubey et al., 2023 [\[16\]](#); Engel & Fries, 2010 [\[48\]](#); Pesaran et al., 2008 [\[22\]](#)).

Despite frontal cortical beta activity being implicated in outcome feedback processing, whether frontal cortical and hippocampal networks are coordinated in the beta frequency range during the goal period remains unknown. Beta frequency coordination of hippocampal-neocortical networks has been reported in olfactory sensory decision-making tasks during the cue presentation period (Igarashi et al., 2014 [\[2\]](#); Jayachandran et al., 2023 [\[3\]](#); Martin et al., 2007 [\[50\]](#); Symanski et al., 2022 [\[8\]](#)), and is hypothesized to support the use of memory-based sensory associations for decision making (Spitzer & Haegens, 2017 [\[7\]](#)). However, goal-related beta frequency oscillations have not been reported in the hippocampus. Beta oscillations in the hippocampus have so far been observed

during the exploration of novel environments (Berke et al., 2004), interaction with novel objects (França et al., 2014; França et al., 2021; Rangel et al., 2015), approaches to goals (Iwasaki et al., 2021; Lansink et al., 2009) as well as sensory stimulus sampling (Fourcaud-Trocmé et al., 2019; Gourévitch et al., 2010; Jayachandran et al., 2023; Kay & Freeman, 1998; Kay et al., 1996; Martin et al., 2007; Rangel et al., 2016; Symanski et al., 2022). Thus, it is unknown if and how hippocampal-neocortical networks are coordinated at the beta frequency during the goal phase of a task, and how this coordination relates to learning.

To understand the relationship between goal-related beta frequency activity in hippocampal-neocortical networks and learning, we recorded local field potentials (LFPs) and single units from the hippocampus (dorsal CA1) and the prefrontal cortex (PFC) in rats learning spatial navigation tasks over five days. We observed beta oscillations in both regions at the goal locations of the tasks. However, we were surprised to find that beta oscillations in the PFC and CA1 had distinct spectral and temporal properties. The mismatch in frequency range and timing is consistent with each region engaging in distinct beta-activity modulation, likely with other brain regions, rather than being coupled with each other by beta. Over days of training, beta oscillations in the PFC and CA1 had distinct correlations with performance, where PFC beta increased in strength and CA1 beta decreased in strength. We also found an inverse relationship between the learning-related properties of PFC beta and a prominent hippocampal marker of learning, the sharp wave-ripple (SWR). Lastly, we found distinct task correlates in a subpopulation of PFC cells that showed modulation by both beta oscillations and hippocampal SWRs.

In contrast to previous results demonstrating coordinated hippocampal-neocortical beta modulation during sensory decision-making (Gourévitch et al., 2010; Jayachandran et al., 2023; Kay & Freeman, 1998; Kay et al., 1996; Martin et al., 2007; Rangel et al., 2016; Symanski et al., 2022), we show that beta oscillations in these networks are likely modulating distinct network processes during the goal phase of a task. Further, beta dynamics in the PFC and CA1 undergo opposite changes across learning. After goal entry, the neocortex and hippocampus are uncoupled at the beta frequency but later coordinate during hippocampal SWRs. Our results support the hypothesis that at the goal, the neocortex is initially engaged in processing outcome-related information before coordinating with hippocampal networks for memory-related processes.

Results

Rats ($n=6$) were trained on two spatial alternation tasks, interleaved across sessions, for five days. In each task, reward was delivered when the three goal locations were visited in an alternating sequence (Fig. 1A). We first asked whether beta oscillations were present in both CA1 and PFC (Fig. 1-1). We saw power in the beta-frequency range (15-30Hz) in both PFC and CA1 after the animal reached the goal locations (Fig. 1B). This was confirmed by the power spectral density (PSD) for periods when the animal was at the goal location (Fig. 1C). The PSD from the PFC showed a peak at approximately 20Hz. Although the PSD in CA1 did not show a peak in the beta frequency range like the one found in PFC, the continuous wavelet transform from single trials showed beta oscillations occurred in bursts (Fig. 1B), which is consistent with beta in other neocortical regions (Sherman et al., 2016; Shin et al., 2017). To characterize the properties of beta-frequency bursts in PFC and CA1, we extracted burst times from the continuous wavelet transform (Fig. 1-2). We found the spectral properties of PFC and CA1 bursts differed significantly. PFC bursts were tightly distributed in frequency (median peak frequency: 19 Hz), whereas the peak frequencies of CA1 bursts were distributed across a wider frequency range (median peak frequency: 22 Hz) (Fig. 1D-E). This explains the peak in the PFC PSD and the lack of such a peak in the CA1 PSD. The burst amplitude profiles also differed between the two regions. In PFC, lower-frequency bursts tended to be higher in amplitude, whereas CA1 bursts were more uniform in size (Fig. 1-3A). Burst durations were similar across the two regions (Fig. 1-3B).

The timing of bursts relative to goal entry also differed between PFC and CA1 (Fig. 1F-G). Bursts tended to start approximately 400ms after reward location entry, but CA1 bursts were more concentrated within the first two seconds compared with PFC bursts, which showed a sustained

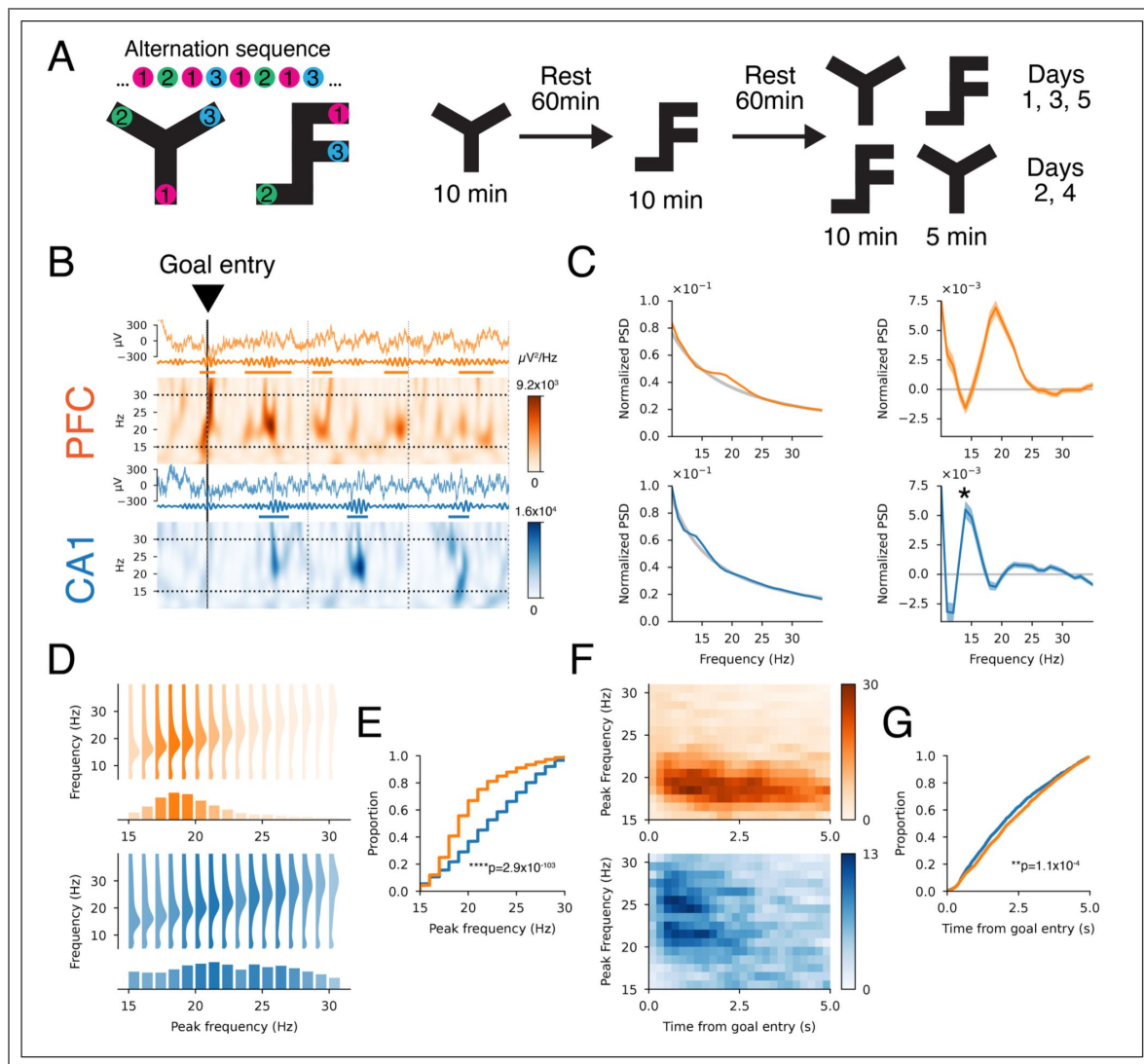


Figure 1. Distinct PFC and CA1 beta frequency activity after the reward location entry during spatial navigation tasks.

a. Spatial learning tasks on Y and F shaped mazes with spatial alternation rules. Animals were trained on the mazes across interleaved sessions. Reward locations (1, 2 and 3) are indicated. The order of visits required to ensure reward on every trial is shown above the maze schematics. The daily training schedule shows the duration, order and separation between sessions.

b. Example PFC (orange) and CA1 (blue) LFP traces aligned to goal location entry (black vertical line). The beta frequency-filtered LFP is shown below the raw LFP. The corresponding continuous wavelet transform spectrogram is included. Beta bursts are indicated by horizontal lines. Dotted vertical lines mark 1 s intervals.

c. Power spectral density for time intervals when the animal is at the reward locations. Left panel shows the PSD, with the aperiodic component shown in gray. Right panel show PSD with aperiodic component subtracted. The peak marked by * in the CA1 PSD at ~15Hz corresponds to the first harmonic of theta (Scheffer-Teixeira & Tort, 2016).

d. Frequency profile for beta bursts grouped by peak power frequency for PFC (orange) and CA1 (blue). Top: the vertical histogram of the mean frequency profiles for bursts at each peak power frequency. Bottom: histograms with the count distribution for bursts within 15-30Hz, grouped by peak power frequency. Shading corresponds to the probability value at each frequency. Bursts occurring within 5s after reward location entry are included.

e. Cumulative distribution of peak burst frequencies for PFC (orange) and CA1 (blue). Kolmogorov-Smirnov test, $p=2.9 \times 10^{-103}$.

f. Distribution of burst times relative to goal location entry grouped by peak frequency for PFC (orange) and CA1 (blue).

g. Cumulative distribution of burst occurrence relative to goal location entry for PFC (orange) and CA1 (blue). Kolmogorov-Smirnov test, $p=1.1 \times 10^{-4}$.

Figure 1-1. Location of recording tetrodes.

a. Representative histology showing location of tetrodes in PFC. b. Representative histology showing location of tetrodes in CA1.

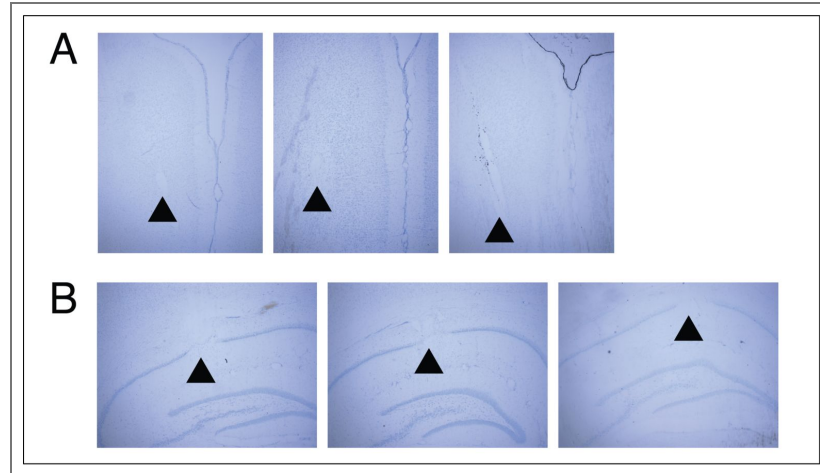
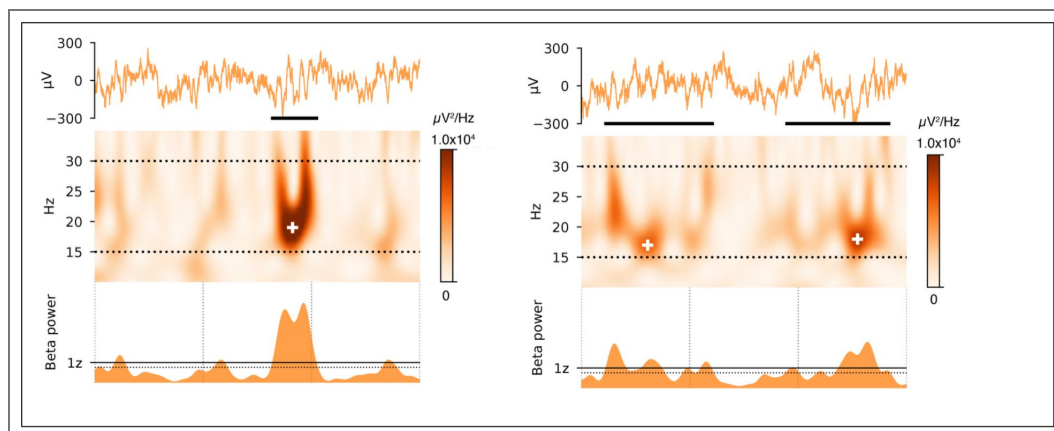


Figure 1-2. Burst detection.

a. Two example bursts with corresponding LFP and continuous wavelet transform from PFC (1.5 s each, top row). The burst is marked by the black horizontal line. The corresponding continuous wavelet transform is shown in the middle row. The white cross marks the frequency and time corresponding to the maximum power in the burst interval. The mean power in the beta band (15-30Hz) from the continuous wavelet transform is shown by the histogram in the bottom row. The solid black line corresponds to 1 standard deviation ($1z$) above the mean ($1z$), and the dotted black line corresponds to 0.5 standard deviation above the mean ($0.5z$). To detect bursts, we identify intervals during which the beta-band power exceeds 0.5 standard deviation above the mean. Intervals are included if the maximum power in the interval exceeds 1 standard deviation above the mean, and the duration of the interval is greater than 100ms. Intervals separated by less than 100ms were merged. The peak frequency for each burst is the frequency corresponding to the maximum power within the burst interval.



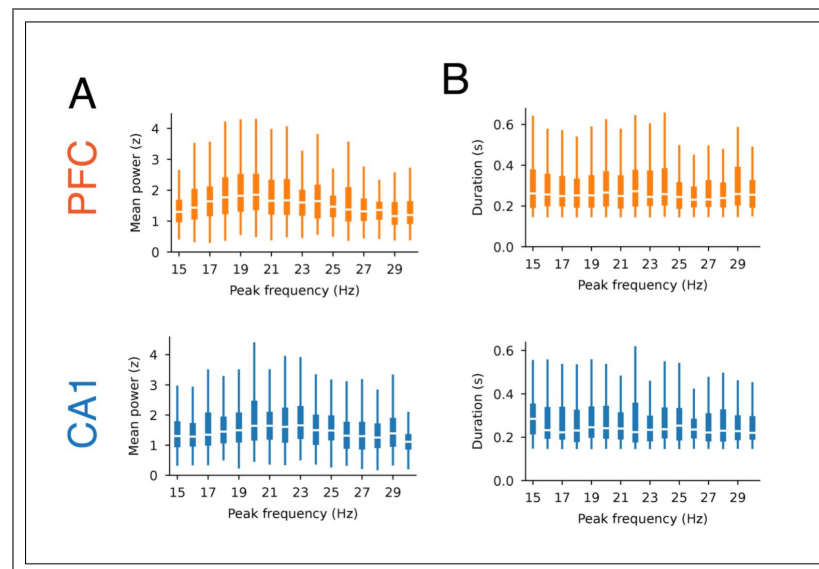


Figure 1-3. Power and duration for beta bursts by frequency.

a. Beta burst power by peak burst frequency. b. Beta bursts duration by peak burst frequency.

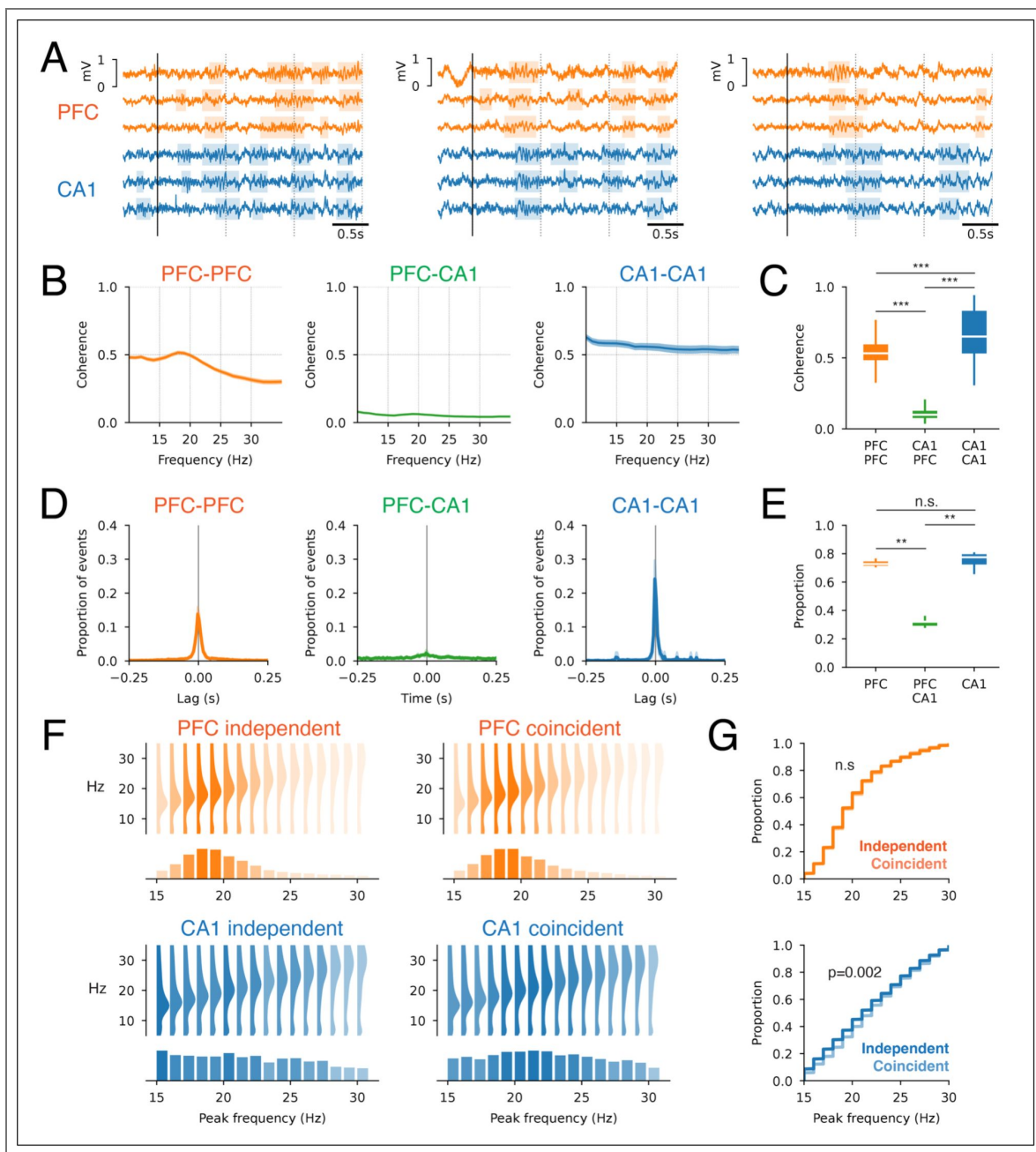


Figure 2. Beta bursts occur independently in both regions.

a. Beta frequency bursts (shaded) detected across multiple electrodes in PFC (orange) and CA1 (blue) relative to reward location entry (black vertical line). Three example trials are shown. b. Coherence (mean±SEM) within PFC (orange), between PFC and CA1 (green), or within CA1 (blue) for periods at the goal location. c. Mean coherence (15-30Hz) across the groups. Pairwise rank sum test with Benjamini-Hochberg false discovery rate correction: $p < 0.001$ for all pairs. d. Cross-correlation (mean±SD) of burst peak times for bursts detected on tetrodes with PFC (orange), across PFC-CA1 (green) and within CA1 (blue). e. Proportion of the cross-correlation density within ± 50 ms lag for PFC (orange), across PFC-CA1 (green) and within CA1 (blue). Pairwise rank sum test with Benjamini-Hochberg false discovery rate correction: PFC versus PFC-CA1 ($p = 0.003^{**}$), PFC versus CA1 ($p = 0.24^{n.s.}$) and PFC-CA1 versus CA1 ($p = 0.003^{**}$). f. Frequency distribution of bursts by peak frequency for independent and coincident bursts in each region. g. Burst peak frequency distribution for coincident and independent bursts. Cumulative distribution burst occurrence relative to goal location entry. Kolmogorov-Smirnov test: PFC ($p = 0.96^{n.s.}$) and CA1 ($p = 0.002^{**}$).

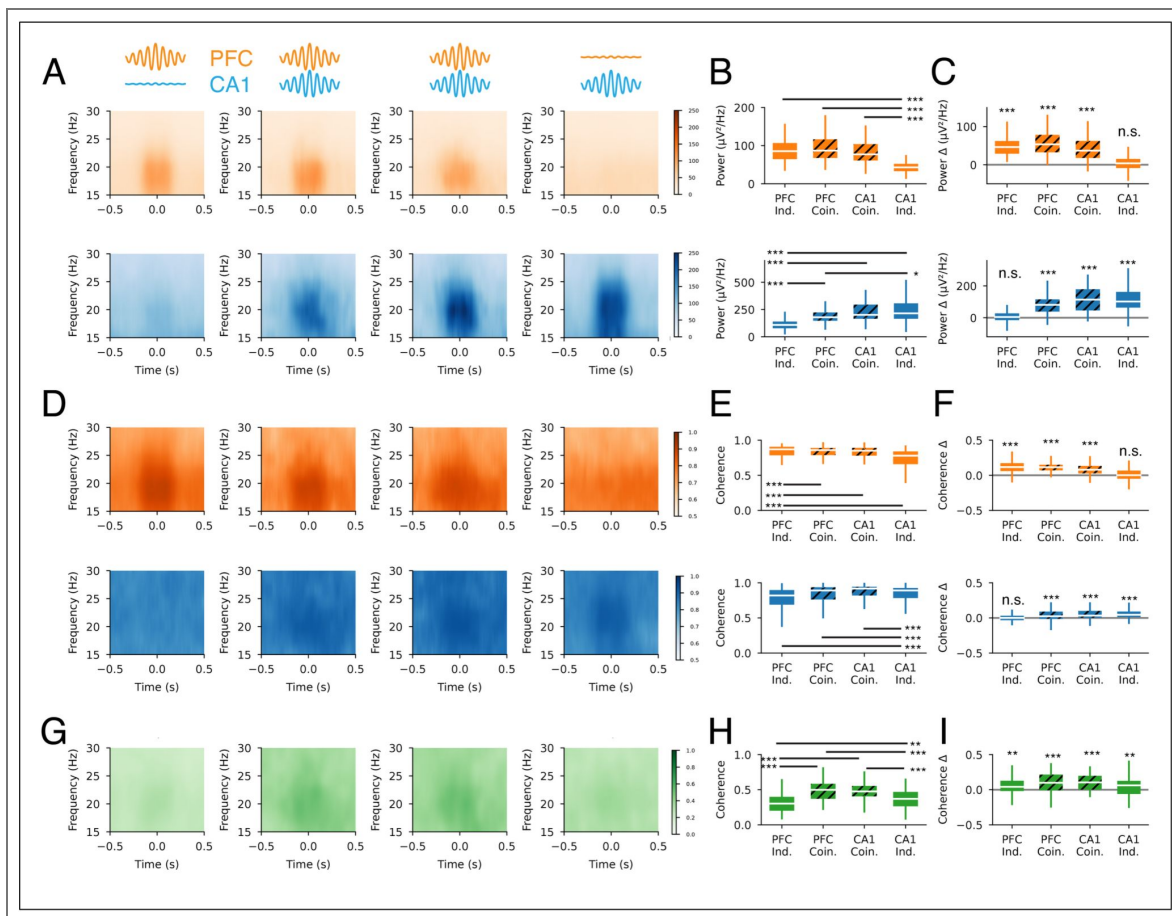


Figure 2-1. Beta burst aligned power and coherence

a. Multi-taper power spectrum within a 1 s window centered on the peaks of independent or coincident beta bursts (columns) in the PFC (top row) and CA1 (bottom row). The heatmap shows the mean across all bursts in each category. b. Power (18-25 Hz) within ± 100 ms of the peak. PFC (orange, top) and CA1 (blue, bottom). Pairwise rank-sum test with Benjamini-Hochberg false discovery rate correction: $p < 0.001^{***}$ and $p < 0.05^*$ for all significant comparisons. c. Change in power within ± 100 ms of the peak relative to baseline (125 ms from -0.5 s). PFC (orange, top) and CA1 (blue, bottom). Wilcoxon signed-rank test with Benjamini-Hochberg false discovery rate correction: $p < 0.001^{***}$. d. Multi-taper coherence in PFC (upper row) and CA1 (lower row) within a 1 s window centered on the peaks of independent or coincident beta bursts. The heatmap shows the mean across all bursts in each category. e. Coherence (18-25 Hz) within ± 100 ms of the peak in PFC (upper row) and CA1 (lower row). Pairwise rank sum test with Benjamini-Hochberg false discovery rate correction: $p < 0.001^{***}$ and $p < 0.05^*$ for all significant comparisons. f. Change in coherence within ± 100 ms of the peak relative to baseline (125 ms from -0.5 s). PFC (orange, top) and CA1 (blue, bottom). Wilcoxon signed-rank test with Benjamini-Hochberg false discovery rate correction: $p < 0.001^{***}$. g. PFC-CA1 coherence within a 1 s window centered on the peaks of independent or coincident beta bursts. The heatmap shows the mean across all bursts in each category. h. PFC-CA1 coherence between (18-25 Hz) within ± 100 ms of the peak in PFC (top row) and CA1 (bottom row). Pairwise rank sum test with Benjamini-Hochberg false discovery rate correction: $p < 0.001^{***}$ and $p < 0.01^{**}$ for all significant comparisons. i. Change in PFC-CA1 coherence within ± 100 ms of the peak relative to baseline (125 ms from -0.5 s). PFC (orange, top) and CA1 (blue, bottom). Wilcoxon signed-rank test with Benjamini-Hochberg false discovery rate correction: $p < 0.001^{***}$ and $p < 0.01^{**}$.

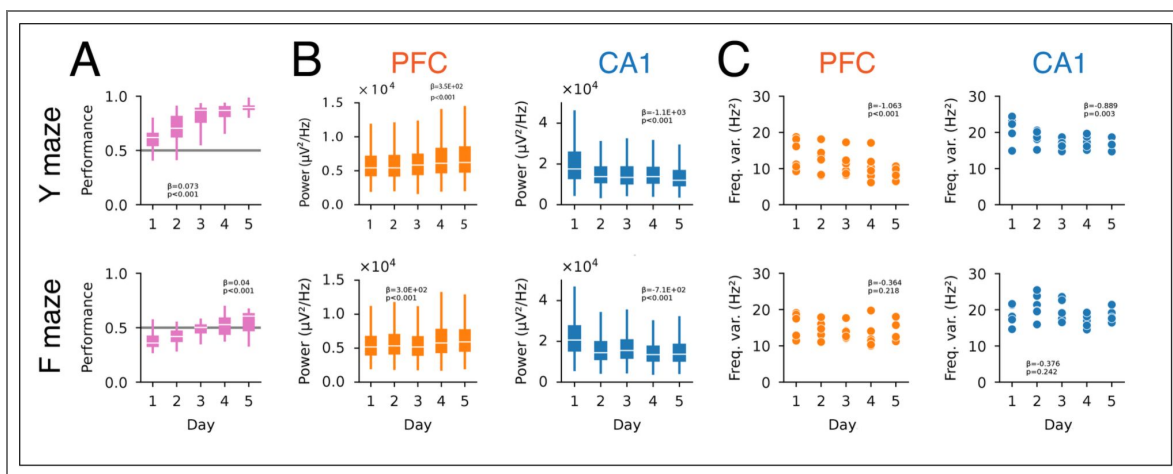


Figure 3. Distinct changes in PFC and CA1 burst properties across days of learning.

a. Performance in each maze task by day. Linear model with fixed (day) and random (animal) effects. Y maze ($\beta_{\text{day}}=0.073$, $\text{SE}=0.001$, 95% $\text{CI}=(0.071, 0.075)$, $z=71.9$ and $p<0.001^{***}$) and F maze ($\beta_{\text{day}}=0.04$, $\text{SE}=0.001$, 95% $\text{CI}=(0.038, 0.042)$, $z=42.4$ and $p<0.001^{***}$). b. Burst power in each maze task by day. Linear model with fixed (day) and random (animal) effects. Y maze PFC ($\beta_{\text{day}}=347.7$, $\text{SE}=38.2$, 95% $\text{CI}=(272.9, -422.5)$, $z=9.1$ and $p<0.001^{***}$) and F maze PFC ($\beta_{\text{day}}=300.3$, $\text{SE}=49.4$, 95% $\text{CI}=(203.5, 397.1)$, $z=6.1$ and $p<0.001^{***}$). Y maze CA1 ($\beta_{\text{day}}=-1133.2$, $\text{SE}=121.5$, 95% $\text{CI}=(-1371.3, -895.0)$, $z=-9.3$ and $p<0.001^{***}$) and F maze CA1 ($\beta_{\text{day}}=-711.7$, $\text{SE}=158.6$, 95% $\text{CI}=(-1022.6, -400.9)$, $z=4.5$ and $p<0.001^{***}$). c. Burst peak frequency variance in each maze task by day. Linear model with fixed (day) and random (animal) effects. Y maze PFC ($\beta_{\text{day}}=-1.1$, $\text{SE}=0.3$, 95% $\text{CI}=(-1.7, -0.48)$, $z=-3.6$ and $p<0.001^{***}$), F maze PFC ($\beta_{\text{day}}=-0.37$, $\text{SE}=0.3$, 95% $\text{CI}=(-.94, .22)$, $z=6.1$ and $p=0.22^{\text{n.s.}}$), Y maze CA1 ($\beta_{\text{day}}=-0.89$, $\text{SE}=0.30$, 95% $\text{CI}=(-1.5, -0.31)$, $z=-3.0$ and $p=0.003^{**}$) and F maze CA1 ($\beta_{\text{day}}=-0.38$, $\text{SE}=0.32$, 95% $\text{CI}=(-1.0, 0.25)$, $z=-1.2$ and $p=0.24^{\text{n.s.}}$).

pattern. The heatmap shows a clear difference in the burst frequency distribution between the two regions and their distribution over time. Although beta is generally defined as oscillations in the 15-30Hz range, it has been separated into a lower-frequency beta1 (~15Hz) and a higher-frequency beta2 (20-30Hz), based on work in cortical regions (Baker et al., 1997 [↗](#); MacKay & Mendonça, 1995 [↗](#); Roopun et al., 2008 [↗](#); Roopun et al., 2006 [↗](#)). However, the frequency of PFC beta bursts described here is higher than beta1 and lower than beta2. The frequency of CA1 beta bursts is consistent with beta2 previously described in the hippocampus (Berke et al., 2008 [↗](#); Igarashi et al., 2014 [↗](#); Iwasaki et al., 2021 [↗](#)). These results indicate that PFC and CA1 beta bursts at the goal have distinct spectral and temporal properties.

Beta oscillations are hypothesized to coordinate neural activity across brain regions (Spitzer & Haegens, 2017 [↗](#)) to support cognitive processes including sensory-guided decisions and reinstatement of context-dependent memory patterns (Igarashi et al., 2014 [↗](#); Jayachandran et al., 2023 [↗](#); Kay & Freeman, 1998 [↗](#); Symanski et al., 2022 [↗](#)). We therefore asked whether beta oscillations can coordinate PFC and CA1 activity at the goal. If so, we would expect coherence in the beta-frequency range between PFC and CA1, and similar burst timing in both regions. Visual inspection of LFP signals from PFC and CA1 tetrode showed that some beta bursts were coincident, while others appeared independent in time (Fig. 2A [↗](#)). To quantify beta-frequency coordination between regions, we first calculated the LFP coherence between tetrodes within each region as well as across regions, for periods when the animal was at the goal. We found higher coherence within PFC or CA1 compared to coherence between PFC and CA1 (Fig. 2B-C [↗](#)). The PFC coherence within the beta range showed a peak centered at approximately 20Hz, whereas the CA1 coherence was similar across the entire beta-frequency range. The across-region coherence was significantly weaker but still showed a small peak at ~20Hz. We then analyzed burst-wise timing and found beta bursts were more coincident within each region compared with across regions (Fig. 2D-E [↗](#)). The cross-correlation of burst peak times showed higher values around 0s lag within each brain region compared with the cross-correlation between PFC and CA1.

Our results so far suggest beta-frequency oscillations are distinct across PFC and CA1 based on their frequency distributions and low burst coincidence. Despite these differences, it is possible that a subset of coincident PFC and CA1 bursts could coordinate activity across the two regions. This hypothesis predicts that coincident bursts have similar frequency distributions and are more coherent between the two regions. We therefore classified each burst as “coincident” across regions, if it overlapped in time with a burst in the other brain region. Bursts that did not overlap were classified as “independent” across the regions. Based on this method, we asked whether coincident bursts were more closely matched in their frequency distribution across the regions compared with independent bursts. However, this was not the case, as coincident bursts in CA1 were higher in peak frequency compared with coincident bursts in PFC (Fig. 2F-G [↗](#)). The difference in frequency distribution for the coincident bursts provides evidence against a common beta-frequency range coordinating PFC and CA1, since there is a significant frequency mismatch. We confirmed our classification of independent and coincident bursts using burst-aligned power and coherence analysis (Fig. 2-1 [↗](#)). Independent bursts in one region were not accompanied by significant increases in beta power in the other region (Fig. 2-1A-B [↗](#)). Coincident bursts, by definition, showed the expected increase in power in both regions. We saw a similar pattern for coherence (Fig. 2-1D-E [↗](#)). Coherence within each region increased during independent bursts but not in the other region. Coherence in both regions increased during coincident bursts. Coherence across regions also increased for coincident bursts more than independent bursts (Fig. 2-1G-H [↗](#)), however, the coherence value across brain regions was lower in comparison with coherence within each region (Fig. 2-1E [↗](#) vs. Fig. 2-1H [↗](#)).

Having established the properties of beta oscillations in PFC and CA1, we next asked how goal-related hippocampal-neocortical beta oscillations changed across task learning. We therefore determined the relationship between beta properties in PFC and CA1 with either days of training or performance in each task. Animals performed better in the Y alternation compared with the F alternation over five days (Fig. 3A [↗](#)). By day five, performance reached greater than 80% on the Y compared with approximately 60% on the F maze tasks, indicating the F maze task was more

challenging. This difference in performance allowed us to examine the effects of both training time and performance improvement on beta dynamics. In both tasks, PFC beta-burst power increased over the five days, whereas CA1 beta-burst power decreased (Fig. 3B). Interestingly, beta bursts became more consistent in their peak frequency across days, but only when performance improved. The variance in PFC and CA1 burst frequency decreased over days of training for the Y but not the F maze (Fig. 3C). We repeated the same set of analyses by partitioning the data based on performance quintiles (Fig. 4A), which allowed us to directly relate beta activity properties with performance. We found similar relationships between burst power (Fig. 4B) and frequency variance (Fig. 4C).

We next found beta bursts occurred earlier after reaching the goal location over days of training (Fig. 5), pointing to temporal changes in beta-frequency modulated processes in PFC and CA1 with learning. We examined rewarded and unrewarded trials separately. During early learning days, bursts in PFC and CA1 on rewarded trials tended to occur several seconds after entry to the goal (Fig. 5A-E). During later days of training, the peak in the probability density shifted to earlier time points relative to goal entry. The same trend across days was found for unrewarded trials, but more strikingly, bursts on unrewarded trials occurred earlier than those on rewarded trials (Fig. 5C, F). These results demonstrate that beta frequency modulation in PFC and CA1 has distinct correlates with performance across the five days of training, suggesting changes to beta frequency activity reflect learning-related dynamics in PFC and CA1 networks.

We next asked how neurons in PFC and CA1 are modulated by beta-frequency oscillations. We found that cells in PFC and CA1 were more strongly phased-locked to beta oscillations within their own region (local) rather than the beta oscillation in the other region (remote). Both PFC (20%) and CA1 (41%) populations showed significant phase locking to beta within each region (Fig. 6A-C). The PFC and CA1 cell populations showed different phase preferences to local beta, with PFC cells showing a bias toward spiking during the rising phases, whereas CA1 cells showed a slight bias for the falling phases (Fig. 6D). Further, we found cells in each region showed higher phase locking to local beta compared with remote beta (Fig. 6E-F). This indicates that spiking in each region is modulated preferentially by local beta oscillations rather than remote beta oscillations. These results provide further evidence supporting that the PFC and CA1 are independently modulated at the beta frequency during the goal period.

The inverse learning-related changes in PFC and CA1 beta oscillations point to complementary processes modulated by beta in each region. We next asked how changes in beta oscillations are related to another prominent neural process supporting learning: awake hippocampal SWRs. Hippocampal SWRs also occur at goal locations (Ambrose et al., 2016; Carey et al., 2019; Diba & Buzsaki, 2007; Foster & Wilson, 2006; Kleinman & Foster, 2025; Singer & Frank, 2009) and are hypothesized to coordinate distributed representations (Jadhav et al., 2016; Shin et al., 2019; Tang et al., 2021; Yu et al., 2017; Yu et al., 2018) to support the formation and use of memory during spatial learning (Cheng & Frank, 2008; Deceuninck & Kloosterman, 2024; Dupret et al., 2010; Gupta et al., 2010; Jadhav et al., 2012; Pfeiffer & Foster, 2013; Singer et al., 2013; Singer & Frank, 2009). Since both beta and SWRs occur at goal locations, this led us to ask how beta-frequency dynamics within PFC and CA1 networks are related to hippocampal SWR dynamics. We found several features of beta-frequency oscillations that show the opposite pattern of change compared with SWRs. Consistent with previous findings, we found SWRs tended to occur several seconds after the animal reached the goal (Fig. 7A, B) (Ambrose et al., 2016; Carey et al., 2019; Diba & Buzsaki, 2007; Foster & Wilson, 2006; Kleinman & Foster, 2025; Singer & Frank, 2009) and the amplitude of SWRs decreased across days (Fig. 7C) (Cheng & Frank, 2008). In contrast to the delayed onset of hippocampal SWRs, beta bursts in PFC and CA1 occurred closer to the time of goal entry (Fig. 7A, D); thus, on average beta bursts in each region occurred earlier than SWRs. We confirmed this relationship occurred on a single-trial timescale by computing the cross-correlation between the timing of beta bursts in each region and SWRs (Fig. 7E). Further, the amplitude of PFC beta-frequency bursts increased across days of training (Fig.

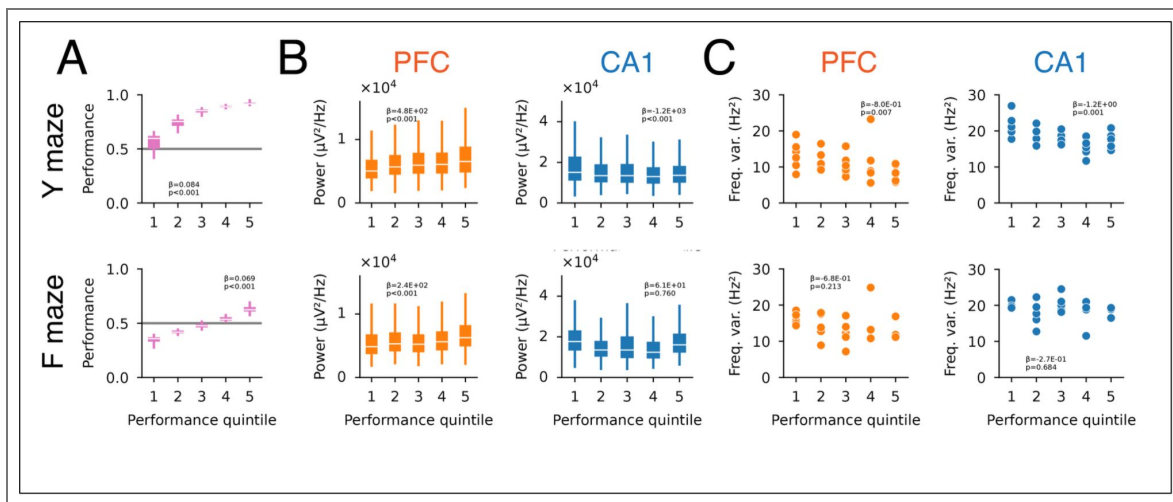


Figure 4. Distinct changes in PFC and CA1 burst properties with performance.

a. Performance in each maze task by performance quintile. Linear model with fixed (performance quintile) and random (animal) effects. Y maze ($\beta_{\text{day}} = 0.084$, $SE = 0.001$, 95% $CI = (0.083, 0.086)$, $z = 103.3$ and $p < 0.001^{***}$) and F maze ($\beta_{\text{day}} = 0.069$, $SE = 0.001$, 95% $CI = (0.068, 0.070)$, $z = 136.9$ and $p < 0.001^{***}$). b. Burst power in each maze task by performance quintile. Linear model with fixed (performance quintile) and random (animal) effects. Y maze PFC ($\beta_{\text{perf.}} = 484.4$, $SE = 40.5$, 95% $CI = (405.1, 563.8)$, $z = 12.0$ and $p < 0.001^{***}$) and F maze PFC ($\beta_{\text{perf.}} = 242.6$, $SE = 60.9$, 95% $CI = (123.2, 362.0)$, $z = 4.0$ and $p < 0.001^{***}$). Y maze CA1 ($\beta_{\text{perf.}} = -1199.6$, $SE = 127.2$, 95% $CI = (-1448.9, -950.3)$, $z = -9.4$ and $p < 0.001^{***}$) and F maze CA1 ($\beta_{\text{perf.}} = 60.6$, $SE = 198.3$, 95% $CI = (-328.1, 449.3)$, $z = 0.3$ and $p = 0.76^{n.s.}$). c. Burst peak frequency variance in each maze task by performance quintile. Linear model with fixed (performance quintile) and random (animal) effects. Y maze PFC ($\beta_{\text{perf.}} = -0.80$, $SE = 0.30$, 95% $CI = (-1.4, -0.22)$, $z = -2.7$ and $p < 0.007^{**}$) and F maze PFC ($\beta_{\text{perf.}} = -0.68$, $SE = 0.54$, 95% $CI = (-1.74, 0.39)$, $z = -1.2$ and $p = 0.21^{n.s.}$). Y maze CA1 ($\beta_{\text{perf.}} = -1.2$, $SE = 0.35$, 95% $CI = (-1.87, -0.50)$, $z = -3.40$ and $p = 0.001^{**}$) and F maze CA1 ($\beta_{\text{perf.}} = -0.27$, $SE = 0.67$, 95% $CI = (-1.57, 1.03)$, $z = -0.41$ and $p = 0.68^{n.s.}$).

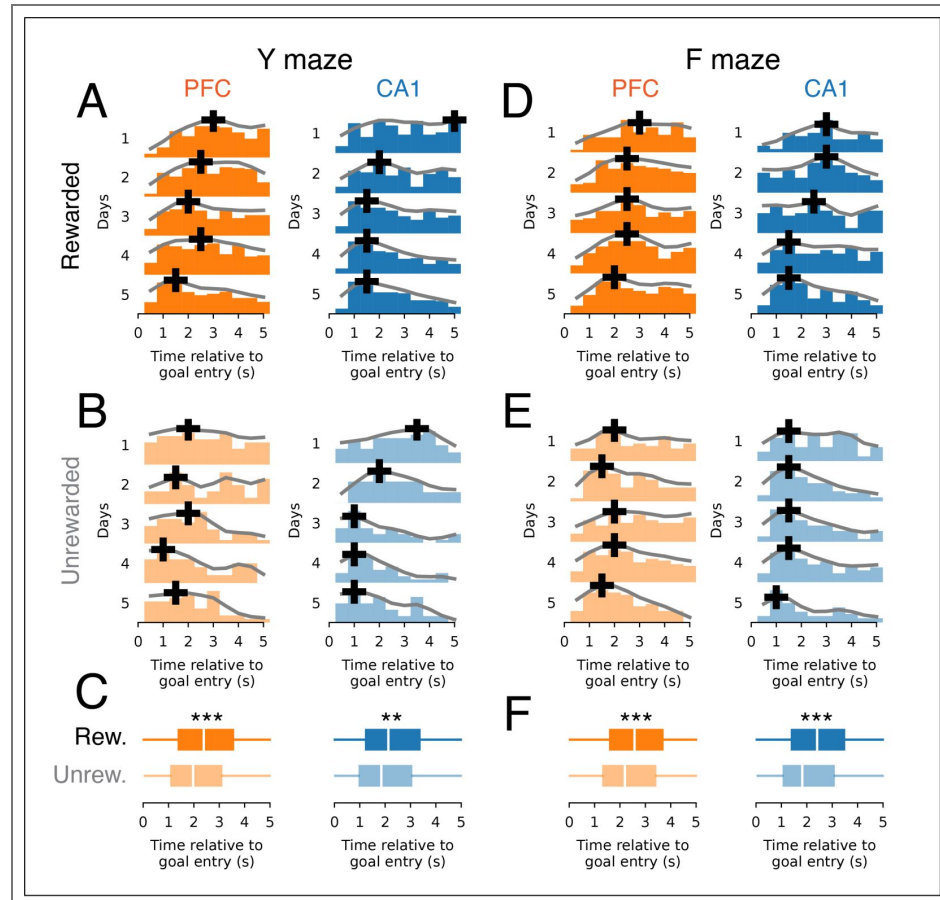


Figure 5. Bursts occur sooner after goal entry over days of training.

a. Y maze burst distribution after goal entry for rewarded trials. PFC (orange) and CA1 (blue). Gray line indicates the smoothed histogram. Black plus marks the peak of the smoothed histogram. Linear model with fixed (day) and random (animal) effects on burst timing: PFC ($\beta_{\text{day}} = -0.127$ SE=0.023, 95% CI=(-0.17, -0.081), $z = -5.45$ and $p < 0.001$) and CA1 ($\beta_{\text{day}} = -0.11$ SE=0.030, 95% CI=(-0.17, -0.048), $z = -3.54$ and $p < 0.001$). b. Y maze burst distribution after goal entry for unrewarded trials. PFC (orange) and CA1 (blue). Linear model with fixed (day) and random (animal) effects on burst timing: PFC ($\beta_{\text{day}} = -0.14$ SE=0.057, 95% CI=(-0.26, -0.031), $z = -2.51$ and $p = 0.012$) and CA1 ($\beta_{\text{day}} = -0.23$ SE=0.065, 95% CI=(-0.34, -0.099), $z = -3.48$ and $p < 0.001$). c. Boxplot comparison for rewarded and unrewarded trials. Wilcoxon rank sum test: $p = 2.20 \times 10^{-4}$ (PFC) and $p = 1.15 \times 10^{-2}$ (CA1). d. F maze burst distribution after goal entry for rewarded trials. PFC (left) and CA1 (right). Gray line indicates the smoothed histogram. Black plus marks the peak of the smoothed histogram. Linear model with fixed (day) and random (animal) effects on burst timing: PFC ($\beta_{\text{day}} = -0.042$ SE=0.037, 95% CI=(-0.12, 0.030), $z = -1.15$ and $p = 0.25$) and CA1 ($\beta_{\text{day}} = -0.05$ SE=0.047, 95% CI=(-0.18, 0.008), $z = -1.78$ and $p = 0.073$). e. F maze burst distribution after goal entry for unrewarded trials. PFC (left) and CA1 (right). Linear model with fixed (day) and random (animal) effects on burst timing: PFC ($\beta_{\text{day}} = -0.082$ SE=0.043, 95% CI=(-0.17, 0.003), $z = -1.9$ and $p = 0.057$) and CA1 ($\beta_{\text{day}} = -0.056$ SE=0.058, 95% CI=(-0.17, -0.057), $z = -0.97$ and $p = 0.33$). f. Boxplot comparison for rewarded and unrewarded trials. Wilcoxon rank sum test: $p = 2.89 \times 10^{-4}$ (PFC) and $p = 8.01 \times 10^{-4}$ (CA1).

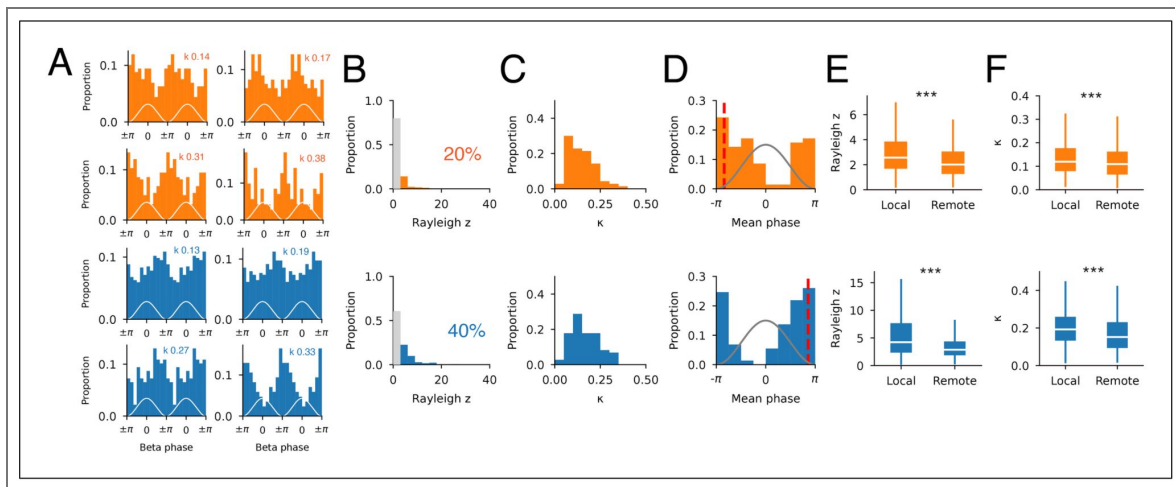


Fig. 6. PFC and CA1 cells show stronger spiking modulation to local beta.

a. Example PFC (orange) and CA1 (blue) spike phase locking histogram, sorted by increasing phase locking strength. The white line indicates the peak and trough of beta. The distributions were duplicated across two cycles of beta to improve visualization. The strength of the concentration parameter k is indicated for each cell. b. Distribution of Rayleigh z for PFC (upper) and CA1 (lower). The proportion of cells showing significant phase locking are shown. c. Distribution of k from a von Mises distribution fit for significantly beta modulated cells (Rayleigh $p < 0.05$ in panel b) in PFC (upper) and CA1 (lower). d. Distribution of phase preference for cells in PFC (upper) and CA1 (lower). Red dotted line shows the mean population phase preference. The gray line indicates the peak and trough of beta. Watson-Williams circular means test for PFC and CA1: $p = 1.01 \times 10^{-10}$. e. Beta phase locking strength (Rayleigh z) to local or remote beta for cells in PFC (upper) and CA1 (lower). Wilcoxon signed-rank test: $p = 3.17 \times 10^{-15}$ (PFC) and $p = 3.64 \times 10^{-31}$ (CA1). f. Beta phase locking strength (k) to local or remote beta for cells in PFC (upper) and CA1 (lower). Wilcoxon signed-rank test: $p = 2.20 \times 10^{-11}$ (PFC) and $p = 6.76 \times 10^{-24}$ (CA1).

3B) in contrast to the decrease in SWR amplitude (Fig. 7C). These differences in the properties of beta-frequency activity and SWRs indicate that these are two neural signatures for complementary learning-related processes during learning.

Since our results suggest that beta frequency activity and SWRs correspond to distinct processes at the goal, do they modulate distinct populations of PFC and CA1 cells? In PFC and CA1, we found cells modulated by both SWRs and beta (Fig. 8A, B). In PFC, 20% of cells showed modulation to beta and 43% showed modulation to SWRs. The subset of PFC cells that are modulated by both SWR and beta (11%) is greater than the expected proportion (8.6%) under the assumption that SWR and beta can modulate the population independently (Fisher exact test, $p=0.021$), although the size of the difference is small. We found PFC cells modulated by both beta and SWRs have distinct firing properties (Fig. 8C-D). For these cells, we found a positive relationship between the spike-phase preference and the direction of SWR modulation (Fig. 8C left). PFC cells with spiking preference for the falling phases of the beta cycle tended to show spiking inhibition during SWRs (negative SWR modulation index) (Fig. 8A, lower row) whereas cells with spiking preference for the rising phases of beta tended to be excited during SWRs (positive SWR modulation index) (Fig. 8A upper row). This relationship was not observed for PFC cells that are modulated by beta but not modulated by SWRs (Fig. 8C, right, Fig. 8-1A). Further, we found a negative relationship between spike-phase preference and the cell's firing pattern relative to goal entry. PFC cells with spiking preference for the falling phases of beta tended to spike later after goal entry whereas cells with phase preference to the rising phase of beta were more active sooner after goal entry (Fig. 8D, left). This again was not observed for PFC cells that were modulated by beta but not SWRs (Fig. 8D, right, Fig. 8-1B, Fig. 8A, compare top and bottom rows). We repeated these analyses for the CA1 population but did not find any statistically significant relationships between beta phase preference and SWR modulation (Fig. 8E-H). In CA1, ~40% of cells showed modulation to beta and 76% of cells showed modulation to SWRs. The subset of CA1 cells that are modulated by both SWR, and beta (31%) was similar to the expected proportion (30%) under the assumption of independence (Fisher exact test, $p=0.983$). Our results show that beta oscillations modulate a subpopulation of PFC neurons active at the goal, and some of these cells are coordinated with hippocampal SWRs. The PFC subset may not be coordinated with the hippocampus at the beta frequency, but they can still be linked with relevant hippocampal representations during SWRs. Together, this subset of PFC cells could form a distinct cell ensemble across hippocampal-cortical networks relevant for learning from goal outcome.

Discussion

Our results show beta-frequency oscillations occurred after entry to goal locations in both CA1 and PFC. However, several properties suggest that beta may not be strongly coordinating both regions at the goal. First, we found that beta bursts had distinct spectral and temporal properties in each region, where PFC beta bursts were lower in frequency than CA1 bursts. Second, PFC burst amplitude increased with training and performance, whereas CA1 burst amplitude decreased. The pattern of learning-related changes for PFC bursts was also opposite to those of SWRs. Lastly, beta activity and SWR modulated PFC cells identified a specific subpopulation with distinct task correlates, but not in CA1.

Our results suggest that the neocortex and hippocampus may participate in distinct functional networks at the goal, and beta oscillations with distinct frequencies may be supporting interactions between each region with their respective network partners. This contrasts with other task periods where the PFC and hippocampus are part of the same functional network modulated by beta, or other frequencies. For example, during spatial navigation, PFC cells show strong phase locking to hippocampal theta (Hyman et al., 2005; Jones & Wilson, 2005; Siapas et al., 2005; Yu & Frank, 2021; Zielinski et al., 2019), a frequency band that has been hypothesized to reflect coordination of distinct task-related representations across these structures during the execution of cognitive tasks. During olfactory sensory decision-making, beta-frequency coherence is observed across neocortical and hippocampal networks, which is thought to coordinate associative memory representations (Fourcaud-Trocmé et al., 2019; Igarashi et al., 2014);

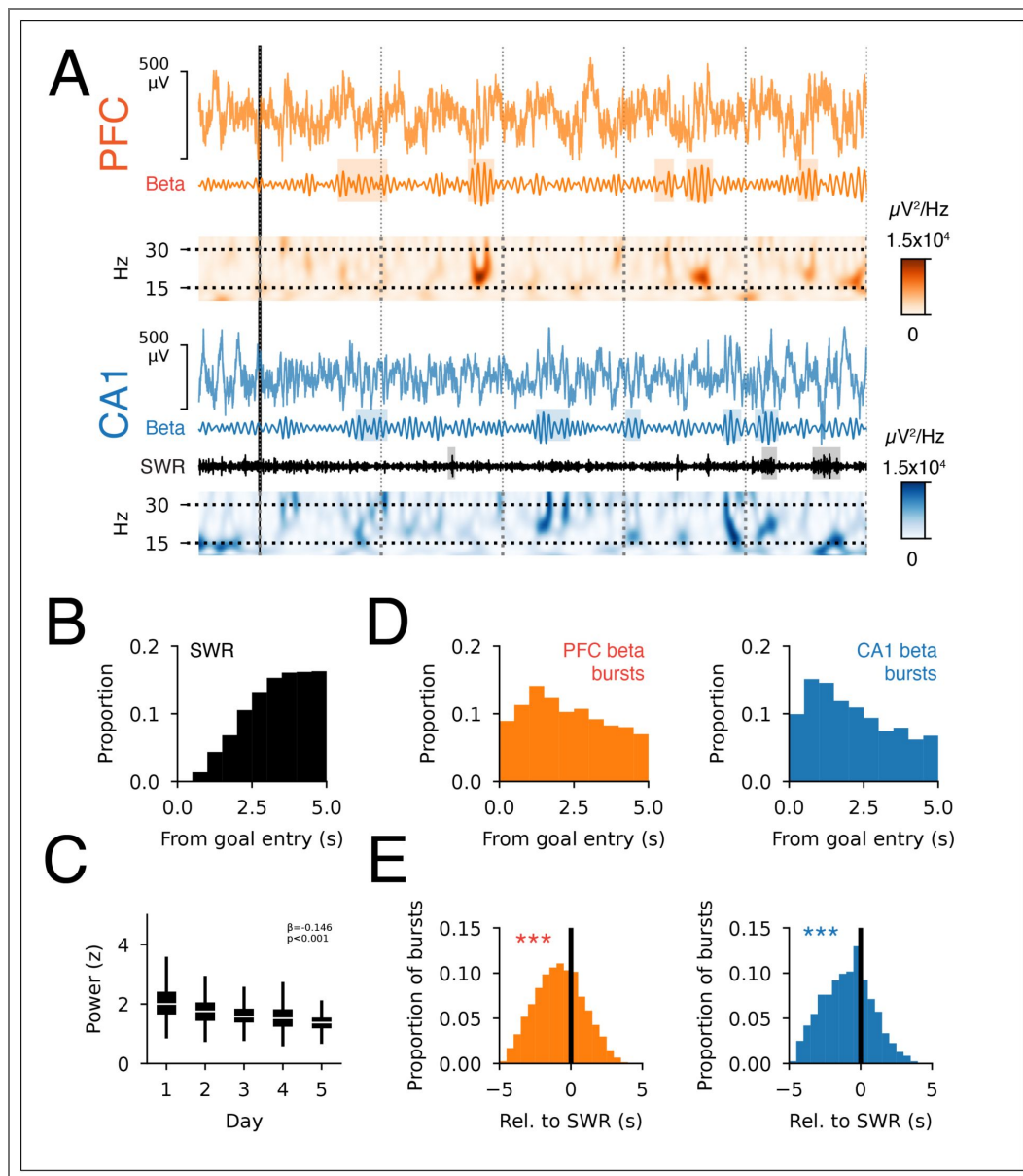


Figure 7. Beta bursts occur earlier than hippocampal SWRs at goal locations and have inverse learning-related changes in amplitude compared with PFC beta bursts.

a. PFC (orange) and CA1 (blue) LFP relative to goal entry (black vertical line). Beta frequency filtered signal is shown below the LFP. Ripple frequency (150-250Hz) filtered CA1 signal is shown in black. b. Goal entry aligned histogram for SWRs. c. SWR size across days of training. Linear model with fixed (day) and random (animal) effects: $\beta_{\text{day}} = -0.15$ SE=0.01, 95% CI=(-0.16, -0.13), $z = -15.3$ and $p < 0.001$. d. Goal entry aligned histogram for PFC beta (orange) or CA1 beta bursts (blue). e. Cross-correlation between PFC (left) or CA1 (right) beta bursts and SWRs. Wilcoxon signed-rank test $p = 3.12 \times 10^{-114}$ (PFC) and $p = 5.64 \times 10^{-78}$ (CA1.)

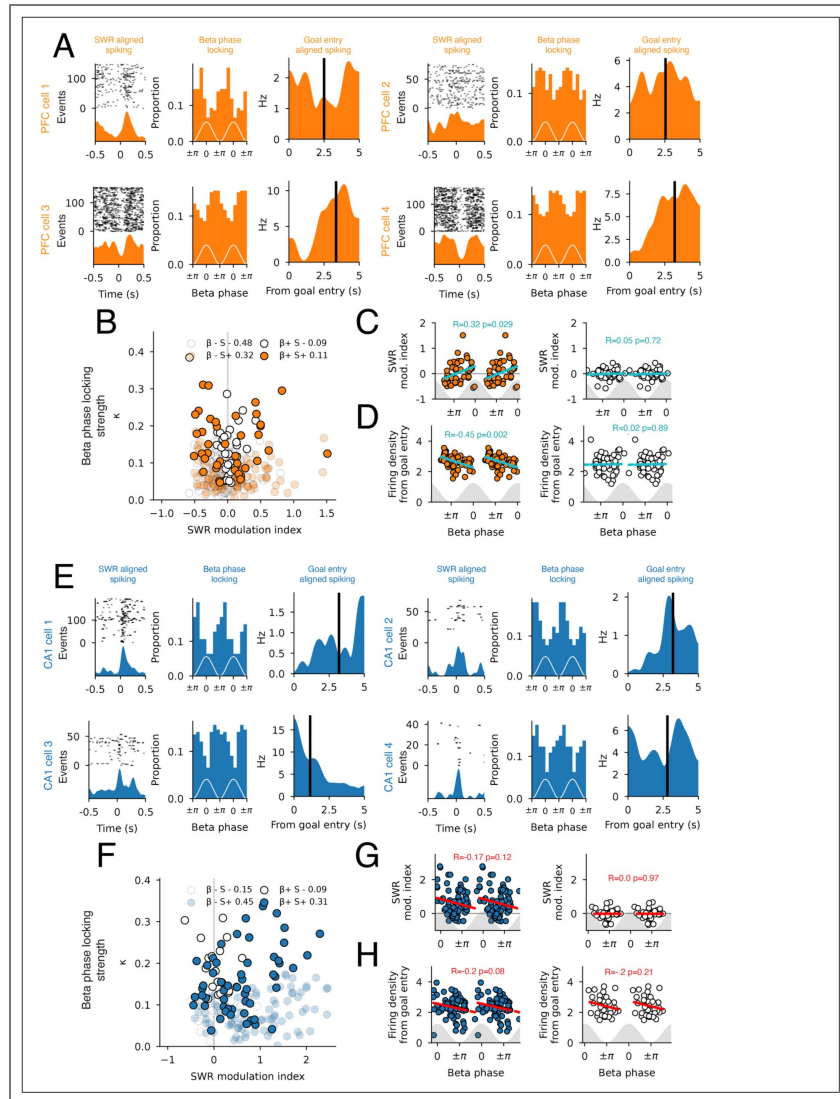


Figure 8. SWR and beta modulation in PFC and CA1.

a. Four example PFC cells showing SWR aligned spiking raster and histogram, spike beta-phase locking histogram and goal entry aligned firing histogram. Top two cells show spiking excitation around SWRs, and bottom two cells show spiking inhibition around SWRs. In the spike beta-phase locking histogram, the distribution is duplicated to improve visualization. The peaks and troughs for the beta cycle is shown in white. For the goal entry aligned firing histogram, the median firing density is shown by the vertical black line. This corresponds to 50% of the firing density relative to goal entry. b. PFC beta modulation strength (κ) versus SWR modulation index. The four combinations of SWR (S) and beta (β) modulation (+: modulated and -: not modulated) and their corresponding proportions are indicated. c. PFC SWR modulation index versus beta phase locking preference for beta and SWR modulated cells ($\beta+S+$) (left) and SWR modulated but not beta modulated cells ($\beta+S-$) (right). The regression line is shown in cyan. The gray shading indicates the peak and trough of beta. Two cycles are repeated for clarity. d. PFC median firing density from goal entry versus beta phase locking preference for beta and SWR modulated cells ($\beta+S+$) (left) and SWR modulated but not beta modulated cells ($\beta+S-$) (right). Median firing density is the time from goal entry corresponding 50% of the firing density within 5 seconds. e. Four example CA1 cells showing SWR aligned spiking raster and histogram, spike beta-phase locking histogram and goal entry aligned firing histogram. f. CA1 beta modulation strength (κ) versus SWR modulation index. The four combinations of SWR and beta (β) modulation (+: modulated and -: not modulated) and their corresponding proportions are indicated. g. CA1 SWR modulation index versus beta phase locking preference for beta and SWR modulated cells ($\beta+S+$) (left) and SWR modulated but not beta modulated cells ($\beta+S-$) (right). The regression line is shown in red. The gray shading indicates the peak and trough of beta. Two cycles are repeated for clarity. h. CA1 median firing density from goal entry versus beta phase locking preference for beta and SWR modulated cells ($\beta+S+$) (left) and SWR modulated but not beta modulated cells ($\beta+S-$) (right). Median firing density is the time from goal entry corresponding 50% of the firing density within 5 seconds.

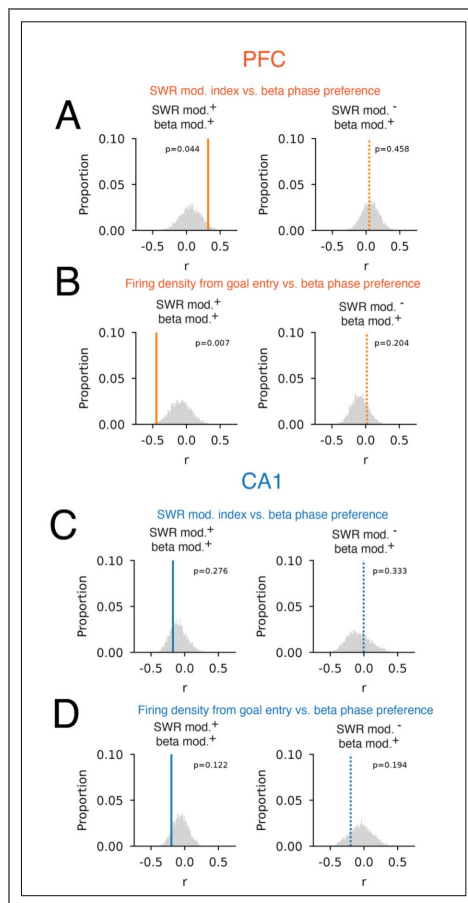


Figure 8-1. Permutation test for the significance of the correlation coefficient.

a. Distribution of the permuted (gray) and observed (vertical line) for PFC SWR modulation index versus beta phase locking preference in Fig. 8C. We performed this additional permutation test to verify the observed value of the correlation coefficient is different to the chance distribution. b. Distribution of the permuted (gray) and observed (vertical line) for PFC median firing density from goal entry versus beta phase locking preference in Fig. 8D. c. Distribution of the permuted (gray) and observed (vertical line) for CA1 SWR modulation index versus beta phase locking preference in Fig. 8G. d. Distribution of the permuted (gray) and observed (vertical line) for CA1 median firing density from goal entry versus beta phase locking preference in Fig. 8H.

Jayachandran et al., 2023 [↗](#); Kay & Freeman, 1998 [↗](#); Martin et al., 2007 [↗](#); Sheriff et al., 2021 [↗](#); Symanski et al., 2022 [↗](#)). During awake quiescence, activity in neocortical and hippocampal networks is transiently synchronized during SWRs (Jadhav et al., 2016 [↗](#); Remondes & Wilson, 2015 [↗](#); Shin et al., 2019 [↗](#); Tang et al., 2017 [↗](#); Yu et al., 2017 [↗](#); Yu et al., 2018 [↗](#)). Coordination at these frequencies and task periods demonstrates hippocampal-neocortical interactions play a central role in supporting diverse cognitive functions. Our results show that the neocortex and hippocampus may be decoupled or only weakly coupled during the goal period at the beta frequency, and each region may be engaged with its own set of functionally connected networks (Cohen et al., 2011 [↗](#)). This was surprising given the extensive coordination across these brain structures during other important task periods. We had expected that stronger coordination during this period would be important for learning-related changes across neocortical-hippocampal networks, similar to SWRs that occur at the goal.

Our results point to another insight on the complementary changes in hippocampal-neocortical beta dynamics. We saw an inverse pattern in the hippocampus and PFC during learning. These results indicate that beta-frequency activity in the neocortex and hippocampus, together with SWRs, are markers of complementary learning-induced changes in these networks, pointing to the contrasting contributions of the hippocampus and neocortex to learning. The hippocampus is hypothesized to play an important role in rapid changes during early learning, whereas the neocortex gradually changes on a longer timescale (Buzsáki, 1996 [↗](#); Mclelland et al., 1995 [↗](#)). In the hippocampus, SWRs are a neural signature of early learning, where larger amplitude events are observed during novel experience (Cheng & Frank, 2008 [↗](#)). With learning, these events become less prominent. We found similar patterns for goal-related beta activity in the hippocampus, which decreases with performance. This mirrors novelty-related beta activity in the hippocampus that occurs during exploration of new environments or objects, which decreases with familiarity (Berke et al., 2008 [↗](#); França et al., 2014 [↗](#); França et al., 2021 [↗](#); Rangel et al., 2015 [↗](#)). In contrast to hippocampal beta oscillations, we hypothesize that beta activity in the PFC reflects the reconfigured state for a given task as learning progresses, where beta amplitude and frequency uniformity increases with experience and performance. This increase parallels findings in the olfactory bulb and piriform cortex, where the strength of beta during odor sampling increases with performance proficiency in olfactory sensory decision-making tasks (Cohen et al., 2015 [↗](#); Fourcaud-Trocmé et al., 2019 [↗](#); Gervais et al., 2007 [↗](#); Martin et al., 2007 [↗](#); Martin et al., 2004 [↗](#)), the ventral striatum (Howe et al., 2011 [↗](#)), as well as the emergence of beta oscillations in the basolateral amygdala with the development of reward preference (Amaya et al., 2024 [↗](#)).

The difference in the frequency distribution of hippocampal and PFC beta raises the question of whether cortical and hippocampal beta have similar origins. Given that beta oscillations have been found in connected cortical, subcortical, and hippocampal regions, do they arise from similar mechanisms? Experimental evidence and computational models indicate that beta oscillations could be generated locally within a network (Bitzenhofer et al., 2017 [↗](#); David et al., 2015 [↗](#); Fourcaud-Trocmé et al., 2011 [↗](#); Osinski & Kay, 2016 [↗](#); Roopun et al., 2008 [↗](#); Roopun et al., 2006 [↗](#); Sherman et al., 2016 [↗](#); Womelsdorf et al., 2014 [↗](#)). Beta was originally partitioned into a lower-frequency ~15Hz (beta1) band and a higher frequency 20-30Hz (beta2) band (Baker et al., 1997 [↗](#); MacKay & Mendonça, 1995 [↗](#); Roopun et al., 2008 [↗](#); Roopun et al., 2006 [↗](#)). Our observations in CA1 are consistent with beta2, with beta bursts having peak frequencies primarily above 20Hz (Berke et al., 2008 [↗](#); Igarashi et al., 2014 [↗](#); Iwasaki et al., 2021 [↗](#)). The PFC beta we observed centers around 19Hz with a narrow frequency distribution. This is closer to beta1 but is higher than the beta1 reported in various neocortical regions. Could the distinct beta frequency distribution in these regions point to distinct origins? PFC beta may be generated locally or from a brain region with a lower frequency beta generator. The wider distribution of CA1 beta burst peak frequencies suggests hippocampal beta may arise from multiple local or remote inputs from a variety of brain regions, each with a range of central frequencies above 20Hz. These may be relayed to CA1, possibly via the midline thalamic regions (Jayachandran et al., 2023 [↗](#)) or via the entorhinal cortex (Kay & Freeman, 1998 [↗](#); Kay et al., 1996 [↗](#)).

There is increasing evidence for the contribution of beta oscillations to a wide range of cognitive processes (Lundqvist et al., 2024 [DOI](#); Miles et al., 2023 [DOI](#)), expanding from prior work focused on sensorimotor control (Barone & Rossiter, 2021 [DOI](#); Engel & Fries, 2010 [DOI](#)) and sensory perception (Kay, 2014 [DOI](#)). While beta has been implicated in coordinating neural activity across brain networks, including the hippocampus and neocortex (Igarashi et al., 2014 [DOI](#); Jayachandran et al., 2023 [DOI](#); Spitzer & Haegens, 2017 [DOI](#); Symanski et al., 2022 [DOI](#)), we identified an important period for learning during which the hippocampus and PFC are modulated independently by distinct frequency bands within the beta range. Thus, identifying functional subnetworks and when they coordinate can provide further insight into the temporal dynamics of distributed neural processes supporting cognition.

Methods

Animals

Long-Evans rats (Charles River Laboratories, 6 males, 4-10 months) were used for the study. All procedures were performed under approval by the university's Institutional Animal Care and Use Committee, according to the guidelines of the Association for Assessment and Accreditation of Laboratory Animal Care.

Neural implants

Animals were chronically implanted with neural recording devices (Voigts et al., 2020 [DOI](#)) with up to 32 adjustable tetrodes. Up to 16 tetrodes targeted the CA1 region of the left hippocampus (AP -3.8, ML -2.75 relative to Bregma), and up to 16 tetrodes targeted both hemispheres of the PFC (AP +3.5, ML +/-1.5 relative to Bregma). The PFC bundle was angled at 15 degrees towards the midline to avoid the superior sagittal sinus. A ground screw was placed in the skull above the right cerebellum. Tetrodes were gradually adjusted into the target regions over two to three weeks after surgery, based on LFP markers and estimated depth of the tetrodes. Once the tetrodes were within the target brain regions, small adjustments of 25µm, when necessary, were made to isolate single cells. Tetrode locations were verified at the end of the experiment. To mark the tip of the tetrode, electrolytic lesions were induced for each tetrode (100µA, 2s). Nissl staining was used to verify the location of the lesion was within the intended area.

Spatial learning apparatus

All tracks and mazes were constructed from acrylic (black DP-9, 8cm wide, 4cm tall walls, 76cm above floor level). Reward delivery in all tasks was automated. Infrared sensors were placed at the ends of the maze arms to detect the rat's arrival and to trigger the reward. Reward was delivered by a syringe pump (100µl at 20ml/min, NE-500, New Era Pump Systems Inc, New York, USA).

Behavioral training

Animals were food restricted to >85-90% of their baseline body weight. For pretraining, animals were first trained to forage for reward in a black open field box (H: 31cm, W: 61cm, L: 61cm), for 10 minutes per day for 3 days. The reward was 70% evaporated milk (Carnation) with 5% sucrose. The reward was randomly dropped inside the open box to encourage foraging. The next pretraining training phase involved the rats learning to run back and forth on an elevated linear track (60cm) to consume reward from the ends. Animals were trained until a performance criterion of 20 rewards per session (10-minute sessions, three times daily, 4 to 7 days).

For the tasks on the Y and F shaped mazes, the animals needed to learn a specific sequence of goal visits to be rewarded on every trial. There were three goal locations in each maze, which were wells at the end of the arms. The animal needed to alternate visits between wells 2 and 3 via well 1 (1, 2, 1, 3, 1, 2, 1, 3 ...), similar to previously described spatial alternation tasks (Frank et al., 2000; Kim and Frank, 2009; Jadhav et al., 2012 [DOI](#)). For example, if the rat was at well 1, it would be rewarded next at well 2 only if it had previously visited well 3. Similarly, if the rat was at well 1, it

would be rewarded next at well 3 only if it had previously visited well 2. If the rat was at wells 2 or 3, it would be rewarded only by going to well 1. Reward delivery was controlled using custom scripts written for the data recording system.

Data recording

Data were collected using the Tredes data acquisition system (SpikeGadgets LLC, California, USA). Neural data were recorded using a 128-channel digitizing headstage. The head stage was tethered via a commutator to the main data acquisition system. The commutator and tether were supported by a passive suspension system. Raw data were recorded at 30KHz. Local field potential (<300Hz) was extracted at 1500Hz. Time-synchronized video (1456 × 1088, 30Hz) was recorded using Allied Vision Manta G-158C cameras.

Behavioral analysis

DeepLabCut (Mathis et al., 2018 [DOI](#)) was used to track the animal in the video. The spatial coordinate for the neck of the animal was used as the animal's location and to calculate the animal's speed. Performance of the animals was derived using a state-space model that estimated the probability of the animal making a correct choice (Smith et al., 2004 [DOI](#)). We then calculated the mean performance for each day grouped performance by quintiles.

Data and statistical analysis packages

We used Python packages for signal processing: Elephant electrophysiology toolkit (<https://elephant.readthedocs.io/> [DOI](#)), fooof tools (<https://fooof-tools.github.io/> [DOI](#)), GhostiPy (<https://github.com/kemerelab/ghostipy> [DOI](#)); circular statistics: PyCircStat (<http://github.com/circstat/pycircstat> [DOI](#)); and statistics: SciPy (scipy.org [DOI](#)), statsmodels (statsmodels.org [DOI](#)) and pingouin (pingouin-stats.org [DOI](#)).

Spectral analysis

We calculated the power spectral density (PSD) using the Welch function, with 1s segments with 50% overlap (`scipy.signal.welch`). We calculated coherence using the coherence function with 1s, with 1s segments and 50% overlap (`scipy.signal.coherence`). We isolated the periodic component of the PSD by subtracting the aperiodic component using Fitting Oscillations & One-Over-F (fooof-tools) (Donoghue et al., 2020 [DOI](#)).

Beta burst detection

Local field potential (LFP) analysis was performed using the Elephant electrophysiology toolkit (Denker et al., 2024 [DOI](#)). We applied a continuous wavelet transform (CWT) using the generalized Morse wavelet ($\gamma = 4$, $\beta = 7.5$) to extract time-resolved spectral power for 0.5–130 Hz in 1 Hz steps. This was done using the Ghostipy package (Chu & Kemere, 2021 [DOI](#)). The average power in the beta-band (15–30 Hz) isolated from the CWT spectrogram was used to detect bursts using a dual-threshold amplitude method (Feingold et al., 2015 [DOI](#)). Bursts were defined as periods when the beta power envelope exceeded 1 standard deviation (SD) above the mean power with a minimum duration of 100ms. The onset and offset of each burst were marked by the first upward and downward crossings of 0.5 SD above the mean, respectively. Burst peaks were characterized by the z-scored amplitude at the power maximum. Events separated by less than 100ms were combined. Periods where the maximum LFP signal amplitude across all tetrodes exceeded 10 standard deviations were classified as noise and excluded from analyses.

We identified the time at which the burst had its peak power, the magnitude of the peak power, and the frequency at the time of peak power. This was done by isolating the CWT spectrogram for each burst and extracting the time and frequency corresponding to the maximum power value within the burst. Bursts were classified as independent or coincident based on overlap. Independent bursts are those without overlap in time, whereas coincident bursts overlap in time.

Burst aligned power and coherence analysis

Event-aligned power and coherence within and across PFC and CA1 were computed using the multi-taper method (2 tapers with a time-bandwidth product of 2) (Python implementation of the coherence function from chronux.org) (Mitra & Bokil, 2008). We calculated the coherence in a 1s window centered at the peak of each burst (500ms moving window, 5ms steps). For within-region coherence, the coherence value was the mean for all pairs of tetrodes. To determine the change in coherence around the peak of the burst, a baseline was defined as the mean coherence in the -500 to -375ms interval relative to the center of the burst. We used linear mixed-effects models (statsmodels.mixedlm) to determine the relationship between burst power or frequency variance and performance (by day or quintiles) while accounting for differences between animals.

Sharp wave ripple detection

Sharp-wave ripples (SWRs) were identified based on previous methods (http://github.com/Eden-Kramer-Lab/ripple_detection) (Kay et al., 2016). LFP from tetrodes in the dorsal CA1 region (oriens and pyramidale) was filtered in the ripple frequency band (150–250 Hz). The median of the smoothed envelope (Gaussian kernel $\sigma = 4$ ms) was calculated. We used a threshold of 2 standard deviations for detecting SWRs, with a minimum duration of 15ms and separation of 50ms. Only SWR events occurring at speed <4 cm/s and at the goal locations were included. We filtered out detection artifacts due to LFP noise by excluding time intervals in which the LFP signal magnitude exceeded 10 standard deviations across any tetrode.

Spike sorting

We used MountainSort (Chung et al., 2017) with manual curation to isolate single cells. The quality of well-isolated cells was determined by having an interspike interval >2ms, consistency of the waveforms, and the stability of the peak voltage values over the sessions.

Spiking phase locking analysis

For each tetrode, the phase of beta oscillations was extracted by first applying a band-pass filter to the raw LFP signal within the beta band range (15-30Hz, acausal 4th order Butterworth), followed by a Hilbert transform using the Elephant toolkit (Denker et al., 2024). For each cell, we calculated the phase at each spike relative to the beta phase for every available tetrode, which allowed us to determine the cell's phase-locking preference to beta within the same brain region (local) and the other region (remote). We used two metrics to quantify the strength of spike phase locking to beta. First, we performed the Rayleigh test for circular non-uniformity and calculated the Rayleigh-z value using PyCircStat (Berens, 2009). Second, we fitted a von Mises distribution to the phase preference histogram to estimate the mean phase and the concentration parameter (kappa) (scipy.stats.vonmises). To determine the local phase-locking strength of a given cell, we chose the maximum values of the phase-locking metric across all tetrodes within the same region as the cell. Similarly, we calculated the remote phase-locking strength as the maximum phase locking value across all tetrodes in the other brain region. Only spikes that occurred when the animal was at the goal location were included for the phase-locking analysis.

SWR modulation of spiking

SWR modulation was determined based on previously described methods (Jadhav et al., 2016; Rothschild et al., 2017; Yu et al., 2017; Yu et al., 2018). For each cell, a SWR event-aligned spiking histogram was created for a 1 s window centered on the start of each SWR. A modulation index was calculated based on the difference in spiking rate within a 200 ms window after the start of the SWR relative to the baseline within the 1s window. A circular-shift permutation test was used to determine the significance of the modulation index. A positive modulation index corresponds to an increase in firing around the time of SWRs, whereas a negative modulation index corresponds to a decrease in firing. A permutation test was used to determine the significance.

Correlation between beta phase locking preference and SWR modulation index or goal-entry firing

We calculated the Pearson's correlation between a cell's beta phase preference and its SWR modulation index or goal-entry firing. Goal-entry firing measures the firing latency relative to goal entry and is defined as the time corresponding to 50% of the firing density in the 5 s from goal entry. To estimate the significance of the correlation coefficient, we performed a permutation test. Each cell was classified based on its phase-locking significance to local beta (β^+ or β^-) and its SWR modulation significance (SWR+ or SWR-). This produces four possible combinations in the population (β -SWR-, β +SWR-, β -SWR+, or β +SWR+). We then permuted the β and SWR significance labels for the population and repeated the calculation. This was done 5000 times to generate a permuted correlation coefficient distribution, which allowed us to estimate the significance to $p=0.0002$. The p value of the observed correlation coefficient is calculated as the proportion of the permuted distribution that is greater or less than the observed value.

Acknowledgements

We thank Leslie Kay for providing helpful feedback on the manuscript; Audrey Kay, and Jaqueline Gutierrez for assisting with histology; and Krish Khana and Rajat Gupta for assisting with DeepLabCut.

Additional information

Author contributions

Experiment design and conceptualization (JYY, NZ and GW). Data collection (ZL and NZ). Data analysis (JYY and GW). Manuscript preparation (JYY) and editing (JYY, NZ, GW and ZL).

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Peer reviews

Reviewer #1 (Public review):

Wang, Zhou et al. investigated coordination between the prefrontal cortex (PFC) and the hippocampus (Hp), during reward delivery, by analyzing beta oscillations. Beta oscillations are associated with various cognitive functions, but their role in coordinating brain networks during learning is still not thoroughly understood. The authors focused on the changes in power, peak frequencies, and coherence of beta oscillations in two regions when rats learn a spatial task over days. Inconsistent with the authors' hypothesis, beta oscillations in those two regions during reward delivery were not coupled in spectral or temporal aspects. They were, however, able to show reverse changes in beta oscillations in PFC and Hp as the animal's performance got better. The authors were also able to show a small subset of cell populations in PFC that are modulated by both beta oscillations in PFC and sharp wave ripples in Hp. A similarly modulated cell population was not observed in Hp. These results are valuable in pointing out distinct periods during a spatial task when two regions modulate their activity independently from each other.

The authors included a detailed analysis of the data to support their conclusions. However, some clarifications would help their presentation, as well as help readers to have a clear understanding.

- (1) The crucial time point of the analysis is the goal entry. However, it needs a better explanation in the methods or in figures of what a goal entry in their behavioral task means.
- (2) Regarding Figure 2, the authors have mentioned in the methods that PFC tetrodes have targeted both hemispheres. It might be trivial, but a supplementary graph or a paragraph

about differences or similarities between contralateral and ipsilateral tetrodes to Hp might help readers.

(3) The authors have looked at changes in burst properties over days of training. For the coincidence of beta bursts between PFC and Hp, is there a change in the coincidence of bursts depending on the day or performance of the animal?

(4) Regarding the changes in performance through days as well as variance of the beta burst frequency variance (Figures 3C and 4C); was there a change in the number of the beta bursts as animals learn the task, which might affect variance indirectly?

(5) In the behavioral task, within a session, animals needed to alternate between two wells, but the central arm (1) was in the same location. Did the authors alternate the location of well number 1 between days to different arms? It is possible that having well number 1 in the same location through days might have an effect on beta bursts, as they would get more rewards in well number 1?

(6) The animals did not increase their performance in the F maze as much as they increased it in the Y maze. It would be more helpful to see a comparison between mazes in Figure 5 in terms of beta burst timing. It seems like in Y maze, unrewarded trials have earlier beta bursts in Y maze compared to F maze. Also, is there a difference in beta burst frequencies of rewarded and unrewarded trials?

(7) For individual cell analysis, the authors recorded from Hp and the behavioral task involved spatial learning. It would be helpful to readers if authors mention about place field properties of the cells they have recorded from. It is known that reward cells firing near reward locations have a higher rate to participate in a sharp wave ripple. Factoring in the place field properties of the cells into the analysis might give a clearer picture of the lack of modulation of HP cells by beta and sharp wave ripples.

<https://doi.org/10.7554/eLife.108623.1.sa3>

Reviewer #2 (Public review):

(1) When presenting the power spectra for the representative example (Figure 1), it would be appropriate to display a broader frequency band-including delta, theta, and gamma (up to ~100 Hz), rather than only the beta band. What was the rat's locomotor state (e.g., running speed) after entering the reward location, during which the LFPs were recorded? If the rats stopped at the goal but still consumed the reward (i.e., exhibited very low running speed), theta rhythms might still occasionally occur, and sharp-wave ripples (SWRs) could be observed during rest. Do beta bursts also occur during navigation prior to goal entry? It would be beneficial to display these rhythmic activities continuously across both the navigation and goal entry phases. Additionally, given that the hippocampal theta rhythm is typically around 7-8 Hz, while a peak at approximately 15-16 Hz is visible in the power spectra in Figure 1C, the authors should clarify whether the 22 Hz beta activity represents a genuine oscillation rather than a harmonic of the theta rhythm.

(2) The authors claim that beta activity is independent between CA1 and PFC, based on the low coherence between these regions. However, it is challenging to discern beta-specific coherence in CA1; instead, coherence appears elevated across a broader frequency band (Figure 2 and Figure 2-1D). An alternative explanation could be that the uncoupled beta between CA1 and PFC results from low local beta coherence within CA1 itself.

(3) In Figure 2-1E-F, visual inspection of the box plots reveals minimal differences between PFC-Ind and PFC-Coin/CA1-Coin conditions, despite reported statistical significance. It may be necessary to verify whether the significance arises from a large sample size.

(4) In Figure 3 and Figure 4, although differences in power and frequency appear to change significantly across days, these changes are not easily discernible by visual inspection. It is worth considering whether these variations are related to increased task familiarity over days, potentially accompanied by higher running speeds.

(5) The stronger spiking modulation by local beta oscillations shown in Figure 6 could also be interpreted in the context of uncoupled beta between CA1 and PFC. In this analysis, only spikes occurring during beta bursts should be included, rather than all spikes within a trial. The authors should verify the dataset used and consider including a representative example illustrating beta modulation of single-unit spiking.

(6) As observed in Figure 7D, CA1 beta bursts continue to occur even after 2.5 seconds following goal entry, when SWRs begin to emerge. Do these oscillations alternate over time, or do they coexist with some form of cross-frequency coupling?

<https://doi.org/10.7554/eLife.108623.1.sa2>

Reviewer #3 (Public review):

Summary:

This paper explored the role of beta rhythms in the context of spatial learning and mPFC-hippocampal dynamics. The authors characterized mPFC and hippocampal beta oscillations, examining how their coordination and their spectral profiles related to learning and prefrontal neuronal firing. Rats performed two tasks, a Y-maze and an F-maze, with the F-maze task being more cognitively demanding. Across learning, prefrontal beta oscillation power increased while beta frequency decreased. In contrast, hippocampal beta power and beta frequency decreased. This was particularly the case for the well-performed and well-learned Y-maze paradigm. The authors identified the timing of beta oscillations, revealing an interesting shift in beta burst timing relative to reward entry as learning progressed. They also discovered an interesting population of prefrontal neurons that were tuned to both prefrontal beta and hippocampal sharp-wave ripple events, revealing a spectrum of SWR-excited and SWR-inhibited neurons that were differentially phase locked to prefrontal beta rhythms.

In sum, the authors set out to examine how beta rhythms and their coordination were related to learning and goal occupancy. The authors identified a set of learning and goal-related correlates at the level of LFP and spike-LFP interactions, but did not report on spike-behavioral correlates.

Strengths:

Pairing dual recordings of medial prefrontal cortex (mPFC) and CA1 with learning of spatial memory tasks is a strength of this paper. The authors also discovered an interesting population of prefrontal neurons modulated by both beta and CA1 sharp-wave ripple (SWR) events, showing a relationship between SWR-excited and SWR-inhibited neurons and beta oscillation phase.

Weaknesses:

The authors report on a task where rats were performing sub-optimally (F-maze), weakening claims. Likewise, it is questionable as to whether mPFC and hippocampus are dually required to perform a no-delay Y-maze task at day 5, where rats are performing near 100%. There would be little reason to suspect strong oscillatory coupling when task performance is poor and/or independent of mPFC-HPC communication (Jones and Wilson, 2005), potentially weakening conclusions about independent beta rhythms. Moreover, there is little detail

provided about sample sizes and how data sampling is being performed (e.g., rats, sessions, or trials), raising generalizability concerns.

<https://doi.org/10.7554/eLife.108623.1.sa1>

Author response:

Public Reviews:

Reviewer #1 (Public review):

Wang, Zhou et al. investigated coordination between the prefrontal cortex (PFC) and the hippocampus (Hp), during reward delivery, by analyzing beta oscillations. Beta oscillations are associated with various cognitive functions, but their role in coordinating brain networks during learning is still not thoroughly understood. The authors focused on the changes in power, peak frequencies, and coherence of beta oscillations in two regions when rats learn a spatial task over days. Inconsistent with the authors' hypothesis, beta oscillations in those two regions during reward delivery were not coupled in spectral or temporal aspects. They were, however, able to show reverse changes in beta oscillations in PFC and Hp as the animal's performance got better. The authors were also able to show a small subset of cell populations in PFC that are modulated by both beta oscillations in PFC and sharp wave ripples in Hp. A similarly modulated cell population was not observed in Hp. These results are valuable in pointing out distinct periods during a spatial task when two regions modulate their activity independently from each other.

The authors included a detailed analysis of the data to support their conclusions. However, some clarifications would help their presentation, as well as help readers to have a clear understanding.

(1) The crucial time point of the analysis is the goal entry. However, it needs a better explanation in the methods or in figures of what a goal entry in their behavioral task means.

We appreciate Reviewer 1 pointing out this shortcoming and will clarify the description in the revised manuscript. Each goal is located at the end of the arm, and is equipped with a reward delivery unit. The unit has an infrared sensor. The rat breaks the infrared beam when it enters the goal.

(2) Regarding Figure 2, the authors have mentioned in the methods that PFC tetrodes have targeted both hemispheres. It might be trivial, but a supplementary graph or a paragraph about differences or similarities between contralateral and ipsilateral tetrodes to Hp might help readers.

We will provide the requested analysis in the full revision. We saw both hemispheres had similar properties.

(3) The authors have looked at changes in burst properties over days of training. For the coincidence of beta bursts between PFC and Hp, is there a change in the coincidence of bursts depending on the day or performance of the animal?

We will provide the requested analysis in the full revision.

(4) Regarding the changes in performance through days as well as variance of the beta burst frequency variance (Figures 3C and 4C); was there a change in the number of the beta bursts as animals learn the task, which might affect variance indirectly?

The analysis we can do here is to control for differences in the number of bursts for each category (days/performance quintile) by resampling the data to match the burst count between categories.

(5) In the behavioral task, within a session, animals needed to alternate between two wells, but the central arm (1) was in the same location. Did the authors alternate the location of well number 1 between days to different arms? It is possible that having well number 1 in the same location through days might have an effect on beta bursts, as they would get more rewards in well number 1?

The central arm remained the same across days since we needed the animals to learn the alternation task. In our experience, the animal needs a few days to learn the alternation rule when we switch the central arm location. For this experiment, we were interested in the initial learning process, and we kept the central constant. Switching the central arm location is a great suggestion for a follow up experiment where we can understand the effects of reward contingency change has on beta bursts.

(6) The animals did not increase their performance in the F maze as much as they increased it in the Y maze. It would be more helpful to see a comparison between mazes in Figure 5 in terms of beta burst timing. It seems like in Y maze, unrewarded trials have earlier beta bursts in Y maze compared to F maze. Also, is there a difference in beta burst frequencies of rewarded and unrewarded trials?

We will add this analysis in the revised manuscript.

(7) For individual cell analysis, the authors recorded from Hp and the behavioral task involved spatial learning. It would be helpful to readers if authors mention about place field properties of the cells they have recorded from. It is known that reward cells firing near reward locations have a higher rate to participate in a sharp wave ripple. Factoring in the place field properties of the cells into the analysis might give a clearer picture of the lack of modulation of HP cells by beta and sharp wave ripples.

This is a great suggestion, and we will address this in the full revision.

Reviewer #2 (Public review):

We thank Reviewer 2 for their helpful comments and will address these in full in the revision. These are great suggestions to provide greater detail on the spectral and behavioral data at the goal.

(1) When presenting the power spectra for the representative example (Figure 1), it would be appropriate to display a broader frequency band-including delta, theta, and gamma (up to ~100 Hz), rather than only the beta band.

We will show more examples of power spectra with a wider frequency range. We did examine the wider spectra and noticed power in the beta frequency band was more prominent than others.

What was the rat's locomotor state (e.g., running speed) after entering the reward location, during which the LFPs were recorded?

We will add the time aligned speed profile to the spectra and raw data examples. Because goal entry is defined as the time the animals break the infrared beam at the goal (response to Reviewer 1), the rat would have come to a stop.

If the rats stopped at the goal but still consumed the reward (i.e., exhibited very low running speed), theta rhythms might still occasionally occur, and sharp-wave ripples

(SWRs) could be observed during rest.

We typically find low theta power in the hippocampus after the animal reaches the goal location and as it consumes reward. Reviewer 2 is correct about occasional theta power at the goal. We have observed this but mostly before the animal leaves the goal location. We did find SWRs during goal periods. One example is shown in Fig. 7A.

Do beta bursts also occur during navigation prior to goal entry?

We did not find consistent beta bursts in PFC or CA1 on approach to goal entry. We can provide the analyses in our full revision. In our initial exploratory analysis, we found beta bursts was most prominent after goal entry, which led us to focus on post-goal entry beta for this manuscript. However, beta oscillations in the hippocampus during locomotion or exploration has been reported (Ahmed & Mehta, 2012; Berke et al., 2008; França et al., 2014; França et al., 2021; Iwasaki et al., 2021; Lansink et al., 2016; Rangel et al., 2015).

It would be beneficial to display these rhythmic activities continuously across both the navigation and goal entry phases. Additionally, given that the hippocampal theta rhythm is typically around 7-8 Hz, while a peak at approximately 15-16 Hz is visible in the power spectra in Figure 1C, the authors should clarify whether the 22 Hz beta activity represents a genuine oscillation rather than a harmonic of the theta rhythm.

To ensure we fully address this concern, we can provide further spectral analysis in our revised manuscript to show theta power in CA1 is reduced after goal entry. We were initially concerned about the possibility that the 22Hz power in CA1 may be a harmonic rather than a standalone oscillation band. If these are harmonics of theta, we should expect to find coincident theta at the time of bursts in the beta frequency. In Fig. 1B, Fig. 2A, we show examples of the raw LFP traces from CA1. Here, the detected bursts are not accompanied by visible theta frequency activity. For PFC, we do not always see persistent theta frequency oscillations like CA1. In PFC, we found beta bursts were frequent and visually identifiable when examining the LFP. We provided examples of the PFC LFP (Fig. 1B, Fig. 1-1, and Fig. 2A). In these cases, we see clear beta frequency oscillations lasting several cycles and these are not accompanied by any oscillations in the theta frequency in the LFP trace.

(2) The authors claim that beta activity is independent between CA1 and PFC, based on the low coherence between these regions. However, it is challenging to discern beta-specific coherence in CA1; instead, coherence appears elevated across a broader frequency band (Figure 2 and Figure 2-1D). An alternative explanation could be that the uncoupled beta between CA1 and PFC results from low local beta coherence within CA1 itself.

This is a legitimate concern, and we used three methods to characterize coherence and coordination between the two regions. First, we calculated coherence for tetrode pairs for times when the animal was at goals (Fig. 2B), which provides a general estimation of coherence across frequencies but lack any temporal resolution. Second, we calculated burst aligned coherence (Fig. 2-1), which provides temporal resolution relative to the burst, but the multi-taper method is constrained by the time-frequency resolution trade off. Third, we quantified the timing between the burst peaks (Fig. 2D), which will describe timing differences but the peaks for the bursts may not be symmetric. Thus, each method has its own caveats, but we drew our conclusion from the combination of results from these three analyses, which pointed to similar conclusions.

Reviewer 2 is correct in pointing out the uniformly high coherence within CA1 across the frequency range we examined. When we inspected the raw LFP across multiple tetrodes in CA1, they were similar to each other (Fig. 2A). This likely reflects the uniformity in the LFP across recording sites in CA1, which is what we saw with coherence values across the frequency range (Fig. 2B). We found CA1 coherence between tetrode pairs within CA1 across

the range, were statistically higher, compared to tetrode pairs in PFC (Fig. 2B and C), thus our results are unlikely to be explained by low beta coherence within CA1 itself. The burst aligned coherence using a multi-taper method also supports this. The coherence values within CA1 at the time of CA1 bursts is ~0.8-0.9.

(3) In Figure 2-1E-F, visual inspection of the box plots reveals minimal differences between PFC-Ind and PFC-Coin/CA1-Coin conditions, despite reported statistical significance. It may be necessary to verify whether the significance arises from a large sample size.

We will include the sample sizes for each of the boxplots, these should be the same as the power comparison in Fig. 2-1 A-C. The LFP within a one second window centered around the bursts are usually very similar, and the multi-taper method will return high coherence values. The p-values from statistical comparisons between the boxes are corrected using the Benjamini-Hochberg method.

(4) In Figure 3 and Figure 4, although differences in power and frequency appear to change significantly across days, these changes are not easily discernible by visual inspection. It is worth considering whether these variations are related to increased task familiarity over days, potentially accompanied by higher running speeds.

We agree with Reviewer 2 that familiarity increases across days, and the animal is likely running faster. The analysis for Fig. 3 and 4 includes only data from periods when the animal was at the goal and was not moving. We used linear mixed effects models to quantify the relationship between power, frequency and day or behavioral quintile.

(5) The stronger spiking modulation by local beta oscillations shown in Figure 6 could also be interpreted in the context of uncoupled beta between CA1 and PFC. In this analysis, only spikes occurring during beta bursts should be included, rather than all spikes within a trial. The authors should verify the dataset used and consider including a representative example illustrating beta modulation of single-unit spiking.

We agree with Reviewer 2 that the stronger modulation to local beta is another piece of evidence indicating uncoupled beta between the two regions. We appreciate this suggestion and will add examples illustrating beta modulation for single units. We want to clarify the spikes were only from periods when the animal is at the goal location on each trial and does not include the running period between goals.

(6) As observed in Figure 7D, CA1 beta bursts continue to occur even after 2.5 seconds following goal entry, when SWRs begin to emerge. Do these oscillations alternate over time, or do they coexist with some form of cross-frequency coupling?

This is a very interesting and helpful suggestion. Although we found SWRs generally appear later than beta bursts, it is possible the two are related on a finer timescale pointing to coordination. Our cross-correlation analysis between PFC and CA1 beta bursts only showed the relationship on the timescale of seconds. We will show a higher time-resolution version of this analysis in the revision.

Reviewer #3 (Public review):

Summary:

This paper explored the role of beta rhythms in the context of spatial learning and mPFC-hippocampal dynamics. The authors characterized mPFC and hippocampal beta oscillations, examining how their coordination and their spectral profiles related to learning and prefrontal neuronal firing. Rats performed two tasks, a Y-maze and an F-maze, with the F-maze task being more cognitively demanding. Across learning,

prefrontal beta oscillation power increased while beta frequency decreased. In contrast, hippocampal beta power and beta frequency decreased. This was particularly the case for the well-performed and well-learned Y-maze paradigm. The authors identified the timing of beta oscillations, revealing an interesting shift in beta burst timing relative to reward entry as learning progressed. They also discovered an interesting population of prefrontal neurons that were tuned to both prefrontal beta and hippocampal sharp-wave ripple events, revealing a spectrum of SWR-excited and SWR-inhibited neurons that were differentially phase locked to prefrontal beta rhythms.

In sum, the authors set out to examine how beta rhythms and their coordination were related to learning and goal occupancy. The authors identified a set of learning and goal-related correlates at the level of LFP and spike-LFP interactions, but did not report on spike-behavioral correlates.

Strengths:

Pairing dual recordings of medial prefrontal cortex (mPFC) and CA1 with learning of spatial memory tasks is a strength of this paper. The authors also discovered an interesting population of prefrontal neurons modulated by both beta and CA1 sharp-wave ripple (SWR) events, showing a relationship between SWR-excited and SWR-inhibited neurons and beta oscillation phase.

Weaknesses:

Moreover, there is little detail provided about sample sizes and how data sampling is being performed (e.g., rats, sessions, or trials), raising generalizability concerns.

We appreciate Reviewer 3's thoughtful suggestions for making our claims convincing. We will include information about sample sizes and address each detailed recommendation in the revised manuscript.

The authors report on a task where rats were performing sub-optimally (F-maze), weakening claims.

Our experiment was designed to allow us to examine within the same animal, a well-performed task (Y) and a less well-performed task (F). This contrast allows us to determine differences in neural correlates. We can further dissect the relevant differences to take advantage of this experiment design.

Likewise, it is questionable as to whether mPFC and hippocampus are dually required to perform a no-delay Y-maze task at day 5, where rats are performing near 100%.

We agree with Reviewer 3 that the mPFC and hippocampus may not be required when the animal reaches stable performance on day 5 (Deceuninck & Kloosterman, 2024). The data we collected spans the full range of early learning (day 1) to proficiency (day 5). We wanted to understand the dynamics of beta across these learning stages.

Recent studies suggest mPFC and hippocampus are likely to be needed, in some capacity, for learning continuous spatial alternation tasks on a range of maze geometries. Lesions, inactivation or waking activity perturbation of hippocampus or hippocampus and mPFC on the W maze alternation task slowed learning (Jadhav et al., 2012; Kim & Frank, 2009; Maharjan et al., 2018). More recently, optogenetic silencing of mPFC after sharp wave ripples on the Y maze alternation affected performance when the center arm was switched (den Bakker et al., 2023). The Y and F mazes in our study both share the continuous alternation rule, where the animal needed to avoid visiting a previously visited location on the outbound choice relative to the center, and always return to the center location.

Further, the performance characteristics on the outbound and inbound components of our Y task is similar to the W task. We have analyzed the “inbound” and “outbound” performance of the animals on the Y maze alternation task, and they are similar to the W maze alternation task. The “inbound” or reference location component is learned quickly whereas the “outbound”, alternation component is learned slowly. We can add this analysis to the revised manuscript.

There would be little reason to suspect strong oscillatory coupling when task performance is poor and/or independent of mPFC-HPC communication (Jones and Wilson, 2005) potentially weakening conclusions about independent beta rhythms.

Although many studies have examined the oscillatory coupling properties at the theta frequency between mPFC-HPC (Hyman et al., 2005; Jones & Wilson, 2005; Siapas et al., 2005), our understanding of beta frequency coordination between the two regions is less established, especially at goal locations. Beta frequency coordination at goal locations may or may not follow similar properties to theta frequency coupling. In this manuscript we are reporting the properties of goal-location beta frequency activity in mPFC-HPC networks. We are not aware of prior work describing these properties at this stage of a spatial navigation task, especially their coordination in time.

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