Highlights

- Neural trajectories in the hippocampus exhibited greater variability during a working memory (WM) task compared to those in the entorhinal cortex and amygdala regions.
- The distance of neural trajectories between encoding and retrieval states in the hippocampus was memory-load dependent during a WM task.
- Hippocampal neural trajectories fluctuated between the encoding and retrieval states in a task-dependent manner during both baseline and sharp-wave ripple (SWR) periods.
- Hippocampal neural trajectories shifted from encoding to retrieval states during SWR period.

Hippocampal Neural Fluctuations Between Memory Encoding and Retrieval States During a Working Memory Task in Humans

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Abstract

Working memory (WM) is crucial for a multitude of cognitive functions, but its underlying neural mechanisms at play remain to be fully understood. Interestingly, the hippocampus and sharp-wave ripples (SWRs)— transient and synchronous oscillation observed in the hippocampus — garner recognition for their significance in memory consolidation and retrieval, albeit their correlation with WM tasks remains to be elucidated. Here we show that during a WM task, multi-unit activity patterns in the hippocampus display distinctive dynamics, especially during SWR periods. This study analyzed intracranial electroencephalography data from the medial temporal lobe (MTL) of nine patients with epilepsy, recorded during an eight-second Sternberg task. Utilizing Gaussian-process factor analysis, we extracted low-dimensional neural representations or trajectories (NT) within MTL regions

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during the Sternberg WM task. The results revealed significant variations in NT of the hippocampus compared to those of the entorhinal cortex and the amygdala. Additionally, the distance of the NT between the encoding and retrieval phases was dependent on memory load. Crucially, hippocampal NT oscillated during the retrieval phase between encoding and retrieval states in a task-dependent manner. Notably, these fluctuations shifted from encoding to retrieval states during SWR episodes. These findings reaffirm the role of the hippocampus in WM tasks and propose a hypothesis: the hippocampus transitions its functional state from encoding to retrieval during SWRs in WM tasks.

Keywords: working memory, memory load, hippocampus, sharp-wave ripples, humans

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7 figures, 3 tables, 221 words for abstract, and 3178 words for main text

1. Introduction

Working memory (WM) is crucial in everyday life; however, its neural mechanism has yet to be fully elucidated. Specifically, the hippocampus's involvement in WM processing, a pivotal region for memory, is the subject of ongoing research [1, 2, 3, 4, 5, 6, 7, 8, 9]. Understanding the hippocampus' role in working memory is instrumental in deepening our comprehension of cognitive processes and could potentially enhance cognitive abilities.

Current evidence suggests that transient, synchronized oscillations, termed sharp-wave ripples (SWRs) [10], are associated with various cognitive functions. SWRs have traditionally been linked with long-term memory functions such as memory replay [11, 12, 13, 14, 15], memory consolidation [16, 17, 18, 19], memory recall [20, 21, 22], and neural plasticity [23, 24]. However, only a subset of studies has investigated the role of SWRs in WM tasks [25, 26]. This gap in our understanding motivates the current study to further investigate the potential involvement of SWRs in WM, particularly given their fundamental computational manifestation in hippocampal

processing.

Recent studies have found that low-dimensional representations in hippocampal neurons can explain WM task performances. Specifically, the firing patterns of place cells [27, 28, 29, 30, 31], found in the hippocampus, have been identified within dynamic, nonlinear three-dimensional hyperbolic spaces in rats [32]. Additionally, grid cells in the entorhinal cortex (EC), which is the main pathway to the hippocampus [33, 34, 35], exhibited a toroidal geometry during exploration in rats [36].

However, these existing studies predominantly focus on spatial navigation in rodents, presenting several limitations. First, the temporal resolution of navigation tasks is insufficient, obscuring the precise timing of memory acquisition and recall. Second, the presence of noise in signals recorded during rodent movement complicates the detection of SWRs [37]. Third, the generalization to humans and tasks other than spatial navigation remains unclear. Given these limitations, it is crucial to explore SWRs in a controlled, less noisy environment to better understand their potential role in WM tasks in humans.

Considering these factors, this study investigates the hypothesis that hippocampal neurons in humans exhibit low-dimensional neural trajectories (NTs) that depend on WM load, particularly during SWR periods. To test this hypothesis, we employed a dataset of patients performing an eight-second Sternberg task (1 s for fixation, 2 s for encoding, 3 s for maintenance, and 2 s for retrieval) with high temporal resolution. Intracranial electroencephalography (iEEG) signals within the medial temporal lobe (MTL) were recorded for these patients [38]. To investigate low-dimensional NTs, we utilized Gaussian-process factor analysis (GPFA), an established method for analyzing neural population dynamics [39, 40, 41, 42, 43, 44, 45, 46, 47].

2. Methods

2.1. Dataset

The dataset used in this study, which is publicly available, comprises nine epilepsy patients performing a modified the Sternberg task [38]. This task includes four phases: fixation (1s), encoding (2s), maintenance (3s), and retrieval (2s). During the encoding phase, participants were presented with a set of four, six, or eight alphabet letters. They were then tasked with determining whether a probe letter displayed during the retrieval phase had previously appeared (the correct response for Match IN task) or not (the correct response for Mismatch OUT task). Intracranial electroencephalography (iEEG) signals were captured with a 32 kHz sampling rate within a 0.5–5,000 Hz frequency range, using depth electrodes in the MTL regions: the anterior head of the left and right hippocampus (AHL and AHR), the posterior body of the hippocampus (PHL and PHR), the entorhinal cortex (ECL and ECR), and the amygdala (AL and AR), as depicted in Figure **??**A and Table 1. The iEEG signals were subsequently downsampled to 2 kHz. Correlations between variables such as set size and correct rate were examined (Figure **??**S1). Multiunit spike timing was determined via a spike sorting algorithm [48] using the Combinato package (`https://github.com/jniediek/combinato`)(Figure **??**C).

2.2. Calculation of NT using GPFA

NTs, also referred to as 'factors', in the hippocampus, EC, and amygdala were determined using GPFA [39] applied to the multi-unit activity data for each session, performed with the elephant package (`https://elephant.readthedocs.io/en/latest/reference/gpfa.html`). The bin size was set to 50 ms, without overlaps. Each factor was z-normalized across all sessions, and the Euclidean distance from the origin (O) was then computed.

For each NT within a region such as AHL, geometric medians (g_F for fixation, g_E for encoding, g_M for maintenance, and g_R for retrieval phase) were calculated by determining the median coordinates of the NT during the

four phases. An optimal GPFA dimensionality was found to be three using the elbow method obtained by examining the log-likelihood values through a three-fold cross-validation approach (Figure **??**B).

2.3. Identifying SWR candidates from hippocampal regions

Potential SWR events within the hippocampus were detected using a widely used method [49]. LFP signals from a region of interest (ROI) like AHL, were re-referenced by deducting the averaged signal from locations outside the ROI (for instance, AHR, PHL, PHR, ECL, ECR, AL, and AR). The re-referenced LFP signals were then filtered with a ripple-band filter (80–140 Hz) to determine SWR candidates, marked as SWR^+ candidates. SWR detection was carried out using a published tool (`https://github.com/Eden-Kramer-Lab/ripple_detection`) [50], with the bandpass range adjusted to 80–140 Hz for humans [21, 22, 49], unlike the initial 150–250 Hz range typically applied to rodents [10].

Control events for SWR^+ candidates, labeled as SWR^- candidates, were detected by randomly shuffling the timestamps of SWR^+ candidates across all trials and subjects. The resulting SWR^+/SWR^- candidates were then visually inspected.

2.4. Defining SWRs from putative hippocampal CA1 regions using UMAP clustering

Potential SWRs were differentiated from SWR candidates in putative CA1 (cornu Ammonis 1) regions. These regions were initially defined as follows: SWR^+/SWR^- candidates in the hippocampus were projected into a two-dimensional space based on overlapping spike counts per unit using a supervised method, UMAP (Uniform Manifold Approximation and Projection) [51]. Clustering validation was performed by calculating the silhouette score [52] from clustered samples. Regions in the hippocampus, which scored above 0.6 on average across sessions (75^{th} percentile), were identified as putative CA1 regions, resulting in the identification of five electrode positions from five patients.

SWR^+/SWR^- candidates in these predetermined CA1 regions were categorized as SWR^+/SWR^-, and thus they no longer retained their candidate status. The duration and ripple band peak amplitude of SWRs were found to follow log-normal distributions. Each time period of SWR was partitioned relative to the time from the SWR center into pre- (at −800 ms to −300 ms from the SWR center), mid- (at −250 to +250 ms), and post-SWR (at +300 to +800 ms) times.

2.5. Statistical Evaluation

Both the Brunner–Munzel test and the Kruskal-Wallis test were executed using the SciPy package in Python [53]. Correlational analysis was conducted by determining the rank of the observed correlation coefficient within its associated set-size-shuffled surrogate using a customized Python script. The bootstrap test was implemented with an in-house Python script.

3. Results

3.1. iEEG Recording and NT in MTL Regions during the Sternberg Task

Our analysis employed a publicly accessible dataset [38], which comprises LFP signals (Figure **??**A) from MTL regions (Table 1) recorded during the execution of the modified Sternberg task. We extracted SWR^+ candidates from LFP signals that were filtered in the 80–140 Hz ripple band (Figure **??**B), originating in all hippocampal regions (refer to Methods section). Meanwhile, SWR^- candidates, control events for SWR^+ candidates, were defined at the same timestamps but distributed across different trials (Figure **??**). The dataset encompassed multi-unit spikes (Figure **??**C), recognized via a spike sorting algorithm [48]. Employing GPFA [39], we applied this to 50-ms windows of binned multi-unit activity without overlaps to determine the NTs, or factors, of MTL regions by session and region (Figure **??**D). We normalized each factor per session and region, for instance, session #2 in AHL of subject #1. We then calculated the Euclidean distance from the origin (O) (Figure **??**E).

3.2. Correlation of Hippocampal NT with the Sternberg Task

Figure **??**A exhibits a distribution of median NTs, comprising 50 trials, within the three main factor spaces. Utilizing the elbow method, we established the optimal embedding dimension for the GPFA model as three (Figure **??**B). The NT distance from the origin (O) — represented as $\|g_F\|$, $\|g_E\|$, $\|g_M\|$, and $\|g_R\|$ — in the hippocampus surpassed the corresponding distances in the EC and amygdala (Figure **??**C & D).[1]

Similarly, we computed the distances between the geometric medians of four phases, namely $\|g_F g_E\|$, $\|g_F g_M\|$, $\|g_F g_R\|$, $\|g_E g_M\|$, $\|g_E g_R\|$, and $\|g_M g_R\|$. The hippocampus showed larger distances between phases than those in the EC and amygdala. [2]

3.3. Memory-Load-Dependent NT Distance between Encoding and Retrieval States in the Hippocampus

Regarding memory load in the Sternberg task, we observed a negative correlation between the correct rate of trials and the set size, which denotes the number of letters to be encoded (Figure **??**A).[3] Concomitantly, a positive correlation was noted between the response time and set size (Figure **??**B).[4].

[1]Hippocampus: Distance = 1.11 [1.01], median [IQR], n = 195,681 timepoints; EC: Distance = 0.94 [1.10], median [IQR], n = 133,761 timepoints; Amygdala: Distance = 0.78 [0.88], median [IQR], n = 165,281 timepoints.

[2]Hippocampus: Distance = 0.60 [0.70], median [IQR], n = 8,772 combinations; EC: Distance = 0.28 [0.52], median [IQR], n = 5,017 combinations ($p < 0.01$; Brunner–Munzel test); Amygdala: Distance = 0.24 [0.42], median [IQR], n = 7,466 combinations ($p < 0.01$; Brunner–Munzel test).

[3]Correct rate: set size four (0.99 ±0.11, mean ±SD; n = 333 trials) vs. set size six (0.93 ±0.26; n = 278 trials; $p < 0.001$, Brunner–Munzel test with Bonferroni correction) and set size eight (0.87 ±0.34; n = 275 trials; $p < 0.05$; Brunner–Munzel test with Bonferroni correction). Generally, $p < 0.001$ for Kruskal–Wallis test; correlation coefficient = - 0.20, $p < 0.001$.

[4]Response time: set size four (1.26 ±0.45 s; n = 333 trials) vs. set size six (1.53 ±0.91 s; n = 278 trials) and set size eight (1.66 ±0.80 s; n = 275 trials). All comparisons $p <$ 0.001, Brunner–Munzel test with Bonferroni correction; $p < 0.001$ for Kruskal–Wallis test;

Next, we discovered a positive correlation between set size and the NT distance separating the encoding and retrieval phases ($\log_{10}\|g_E g_R\|$) (Figure **??**C).[5]. However, distances between other phase combinations did not highlight statistically significant correlations (Figures **??**D and **??**).

3.4. Detection of Hippocampal SWRs from Putative CA1 Regions

To enhance the precision of recording sites and SWR detection, we approximated the electrode placements in the CA1 regions of the hippocampus using distinguished multi-unit spike patterns during SWR events. SWR^+/SWR^- candidates from each session and hippocampal region were embedded in two-dimensional space using UMAP (Figure **??**A).[6] With the silhouette score as a quality metric for clustering (Figure **??**B and Table 2), recording sites demonstrating an average silhouette score exceeding 0.6 across all sessions were identified as putative CA1 regions.[7] (Tables 2 and 3). We identified five putative CA1 regions, four of which were not indicated as seizure onset zones (Table 1).

Subsequently, SWR^+/SWR^- candidates within these putative CA1 regions were labeled as SWR^+ and SWR^-, respectively[8] (Table 3). Both SWR^+ and SWR^- manifested identical durations [9] due to their definitions and followed a log-normal distribution (Figure **??**C). During the initial 400 ms of the retrieval phase, an increase in SWR^+ incidence was found[10] (Figure **??**D).

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correlation coefficient = 0.22, $p < 0.001$

[5]Correlation between set size and $\log_{10}(\|g_E g_R\|)$: correlation coefficient = 0.05, $p < 0.001$. Specific values: $\|g_E g_R\| = 0.54$ [0.70] for set size four, $n = 447$; $\|g_E g_R\| = 0.58$ [0.66] for set size six, $n = 381$; $\|g_E g_R\| = 0.61$ [0.63] for set size eight, $n = 395$.

[6]Consider the AHL in session #1 of subject #1 as a case in point.

[7]The identified regions were the AHL of subject #1, AHR of subject #3, PHL of subject #4, AHL of subject #6, and AHR of subject #9.

[8]These definitions produced equal counts for both categories: SWR^+ (n = 1,170) and SWR^- (n = 1,170).

[9]These definitions result in equal durations for both categories: SWR^+ (93.0 [65.4] ms) and SWR^- (93.0 [65.4] ms).

[10]SWR^+ increased against the bootstrap sample; 95th percentile = 0.42 [Hz]; $p < 0.05$.

The peak ripple band amplitude of SWR^+ surpassed that of SWR^- and followed a log-normal distribution (Figure **??**E).[11].

3.5. Transient Change in Hippocampal NT during SWR

We assessed the 'distance' of the NT from the origin (O) during SWR events in both encoding and retrieval phases (Figure **??**A). Observing the increase in distance during SWR, as illustrated in Figure **??**A, we categorized each SWR into three stages: pre-, mid-, and post-SWR. Hence, the distances from the origin O during those SWR intervals are identified as $\|\text{pre-eSWR}^+\|$, $\|\text{mid-eSWR}^+\|$ and others.

As a result, $\|\text{mid-eSWR}^+\|$[12] exceeded $\|\text{pre-eSWR}^+\|$[13], and $\|\text{mid-rSWR}^+\|$[14] was larger than $\|\text{pre-rSWR}^+\|$ in both the Match IN and Mismatch OUT tasks.[15].

3.6. Visualization of Hippocampal NT during SWR in Two-Dimensional Spaces

Having observed NT 'jumping' during SWR (Figure **??**), we visualized the three-dimensional NTs of pre-, mid-, and post-SWR events during the encoding and retrieval phases (Figure **??**). The distance between these was found to be memory-load dependent (Figure **??**).

To provide two-dimensional visualization, we linearly aligned peri-SWR NTs by setting g_E at the origin (0, 0) and g_R at ($\|g_E g_R\|$, 0). Subsequently, we rotated these aligned NTs around the $g_E g_R$ axis (the x axis), ensuring that the distances from the origin O in the original three-dimensional spaces

[11] SWR^+ (3.05 [0.85] SD of baseline, median [IQR]; n = 1,170) vs. SWR^- (2.37 [0.33] SD of baseline, median [IQR]; n = 1,170; $p < 0.001$; Brunner–Munzel test).

[12] 1.25 [1.30], median [IQR], n = 1,281 in Match IN task; 1.12 [1.35], median [IQR], n = 1,163 in Mismatch OUT task

[13] 1.08 [1.07], median [IQR], n = 1,149 in Match IN task; 0.90 [1.12], median [IQR], n = 1,088 in Mismatch OUT task

[14] 1.32 [1.24], median [IQR], n = 935 in Match IN task; 1.15 [1.26], median [IQR], n = 891 in Mismatch OUT task

[15] 1.19 [0.96], median [IQR], n = 673 in Match IN task; 0.94 [0.88], median [IQR], n = 664 in Mismatch OUT task

and angles from $\overrightarrow{g_E g_R}$ are retained in the two-dimensional equivalent.

Scatter plot visualization of NTs within these two-dimensional spaces revealed distinct distributions of peri-SWR NTs based on phases and task types. A notable example of this is the observation that the magnitude of $\|\text{mid-eSWR}^+\|$ exceeds that of $\|\text{pre-eSWR}^+\|$ (Figure **??**B), which is consistent with our previous observations (Figure **??**).

3.7. Fluctuations of Hippocampal NTs between Encoding and Retrieval States

Subsequently, we investigated the 'direction' of the NT in relation to $\overrightarrow{g_E g_R}$, which was found to be dependent on memory load (Figure **??**). The directions of the SWRs were determined by the NT at −250 ms and +250 ms from their center, denoted as, for example, $\overrightarrow{\text{eSWR}^+}$. We calculated the cosine similarities between $\overrightarrow{g_E g_R}$, $\overrightarrow{\text{eSWR}}$, and $\overrightarrow{\text{rSWR}}$ in both SWR (SWR^+) and baseline periods (SWR^-) (Figure **??**A–D).

$\overrightarrow{\text{rSWR}^-} \cdot \overrightarrow{g_E g_R}$ exhibited a biphasic distribution. By computing the difference between the distribution of $\overrightarrow{\text{rSWR}^+} \cdot \overrightarrow{g_E g_R}$ (Figure **??**A & B) and that of $\overrightarrow{\text{rSWR}^-} \cdot \overrightarrow{g_E g_R}$ (Figure **??**C & D), we were able to determine the contributions of SWR (Figure **??**E & F), which indicated a shift in the direction of $\overrightarrow{g_E g_R}$ (Figure **??**E & F: *red rectangles*).

Furthermore, $\overrightarrow{\text{eSWR}^+} \cdot \overrightarrow{\text{rSWR}^+}$ was less than $\overrightarrow{\text{eSWR}^-} \cdot \overrightarrow{\text{rSWR}^-}$ strictly in Mismatch OUT task (Figure **??**F: *pink circles*). In other words, eSWR and rSWR pointed in the opposite direction exclusively in Mismatch OUT task but not Match IN task (Figure **??**E: *pink circles*).

4. Discussion

This study hypothesizes that in low-dimensional spaces during a WM task in humans, hippocampal neurons form unique NTs, primarily during SWR periods. Initially, multi-unit spikes in the MTL regions were projected onto three-dimensional spaces during a Sternberg task using GPFA (Figure **??**D–E & Figure **??**A). The NT distances across WM phases ($\|g_F g_E\|$, $\|g_F g_M\|$, $\|g_F g_R\|$, $\|g_E g_M\|$, $\|g_E g_R\|$, and $\|g_M g_R\|$) were significantly larger in

the hippocampus compared to the EC and amygdala (Figure **??**C–E), indicating dynamic and responsive neural activity in the hippocampus during the WM task. Also, in the hippocampus, the NT distance between the encoding and retrieval phases ($\|g_F g_E\|$) correlated positively with memory load (Figure **??**C–D), reflecting WM processing. The hippocampal neural NT transiently expanded during SWRs (Figure **??**). Lastly, the hippocampal neural NT alternated between encoding and retrieval states, transitioning from encoding to retrieval during SWR events (Figure **??**). These findings explain aspects of hippocampal neural activity during a WM task in humans and offer new insights into SWRs as a state-switching element in hippocampal neural states.

The distance of the neural NT across the phases was significantly longer in the hippocampus compared to the EC and amygdala, even when considering the distance from O in these regions (Figure **??**C–E). This establishes the involvement of the hippocampus in the WM task, corroborating previous studies indicating hippocampal persistent firing during the maintenance phase [4, 5, 6, 3]. However, in the present study, applying GPFA to multi-unit activity during a one-second level resolution of the WM task revealed that the neural NT in low-dimensional space presented a memory-load dependency between the encoding and retrieval phases, denoted as $\|g_E g_R\|$ (Figure **??**). These findings support the association of the hippocampus with WM processing.

Our analysis focused on putative CA1 regions (Figure **??**) in order to enhance the validity of recording site and the true positive rate of SWR detection. This criterion is supported by accumulated evidence. For instance, SWRs synchronize with spike bursts of interneuron and pyramidal neuron [54, 55, 56, 57], potentially within a 50 μm radius of the recording site [58]. Additionally, we identified increased incidence of SWRs during the first 0–400 ms of the retrieval phase (Figure **??**D). This finding aligns with previous reports of heightened SWR occurrence preceding spontaneous verbal recall [21, 22], extending our understanding to a triggered retrieval

condition. Moreover, the log-normal distributions of both SWR duration and ripple band peak amplitude observed in this study (Figure **??**C & E) coincide with the consensus in this field [49]. Therefore, these results support the electrode placement and detected SWRs in this study. One could argue that the neural trajectory (NT) distance increase from O during sharp wave-ripples (SWRs) (Figure **??**) may be artificially inflated towards higher values due to channel selection using UMAP clustering on spike counts. However, this potential bias does not affect the direction of NT, the memory-load dependency, nor the WM task dependency identified in this study.

Interestingly, during the retrieval phase, NT directions alternated between encoding and retrieval states during both baseline and SWR periods in a task-dependent manner (Figure **??**C & D). Additionally, the balance of this fluctuation transitioned from encoding to retrieval state during SWR events (Figure **??** E & F). These results align with previous studies on the role of SWR in memory retrieval [21, 22]. Our findings suggest that (i) neuronal oscillation between encoding and retrieval states occurs during a WM task and (ii) SWR events serve as indicators of the transition in hippocampal neural states from encoding to retrieval during a WM task.

Moreover, our study noted differences specific to the WM-task type between encoding- and retrieval-SWRs (Figure **??**E–F). Notably, opposing movements of encoding-SWR (eSWR) and retrieval-SWR (rSWR) were not observed in Match IN task but were apparent in Mismatch OUT task. Memory engram theory [59] might explain these observations: Match In task presented participants with previously shown letters, while Mismatch OUT task introduced a new letter absent in the encoding phase. This explanation underscores the significant role of SWR in human cognitive processes.

In conclusion, this study illustrates that during a WM task in humans, hippocampal activity fluctuate between encoding and retrieval states, uniquely transitioning from encoding to retrieval during SWR events. These findings offer novel insights into the neural correlates and functionality of working memory within the hippocampus.

Data Availability Statement

The data is available on G-Node (https://doi. gin.g-node.org/10.12751/g-node.d76994/). The source code is available on GitHub (https://github.com/yanagisawa-lab/ hippocampal-neural-fluctuations-during-a-WM-task-in-humans).

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Ethics Declarations

All study participants provided their written informed consent, subsequent to the approval from the pertinent institutional ethics review board (Kantonale Ethikkommission Zürich, PB 2016–02055).

Author Contributions

Y.W. and T.Y. conceptualized the study; Y.W. performed the data analysis; Y.W. and T.Y. wrote the original draft; and all authors reviewed the final manuscript.

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Declaration of Interests

The authors declare that they have no competing interests.

Inclusion and Diversity Statement

We support inclusive, diverse, and equitable conduct of research.

Declaration of Generative AI in Scientific Writing

The authors employed ChatGPT, provided by OpenAI, for enhancing the manuscript's English language quality. After incorporating the suggested improvements, the authors meticulously revised the content. Ultimate responsibility for the final content of this publication rests entirely with the authors.

Tables

Subject ID	# of sessions	AHL	AHR	PHL	PHR	ECL	ECR	AL	AR	
1	4	✓	n.a.	✓	✓	✓	n.a.	✓	n.a.	A
2	7	✓	✓	✓	✓	✓	✓	✓	✓	AH
3	3	✓	✓	✓	✓	✓	✓	✓	n.a.	AH
4	2	✓	✓	✓	✓	✓	✓	✓	✓	AHL & AH
5	3	✓	n.a.	n.a.	✓	n.a.	n.a.	✓	n.a.	
6	6	✓	✓	✓	✓	✓	✓	✓	✓	AHL & P
7	4	✓	✓	✓	✓	✓	✓	✓	✓	AH
8	5	✓	✓	✓	✓	✓	✓	✓	✓	
9	2	✓	✓	✓	✓	✓	✓	✓	✓	E

Table 1 – Electrode Distribution within the Dataset

This figure denotes the placements of electrodes and seizure onset zones. Regions marked with ✓were included in the dataset, while those imprinted with n.a. were absent. The abbreviations used are as follows: AHL, left hippocampal head; AHR, right hippocampal head; PHL, left hippocampal body; PHR, right hippocampal body; ECL, left entorhinal cortex; ECR, right entorhinal cortex; AL, left amygdala; AR, right amygdala; SOZ represents the seizure onset zone.

Subject	AHL	AHR	PHL	PHR
1	0.60 ± 0.14	n.a.	n.a.	0.1 ± 0
2	0.21 ± 0.16	0.17 ± 0.21	0.18 ± 0.22	0.20 ± 0.15
3	0.40 ± 0.42	0.83 ± 0.12	n.a.	n.a.
4	0.10 ± 0.00	0.10 ± 0.00	0.90 ± 0.00	0.10 ± 0.14
5	n.a.	n.a.	n.a.	n.a.
6	0.63 ± 0.06	n.a.	n.a.	0.27 ± 0.06
7	0.10 ± 0.00	0.35 ± 0.35	0.37 ± 0.47	0.10 ± 0.00
8	0.13 ± 0.10	n.a.	0.28 ± 0.49	n.a.
9	n.a.	0.85 ± 0.07	0.15 ± 0.07	n.a.

Table 2 – Silhouette Score of UMAP Clustering for SWR^{+} Candidates and SWR^{-} Candidates

The silhouette scores (mean ±SD across sessions per subject) for UMAP clustering of SWR^{+} candidates and SWR^{-} candidates are based on their respective multi-unit spike patterns (Figure **??**A). The mean scores were 0.205 and the standard deviation was 0.285, calculated for the interquartile range (IQR; Figure **??**B).

Subject ID	# of sessions	# of trials	ROI	# of SWRs	SWR incidence [Hz]
#1	2	100	AHL	274	0.34
#3	2	97	AHR	325	0.42
#4	2	99	PHL	202	0.26
#6	2	100	AHL	297	0.37
#9	2	97	AHR	72	0.09
	Total = 10	Total = 493		Total = 1170	0.30 ± 0.13 (mean ± SD)

Table 3 – Summary of Detected SWRs

The table provides statistics of presumptive CA1 regions and SWR events. Only the initial two sessions (sessions 1 and 2) from each subject were included in our analysis to reduce sampling bias.

Figures