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Bc. Lucie Drahoňovská

REM Sleep and Emotional Processing:

Insights from the Ventral Hippocampus in Rats

Master's thesis

Supervisor: Karolína Korvasová, M.Sc., Dr. rer. nat.

Advisor: Ing. Katarína Studeničová

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PROHLÁŠENÍ

Prohlašuji, že jsem závěrečnou práci zpracovala samostatně a že jsem uvedla všechny použité informační zdroje a literaturu. Tato práce ani její podstatná část nebyla předložena k získání jiného nebo stejného akademického titulu.

V Praze, 2.8.2025

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ABSTRACT

In memory-related processes, sleep plays a pivotal role, with most studies focusing on non-rapid eye movement (NREM) sleep. On the other hand, rapid eye movement (REM) sleep has been hypothesized to contribute uniquely to emotional processing. The hippocampus is a neural structure critical for memory and spatial navigation, with extensive literature documenting the dorsal hippocampus's involvement in these domains. In contrast, the ventral hippocampus remains comparatively understudied, although emerging evidence implicates its roles in emotional regulation. This thesis seeks to bridge these ideas by investigating how emotional experiences modulate ventral hippocampal activity during REM sleep. Using electrophysiological data recorded from the rat hippocampus after either rewarding or aversive waking experiences, we examine changes in sleep architecture and neural dynamics. First, we characterize sleep structure, such as the duration of sleep epochs and sleep depth. We found minor variations linked to the valence of the preceding experience, with more prominent effects arising from circadian factors. Subsequent analyses of local field potentials focused on spectral power and phase locking within hippocampal oscillations, revealing no significant differences between reward and aversion conditions. Crucially, correlation analyses between anatomical locations within the gamma frequency band identified a reduction in dorso-ventral hippocampal coordination following aversive experiences. These findings suggest the active role of REM sleep in emotional regulation, as implemented across subcortical regions.

KEYWORDS

Hippocampus, emotional memory, ventral hippocampus, REM sleep, local field potential

ABSTRAKT

V procesech spojených s emoční pamětí hraje spánek vždy klíčovou roli, přičemž většina studií se zaměřuje především na non-rapid eye movement (NREM) spánek. Na druhou stranu existují hypotézy, že rapid eye movement (REM) spánek přispívá výlučně ke zpracování emocí. Hipokampus je mozková struktura klíčová pro paměť a prostorovou orientaci. Zapojení dorzální části hipokampu v těchto oblastech je v literatuře důsledně zdokumentováno a ačkoli v prostudování ventrálního hipokampu zůstávají značné mezery, nově vznikající studie mu přisuzují roli v emoční regulaci. Tato diplomová práce si dává za cíl propojit tyto poznatky pomocí analýzy toho, jak emoční zkušenosti modulují aktivitu ventrálního hipokampu po během REM spánku. Pomocí elektrofyziologických dat nahraných z krysího hipokampu po odměňující nebo averzivní zážitcích z bdělého stavu zkoumáme změny ve spánkové architektuře a nervové dynamice. Nejprve charakterizujeme spánkovou strukturu, například délku jednotlivých spánkových epoch a hloubku spánku. Zjistili jsme drobné rozdíly související valencí předchozí zkušenosti, přičemž výraznější efekty však vyplývaly z cirkadiánních faktorů. Následné analýzy local field potentials se zaměřili na spectral power - sílu signálu, a phase locking value - míru koordinace fází více frekvencí, v rámci hipokampálních oscilací, přičemž mezi podmínkami zahrnujícími odměny a tresty nebyly nalezeny žádné významné rozdíly. Klíčové výsledky však odhalila korelační analýza mezi anatomickými oblastmi v gamma frekvenčním pásmu odhalila sníženou koordinaci mezi dorzálním a ventrálním hipokampem po averzivních zážitcích. Tato zjištění naznačují aktivní roli REM spánku v regulaci emocí, která se uskutečňuje prostřednictvím subkortikálních oblastí

KLÍČOVÁ SLOVA

Hipokampus, emoční paměť, ventrální hipokampus, REM spánek, local field potential

ABBREVIATIONS

REM	rapid eye movement
NREM	non-rapid eye movement
LFP	local field potential
vHPC	ventral hippocampus
dHPC	dorsal hippocampus
mPFC	medial prefrontal cortex
PSD	power spectral density
M/E normalization	morning / evening normalization
norm.u.	normalized units
a.u.	arbitrary units
PLV	phase locking value

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1. INTRODUCTION

1.1. MOTIVATION

Newly acquired experiences are consolidated into long-term memories mostly during sleep. Daily life experience and research (Kensinger & Ford, 2020; Talmi, 2013) show that the brain prefers to remember memories with emotional relevance, but the precise mechanism of the memory selection process so far remains unknown. In this thesis, we investigate the neural response to positively and negatively motivated learning during subsequent sleep.

The hippocampus is a structure well known for its roles in memory formation and spatial navigation. Due to historical and technical reasons, most studies have focused on the dorsal hippocampus (dHPC), leaving the ventral hippocampus (vHPC) comparatively less explored. Anatomically and functionally, the ventral hippocampus is hypothesized to act as an interface between the amygdala, dHPC, and other limbic structures, providing emotional context to spatial memories formed in the dorsal regions.

Substantial progress has been made in understanding emotional memory processing in the hippocampus during active wakefulness, and recent efforts of Morici and colleagues (Sleep and emotional memory lab, Sorbonne University, INSERM, Paris) have expanded this investigation into NREM sleep (Morici et al., 2024). It has been proposed that REM sleep also plays a key role in the consolidation of emotional memories (Wagner et al., 2001). However, to our knowledge, no studies have specifically examined the connection between the properties of rodent vHPC during REM sleep and emotional valence.

This thesis aims to address the gap by complementing F. Morici's NREM analysis with an investigation of REM sleep using the same electrophysiological dataset. The goal is to further test the hypothesis that vHPC facilitates the flow of emotional memory components across structures and their incorporation with spatial memories from dHPC.

1.2. HIPPOCAMPUS

The hippocampus is a highly studied part of the mammal brain, primarily linked to declarative memory (Packard & Knowlton, 2002). Its name originates from its curved shape, which resembles a seahorse in humans. In rats, the hippocampus lies beneath the neocortex and has a characteristic cashew-like shape. It is commonly divided into two functionally distinct subregions: the dorsal hippocampus (dHPC) and the ventral hippocampus (vHPC) (Figure 1.). The dHPC is closely connected to the entorhinal cortex, which contains spatially tuned neurons called grid cells (Hafting et al., 2005). These connections make the dHPC essential for spatial processing (Fyhn et al., 2004). The dHPC also contains place cells - neurons that become active when the rat is at a particular location (O'Keefe, 1976) and are reactivated during sleep as a part of memory consolidation (Wilson & McNaughton, 1994).

In contrast, the vHPC is anatomically connected to the prefrontal cortex (Verwer et al., 1997) and amygdala (Cenquizca & Swanson, 2007), which together with other structures form a fundamental circuit involved in emotional processing and fear-related behavior (Han et al., 2023). The role of vHPC in emotion has been supported by numerous studies involving lesions or pharmacological inhibition, which often lead to alterations in anxiety-like or emotional behavior (Bannerman et al., 2004; Kjelstrup et al., 2002). Similarly, the spatial role of dHPC has been validated through lesion studies showing impairment in navigation tasks (Ferbinteanu & McDonald, 2001; Pothuizen et al., 2004).

As reviewed in (Pronier et al., 2023; Strange et al., 2014), studies suggest that this dichotomy may be overly simplistic. Instead, the hippocampus may be organized along a functional gradient, with spatial processing dominant in the dorsal region and emotional processing increasingly represented toward the ventral pole.

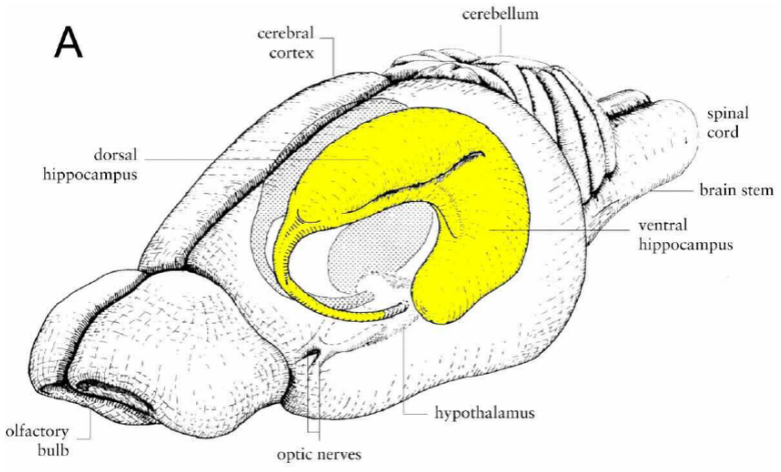

Figure 1. *Diagram of the rats' brain with highlighted hippocampus. Original from (Cheung & Cardinal, 2005) adapted in (Little, n.d.)*

1.3. LOCAL FIELD POTENTIAL

Local field potential (LFP) is an electric potential primarily reflecting extracellular currents generated by neural activity in the brain. LFPs are recorded in the extracellular medium of the brain tissue using intracranial electrodes placed directly into the brain(Buzsáki et al., 2012; Herreras, 2016). These signals are shaped by a combination of multiple sources, with synaptic activity as the most prominent contributor. Synaptic activity alters the membrane potential near synapses, sites of communication between neurons, through the flow of ions into or out of cells. This ionic movement produces extracellular sources or sinks, which, if synchronized across enough neurons, can then be detected by the electrodes and recorded as LFPs (Buzsáki et al., 2012).

Most studies focus on specific frequency components rather than analyzing the raw composite signal, which can be extracted using various signal processing techniques.

1.4. BRAIN OSCILLATIONS

Brain oscillations are rhythmic changes in electrical voltages present in different parts of the brain. They are formed by synchronized neuronal activity of a large number of neurons firing with the same frequency. There are at least five main frequency ranges with different characteristics and functions, of which three are important for our study: delta, theta, and gamma (Figure 2.) (Abhang et al., 2016, p. 20). After decades-long disputes about the functional importance of brain oscillations (Singer, 2018), emerging evidence suggests that rhythmic synchronization may be necessary for certain cognitive operations (Colgin, 2016).

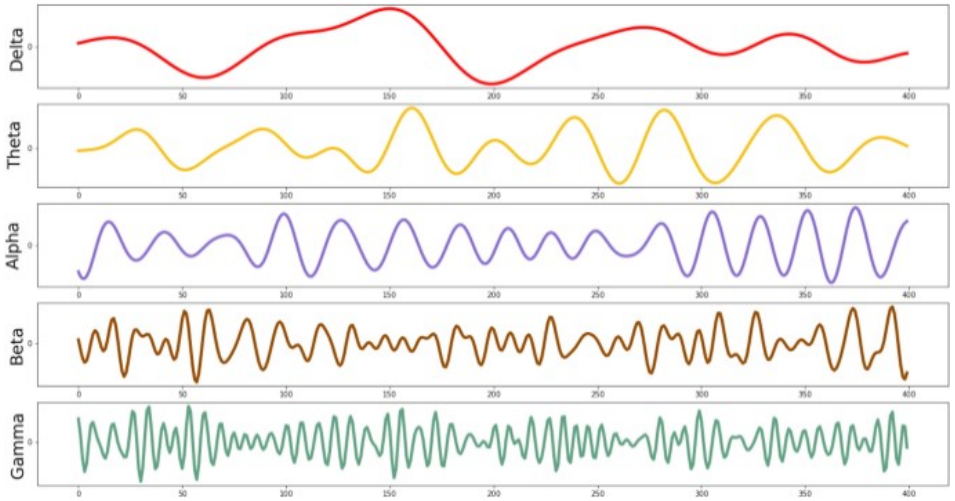

Figure 2. *An illustration of different oscillation frequencies (Pandey et al., 2022), reused for illustrative purposes.*

1.4.1. Delta (0-4 Hz)

Delta oscillations are mainly associated with NREM sleep, where they are significantly stronger than during REM sleep. In fact, delta power serves as a key metric in distinguishing REM from NREM epochs in automated sleep classification (Bastianini et al., 2014; Sunagawa et al., 2013).

Apart from serving as a sleep-stage marker, delta activity has been implicated in memory-related processes. For example, Moroni et al. (2014) demonstrated that hippocampal delta activity (2-4 Hz) increases during NREM following spatial learning, suggesting its role in memory consolidation.

Additionally, delta rhythms are known to synchronize with theta oscillations in various behavioral and cognitive contexts. For example, delta-theta cross-frequency coupling has been observed during auditory stimulus processing (Lakatos et al., 2005) and during the perception of both positive and negative emotional stimuli (Knyazev et al., 2009).

1.4.2. Theta (4-12 Hz)

Theta oscillations occur during rapid eye movement (REM) and active exploration (Buzsáki, 2002). They represent one of the most extensively studied rodent hippocampal rhythms. In

the hippocampus, theta oscillations seem to be necessary for the acquisition of new memories (McNaughton et al., 2006) and accurate navigation (Bolding et al., 2020; O'Keefe & Recce, 1993). It is also known to organize neuronal firing and coordinate the activity of place cells during planning and imagined trajectories (Pfeiffer & Foster, 2013).

Apart from the hippocampus, theta oscillations are also observed in regions such as the amygdala and prefrontal cortex (mPFC) (Han et al., 2023), and often synchronize across these structures (O'Neill et al., 2013; Popa et al., 2010). During wakefulness, synchronized theta rhythms across the hippocampus, amygdala, and mPFC have been linked to the fear memory retrieval (Seidenbecher et al., 2003), and during REM, they are hypothesized to play a role in the consolidation of emotional memories (Popa et al., 2010).

A critical feature of theta rhythm is its interaction with faster gamma oscillations, known as phase-amplitude coupling (Bragin et al., 1995). Theta-gamma coupling is observed both during wake and REM, but it appears to be stronger in REM (Scheffzük et al., 2011). This interaction has been proposed to help organize items in short-term memory by assigning them to different phases of the theta cycle (Lisman & Idiart, 1995). Moreover, theta-gamma coupling has been shown to increase during the retrieval of conditioned fear memories (Lesting et al., 2011), suggesting its involvement in emotionally salient processes.

1.4.3. Gamma (30-47 Hz) and High gamma (53-80 Hz)

In early studies, gamma oscillations were typically treated as a single frequency band with the span of approximately 40-100 Hz (Bragin et al., 1995). However, later work has shown that gamma activity comprises at least two distinct frequency subbands, likely with differing origins and physiological relevance (Csicsvari et al., 2003).

The precise division of gamma subbands differs across studies. For example Colgin et al., (2009) distinguish between low gamma (20-50 Hz) and high gamma (65-140 Hz), while others define three bands, including low gamma (25-50 Hz), mid gamma (50-100 Hz) and high gamma (100 - 150 Hz) (Bergel et al., 2018).

In our analysis, we selected the ranges 30-47 Hz and 53-80 Hz to represent low and high gamma, respectively. This choice was driven by the need to avoid contamination from artificial amplitude amplification at around 50 Hz, caused by power line interference. The low gamma will be called just gamma.

The functional role of hippocampal gamma oscillation, particularly the functional distinction of high and low gamma, remains an active topic of investigation. Gamma oscillations, coupled with theta, are believed to support temporal coordination of neuronal firing, enabling efficient transmission of information across different brain regions (Buzsáki & Chrobak, 1995; Colgin et al., 2009). In human studies, increases of gamma power and gamma phase synchrony have been linked to both memory encoding and retrieval (Fell et al., 2001; Sederberg et al., 2007). Moreover, gamma power has been shown to increase in response to emotionally salient stimuli in regions such as the amygdala and neocortex (Keil et al., 2001). However, a similar effect has not yet been consistently demonstrated in the hippocampus (Lu et al., 2011).

Recent studies suggest that high and low gamma may subserve different cognitive functions. These two bands couple with different phases of the theta cycle. This property has been proposed to reflect their differential involvement in memory processes, with high gamma associated with encoding and low gamma with retrieval (Bieri et al., 2014; Colgin et al., 2009).

In this thesis, the term “gamma” will, from now on refer specifically to low gamma oscillations (30-47Hz), while the term “high gamma” will denote high gamma oscillations (53-80 Hz).

1.5. EMOTIONAL MEMORY AND SLEEP

There are two types of memory: declarative and procedural (Squire, 1992). Procedural memory includes acquired skills, habits, or forms of associative learning such as conditioning. Declarative memory can be further divided into episodic memory, which regards personally experienced events in a spatiotemporal context, and semantic memory, which involves general knowledge that is independent of context (Tulving, 1972). Emotional arousal can positively impact the strength of retention of an associated memory (Kensinger & Ford, 2020).

Emotional memory refers to the processes underlying the consolidation of emotionally charged memories, the modulation of episodic memories by emotional context, and the regulation of regulation responses (Tempesta et al., 2018). Sleep plays a critical role in these processes (Klinzing et al., 2019).

Emotional memory engages a network of brain regions, including the amygdala, medial prefrontal cortex, and hippocampus, especially its ventral part. The coordination among these regions is believed to contribute to the consolidation of conditioned fear memories

during REM sleep (Popa et al., 2010). Interestingly, REM has been found to be modified not only following aversive conditioning (Datta, 2000), but also after appetitive experiences (Perogamvros & Schwartz, 2012), highlighting its role in the consolidation of emotional memory across a broader spectrum of valence.

Another interesting feature of REM sleep in emotional memory is that REM sleep may represent a critical window, during which the network for systems consolidation is being configured. Sleep deprivation immediately following contextual fear conditioning selectively impairs the retrieval of remote, but not recent, emotional memories (Rosier et al., 2018), suggesting that sleep shortly after encoding is essential for long-term emotional memory stabilization.

2. MATERIAL AND METHODS

2.1. EXPERIMENT

Rats were subjected to seven training days on a linear track under rewarding and aversive conditions (Morici et al., 2024). Starting with the reward training, the rats were water-deprived and trained to run back and forth along the track for a drop of water at the end. Later, they were introduced to aversive conditions, in which an electric shock was delivered to their eyelid if the animal remained motionless for a certain time. Animals were able to recognise which condition they were subjected to based on the constant light cue, which was either on (aversive) or off (reward).

Each recording day follows a consistent structure. It began with a baseline sleep used to record neural activity without any prior valence influence. This was followed by the first run on the linear track, then a first recorded post-run sleep, then a second run and a second recorded sleep. Each session had one aversive and one reward run, and their order was chosen pseudorandomly.

2.2. DATASET

The dataset was provided by J.F. Morici from the *Institut du Fer à Moulin, Inserm, Sorbonne Université, Paris*. It consists of electrophysiological local field potential (LFP) recordings from five female rats with 8-shank electrodes implanted in their ventral hippocampus (NeuroNexus Buzsaki64L) and 4-shank electrodes in their dorsal hippocampus (NeuroNexus Buzsaki32). One dorsal and five ventral channels were used for our analysis. One rat was removed from the analysis due to missing data from the dorsal channel, and one recording session (number 20230830 of rat number 165) was removed due to unusual spectral artifacts appearing on the signal recorded from one of the ventral channels. Original 20 kHz data were resampled at a 1250 Hz sampling rate, and sleep stages were manually assigned by the author based on the visual examination of ventral hippocampal (vHPC) and dorsal hippocampal (dHPC) spectrograms and the output from the accelerometer.

2.3. DATA PREPROCESSING

As a first preprocessing step, we standardized LFP signals by computing z-scores across each recording day, channel by channel. This normalization step controlled for variability in

signal amplitude across different recording days and ensured future comparability across epochs and channels. The resulting z-scored LFP data were then segmented into sleep sessions and further subdivided into sleep epochs based on sleep stage classification. Then we omitted the first and last epochs of each sleep session because those were the periods of complete wakefulness before falling asleep and after waking up, and their length was controlled by the technician.

2.4. SLEEP STRUCTURE ANALYSIS

In the sleep structure analysis, we examined several quantitative metrics to assess changes across experimental conditions. These included:

- **Total duration** of each sleep phase per session (REM, NREM, and REM + NREM)
- **Length of individual epochs** (REM, NREM, wake)
- **Number of epochs** of a particular sleep phase (REM, NREM, wake)
- **Latency to sleep onset**
- **Ratio of total REM to NREM duration**
- **Ratio of total (REM + NREM) to total wake duration**
- **Linear slope of epoch lengths** over time within each sleep session

Some of those, if stated, were normalized using one or both normalization procedures, namely:

1. **Morning/evening (M/E) normalization:**
   The target value from every epoch is divided by the mean value across all sleep sessions from the same rat in the corresponding day phase (morning or evening) and sleep stage (REM or NREM).
2. **Sleep length:**
   The length of every epoch is divided by the total length of the whole sleep period within the corresponding sleep session. By the sleep period, we understand the time between the onset of the first and the end of the last REM or NREM epoch in that session.

Group comparisons were computed using the Kruskal-Wallis test.

2.5. POWER STATISTICS

In this part of the analysis, we focused exclusively on REM sleep epochs. The signal from each epoch was processed using Welch's method (scipy.signal.welch) to estimate the average power spectral density (PSD) across a range of frequencies. From the PSDs for all the epochs pooling across all the sessions, the mean spectral power was computed, and the variability across epochs was expressed using standard error of the mean as the error margin.
From the resulting spectra, we retained only the frequency bands of interest: delta (0-4 Hz), theta (4-12 Hz), gamma (30 - 47 Hz), and high gamma (53 - 80 Hz).

To minimize bias, we applied different normalisation strategies depending on the analysis context. In some cases, more than one was used. If so, they were executed in the following order:

1. **Baseline normalisation**:
   The power of the signal in each REM epoch in a given frequency band was divided by the mean power of the signal in that frequency band across all REM epochs from the baseline sleep session within the same recording day.
2. **Morning/evening (M/E) normalisation**:
   Each REM sleep epoch's power was divided by the mean power of the signal in the corresponding frequency band from all epochs in the same day phase (morning or evening) sleep sessions, from all recording days of the same rat.

2.6. CORRELATION STATISTICS

Next, we investigate temporal changes in frequency-band power, synchrony between ventral and dorsal hippocampal channels in REM, and potential context-dependent differences in this synchrony.

For this analysis, we used data in the same format as in the power analysis - namely, one average power value per REM epoch for each frequency band. We investigated whether temporal changes in average power across REM epochs within a sleep session were correlated between the dorsal and ventral hippocampal channels.

For each session, we constructed a time series of frequency-band power of the signal in each REM epoch for the dHPC and every vHPC channel. We then computed the Pearson correlation coefficient (scipy.stats.pearsonr) between the dorsal series and each of the five

ventral series individually. This yielded five Pearson coefficients per session corresponding to the five ventral hippocampal channels.

These values formed a distribution of dorso-ventral correlation of strengths across sessions and rats. We compared these correlation distributions across conditions using the Kruskal-Wallis test to assess whether the degree of dorso-ventral coupling of any frequency band varied by experimental context (baseline, aversive, reward).

2.7. CROSS-FREQUENCY COUPLING ANALYSIS

To examine the relationship between frequency bands, we analyzed the cross-frequency coupling of the theta oscillation phase and the gamma amplitude envelope phase.

LFP signals were first bandpass-filtered using a 4th-order Butterworth filter (elephant.signal_processing.butter) to isolate distinct frequency bands. The theta band signal was then transformed into analytic form using the Hilbert transform (scipy.signal.hilbert). The phase represents the shift of the signal within its oscillatory cycle at a given time point and was computed as the angle of the analytic signal using np.angle.

To compute the gamma amplitude envelope, we also applied the Hilbert transform (scipy.signal.hilbert), this time to the gamma-filtered signal, took the absolute value of the resulting signal, and z-scored it to match the range of values of the gamma envelope to that of theta. A second Hilbert transform was applied to the z-scored envelope to obtain its analytic representation, from which the phase of the gamma envelope was extracted using np.angle.

Finally, we quantified the coupling of the phases of slower theta oscillations and faster gamma oscillations' envelope by computing the phase locking value (elephant.phase_analysis.phase_locking_value) of those two features.

To assess the statistical significance of our phase-locking value (PLV) results, we performed a surrogate analysis using a shuffle distribution. Specially, for each epoch, we randomly selected a cut point within the list of gamma envelope phase values, circularly shifted the sequence by swapping the two resulting sublists, and then computed the phase locking value between the shuffled gamma envelope phase data and the original theta phase data from the same epoch. This process effectively destroyed any possible phase-phase relationship, while maintaining the overall phase properties.

For ventral channel analysis, the shuffle distribution was constructed from 2000 surrogate PLVs, generated from the first four REM epochs of the first aversive sleep session of channel v0. A similar procedure was applied to create the dorsal shuffle distribution, using the first four REM epochs of the dorsal channel instead. All surrogate PLVs were derived from recordings of the rat 103.

2.8. SOURCE CODE

The python script for the whole analysis can be found in the GitHub repository.

3. RESULTS

3.1. SLEEP STRUCTURE ANALYSIS

The vast majority of memory consolidation happens during sleep, where each sleep phase plays its role. Many studies that focused on the sleep structure in a neutral environment have shown that the duration and the probability of transition between the REM, NREM, and wake epochs are stochastic (Kim et al., 2009; Lo et al., 2002; Stephenson et al., 2013). In the first part of this section, we will, therefore, focus on analyzing the rats' sleep structure to search for substantial deviations from this neutral state, which could be connected to the processing of memories with emotional valence.

Each recording day comprises a baseline extended sleep period, an aversive run, an extended aversive sleep period, a reward run, and an extended reward sleep period. Each extended sleep period comprises multiple sleep epochs of one of three sleep phases: REM, NREM, or wake. Epochs vary in length, number, and order (Figure 3.). An extended sleep period denotes one sleep recording, including the wake epoch before the animal falls asleep and the one after it completely wakes up. Data in this form is used in Figure 3 for visualization purposes, but for later analyses, the flanking wake epochs will be removed, unless stated otherwise. Extended sleep periods after such truncation will be called sleep sessions.

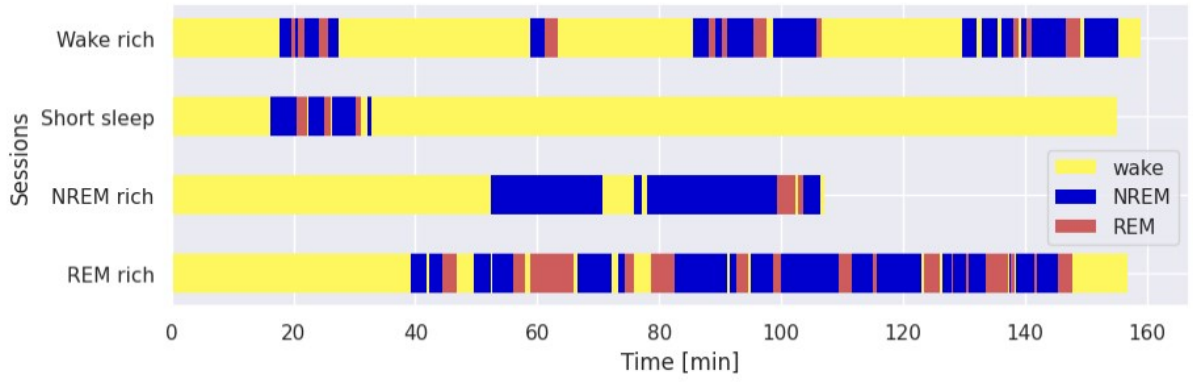

Figure 3. *Visualization of extended sleep periods with different characteristics of sleep architecture.*

Our main interest is to identify the differences between the characteristics of sleep sessions following aversive and reward experiences. We therefore categorize the recordings into three datasets, whose distributions are tested against each other:

- **Baseline** - first sleep sessions of each recording day, unaffected by prior emotional experience
- **Aversive** - sleep sessions following an aversive run
- **Reward** - sleep sessions following a reward run

The order of reward and aversive runs was alternated across recording days. However, the time of the day may also influence sleep architecture. To account for this, we subdivide the original dataset again into two new ones:

- **Morning** - sleep sessions after the first run of the day, regardless of the preceding run type
- **Evening** - sleep sessions after the second run of the day, regardless of the preceding run type

Those are compared both with each other and with the baseline dataset. Although the terms “morning” and “evening” do not necessarily reflect the exact time of recording, they were chosen for clarity in distinguishing between earlier and later sleep sessions within a day.

In (Figure 4.), we can see the aforementioned morning/evening bias in all the tested parameters: total time spent in the REM phase, total time spent in the NREM phase, and total time spent in the REM and NREM phases combined, calculated for each experimental session. In all three cases, the aversive one seems higher than the reward one, but without statistical significance. When we look at the morning and evening distributions, on the other hand, the graph shows that the animals spent significantly more time in REM and NREM phases during the morning sessions than during baseline and evening sessions.

In order to remove the confounding factor of morning VS evening sessions from the analysis, we normalized the investigated variables by their averages across the morning and evening sessions, respectively (further described in the Material and Methods section 2.4). When we correct the total time spent in REM or NREM sleep in each session for the influence of the daytime (Figure 5.), we can see that the animals spent significantly more time in REM and NREM phases after the reward run compared to the aversive run, and that the total sleep length increased. To reject the hypothesis that the difference in the sleep structure is caused solely by the total length of the sleeping session, which could originate from a potential

technical bias, we corrected it for that as well (see Material and methods 2.4.). We can see that the corrected medians are even further apart and have a bigger significance (Figure 6.)

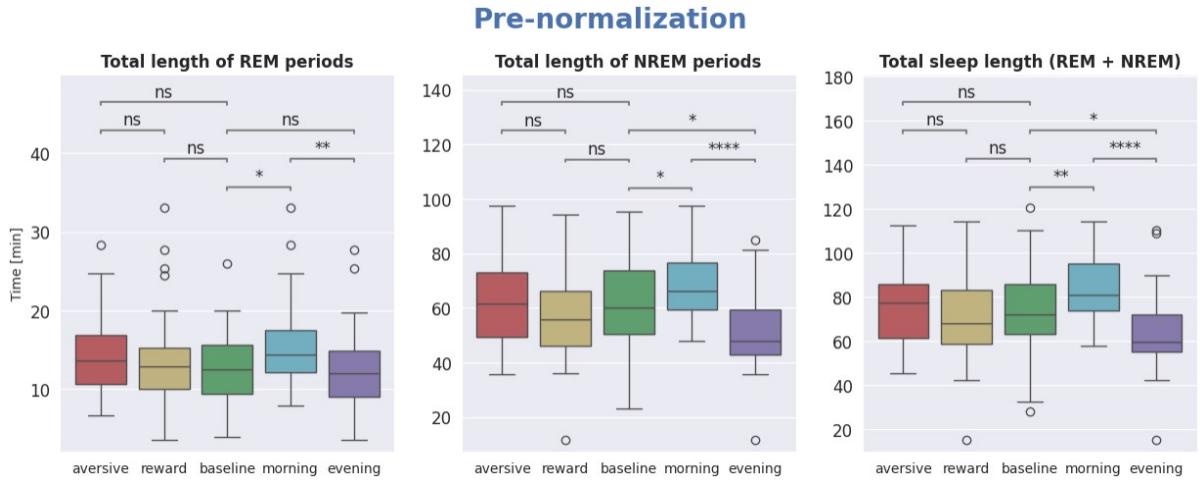

Figure 4. Comparison of the total amount of REM and NREM sleep in a session. Tested by the Kruskal-Wallis test.

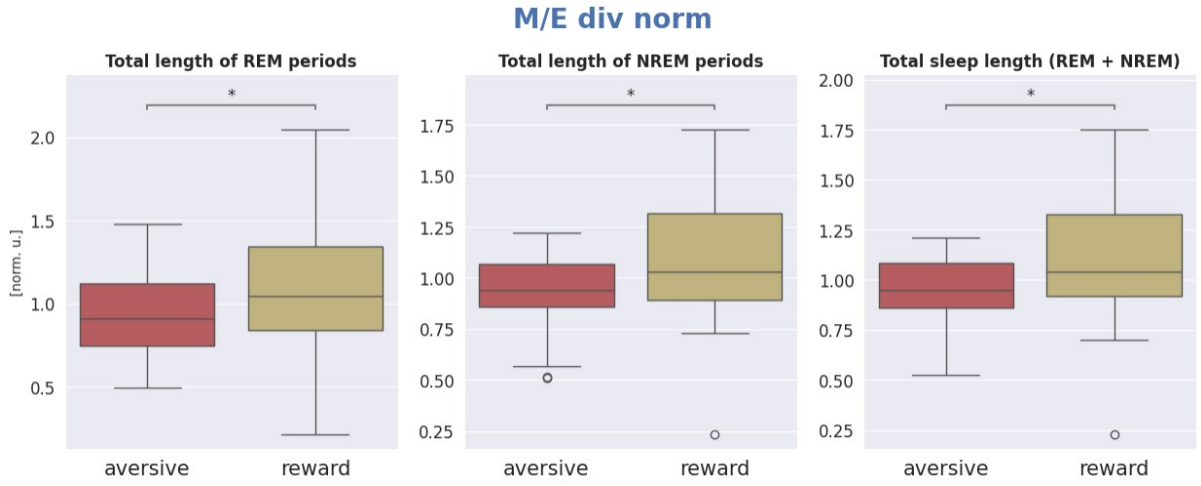

Figure 5. *Comparison of the total amount of REM and NREM sleep in a session after implementing normalization by the day time in which the experiment has been run and tested by the Kruskal-Wallis test.*

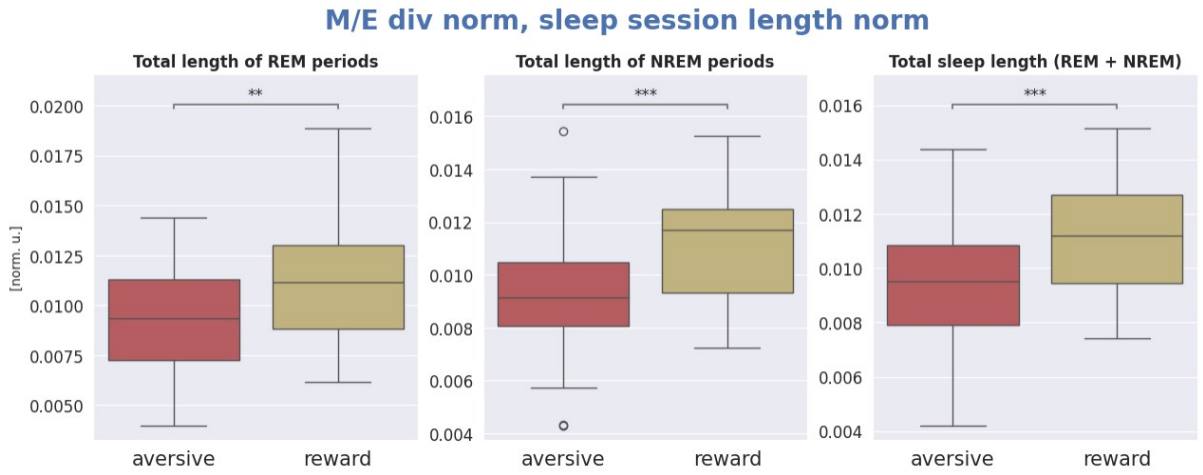

Figure 6. *(total ME length) Comparison of the total amount of REM and NREM sleep in a session after implementing M/E normalization and normalization by the length of the sleep session. Tested by the Kruskal-Wallis test.*

Next, we focus on the length and number of epochs. Although the daytime influence seems to be the strongest factor affecting the length of the epochs, as shown in Figure 7. , we hypothesize that the aversive experience has an additional effect, like REM fragmentation (DaSilva et al., 2011), or increased number of REM epochs after aversive runs (Fogel et al., 2009) that may be masked by the daytime bias. After M/E normalization, we see that the length of REM and NREM epochs is significantly larger, and the length of wake epochs is significantly smaller during reward sleep (Figure 8.) compared to the aversive one. The numbers of different epochs appear the same in all sleep session contexts, even after normalization by the length of the whole sleep session (Figure 9).

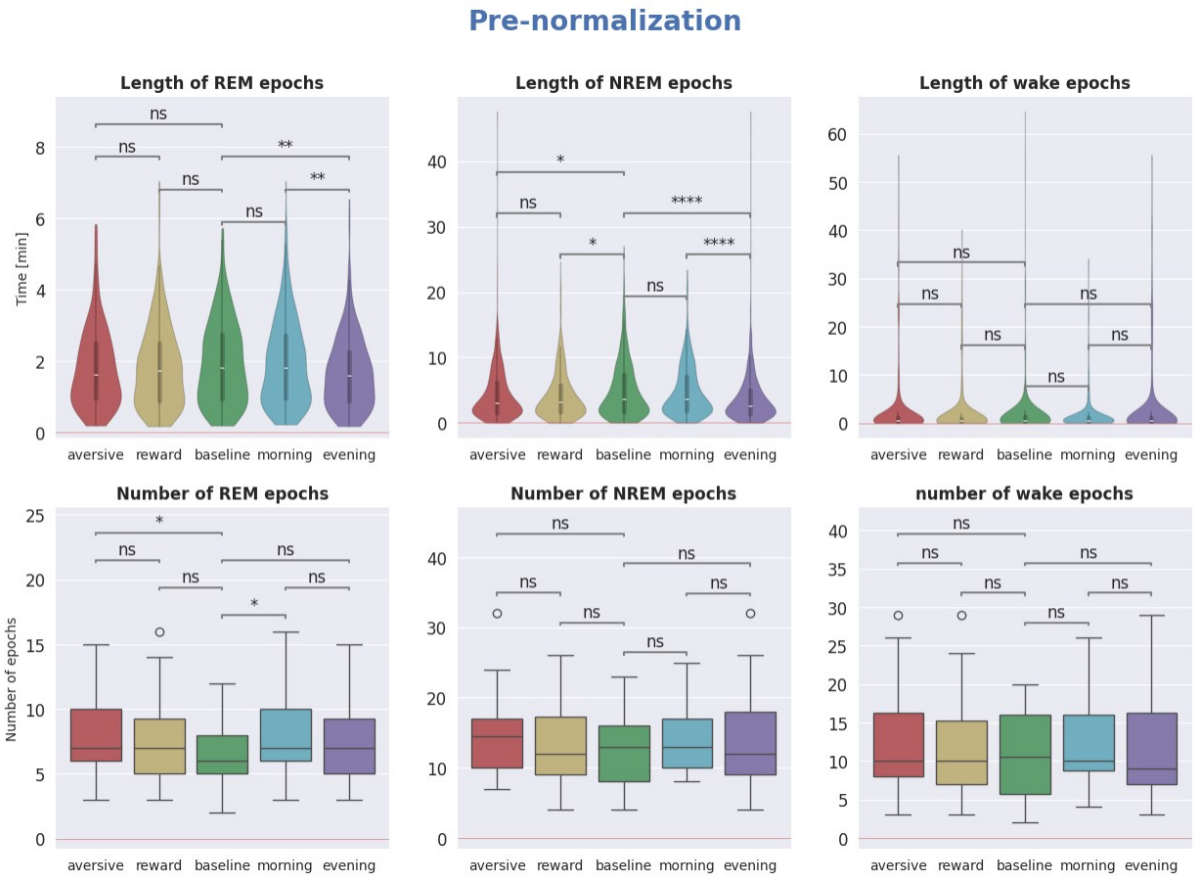

Figure 7. *(length and number pre) Comparison of the length and number of epochs in a sleep session. Tested by the Kruskal-Wallis test*

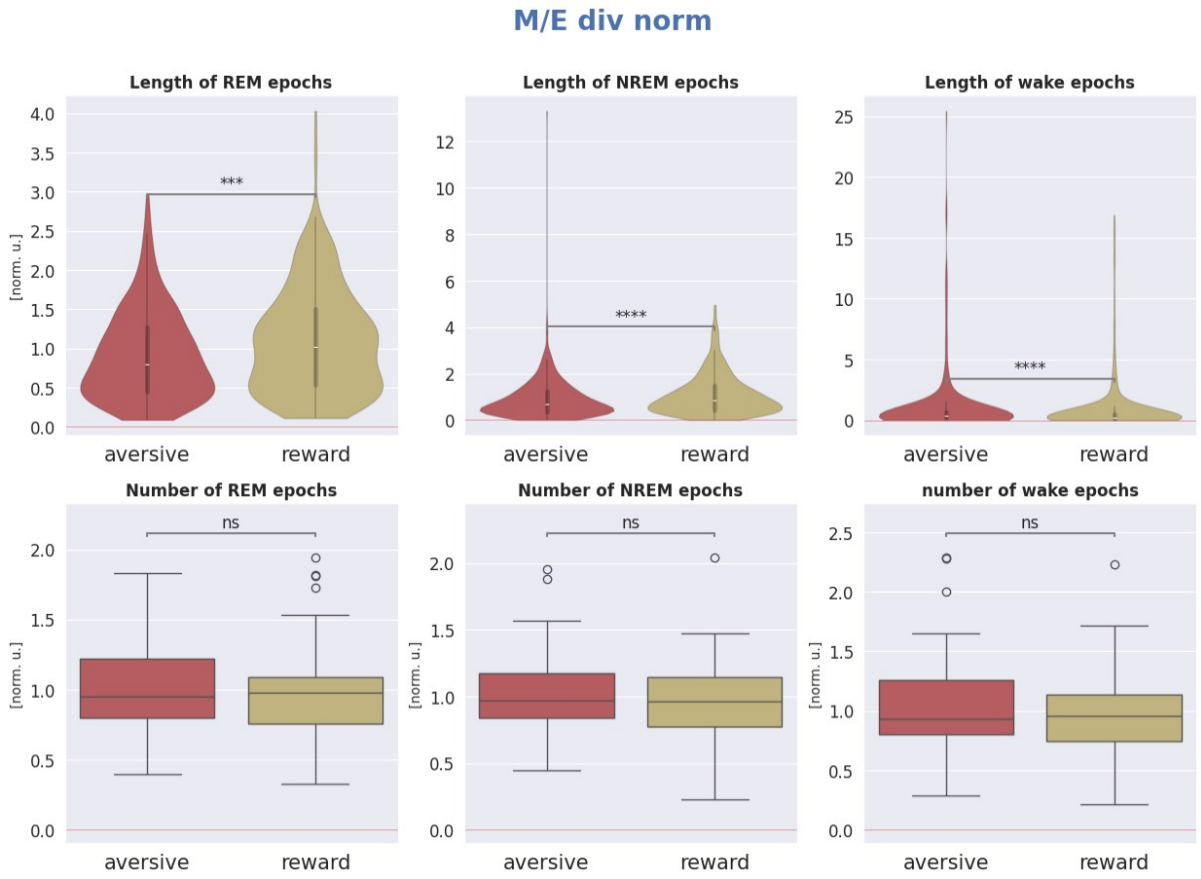

Figure 8. *(length and number ME) Comparison of the length and number of epochs in a sleep session after implementing normalization by the day time in which the experiment has been run and tested by the Kruskal-Wallis test.*

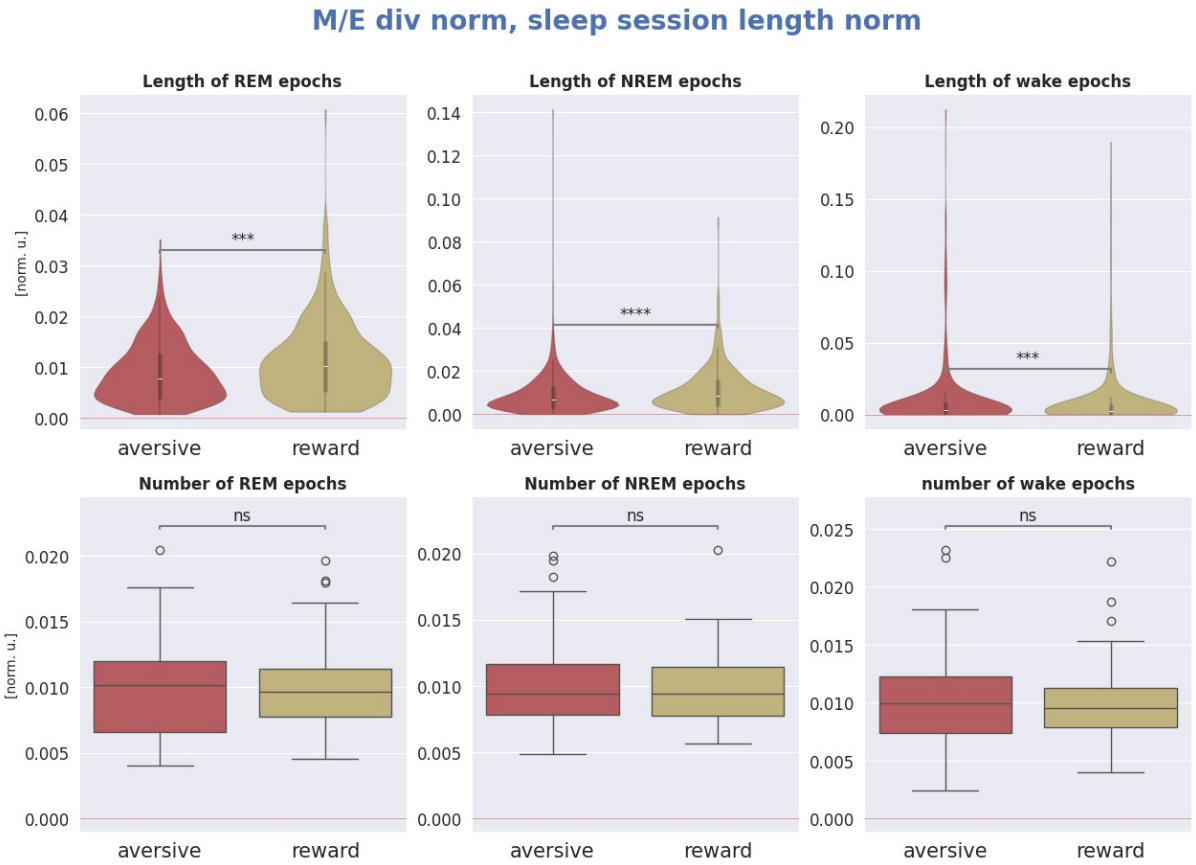

Figure 9. *(length and number ME length) Comparison of the length and number of epochs in a sleep session after implementing M/E normalization and normalization by the length of the sleep session. Tested by the Kruskal-Wallis test.*

Further, we examine how long it takes rats to fall asleep, i.e., the length of the first wake epoch. In all cases of post-run sleep, sleep onset latency is significantly longer compared to baseline sleep. Additionally, the rats fell asleep faster after aversive runs than after reward runs (Figure10.). Although the result is significant, it may have been caused by differences in the experimental protocols of the two run types. Therefore, further validation would be necessary before drawing definitive conclusions.

Regarding the ratio of the total time spent in REM phase to the total time spent in NREM phase, the distributions appear similar across the contexts of interest (Figure 10.), and neither M/E normalization (Figure 11.), nor normalization by total sleep session length (Figure 12.) reveals any substantial differences.

On the other hand, the ratio of total time spent in REM + total NREM phases to wake time seems heavily influenced by the daytime bias (Figure 10.). Given this, we apply M/E normalization (see Materials and methods section 2.4.), which uncovers a higher proportion

of REM and NREM epochs during the reward sleep sessions (Figure 11.), indicating a robust difference independent of overall session duration (Figure 12.)

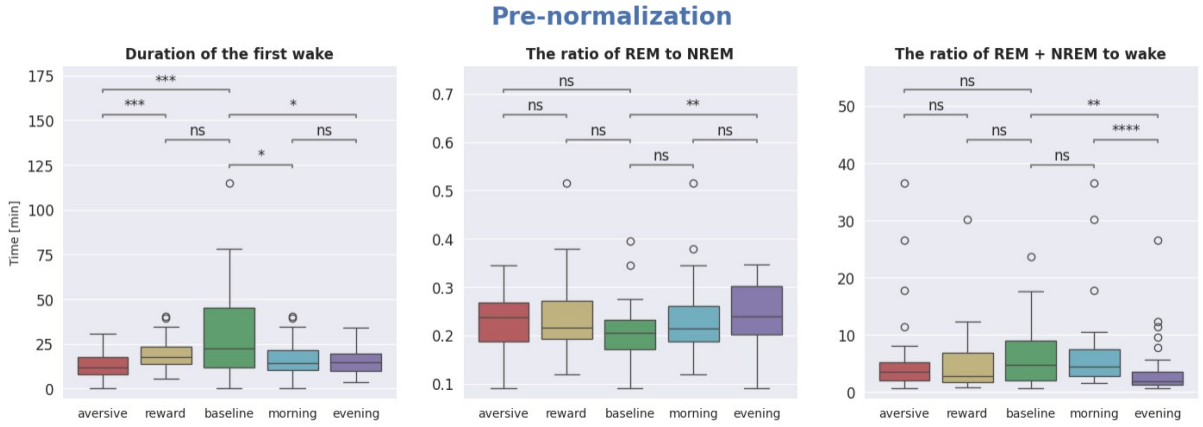

Figure 10. *of the duration of the first wake, the ratio of the duration of REM to NREM epochs in a sleep session, and the ratio of the duration of wake epochs to REM + NREM epochs. Tested by the Kruskal-Wallis test.*

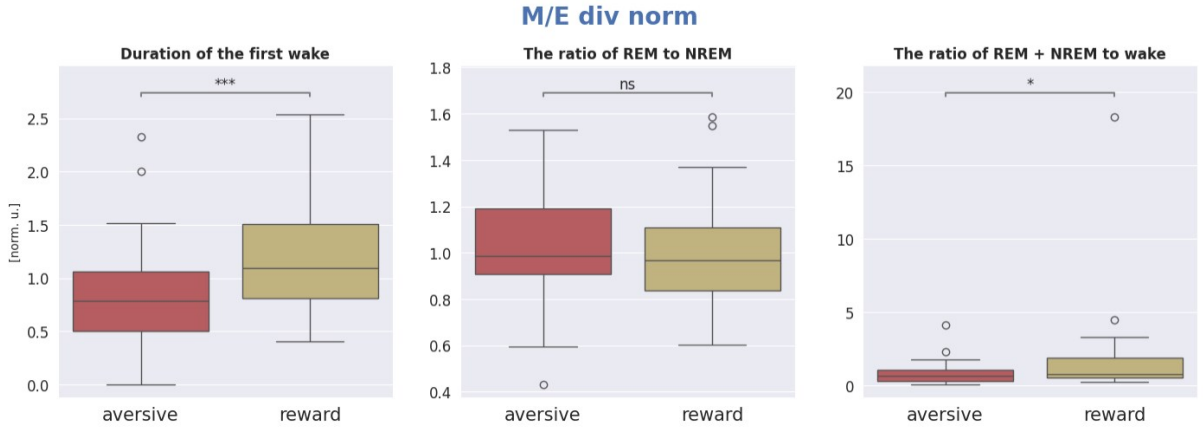

Figure 11. *Comparison of the duration of the first wake, the ratio of the duration of REM to NREM epochs in a sleep session, and the ratio of the duration of wake epochs to REM + NREM epochs after implementing normalization by the day time in which the experiment has been run and tested by the Kruskal-Wallis test.*

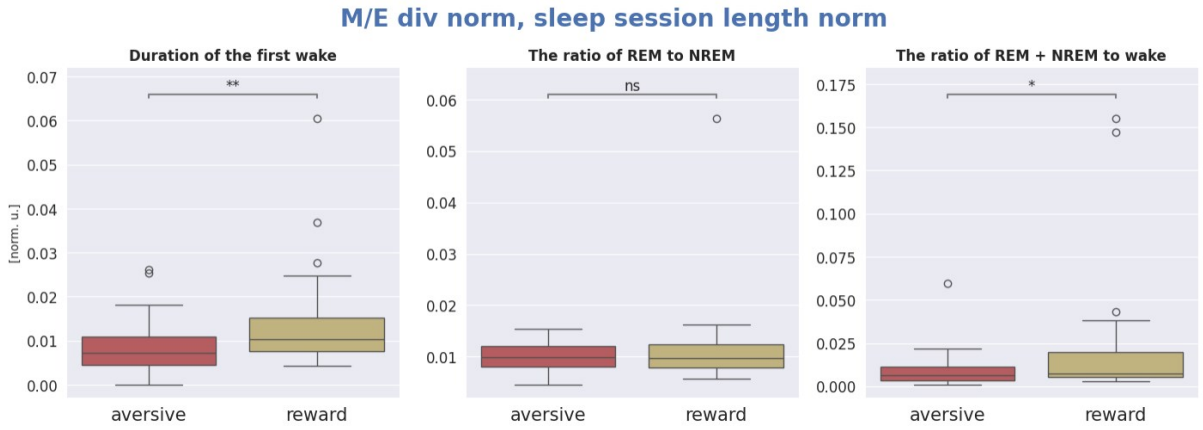

Figure 12. *Comparison of the duration of the first wake, the ratio of the duration of REM to NREM epochs in a sleep session, and the ratio of the duration of wake epochs to REM + NREM epochs, implementing M/E normalization and normalization by the length of the sleep session. Tested by the Kruskal-Wallis test.*

The final area of our sleep structure exploration focuses on the sleep session trends. We hypothesize that the length of the REM and NREM epochs might consistently change during the sleep session, just as was shown by Borbély (1980), where they found NREM epochs to initially be long and then progressively shorten. To test this hypothesis, we compute slopes of the length of epochs (Figure 13.) for each sleep session and then test them context by context using the Wilcoxon statistic against a zero distribution (Figure 14.). According to those tests, only aversive REM epochs' slopes are significantly different from zero. However, when we statistically test it against slope distributions of other contexts, we do not find any significant difference (Figure 16.). The variability of the slopes per animal is further illustrated in (Figure 15.).

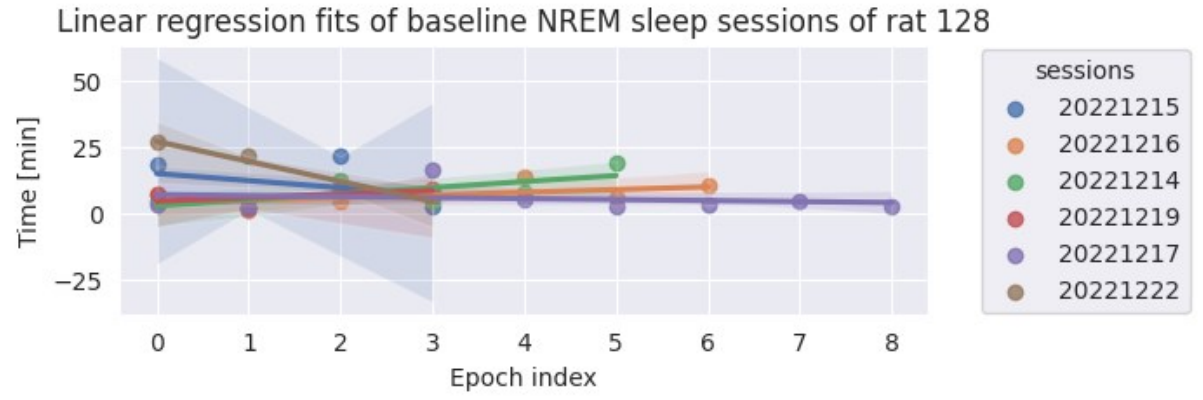

Figure 13. *An illustration of the computation of epoch length slopes. Each line is a linear regression fit of the lengths of all NREM epochs in one baseline session from the recording of rat 128.*

```
wilcoxon statistics against zero

REM

        testing aversive vs zero:
                P-value: 0.00028057557574356906
                Reject null hypothesis:  'The two samples are significantly different.
        testing reward vs zero:
                P-value: 0.5185272742000961
                Fail to reject null hypothesis:  The two samples are not significantly different.
        testing aversive vs reward:
                P-value: 0.1149664051754371
                Fail to reject null hypothesis:  The two samples are not significantly different.
NREM

        testing aversive vs zero:
                P-value: 0.18311741828802042
                Fail to reject null hypothesis:  The two samples are not significantly different.
        testing reward vs zero:
                P-value: 0.5448004511072213
                Fail to reject null hypothesis:  The two samples are not significantly different.
        testing aversive vs reward:
                P-value: 0.9628961195248849
                Fail to reject null hypothesis:  The two samples are not significantly different.
```

Figure 14. *Testing of the slope distributions against zero and comparing different valence contexts using Wilcoxon test*

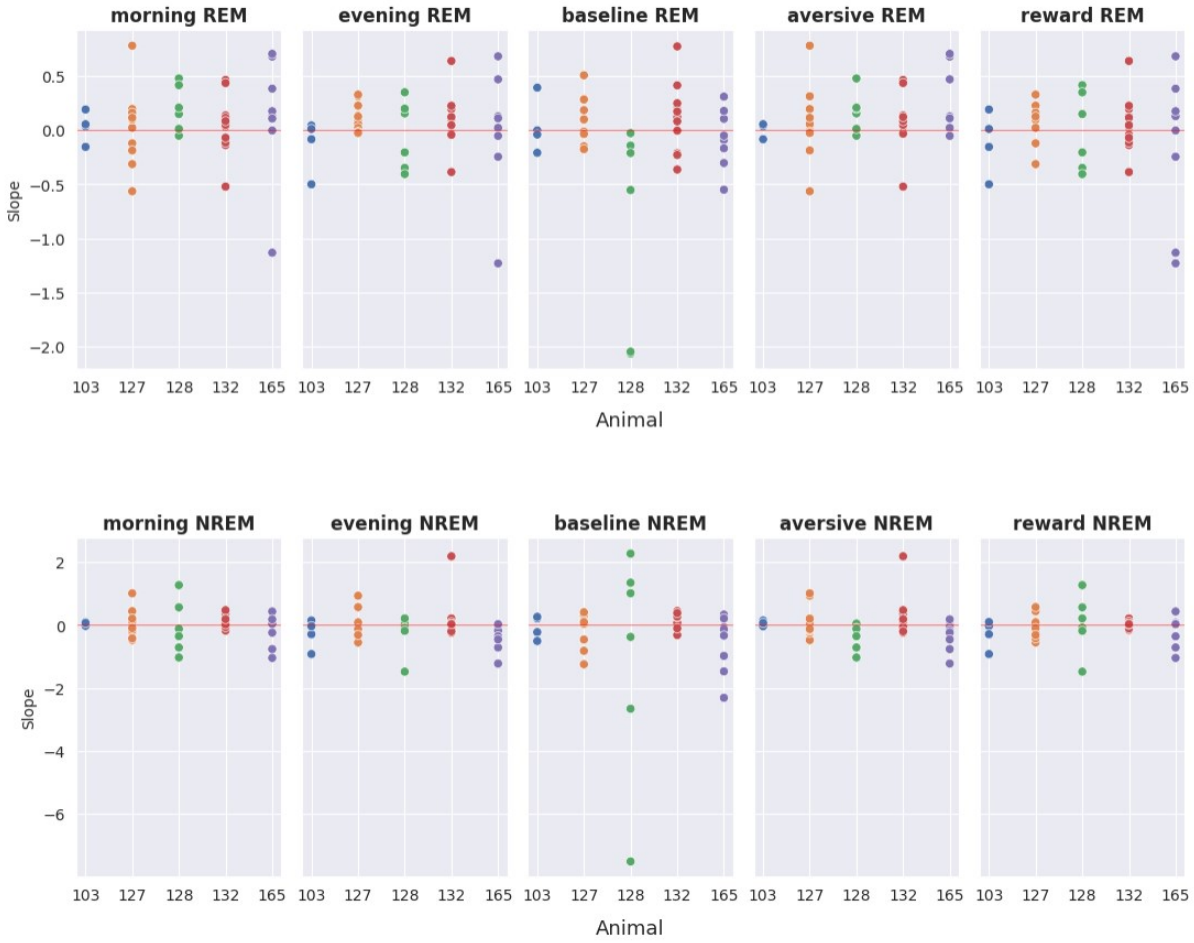

Figure 15. *Distributions of slopes of the lengths of epochs for every sleep session. A red line highlights zero.*

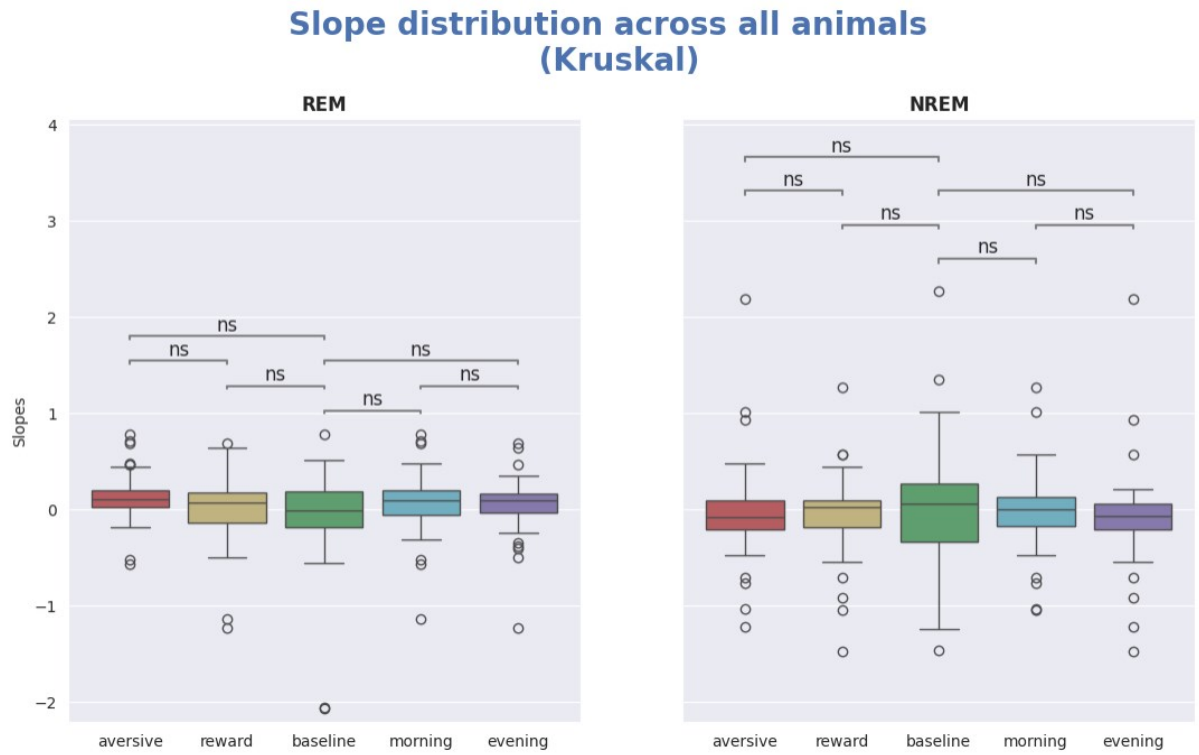

Figure 16. *Comparison of slopes of lengths of epochs in sleep sessions. Tested by the Kruskal-Wallis test.*

In conclusion, our analysis revealed that while the number of sleep epochs remains consistent across emotional contexts, the durations of these epochs differ significantly. In the aversive condition, rats exhibited shorter REM and NREM epochs and longer wake epochs, resulting in a reduced total sleep time and a lower REM+NREM to wake ratio. No consistent temporal trends in epoch length were observed throughout sleep sessions. These findings suggest that the aversive experience affects the quality and depth of sleep without altering its stochastic structural pattern.

3.2. SPECTRUM ANALYSIS

Local field potential is a signal that reflects the sum of the extracellular activity in the recording electrode's nearest and more remote neighborhood (Buzsáki, 2006; Herreras, 2016). Such a composite signal must be processed to obtain information about individual frequency bands. One way to do that is by using a Fourier transform, in our case, a modified one in the form of Welch's method, that decomposes the signal into individual sine waves of various frequencies and computes the relative dominance of such waves over a particular recording time (Buzsáki, 2006, p. 105). We call that the power spectral density (PSD).

The plot (Figure 17.) depicts the PSD averaged across all epochs pooling across all animals. As expected, theta power is elevated in REM epochs compared to wake and NREM (Grastyan & Karmos, 1961). The power on the theta band is substantially higher in the dorsal part of the hippocampus in comparison to the ventral side, which could also be expected according to the studies (Lai-Wo Stan Leung, 1984; Royer et al., 2010). In all sleep phases, but most prominently in REM, the delta power in vHPC is significantly lower than in dHPC, and delta power overall is lower in REM compared to NREM and wake. The peak at 50Hz is a technical artifact caused by interference with the power line that in Europe operates on 50Hz.

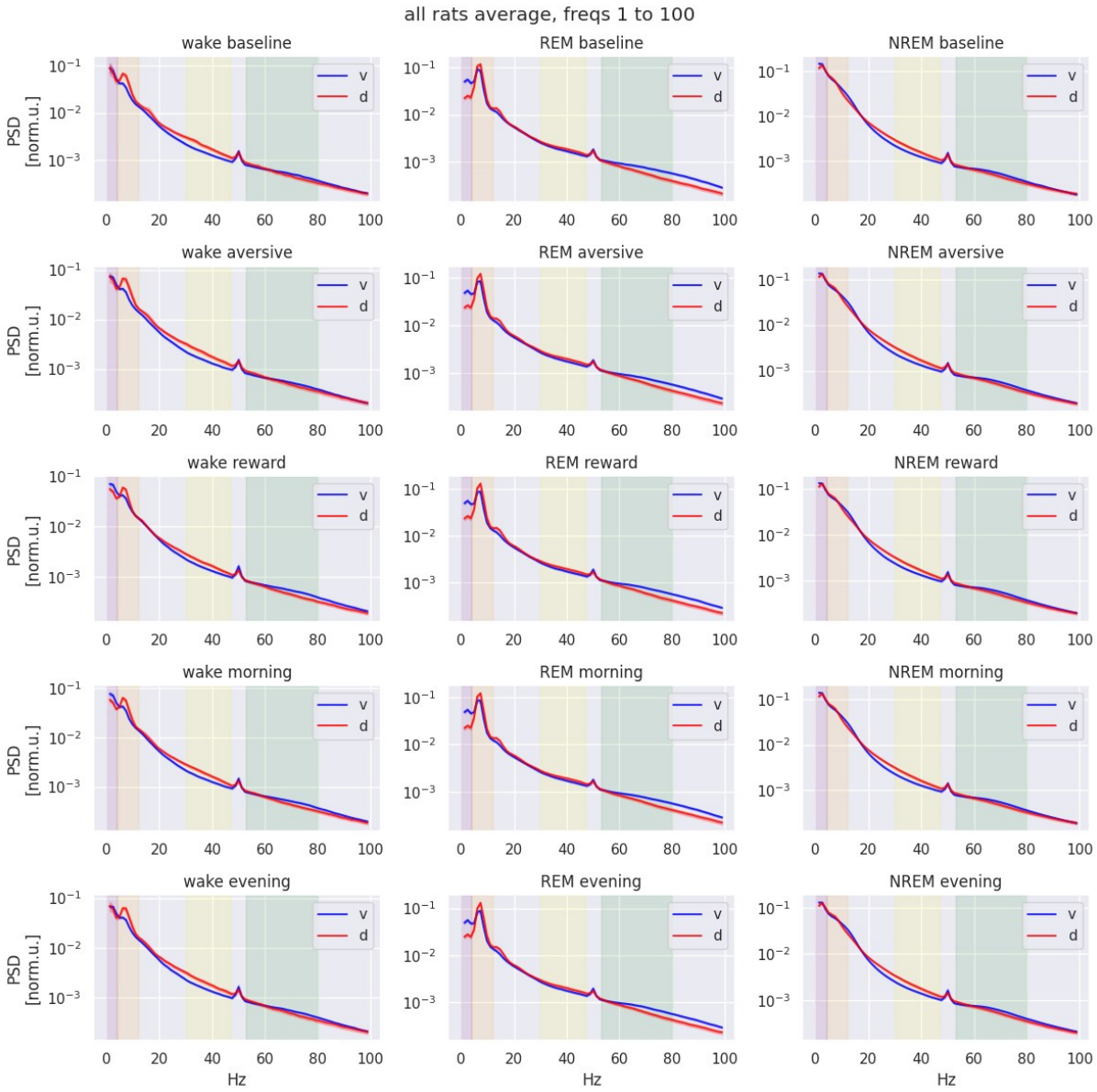

Figure 17. *The average power spectral density across all epochs of a specific sleep phase, aggregated from all sessions within a specific context. Shaded frequency bands indicate delta (0-4 Hz, purple), theta (4-12 Hz, orange), gamma (30-47 Hz, yellow), and high gamma (53-80 Hz, green). Error bars are ± sem.*

According to Ackermann & Rasch (2014), numerous studies suggest that the REM phase plays a vital role in the consolidation of non-procedural and emotional memories. During REM, the most prominent oscillation is theta (Headley & Paré, 2017), which has been shown to increase in power following aversive learning experiences (Fogel et al., 2009). Gamma activity is also present during REM sleep (Bragin et al., 1995) and is often coupled with theta in sleep following fear conditioning, which may alter gamma power (Belluscio et al., 2012). According to some studies (Bódizs et al., 2001). There is limited evidence supporting a functional relevance for delta oscillation in the hippocampus during REM. Some of the

studies have even reported null findings (MacLean & Datta, 2007). Therefore, in our analysis, we included delta primarily as a control frequency band, rather than a candidate for functional interpretation.

In our comparison of the baseline normalized spectral power distributions across different sleep contexts, we found no significant differences between any of the tested distributions in the ventral hippocampus. In the dorsal part, the average powers of epochs on all examined frequencies are higher in the evening sessions (Figure 18.). This aligns with the findings from (Munn et al., 2015), who reported a strong circadian modulation of theta oscillation's power in rats. Our observation suggests that the time of day the experiment was conducted might have a similar effect on delta, gamma, and high gamma power.

To ensure the M/E bias does not overpower any possible differences between the aversive and reward distribution, we apply the M/E normalization (Figure 19.). However, this correction did not reveal any significant differences between the aversive and reward distributions.

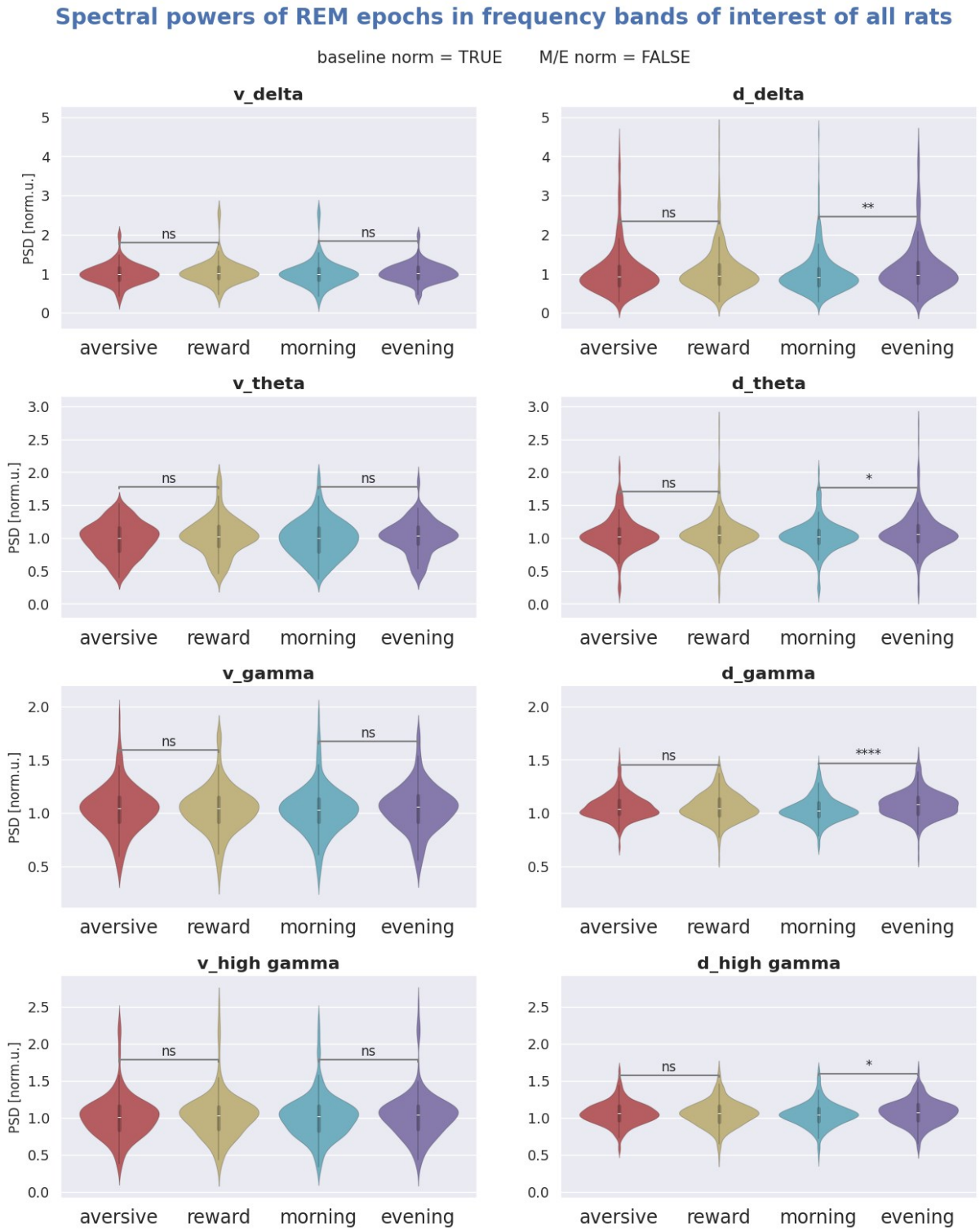

Figure 18. *Comparison of REM spectral power in vHPC on the left and dHPC on the right across context conditions. Violin plots depict baseline normalized spectral power distributions in the delta, theta, gamma, and high gamma bands for aversive (red) and reward (yellow) sessions. Each datapoint represents average spectral power over a single REM epoch. Y-axis units are normalized PSD, and the Kruskal-Wallis test was used for statistical testing.*

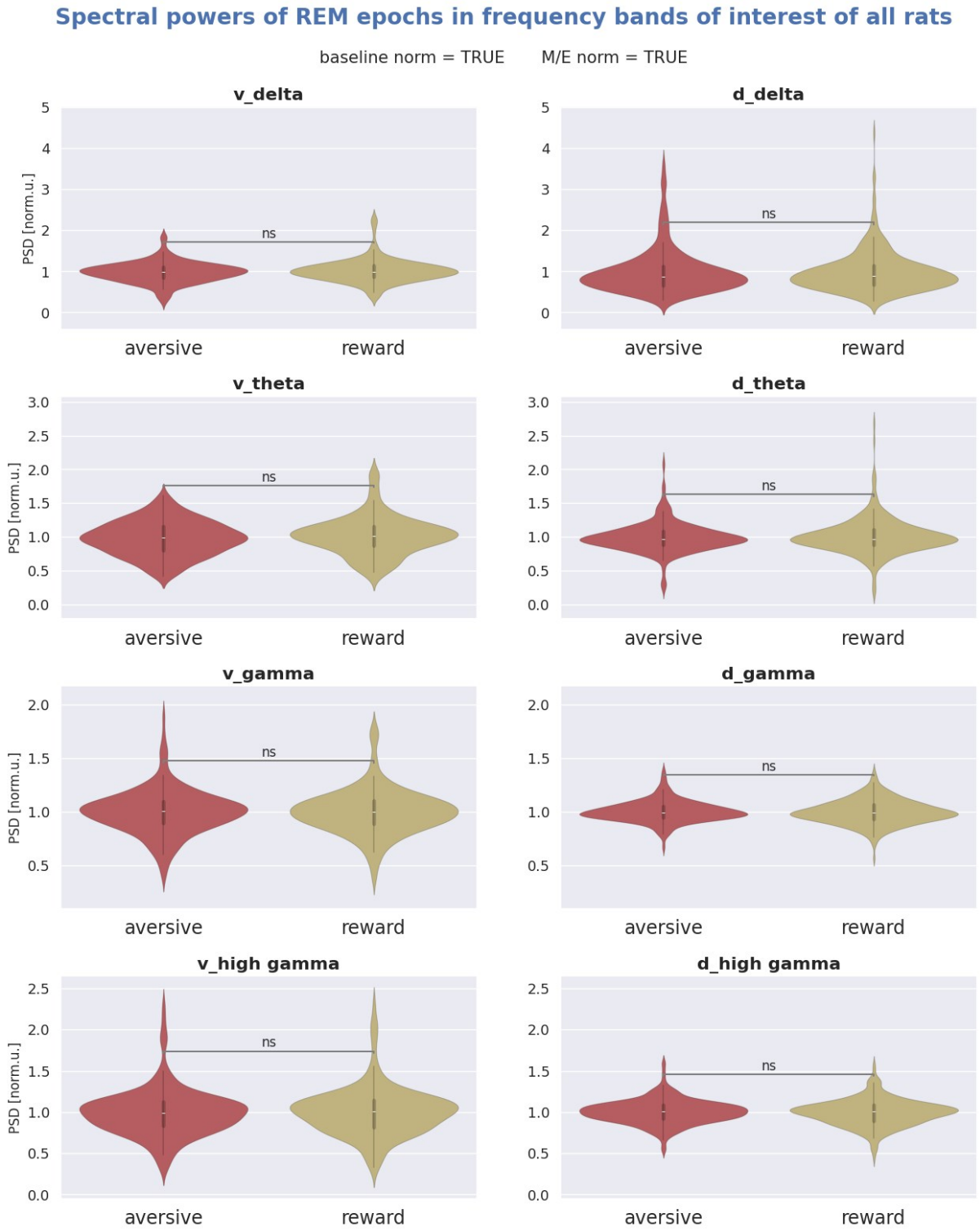

Figure 19. *Comparison of REM spectral power in vHPC (left) and dHPC (right) across different experimental contexts. Violin plots represent baseline and M/E normalized spectral power distributions in the delta, theta, gamma, and high gamma bands for aversive (red) and reward (yellow) sleep sessions. Each data point corresponds to the average spectral power of the signal of a single REM epoch. The y-axis represents normalized power spectral density (PSD), and statistical comparisons were performed using the Kruskal–Wallis test.*

3.3. CORRELATION STATISTICS

So far, we have analyzed spectral power within each hippocampal region independently. In the following analysis, we assess the relationship between oscillatory dynamics in the ventral and dorsal hippocampus. Specifically, we ask whether power fluctuation in defined frequency bands is temporally correlated between the two regions across REM sleep epochs. High correlation would suggest shared modulation or functional coordination, whereas low correlation would imply functional dissociation, supporting the hypothesis that vHPC and dHPC operate more independently under certain conditions. To test this, we compute the Pearson correlation coefficient for the time series of spectral power values in a given frequency band between ventral and dorsal channels within each sleep session. The resulting correlation values are then compared across experimental conditions to assess context-dependent differences in dorso-ventral coupling.

The most prominent finding in this analysis is the divergence of gamma power correlations in the aversive condition compared to the baseline and reward contexts (Figure 20.). Specifically, in REM epochs following aversive runs, gamma-band power in REM epochs exhibits significantly weaker correlation between the dorsal and ventral hippocampal channels compared to reward and baseline sleep, indicating reduced synchrony in their temporal fluctuations. In contrast, gamma power correlations during baseline and reward sleep are comparable, suggesting more consistent dorso-ventral coupling under those conditions. Notably, this effect is restricted to the lower gamma band, no such difference was observed in the high gamma range. This finding reinforces the view that gamma oscillations should not be treated as a single broad frequency band but rather as comprising functionally distinct subcomponents (see Introduction 1.2.3.).

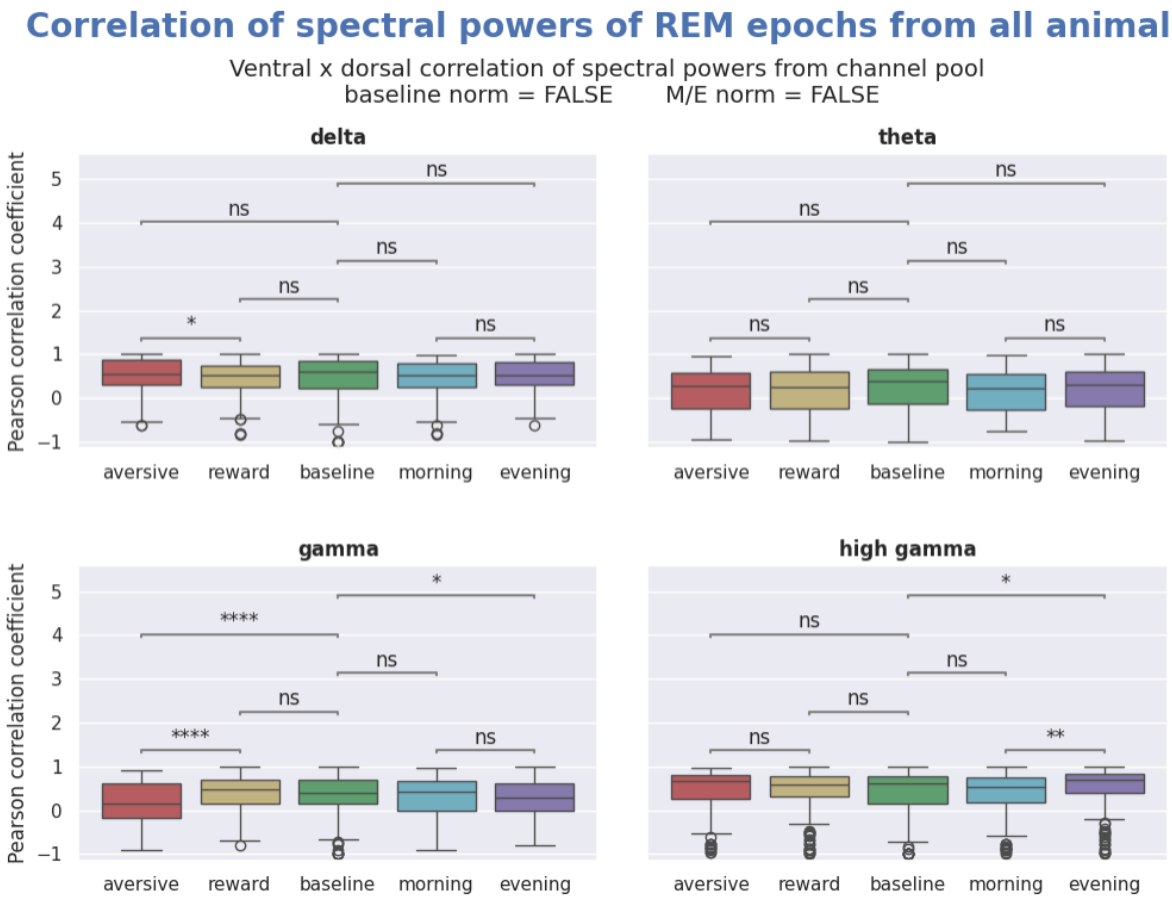

Figure 20. *Comparison of the Pearson correlation coefficient of spectral powers. One data point is a Pearson correlation coefficient of a time series of spectral powers of all REM epochs in one sleep session. Tested by the Kruskal-Wallis test.*

3.4. CROSS-FREQUENCY COUPLING ANALYSIS

Theta activity is known to play a key role in emotional memory consolidation during REM sleep (Popa et al., 2010). It is also known to modulate gamma oscillations through a mechanism called phase-amplitude coupling (Bragin et al., 1995), which has also been implicated in emotional memory processes (Ahlgrim & Manns, 2019; Costa et al., 2022). In this coupling, the phase of the slower theta rhythm modulates the amplitude of the faster gamma oscillation. This modulation can be captured using the phase locking value (PLV) between the phase of theta and the phase of the gamma envelope, a smooth curve outlining the amplitude peaks of the gamma oscillation (Figure 21.). The exact computational procedure is described in the Material and Methods section 2.7.

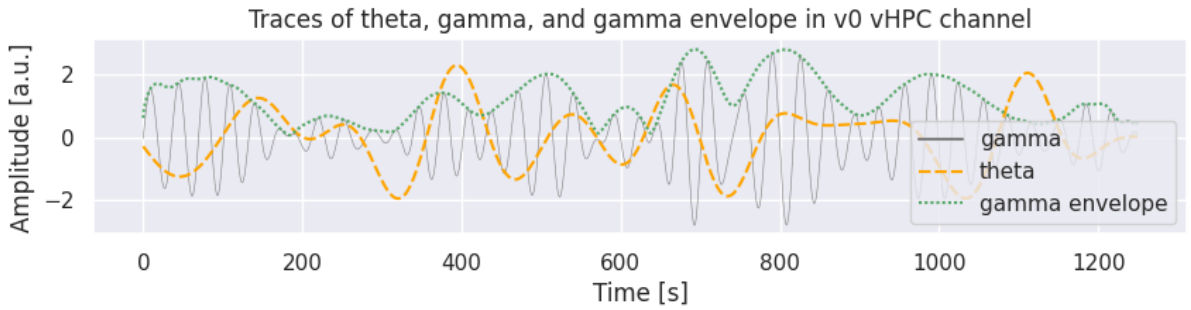

Figure 21. *Time series of gamma (gray), theta (orange), and gamma envelope (green dotted) signals from the ventral v0 channel over time during a chosen part of a random REM epoch. (rat 103, session 220715, aversive sleep, channel v0, first REM epoch, 6250 - 7500s)*

Based on a preliminary inspection of the heatmaps illustrating theta and gamma phase dynamics (Figure 22.), we observed patterns suggestive of phase relationships that we anticipated would be reflected in the PLV results. While the comparison of PLVs across sleep contexts (Figure 23., Figure 24.) revealed a slightly elevated degree of phase synchrony in all sleep contexts relative to the shuffle distribution, the differences among experimental conditions were not substantial. This suggests that although some degree of theta-gamma coupling is present during REM sleep, it does not appear to vary meaningfully with emotional context under the conditions tested. Interestingly, the effects found in the gamma frequency band were anatomically localised in the ventral hippocampus, whereas the high-gamma modulation was especially visible in the dorsal part.

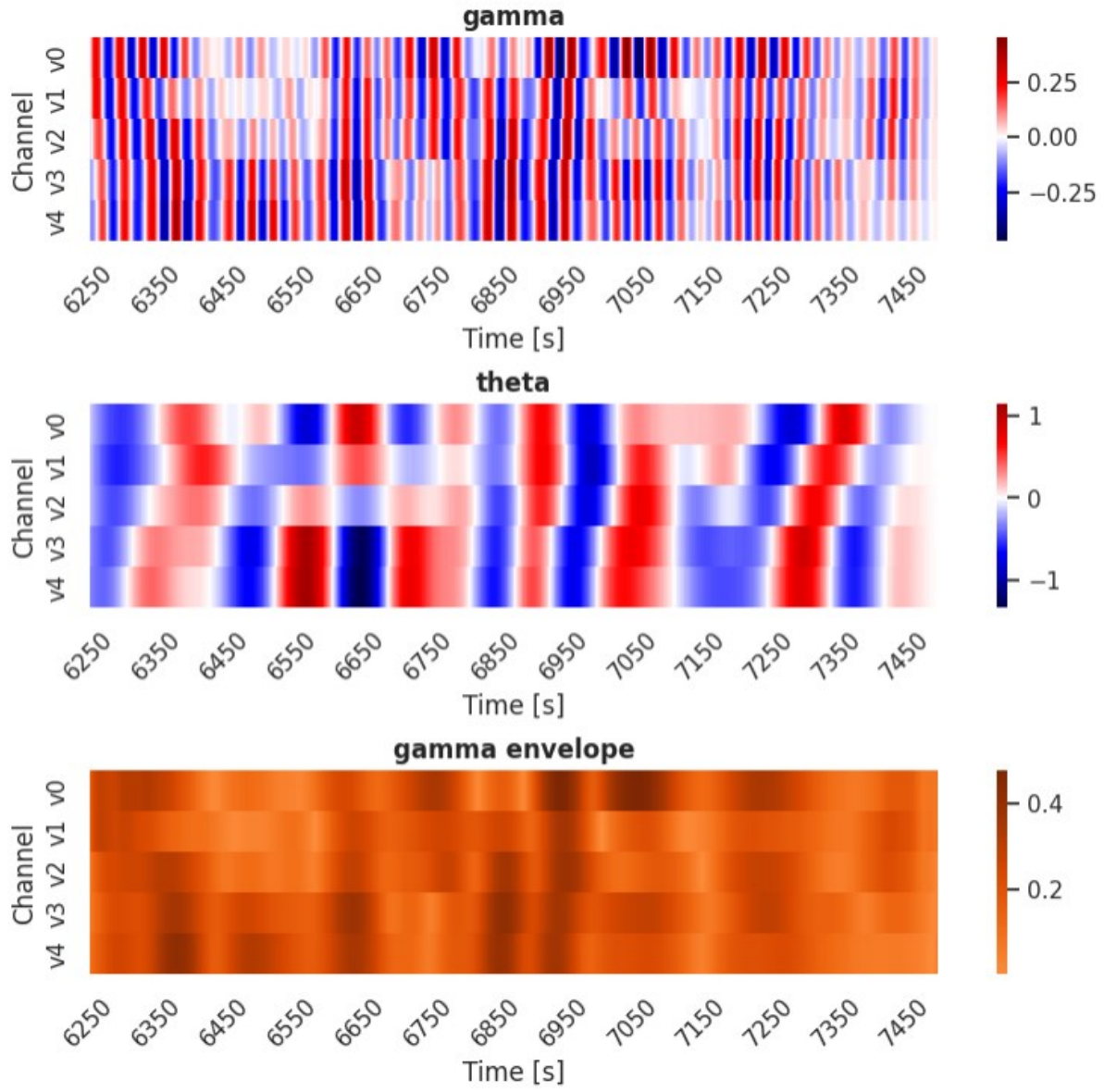

Figure 22. *Heatmaps showing gamma (top), theta (middle), and gamma envelope (bottom) signals across ventral hippocampal channels (v0 - v4) over time during a chosen part of a random REM epoch. (rat 103, session 220715, aversive sleep, first REM epoch, 6250 - 7500s)*

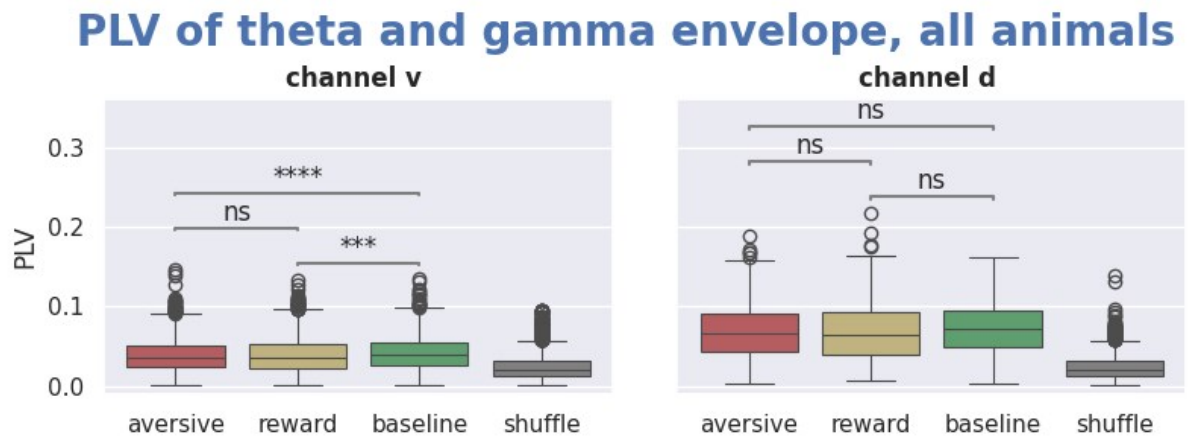

Figure 23. *Comparison of the PLV of the theta phase and the gamma envelope. One datapoint in the boxplot is a PLV of the phases of theta and gamma envelope phase of a single REM epoch. Surrogate shuffle distribution to estimate significance. Tested by the Kruskal-Wallis test.*

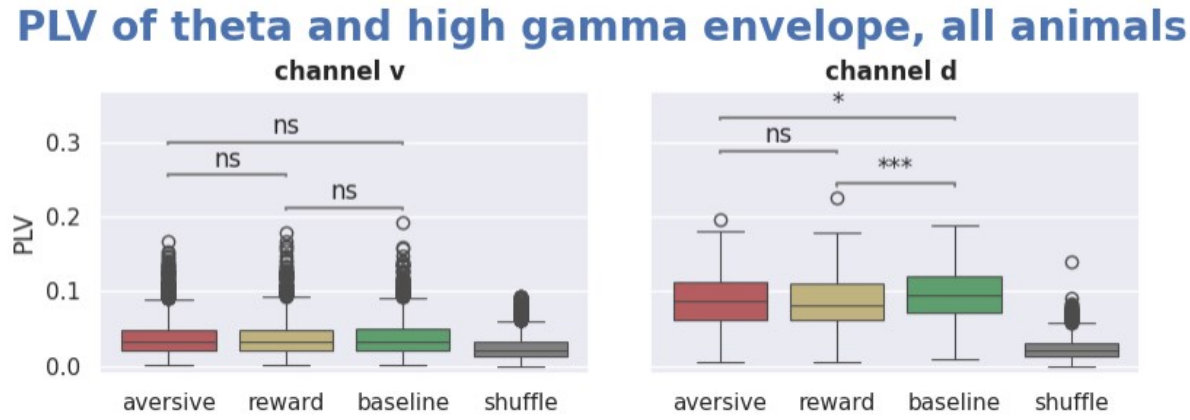

Figure 24. *Comparison of the PLV of the theta phase and the high gamma envelope. One datapoint in the boxplot is a PLV of the phases of theta and high gamma envelope phase of a single REM epoch. Surrogate shuffle distribution to estimate significance. Tested by the Kruskal-Wallis test.*

4. DISCUSSION

This thesis investigated the properties of sleep in rats in relation to emotional memory processing following a behavioral task with either aversive or rewarding valence. Specifically, we aimed to determine whether there are signs of emotional memory processing in REM sleep, focusing on neural activity in the dorsal and ventral hippocampus.

Our initial analysis showed stronger circadian modulation of the sleep structure, than the modification by the context of the preceding run. Nevertheless, when corrected, sleep structure revealed that rats spent more time in REM and NREM sleep following reward run seasons. Moreover, both REM and NREM sleep epochs were, on average, longer in the reward condition compared to the aversive one. However, the number of sleep epochs of each type did not differ significantly across contexts. We also observed that the sleep onset latency was markedly prolonged following aversive runs, although this finding may be influenced by differences in the experimental protocol preceding the sleep session.

Spectral analysis across ventral hippocampal channels did not reveal significant differences in the power of delta, theta, gamma, or high gamma bands across sleep valence contexts. Computation of the PLV revealed that the theta-gamma envelope phase locking was present in all sleep contexts and without any contextual disparity.

The most notable result emerged from our correlation statistics. Specifically, the correlation of gamma-band power across REM epochs between dorsal and ventral hippocampal channels was reduced in the aversive condition compared to both baseline and reward. We hypothesized that this reduction in dorsoventral synchrony may be due to the physiological connection of the ventral hippocampus with mPFC, allowing for enhanced coupling of vHPC gamma with the mPFC activity which has been found to occur more in an aversive experience environment. In contrast, higher dorsoventral synchrony in the reward and baseline conditions may be maintained through shared theta-gamma phase coordination.

A potential explanation for this dissociation lies in the distinct functional connectivity between the hippocampus and the medial prefrontal cortex (mPFC). According to Adhikari et al. (2010), the LFPs in vHPC are more strongly synchronized with the mPFC activity than those in dHPC, even in an environment with no valence. This vHPC–mPFC coupling becomes further enhanced by anxiety. This relationship holds across broadband LFP signals, as well as within the theta and gamma frequency bands.

Under baseline and reward conditions (presumably low in anxiety), the vHPC may not strongly engage with mPFC, allowing both hippocampal poles to remain co-modulated,

possibly via shared theta rhythms for which we have found supporting evidence. However, during aversive contexts, anxiety-related activation of mPFC may strengthen its functional coupling with vHPC, leading to gamma activity in the ventral hippocampus becoming more entrained by mPFC dynamics. This may, in turn, reduce synchrony with dorsal hippocampal oscillations, effectively decoupling the two regions' gamma-band coordination. Such a mechanism would be consistent with the mPFC's established role in regulating anxiety-related behavior and its preferential interaction with vHPC under stress conditions (Adhikari et al., 2010; Padilla-Coreano et al., 2016). However, this interpretation is based on findings obtained during the state of active wakefulness. Since our data were collected during REM sleep, and direct empirical studies focusing on vHPC-mPFC vs dHPC-mPFC gamma interactions are sparse, whether the same hippocampal-mPFC coordination patterns hold across brain states remains uncertain.

Overall, our findings support the hypothesis that the connection of the ventral hippocampus to other brain regions that are considered to have a fundamental role in emotional memory is indeed functionally important. The vHPC might work as an intraregional hub connecting the regions of emotional memory circuits with the dorsal hippocampus and therefore provides the emotional component of memories to be processed together with the spatial component from dHPC.

5. REFERENCES

https://doi.org/10.1126/science.8036517

Abhang, P. A., Gawali, B. W., & Mehrotra, S. C. (2016). *Introduction to EEG- and Speech-Based Emotion Recognition*. Elsevier Science & Technology. http://ebookcentral.proquest.com/lib/cuni/detail.action?docID=4458824

Ackermann, S., & Rasch, B. (2014). Differential Effects of Non-REM and REM Sleep on Memory Consolidation? *Current Neurology and Neuroscience Reports*, *14*(2), 430. https://doi.org/10.1007/s11910-013-0430-8

Adhikari, A., Topiwala, M. A., & Gordon, J. A. (2010). Synchronized activity between the ventral hippocampus and the medial prefrontal cortex during anxiety. *Neuron*, *65*(2), 257. https://doi.org/10.1016/j.neuron.2009.12.002

Ahlgrim, N. S., & Manns, J. R. (2019). Optogenetic Stimulation of the Basolateral Amygdala Increased Theta-Modulated Gamma Oscillations in the Hippocampus. *Frontiers in Behavioral Neuroscience*, *13*, 87. https://doi.org/10.3389/fnbeh.2019.00087

Bannerman, D. M., Rawlins, J. N. P., McHugh, S. B., Deacon, R. M. J., Yee, B. K., Bast, T., Zhang, W.-N., Pothuizen, H. H. J., & Feldon, J. (2004). Regional dissociations within the hippocampus—Memory and anxiety. *Neuroscience and Biobehavioral Reviews*, *28*(3), 273–283. https://doi.org/10.1016/j.neubiorev.2004.03.004

Bastianini, S., Berteotti, C., Gabrielli, A., Del Vecchio, F., Amici, R., Alexandre, C., Scammell, T. E., Gazea, M., Kimura, M., Lo Martire, V., Silvani, A., & Zoccoli, G. (2014). SCOPRISM: A new algorithm for automatic sleep scoring in mice. *Journal of Neuroscience Methods*, *235*, 277–284. https://doi.org/10.1016/j.jneumeth.2014.07.018

Belluscio, M. A., Mizuseki, K., Schmidt, R., Kempter, R., & Buzsáki, G. (2012). Cross-frequency phase-phase coupling between θ and γ oscillations in the hippocampus. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *32*(2), 423–435. https://doi.org/10.1523/JNEUROSCI.4122-11.2012

Bergel, A., Deffieux, T., Demené, C., Tanter, M., & Cohen, I. (2018). Local hippocampal fast gamma rhythms precede brain-wide hyperemic patterns during spontaneous rodent REM sleep. *Nature Communications*, *9*(1), 5364. https://doi.org/10.1038/s41467-018-07752-3

Bieri, K. W., Bobbitt, K. N., & Colgin, L. L. (2014). Slow and Fast Gamma Rhythms Coordinate Different Spatial Coding Modes in Hippocampal Place Cells. *Neuron*, *82*(3), 670–681. https://doi.org/10.1016/j.neuron.2014.03.013

Bódizs, R., Kántor, S., Szabó, G., Szûcs, A., Erõss, L., & Halász, P. (2001). Rhythmic hippocampal slow oscillation characterizes REM sleep in humans. *Hippocampus*, *11*(6), 747–753. https://doi.org/10.1002/hipo.1090

Bolding, K. A., Ferbinteanu, J., Fox, S. E., & Muller, R. U. (2020). Place cell firing cannot support navigation without intact septal circuits. *Hippocampus*, *30*(3), 175–191. https://doi.org/10.1002/hipo.23136

Borbély, A. A. (1980). Effects of light and circadian rhythm on the occurrence of REM sleep in the rat. *Sleep*, *2*(3), 289–298.

Bragin, A., Jando, G., Nadasdy, Z., Hetke, J., Wise, K., & Buzsaki, G. (1995). Gamma (40-100 Hz) oscillation in the hippocampus of the behaving rat. *Journal of Neuroscience*, *15*(1), 47–60. https://doi.org/10.1523/JNEUROSCI.15-01-00047.1995

Buzsáki, G. (2002). Theta Oscillations in the Hippocampus. *Neuron*, *33*(3), 325–340. https://doi.org/10.1016/S0896-6273(02)00586-X

Buzsáki, G. (2006). *Rhythms of the Brain*. Oxford University Press. https://doi.org/10.1093/acprof:oso/9780195301069.001.0001

Buzsáki, G., Anastassiou, C. A., & Koch, C. (2012). The origin of extracellular fields and currents—EEG, ECoG, LFP and spikes. *Nature Reviews Neuroscience*, *13*(6), 407–420. https://doi.org/10.1038/nrn3241

Buzsáki, G., & Chrobak, J. J. (1995). Temporal structure in spatially organized neuronal ensembles: A role for interneuronal networks. *Current Opinion in Neurobiology*, *5*(4), 504–510. https://doi.org/10.1016/0959-4388(95)80012-3

Cenquizca, L. A., & Swanson, L. W. (2007). Spatial organization of direct hippocampal field CA1 axonal projections to the rest of the cerebral cortex. *Brain Research Reviews*, *56*(1), 1–26. https://doi.org/10.1016/j.brainresrev.2007.05.002

Cheung, T. H., & Cardinal, R. N. (2005). Hippocampal lesions facilitate instrumental learning with delayed reinforcement but induce impulsive choice in rats. *BMC Neuroscience*, *6*, 36. https://doi.org/10.1186/1471-2202-6-36

Colgin, L. L. (2016). Rhythms of the hippocampal network. *Nature Reviews Neuroscience*, *17*(4), 239–249. https://doi.org/10.1038/nrn.2016.21

Colgin, L. L., Denninger, T., Fyhn, M., Hafting, T., Bonnevie, T., Jensen, O., Moser, M.-B., & Moser, E. I. (2009). Frequency of gamma oscillations routes flow of information in the hippocampus. *Nature*, *462*(7271), 353–357. https://doi.org/10.1038/nature08573

Costa, M., Lozano-Soldevilla, D., Gil-Nagel, A., Toledano, R., Oehrn, C. R., Kunz, L., Yebra, M., Mendez-Bertolo, C., Stieglitz, L., Sarnthein, J., Axmacher, N., Moratti, S., & Strange, B. A. (2022). Aversive memory formation in humans involves an amygdala-hippocampus phase code. *Nature Communications*, *13*(1). https://doi.org/10.1038/s41467-022-33828-2

Csicsvari, J., Jamieson, B., Wise, K. D., & Buzsáki, G. (2003). Mechanisms of Gamma Oscillations in the Hippocampus of the Behaving Rat. *Neuron*, *37*(2), 311–322. https://doi.org/10.1016/S0896-6273(02)01169-8

DaSilva, J. K., Lei, Y., Madan, V., Mann, G. L., Ross, R. J., Tejani-Butt, S., & Morrison, A. R. (2011). Fear conditioning fragments REM sleep in stress-sensitive Wistar–Kyoto, but not Wistar, rats. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *35*(1), 67–73. https://doi.org/10.1016/j.pnpbp.2010.08.023

Datta, S. (2000). Avoidance task training potentiates phasic pontine-wave density in the rat: A mechanism for sleep-dependent plasticity. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *20*(22), 8607–8613. https://doi.org/10.1523/JNEUROSCI.20-22-08607.2000

Fell, J., Klaver, P., Lehnertz, K., Grunwald, T., Schaller, C., Elger, C. E., & Fernández, G.

(2001). Human memory formation is accompanied by rhinal–hippocampal coupling and decoupling. *Nature Neuroscience*, *4*(12), 1259–1264. https://doi.org/10.1038/nn759

Ferbinteanu, J., & McDonald, R. J. (2001). Dorsal/ventral hippocampus, fornix and conditioned place preference. *Hippocampus*, *11*(2), 187–200. https://doi.org/10.1002/hipo.1036

Fogel, S. M., Smith, C. T., & Beninger, R. J. (2009). Evidence for 2-stage models of sleep and memory: Learning-dependent changes in spindles and theta in rats. *Brain Research Bulletin*, *79*(6), 445–451. https://doi.org/10.1016/j.brainresbull.2009.03.002

Fyhn, M., Molden, S., Witter, M. P., Moser, E. I., & Moser, M.-B. (2004). Spatial representation in the entorhinal cortex. *Science (New York, N.Y.)*, *305*(5688), 1258–1264. https://doi.org/10.1126/science.1099901

GRASTYAN, E., & KARMOS, G. (1961). A study of a possible “dreaming” mechanism in the cat. *Acta Physiologica Academiae Scientiarum Hungaricae*, *20*, 41–50.

Hafting, T., Fyhn, M., Molden, S., Moser, M.-B., & Moser, E. I. (2005). Microstructure of a spatial map in the entorhinal cortex. *Nature*, *436*(7052), 801–806. https://doi.org/10.1038/nature03721

Han, H.-B., Shin, H.-S., Jeong, Y., Kim, J., & Choi, J. H. (2023). Dynamic switching of neural oscillations in the prefrontal–amygdala circuit for naturalistic freeze-or-flight. *Proceedings of the National Academy of Sciences*, *120*(37), e2308762120. https://doi.org/10.1073/pnas.2308762120

Headley, D. B., & Paré, D. (2017). Common oscillatory mechanisms across multiple memory systems. *Npj Science of Learning*, *2*(1), 1–8. https://doi.org/10.1038/s41539-016-0001-2

Herreras, O. (2016). Local Field Potentials: Myths and Misunderstandings. *Frontiers in Neural Circuits*, *10*. https://doi.org/10.3389/fncir.2016.00101

Keil, A., Müller, M. M., Gruber, T., Wienbruch, C., Stolarova, M., & Elbert, T. (2001). Effects of emotional arousal in the cerebral hemispheres: A study of oscillatory brain activity

and event-related potentials. *Clinical Neurophysiology*, *112*(11), 2057–2068. https://doi.org/10.1016/S1388-2457(01)00654-X

Kensinger, E. A., & Ford, J. H. (2020). Retrieval of Emotional Events from Memory. *Annual Review of Psychology*, *71*(1), 251–272. https://doi.org/10.1146/annurev-psych-010419-051123

Kim, J. W., Lee, J.-S., Robinson, P. A., & Jeong, D.-U. (2009). Markov Analysis of Sleep Dynamics. *Physical Review Letters*, *102*(17), 178104. https://doi.org/10.1103/PhysRevLett.102.178104

Kjelstrup, K. G., Tuvnes, F. A., Steffenach, H.-A., Murison, R., Moser, E. I., & Moser, M.-B. (2002). Reduced fear expression after lesions of the ventral hippocampus. *Proceedings of the National Academy of Sciences of the United States of America*, *99*(16), 10825–10830. https://doi.org/10.1073/pnas.152112399

Klinzing, J. G., Niethard, N., & Born, J. (2019). Mechanisms of systems memory consolidation during sleep. *Nature Neuroscience*, *22*(10), 1598–1610. https://doi.org/10.1038/s41593-019-0467-3

Knyazev, G. G., Slobodskoj-Plusnin, J. Y., & Bocharov, A. V. (2009). Event-related delta and theta synchronization during explicit and implicit emotion processing. *Neuroscience*, *164*(4), 1588–1600. https://doi.org/10.1016/j.neuroscience.2009.09.057

Lai-Wo Stan Leung. (1984). Theta rhythm during REM sleep and waking: Correlations between power, phase and frequency. *Electroencephalography and Clinical Neurophysiology*, *58*(6), 553–564. https://doi.org/10.1016/0013-4694(84)90045-2

Lakatos, P., Shah, A. S., Knuth, K. H., Ulbert, I., Karmos, G., & Schroeder, C. E. (2005). An Oscillatory Hierarchy Controlling Neuronal Excitability and Stimulus Processing in the Auditory Cortex. *Journal of Neurophysiology*, *94*(3), 1904–1911. https://doi.org/10.1152/jn.00263.2005

Lesting, J., Narayanan, R. T., Kluge, C., Sangha, S., Seidenbecher, T., & Pape, H.-C. (2011). Patterns of Coupled Theta Activity in Amygdala-Hippocampal-Prefrontal Cortical Circuits during Fear Extinction. *PLoS ONE*, *6*(6), e21714.

https://doi.org/10.1371/journal.pone.0021714

Lisman, J. E., & Idiart, M. A. P. (1995). Storage of 7 ± 2 Short-Term Memories in Oscillatory Subcycles. *Science*, *267*(5203), 1512–1515. https://doi.org/10.1126/science.7878473

Little, K. C. (n.d.). *A Rat Model of Sytemic Chemotherapy for Breast Cancer to Evaluate and Treat Chemobrain*.

Lo, C.-C., Amaral, L. A. N., Havlin, S., Ivanov, P. C., Penzel, T., Peter, J.-H., & Stanley, H. E. (2002). Dynamics of Sleep-Wake Transitions During Sleep. *Europhysics Letters (EPL)*, *57*(5), 625–631. https://doi.org/10.1209/epl/i2002-00508-7

Lu, C. B., Jefferys, J. G. R., Toescu, E. C., & Vreugdenhil, M. (2011). *In vitro* hippocampal gamma oscillation power as an index of *in vivo* CA3 gamma oscillation strength and spatial reference memory. *Neurobiology of Learning and Memory*, *95*(3), 221–230. https://doi.org/10.1016/j.nlm.2010.11.008

MacLean, R. R., & Datta, S. (2007). The relationship between anxiety and sleep–wake behavior after stressor exposure in the rat. *Brain Research*, *1164*, 72–80. https://doi.org/10.1016/j.brainres.2007.06.034

McNaughton, N., Ruan, M., & Woodnorth, M.-A. (2006). Restoring theta-like rhythmicity in rats restores initial learning in the Morris water maze. *Hippocampus*, *16*(12), 1102–1110. https://doi.org/10.1002/hipo.20235

Morici, J. F., Paiva-Lima, I., Pronier, É., & Girardeau, G. (2024). *Dorso-ventral hippocampal neural assemblies are preferentially reactivated during NREM sleep following an aversive experience* (p. 2024.06.13.598918). bioRxiv. https://doi.org/10.1101/2024.06.13.598918

Moroni, F., Nobili, L., Iaria, G., Sartori, I., Marzano, C., Tempesta, D., Proserpio, P., Lo Russo, G., Gozzo, F., Cipolli, C., De Gennaro, L., & Ferrara, M. (2014). Hippocampal slow EEG frequencies during NREM sleep are involved in spatial memory consolidation in humans. *Hippocampus*, *24*(10), 1157–1168. https://doi.org/10.1002/hipo.22299

Munn, R. G. K., Tyree, S. M., McNaughton, N., & Bilkey, D. K. (2015). The frequency of

hippocampal theta rhythm is modulated on a circadian period and is entrained by food availability. *Frontiers in Behavioral Neuroscience*, *9*. https://doi.org/10.3389/fnbeh.2015.00061

O'Keefe, J. (1976). Place units in the hippocampus of the freely moving rat. *Experimental Neurology*, *51*(1), 78–109. https://doi.org/10.1016/0014-4886(76)90055-8

O'Keefe, J., & Recce, M. L. (1993). Phase relationship between hippocampal place units and the EEG theta rhythm. *Hippocampus*, *3*(3), 317–330. https://doi.org/10.1002/hipo.450030307

O'Neill, P.-K., Gordon, J. A., & Sigurdsson, T. (2013). Theta oscillations in the medial prefrontal cortex are modulated by spatial working memory and synchronize with the hippocampus through its ventral subregion. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *33*(35), 14211–14224. https://doi.org/10.1523/JNEUROSCI.2378-13.2013

Packard, M. G., & Knowlton, B. J. (2002). Learning and memory functions of the Basal Ganglia. *Annual Review of Neuroscience*, *25*, 563–593. https://doi.org/10.1146/annurev.neuro.25.112701.142937

Padilla-Coreano, N., Bolkan, S. S., Pierce, G. M., Blackman, D. R., Hardin, W. D., Garcia-Garcia, A. L., Spellman, T. J., & Gordon, J. A. (2016). Direct Ventral Hippocampal-Prefrontal Input Is Required for Anxiety-Related Neural Activity and Behavior. *Neuron*, *89*(4), 857–866. https://doi.org/10.1016/j.neuron.2016.01.011

Pandey, P., Tripathi, R., & Miyapuram, K. P. (2022). Classifying oscillatory brain activity associated with Indian Rasas using network metrics. *Brain Informatics*, *9*(1), 15. https://doi.org/10.1186/s40708-022-00163-7

Perogamvros, L., & Schwartz, S. (2012). The roles of the reward system in sleep and dreaming. *Neuroscience & Biobehavioral Reviews*, *36*(8), 1934–1951. https://doi.org/10.1016/j.neubiorev.2012.05.010

Pfeiffer, B. E., & Foster, D. J. (2013). Hippocampal place cell sequences depict future paths to remembered goals. *Nature*, *497*(7447), 74–79.

https://doi.org/10.1038/nature12112

Popa, D., Duvarci, S., Popescu, A. T., Léna, C., & Paré, D. (2010). Coherent amygdalocortical theta promotes fear memory consolidation during paradoxical sleep. *Proceedings of the National Academy of Sciences*, *107*(14), 6516–6519. https://doi.org/10.1073/pnas.0913016107

Pothuizen, H. H. J., Zhang, W.-N., Jongen-Rêlo, A. L., Feldon, J., & Yee, B. K. (2004). Dissociation of function between the dorsal and the ventral hippocampus in spatial learning abilities of the rat: A within-subject, within-task comparison of reference and working spatial memory. *The European Journal of Neuroscience*, *19*(3), 705–712. https://doi.org/10.1111/j.0953-816x.2004.03170.x

Pronier, É., Morici, J. F., & Girardeau, G. (2023). The role of the hippocampus in the consolidation of emotional memories during sleep. *Trends in Neurosciences*, *46*(11), 912–925. https://doi.org/10.1016/j.tins.2023.08.003

Rosier, M., Le Barillier, L., Meunier, D., El Yacoubi, M., Malleret, G., & Salin, P.-A. (2018). Post-learning paradoxical sleep deprivation impairs reorganization of limbic and cortical networks associated with consolidation of remote contextual fear memory in mice. *Sleep*, *41*(12), zsy188. https://doi.org/10.1093/sleep/zsy188

Royer, S., Sirota, A., Patel, J., & Buzsáki, G. (2010). Distinct Representations and Theta Dynamics in Dorsal and Ventral Hippocampus. *The Journal of Neuroscience*, *30*(5), 1777–1787. https://doi.org/10.1523/jneurosci.4681-09.2010

Scheffzük, C., Kukushka, V. I., Vyssotski, A. L., Draguhn, A., Tort, A. B. L., & Brankačk, J. (2011). Selective Coupling between Theta Phase and Neocortical Fast Gamma Oscillations during REM-Sleep in Mice. *PLOS ONE*, *6*(12), e28489. https://doi.org/10.1371/journal.pone.0028489

Sederberg, P. B., Schulze-Bonhage, A., Madsen, J. R., Bromfield, E. B., Litt, B., Brandt, A., & Kahana, M. J. (2007). Gamma Oscillations Distinguish True From False Memories. *Psychological Science*, *18*(11), 927–932. https://doi.org/10.1111/j.1467-9280.2007.02003.x

Seidenbecher, T., Laxmi, T. R., Stork, O., & Pape, H.-C. (2003). Amygdalar and Hippocampal Theta Rhythm Synchronization During Fear Memory Retrieval. *Science*, *301*(5634), 846–850. https://doi.org/10.1126/science.1085818

Singer, W. (2018). Neuronal oscillations: Unavoidable and useful? *The European Journal of Neuroscience*, *48*(7), 2389–2398. https://doi.org/10.1111/ejn.13796

Stephenson, R., Famina, S., Caron, A. M., & Lim, J. (2013). Statistical Properties of Sleep-Wake Behavior in the Rat and Their Relation to Circadian and Ultradian Phases. *Sleep*, *36*(9), 1377–1390. https://doi.org/10.5665/sleep.2970

Strange, B. A., Witter, M. P., Lein, E. S., & Moser, E. I. (2014). Functional organization of the hippocampal longitudinal axis. *Nature Reviews Neuroscience*, *15*(10), 655–669.

Sunagawa, G. A., Séi, H., Shimba, S., Urade, Y., & Ueda, H. R. (2013). FASTER: An unsupervised fully automated sleep staging method for mice. *Genes to Cells*, *18*(6), 502–518. https://doi.org/10.1111/gtc.12053

Tempesta, D., Socci, V., De Gennaro, L., & Ferrara, M. (2018). Sleep and emotional processing. *Sleep Medicine Reviews*, *40*, 183–195. https://doi.org/10.1016/j.smrv.2017.12.005

Verwer, R. W., Meijer, R. J., Van Uum, H. F., & Witter, M. P. (1997). Collateral projections from the rat hippocampal formation to the lateral and medial prefrontal cortex. *Hippocampus*, *7*(4), 397–402. https://doi.org/10.1002/(SICI)1098-1063(1997)7:4<397::AID-HIPO5>3.0.CO;2-G

Wagner, U., Gais, S., & Born, J. (2001). Emotional Memory Formation Is Enhanced across Sleep Intervals with High Amounts of Rapid Eye Movement Sleep. *Learning & Memory*, *8*(2), 112–119. https://doi.org/10.1101/lm.36801

Wilson, M. A., & McNaughton, B. L. (1994). Reactivation of hippocampal ensemble memories during sleep. *Science (New York, N.Y.)*, *265*(5172), 676–679. https://doi.org/10.1126/science.8036517

Tulving, E. (1972). Episodic and semantic memory. In E. Tulving & W. Donaldson, *Organization of memory.* Academic Press.