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1                                   **The role of the hippocampus in the consolidation**  
2                                   **of emotional memories during sleep**

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6    **Keywords**

7    Oscillations; Reactivation; REM sleep; rodent; consolidation; engram; sharp-wave ripples

8    **Abstract**

9    Episodic memory relies on the hippocampus, a heterogeneous brain region with distinct functions.  
10   Spatial representations in the dorsal hippocampus are crucial for contextual memory, while the  
11   ventral hippocampus is more involved in emotional processing. Here, we review the literature in  
12   rodents highlighting the anatomical and functional properties of the hippocampus along its dorso-  
13   ventral axis that underlie its role in contextual and emotional memory encoding, consolidation, and  
14   retrieval. We propose that the coordination between the dorsal and ventral hippocampus through  
15   theta oscillations during REM sleep, and through sharp-wave ripples during non-REM sleep, might  
16   facilitate the transfer of contextual information for integration with valence-related processing in  
17   other structures of the network. Further investigation into the physiology of the ventral  
18   hippocampus and its connections with other brain areas is needed to deepen the current  
19   understanding of emotional memory consolidation during sleep.

20   **Main Text**

21   **The hippocampus and spatial and emotional memory consolidation during sleep**

22   Sleep is a physiological state present throughout the entire animal kingdom. In mammals, a  
23   characteristic feature of sleep is a reversible loss of consciousness associated with behavioral  
24   quiescence. This vulnerable state plays a vital role in the proper functioning of various organs,  
25   particularly the brain. Sleep deprivation notably impairs two interconnected cognitive processes:  
26   memory consolidation, i.e. the gradual strengthening of memories over time, and emotional  
27   processing [1]. Emotions have the potential to enhance memory formation, as experiences that  
28   evoke positive or negative emotional responses are more effectively remembered [2]. Specific  
29   contexts can also be associated with emotions, forming direct associations so that the emotion is re-  
30   experienced when exposed to the same context, a phenomenon modeled in rodents with contextual

31 fear conditioning. Emotions are characterized by their valence, which can range from negative to  
32 positive, and by their intensity, which will in turn influence the arousal level triggered by the  
33 emotion. Both valence and intensity will influence the processing of the emotion and its effect on  
34 memory.. Extensive research in rodents has focused on studying how the physiology of the dorsal  
35 hippocampus (dHPC), a central structure for contextual memory, contributes to the encoding,  
36 consolidation, and retrieval of spatial memories during both wakefulness and sleep. The ventral  
37 hippocampus (vHPC) is considered functionally distinct from the dHPC, and a large body of selective  
38 lesions and pharmacological inactivation studies established its role in emotional processing,  
39 especially stress-, fear-, and anxiety-related behaviors [3–9]. Here, we review the rodent literature to  
40 first, compare the known spatial and emotional features of the dorsal and ventral hippocampus. We  
41 then discuss evidence supporting the notion that the interactions between the hippocampus and  
42 other core valence-processing structures, such as the basolateral amygdala (BLA), nucleus  
43 accumbens (NAc), anterior cingulate cortex (ACC) and medial prefrontal cortex (mPFC), are crucial  
44 for the processing of spatial and emotional information during sleep. Notably, we argue for a  
45 potential role of the vHPC as a central hub for integrating context and valence information,  
46 contributing to emotional memory acquisition and retrieval, as well as consolidation during sleep.  
47 Investigating well-known mechanisms of the dHPC like neural reactivation, non-REM sleep sharp-  
48 wave ripples, and REM sleep theta oscillation in the vHPC in the context of emotional memory  
49 consolidation and exploring how the valence of an experience modulates dorso-ventral coordination  
50 during sleep will deepen current understanding of how contextual information is processed in  
51 parallel or convergence across the hippocampus dorso-ventral axis and associated with emotional  
52 information to consolidate the memory of emotional experiences.

### 53 **Spatial and emotional neural representations along the hippocampus dorso-ventral axis**

54 The hippocampus contains place cells that selectively activate at particular locations of an  
55 environment, called the place field [10,11]. Altogether, hippocampal place cells form cognitive maps  
56 [12,13] believed to sustain spatial learning. The exposure to a completely different environment can  
57 lead to drastic reconfiguration of the hippocampal cognitive map, a process referred to as global  
58 remapping, but more moderate changes in the environment, like spatial ‘stretching’, re-shaping, and  
59 adding or removing sensory cues lead to more subtle changes in the spatial representation: in some  
60 cases, place cells only change their firing rate (referred to as rate remapping), and in other cases a  
61 subset of cells changes the location of their place-fields (referred to as partial remapping; see [14]  
62 for review). In the dHPC, spatial representations can be modulated by the emotional valence of an  
63 experience. For instance, the introduction or removal of an aversive footshock in an environment,

64 such as in contextual fear conditioning and extinction, respectively, triggers remapping [15–17].  
65 Place fields tend to relocate towards locations associated with positive valence (or reward), referred  
66 to as “goal-directed remapping”, or towards locations associated with negative valence (e.g. due to a  
67 air puff), leading to a higher density of place fields around emotionally salient zones [18,19]. A  
68 subset of dHPC cells activates specifically at reward sites, independently of their location, thus  
69 directly encoding positive valence independently of space (“reward cells”, [20]). In addition, there  
70 are dHPC cells specifically active during freezing, a typical fear-related behavior [17].  
71 Representations in the dHPC are therefore mostly spatial but can adapt to integrate valence-related  
72 information.

73 Compared to the dorsal part of the hippocampus, the vHPC contains a smaller number of place cells  
74 with larger place fields [21–23]. During wakefulness, the hippocampal local field potential (LFP)  
75 displays 6-12Hz theta oscillations, and place cell activity occurs at gradually earlier phases of theta as  
76 the animal crosses the place field. This mechanism, called “phase precession” [24], contributes to  
77 the organization of place cell activity into “theta-sequences” at a timescale compatible with  
78 plasticity [25,26]. Phase precession is slower in the vHPC [22]. During spatial navigation, ventral  
79 neurons are less theta-modulated than dorsal ones, but theta power is also overall lower in the vHPC  
80 [27]. In the dHPC, but not in the vHPC, theta amplitude and frequency correlate with features of the  
81 animal’s locomotion (e.g. speed and acceleration) [28,29]. The changes along the dorso-ventral axis  
82 at the single neuron level pervade into the population dynamics, with a reduced dimensionality in  
83 the vHPC [30] corroborating a decreased spatial accuracy (but see [23]). Paralleling this decrease in  
84 spatial features (Fig. 1), there is an increase in valence-related activity in the vHPC: the number of  
85 place cells remapping towards rewards and neurons directly encoding reward increases from the  
86 dorsal to the intermediate hippocampus [31,32], and the vHPC displays specific neuronal patterns in  
87 response to anxiogenic vs. safe environments, or close to rewards [33–35]. vHPC inhibition is  
88 anxiolytic [34], and a reduced vHPC activation was observed in mice resilient to stress [36]. There are  
89 shock-responsive cells in the vHPC [37], and different subpopulations respond to aversive stimuli vs.  
90 reward [38,39].

91 In ethological contexts, it is crucial to associate specific places with salient emotional experiences, to  
92 find food or stay hyper-vigilant in a zone where a predator was previously encountered. It is  
93 therefore difficult to disambiguate spatial and emotional learning. The vast majority of studies on  
94 spatial coding and memory use rewards to stimulate exploration, making them inherently positively  
95 valenced. Still, it is possible to design experiments to reveal non-spatial emotional properties of the  
96 hippocampus. For example, two recent studies in head-fixed animals using odors associated with

97 reward or punishment found that the vHPC was more responsive to the predicted positive or  
98 negative outcome of the odor [40,41]. vHPC neurons also respond to the sound stimulus predicting  
99 the shock during cued fear extinction [42]. Thus, both the dorsal and ventral hippocampus display a  
100 mix of valence-related and spatial features, but the representations are heavily biased towards  
101 space in the dHPC and towards valence and salience in the vHPC, sustaining the functional gradient  
102 from spatial to emotional along the dorso-ventral axis.

### 103 **Hippocampal representations support the retrieval of emotional memories**

104 The term ‘engram’ has been often used to indicate the population of neurons that constitute the  
105 physical trace of a memory in the brain and whose activation supports the retrieval of this memory.  
106 Can hippocampal space and valence representations be seen as engrams for emotional memories?  
107 In other words, can the activation of dHPC or vHPC representations trigger emotion-related  
108 behaviors, effectively constituting the support of emotional memory recall? A series of studies  
109 leveraged tagging and optogenetics methods to address this question. In the dHPC, optogenetic  
110 activation of neuronal ensembles previously associated with a positive (reward) or negative  
111 (footshock) environment is sufficient to trigger the behavior related to the emotional experience (e.g  
112 licking for reward or freezing) in another, neutral environment [43, 44]. These associations between  
113 the valence and the spatial representation can also be artificially manipulated : for example, when the  
114 opto- activation of a neutral spatial representation is paired with a footshock, the activation of this  
115 initially neutral representation subsequently triggers freezing in an neutral environment [45]. The  
116 associations between hippocampal neurons representing a specific context and an emotional  
117 valence, can also be reversed from positive to negative, and a freezing response in a negatively  
118 valenced environment can be reduced by the opto-activation of a competitive engram associated  
119 with a positive valence [46, 47]. Finally, extinction training, i.e. reexposing an animal to a  
120 conditioned stimulus without any threat, suppresses the activation of a dHPC “fear” engram while  
121 activating a new “extinction” engram: manipulating those distinct engrams directly impacts  
122 extinction and relapse of fear memory [48]. vHPC engram studies are still sparse, but seem to  
123 indicate that the activation of ventral hippocampus engrams can also drive valence-related  
124 behaviors: artificially reactivating vHPC cells active during encoding enhances behavioral expression  
125 of fear or reward place preference during retrieval, through interactions with the BLA [49]. Hence,  
126 activation of either the dHPC or vHPC engrams can sustain the recall of contextualized emotional  
127 memories, likely through the recruitment of a larger engram spanning other valence-related  
128 structures. The limited connectivity of the dHPC and extended connectivity of the vHPC (see Box 1)

129 places the vHPC in a strategic position for the transmission and integration of dHPC contextual inf  
130 ormation with valence information.

### 131 **The vHPC selectively receives and routes information from/to other valence-processing structures**

132 The valence-related activity of the vHPC is sustained by vHPC's direct connections with other brain  
133 regions involved in valence processing. Different neuronal pathways sustain distinct behaviors. The  
134 pathways between the vHPC, basal amygdala (BA) and BLA, mPFC, ACC, and NAc have received  
135 particular attention. Manipulating vHPC inputs to BA or BLA in mice modulates contextual fear  
136 response [50,51], without affecting anxiety-like behaviors, potentially sustained by another pathway  
137 including the lateral hypothalamus [37], and the medial prefrontal cortex [52]. In the vHPC, the  
138 neurons responding to shock during contextual fear conditioning preferentially project to BLA [37].  
139 Contextual fear conditioning induces a strengthening of vHPC-BA synapses, especially for a subset of  
140 BA neurons that receive monosynaptic inputs from context-responding vHPC cells [53]. These vHPC  
141 inputs to the BA are necessary for contextual fear retrieval [54]. The inputs from vHPC to the NAc  
142 promote susceptibility to chronic stress [36], but also mediate cocaine-induced place preference and  
143 reward-oriented behavior, potentially linking a spatial-emotional joint engram in the vHPC with a  
144 valence engram in the NAc [35,55]. Inputs from the vHPC to the mPFC modulate the acquisition and  
145 retrieval of fear and fear extinction memory [56–58], probably through the transfer of contextual  
146 information. vHPC to mPFC inputs are also involved in the bi-directional modulation of anxiety-  
147 related behavior in the absence of learning [52,59]. Finally, parallel vHPC to lateral septum  
148 projections are involved in approach/avoidance behavior [60].

149 The vHPC sends projections to multiple valence-related structures along segregated paths, but also  
150 receives inputs from these structures. Manipulating BLA inputs to the vHPC in mice modulates  
151 anxiety-like behaviors, depressive-like behaviors, and fear extinction [61–63]. Post-training  
152 manipulation of the BLA inputs to the vHPC modulates aversive memory consolidation [64,65]. The  
153 BLA neurons projecting to the vHPC encode positive and negative valence in the same proportion  
154 [66]. The vHPC was also shown to be important for contextual fear generalization, a form of long-  
155 term memory, through its connections with the ACC [67,68]. Using tracing and selective optogenetic  
156 manipulations, these studies have established the vHPC as a strategic outpost for the circulation of  
157 valence information within a larger network during wakefulness. Sleep is crucial for spatial memory  
158 consolidation, but the mechanisms underlying the consolidation of emotional memory along the  
159 anatomo-functional pathways described in this section are mostly unknown.

### 160 **The reactivation of hippocampal representations during sleep sustains memory consolidation**

161 Memory consolidation is believed to occur partially during sleep through the “off-line” activation of  
162 patterns of neural activity previously elicited during learning, a phenomenon referred to as  
163 reactivation. Early reactivation studies in rats described that the firing rates or pairwise correlated  
164 activity observed during wakefulness in the dHPC were maintained during the following non-REM  
165 (NREM) sleep epoch [69,70]. It is now known that the temporal order of place cell firing can be  
166 conserved during reactivation, replaying entire trajectories during NREM following exploration  
167 [71,72]; this type of sequence reactivation is called “replay” [73–75]. Hippocampal reactivation  
168 preferentially occurs during hippocampal sharp wave-ripple complexes (SWRs) generated by the  
169 synchronous, spontaneous activation of CA3 pyramidal neurons propagating to the CA1 region [76].  
170 SWRs are believed to enable a decrease in the synaptic strength of irrelevant neuronal connection  
171 by promoting network long-term depression (LTD;[77]), and the strengthening of relevant neuronal  
172 connections through selective long-term potentiation (LT;[78]), effectively enhancing the signal-to-  
173 noise ratio and therefore supporting memory consolidation [79]. In rats, the blockade of dHPC SWRs  
174 during post-learning NREM, which concomitantly silences hippocampal activity and therefore the  
175 associated reactivation, impairs spatial memory consolidation in rats [80,81]. On the contrary, the  
176 selective sparing of reactivation associated with an environment by suppressing all other  
177 synchronized events including reactivation of a second environment induces a learning impairment  
178 restricted to the suppressed environment [83]. The indirect suppression of dHPC SWRs during NREM  
179 sleep also impairs contextual fear conditioning in mice [82]. . NREM sleep SWRs and reactivation in  
180 the dHPC thus sustain spatial memory consolidation.

181 How does emotional valence influence reactivations? During sleep ripples, stimulating dopaminergic  
182 inputs to the dHPC increases pairwise reactivation [84], suggesting an influence of valence or  
183 salience on sleep replay [85]. Artificially pairing place-cell activity during sleep with middle forebrain  
184 bundle (MFB) stimulations, thought to be intrinsically pleasurable through the activation of  
185 dopaminergic fibers, induces subsequent reward-related behavior toward the associated place field  
186 locations [86]. Thus, the activation of the dopaminergic system during sleep directly influences  
187 spatial memory consolidation, but the effect of valence on sleep reactivation is likely initiated during  
188 the encoding phase, a process conceptualized as “emotional tagging” [87]. Indeed, a study in rats  
189 underscored a preferential role of hippocampal replay for the consolidation of large rewards  
190 compared to small ones during a 2 hours delay period between acquisition and retrieval [88].  
191 Dopamine release is modulated by reward, aversive stimuli, salience, uncertainty, and novelty [89],  
192 and mediates hippocampal synaptic potentiation and neuron excitability [90], potentially enhancing  
193 the hippocampal representations of relevant locations and influencing the replay content of awake  
194 SWRs occurring during non-exploratory states of wakefulness [73,91,92]. Awake ripples and reverse

195 replay are enhanced by the presence of reward [93,94], and awake replay will preferentially  
196 represent trajectories leading to a reward [95] (but see [96]). Replay has been detected during the  
197 avoidance of a shock zone [97], suggesting that it might sustain aversive memory retrieval. Finally,  
198 place cells that remap in a spatial avoidance task increase their participation in awake ripples during  
199 training [98], suggesting a link between the integration of aversive elements into the hippocampal  
200 representation and its immediate preferential processing. Another parameter to consider is that  
201 animals will avoid an aversive zone, and spend more time around rewarded areas, effectively  
202 reducing or increasing, respectively, the activity of the corresponding place cells, which could  
203 directly affect later reactivation. The acute stress triggered by an aversive experience could also  
204 influence reactivation, as suggested by the fact that repeated restraint stress decreases CA1  
205 pyramidal activity, but increases participation in SWRs during wake and sleep [99]. Of note, chronic  
206 stress might have longer-term deleterious effects on memory, which differ widely from those of  
207 acute stress [100].

208 Like the dHPC, the vHPC also displays ripples during non-exploratory wakefulness and NREM sleep.  
209 However, it remains unknown whether vHPC ripples are associated with reactivation (see  
210 Outstanding Questions). We propose that the vHPC relies on consolidation principles similar to those  
211 established in the dHPC for spatial memory consolidation [74], but applied in the vHPC to  
212 consolidate valence-related information. To what extent this valence information would be  
213 contextualized remains to be established, as well as the mechanisms involving neuromodulatory  
214 systems by which valence during an experience will influence later dHPC and vHPC sleep-dependent  
215 reactivation.

## 216 **Neural oscillations coordinate the hippocampus and other valence-processing structures**

### 217 *Theta oscillations during encoding and retrieval*

218 Various models of contextual emotional learning involve the hippocampus in combination with other  
219 valence-related structures. Contextual fear conditioning (CFC) is the canonical model for  
220 contextualized aversive memory, i.e. the association of a specific context with an aversive stimulus,  
221 usually a footshock, in the context of rodent studies. CFC requires both the dHPC, believed to  
222 process the context, and the BLA [101], one of the core structures of the network processing fear  
223 and anxiety [102], including fear memory. Conditioning an animal to a simple auditory cue does not  
224 appear to require the hippocampus, suggesting that the hippocampus and the BLA interact to  
225 integrate aversive with context information. In addition, the mPFC, which has limited connectivity  
226 with the dHPC, is involved in the control of the expression of conditioned fear [103]. Observational



227 fear learning (OFC) is a complex behavior that involves context, valence, and social processing.  
228 Animals having experienced shocks in a given context exhibit freezing when watching a conspecific  
229 experiencing the shock. The initial formation of the memory trace of the context in the dHPC is  
230 required and drives the formation of a memory trace in the BLA. A study in mice has shown that the  
231 expression of OFC involves the vHPC and BLA [104], and highlights the joint involvement of both the  
232 dHPC and vHPC in processing memories involving context and valence, in coordination with other  
233 structures of the network, in this case, the BLA [64]. What are the neural mechanisms underlying  
234 these interactions? Oscillations are believed to synchronize neural activity within and across  
235 structures, and phase-locking (i.e. the firing of neurons at specific phases of the LFP oscillation) is a  
236 marker of this synchronization. Within the hippocampus during exploration and movement, theta  
237 paces place-cell activity, organizing the neuronal assemblies that will later be reactivated during  
238 sleep [25]. The peak and troughs of the theta rhythm are favorable to LTP and LTD, respectively, in  
239 awake and anesthetized animals [105–107]. Coordination in the theta band between the dHPC, the  
240 amygdala, and the mPFC correlates with the acquisition and retrieval of cued and contextual fear  
241 conditioning [108–111]. Of note, however, the theta band as defined in these publications  
242 potentially overlapped with the 4-Hz coordinated oscillation between the mPFC and amygdala that  
243 was later shown to control the expression of freezing [112,113]. In a study in mice, manipulating  
244 theta power in the vHPC was shown to modify the amount of exploration of odor predator-  
245 associated zones [114]. In addition, theta coordination between the vHPC and mPFC is increased in  
246 anxiogenic environments [115], and mPFC units responding to aversive or safe stimuli in anxiogenic  
247 tasks are strongly locked to vHPC theta, but not dHPC theta [116]. In another study, optogenetic  
248 stimulation at theta frequency of vHPC inputs to mPFC activity was associated with increased  
249 synchronicity between vHPC theta and mPFC spiking activity and enhanced avoidance behavior in  
250 the elevated plus-maze [117]. Theta oscillations during wakefulness thus emerge as a key  
251 mechanism for the synchronization of dHPC and vHPC with other structures sustaining innate and  
252 learned emotional behaviors.

### 253 *Theta oscillations during REM sleep*

254 Theta oscillations are also a hallmark of REM sleep. Studies in humans point towards a role for REM  
255 sleep in emotional memory consolidation ([118], but see [119]). The underlying physiological  
256 mechanisms, however, are still largely unknown (see Outstanding questions). Studies in mice and  
257 rats have shown that selective REM sleep deprivation or inhibiting theta oscillations during post-  
258 learning REM induces contextual memory impairments [120,121]. However, classical, NREM-like  
259 dHPC reactivation has not yet been widely found during REM sleep [122], although there are some

260 similarities between awake and REM sleep neuronal patterns [123,124]. Theta power in the dHPC  
261 during a REM-sleep episode correlates with an increase in the synchrony and firing rate of pyramidal  
262 cells during the SWRs of the following NREM epoch [125], suggesting that REM sleep might initiate  
263 plastic changes implemented during NREM sleep. Aversive learning and extinction trigger changes in  
264 theta synchronization during REM across the dHPC, vHPC, BLA, and mPFC, especially in the dHPC-BLA  
265 coherence and vHPC-LA phase shift [126,127], but in the absence of structured dHPC-BLA  
266 reactivation [128]. Hippocampal theta oscillations are traveling waves [129], the propagation of  
267 which across the dorso-ventral axis [29] could mediate communication between the dHPC, vHPC,  
268 and the rest of the valence-related network through the vHPC connections. Indeed, theta  
269 synchronization between the dorsal and ventral hippocampus increases during the retrieval of trace  
270 fear conditioning [130]. Thus, further investigation is required to elucidate how changes in the  
271 organization of neural activity by REM theta oscillations within the hippocampus and across  
272 structures might contribute to the consolidation of experiences of different emotional valence and  
273 salience.

#### 274 *SWRs during non-exploratory wakefulness and non-REM sleep*

275 During training on a rewarded spatial task, dorsal and ventral SWRs activate distinct and opposing  
276 patterns of NAc spiking. NAc neurons responding to dHPC SWRs show more location and reward-  
277 related activity [131], and the coupling between dHPC and NAc neurons encoding a location  
278 associated with cocaine administration increases during wakefulness and sleep [132]. This suggests  
279 that awake and sleep SPWs originating from the dHPC vs. vHPC could play distinct roles in the  
280 integration of space and valence information, supported by the respective anatomical connexions  
281 between the dHPC, vHPC, and NAc [133]. Reward-responsive ventral tegmental area (VTA) neurons  
282 activate synchronously with dorsal hippocampal reactivation events of appetitive spatial experience  
283 during quiet wakefulness [134], and ventral striatum reward-related cells also reactivate in  
284 coordination with dHPC place cells during SWRs [135,136], probably primed by the coordination of  
285 dHPC-striatal neural activity by theta phase-precession during learning [137]. Thus, interactions  
286 between the dHPC and other structures related to reward processing might sustain the  
287 consolidation of place-reward associations [86]. On the other end of the valence spectrum, the  
288 dHPC-BLA pairwise representation of an aversive experience is reactivated during NREM sleep SWRs  
289 [128]. In the absence of direct connections between the dHPC and BLA [138,139], these joint  
290 reactivations necessarily involve at least one relay structure, potentially the vHPC. Indeed,  
291 inactivating vHPC neurons after training impairs the consolidation of contextual fear memory [140],  
292 potentially by impairing the vHPC NREM reactivation of stimulus-related activity which is modulated  
293 by BLA inputs [42]. During NREM sleep following fear conditioning, there are also multi-structure

294 reactivations involving the vHPC, BLA, and infralimbic part of the mPFC associated with high-  
295 frequency oscillations in vHPC and BLA and modulated by cortical slow waves [141]. Because they  
296 propagate along the dorso-ventral axis [142], SWRs are a likely candidate for binding dorsal and  
297 ventral hippocampus activity during NREM sleep. There is a progressive decrease in the dorso-  
298 ventral coordination of SWRs along the dorso-ventral axis, reaching marginal coordination between  
299 the most dorsal and ventral zones (Fig. 2). However, this has only been examined in the absence of  
300 previous spatial or emotional learning, and the need for joint consolidation of spatial and valence  
301 information could affect dorso-ventral SWR coordination.

302 In the cortex, NREM sleep is characterized by thalamo-cortical spindles and slow oscillations arising  
303 from the synchronized alternation of periods of high activity and quiescence in cortical neurons,  
304 referred to as “up” and “down” states. Systems consolidation involves a transfer of information from  
305 the hippocampus to cortical areas and is mediated by the temporal organization of neural activity by  
306 dorsal hippocampal SWRs, thalamo-cortical spindles, and cortical slow oscillations [143]. Notably,  
307 the artificial enhancement of the coordination between dHPC ripples and down-state-spindle  
308 complexes in the mPFC improves memory consolidation [144]. Thus, dHPC-cortical coordination is a  
309 crucial mechanism for memory consolidation despite the limited anatomical connections between  
310 the dHPC and mPFC [145,146]. The coordination between ventral ripples and cortical/thalamic slow  
311 waves also increases after contextual fear learning, as well as ventral ripple events phase-locking to  
312 cortical/thalamic spindles, albeit uncorrelated with memory performance at retrieval [147]. The  
313 thalamic nucleus reuniens is emerging as a relay structure for the coordination between the ventral  
314 and intermediate hippocampus and the mPFC [147,148]. To our knowledge, only one study has  
315 established the functional implication of the monosynaptic connections from the ventral and  
316 intermediate hippocampus to the mPFC during memory consolidation [149]. Systems consolidation  
317 of emotional memories could thus involve direct or indirect coordination between the vHPC and  
318 cortical areas, and/or triple coordination of dorsal and ventral hippocampus SWRs with cortical  
319 oscillations.

## 320 **Concluding remarks and future perspectives**

321 The features of neurons along the dorso-ventral axis of the hippocampus display a gradient from  
322 mostly spatial to mostly emotional, and the neural representations in the dHPC and vHPC are  
323 involved in the expression of contextual and valenced memories through their connectivity with  
324 other valence-related structures. Spatial memories are consolidated during sleep through neural  
325 reactivation and the organization of neural activity by non-REM sleep SWRs and REM sleep theta  
326 oscillations. Although these phenomena have been mostly studied in the dHPC, there are

327 preliminary indications that the same principles could hold for emotional memory consolidation in  
328 the vHPC. However, most memories are complex and combine contextual and emotional  
329 information. How is the contextual information transferred to structures that lack direct connectivity  
330 with the dHPC? We propose that changes in the coordination between the dorsal and ventral  
331 hippocampus through theta oscillations and SWRs might underlie the gating of contextual  
332 information for their integration with valence information processed in the rest of the network,  
333 including the BLA and mPFC. To directly test this hypothesis and more generally refine theories of  
334 the processing of emotional information, the physiology of the vHPC and this area's connections  
335 with the rest of the valence network deserve further investigation. For example, vHPC inputs to the  
336 mPFC are anatomically and functionally segregated according to the depth of the projecting neurons  
337 in the pyramidal layer: superficial neurons are preferentially connected to PFC inhibitory  
338 interneurons and promote exploration, whereas deeper neuronal populations project to PFC  
339 pyramidal neurons and fast-spiking interneurons, and promote avoidance [59]. In the dHPC, CA1  
340 pyramidal neurons have different spatial properties depending on their depth [150,151], influencing  
341 their recruitment into slow oscillations, SWRs, reactivation, and REM theta [146,152,153]. Can  
342 similar gradients be found in the vHPC for spatial or valence-related properties? Crucially, it is still  
343 unknown whether vHPC neuronal assemblies reactivate during vHPC ripples. If so, would the content  
344 of the reactivation be exclusively valence-related or exhibit a mix of valence and contextual  
345 information? Would vHPC reactivation be coordinated with contextual reactivation in the dHPC?  
346 Overall, a better understanding of how ventral and dorsal hippocampal sleep SWRs and reactivation  
347 differentially recruit other brain areas would help refine their respective roles during emotional  
348 memory consolidation. Of note, a longstanding bias has restricted research on memory  
349 consolidation to mostly males. While it is unclear how sex and hormonal variations affect spatial  
350 memory, it is known that there are sex-dependent differences in fear conditioning [154] and that  
351 hippocampal plasticity is susceptible to hormonal changes [155]. Because women are more  
352 susceptible to PTSD and anxiety disorders, future research on emotional memory consolidation in  
353 rodent models should strive to balance the sexes and carefully examine potential sex differences.  
354 Finally, there is still a lack of both causal and physiological evidence supporting the involvement of  
355 ventral theta oscillations during REM in memory consolidation. Overall, the vHPC holds significant  
356 potential as a focal point for future research on emotional memory consolidation during sleep, with  
357 particular attention to be paid to the pertinent anatomical connections between neural circuits.

358 **Box 1: Intrinsic and extrinsic hippocampal anatomical connectivity.** Anatomical studies have  
359 revealed distinct connectivity patterns along the dorso-ventral axis of the rodent hippocampus and  
360 the brain structures of the valence-processing network mentioned in this review. Unless specified,

361 these connections are glutamatergic. There are bidirectional connections all along the dorso-ventral  
362 axis with the thalamic nucleus reuniens [156], thus considered the main relay between the  
363 hippocampus and cortical areas. However, the medial prefrontal cortex receives direct input  
364 from the intermediate and ventral hippocampus [53, 60], and has also marginal connections  
365 with the dHPC [145,146].

366 . The NAc, part of the ventral striatum, receives inputs from all hippocampal subregions [131,133],  
367 but no projections from the NAc to the hippocampus have been identified. The VTA is a  
368 heterogeneous structure with intermingled dopaminergic, GABAergic, and a small population of  
369 glutamatergic neurons. The VTA sends sparse dopaminergic innervation to the whole hippocampus  
370 and glutamatergic projections to the dHPC which are thought to instruct the dHPC with reward  
371 signals [157]. The VTA doesn't receive direct hippocampal inputs [158]. The BLA, a core structure of  
372 the valence-processing network, has bidirectional connections with the ventral part of the  
373 hippocampus only [138](Fig. 2B).

374 In this review, we hypothesize that the association of spatial information with valence information  
375 might involve the transfer of spatial and emotional information along the dorso-ventral axis. These  
376 could rely on at least two forms of intra-hippocampal anatomical connectivity. The first one is direct  
377 long-range monosynaptic connections between the dorsal and ventral poles. Notably, dorsal CA2  
378 neurons were shown to project to the ventral CA1 region implicated in social memory [159].  
379 Additional long-range projections remain to be established. The second one is overlapping local  
380 excitatory/inhibitory circuits along the dorsal-ventral axis that could synchronize through the  
381 inhibitory interneurons and the recurrent collaterals of the CA3 pyramidal cells [76]. This indirect  
382 path potentially underlies the coordination of SWRs and the traveling of theta waves. However, both  
383 theta coherence and SWR coordination decrease drastically in the ventral pole [29,142], suggesting a  
384 partial disconnection between the dorsal/intermediate and ventral hippocampus. Given the high  
385 genomic, proteomics, cellular, and connectivity heterogeneity across the dorsal-ventral axis [5], and  
386 the variation in the delineation of the hippocampal segments as a function of the chosen criteria, it  
387 is difficult to identify the anatomical, cellular, and/or electrophysiological factors explaining this  
388 coordination drop and the exact location of the ventral border. Because the excitability and GABA  
389 release change along the dorso-ventral axis [160] and are modulated by learning, one may speculate  
390 that environmental factors, such as learning from a highly emotional experience, may temporarily  
391 modulate the excitability of dorsal and ventral neurons around the intermediate-ventral zone to  
392 control for the coordination between the dorsal and ventral hippocampus (see Outstanding

393 questions). Alternatively, the dorsal and ventral poles could synchronize through the coordinating  
394 influence of external structures.

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401

### 402 **Declaration of interests**

403 The authors declare no competing interest .

404

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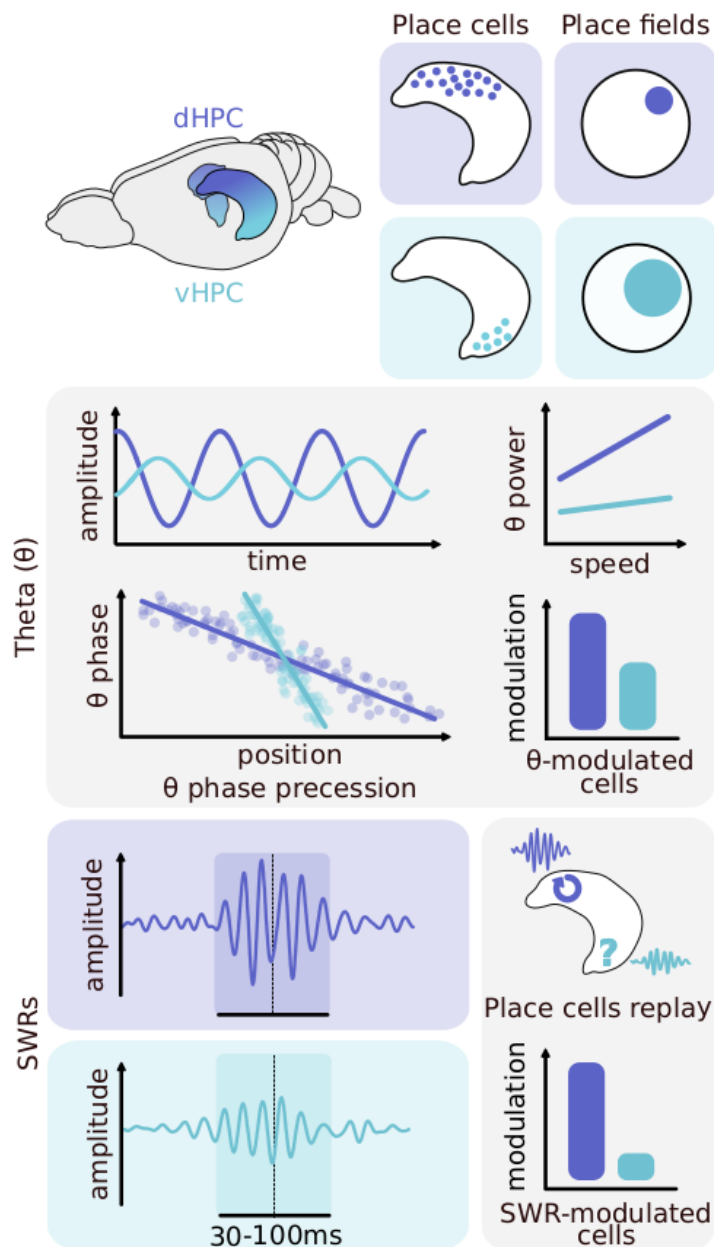
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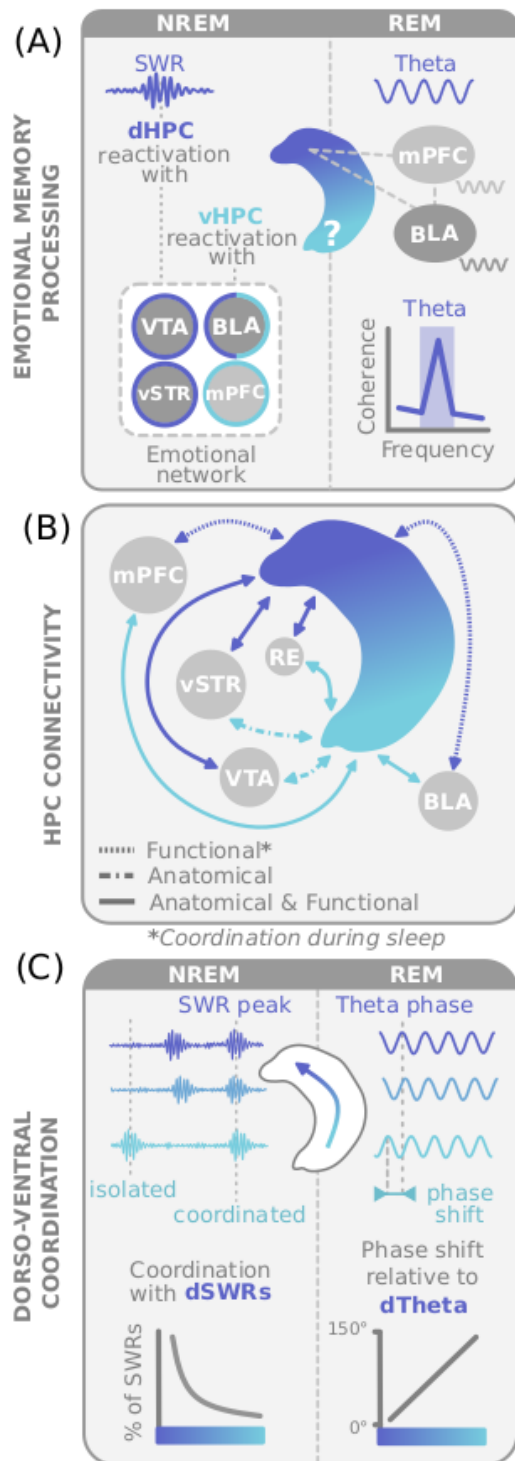
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**Figure 1. Firing properties of rodent hippocampal neurons along the dorso-ventral axis.** Compared  
 740 to the dHPC, vHPC place cells are fewer and have larger place fields [21,22]. Phase precession, the  
 741 process by which place cell activity occurs at earlier phases of theta ( $\theta$ ) as the animal crosses the  
 742 place field, is slower in the vHPC [22]. During navigation,  $\theta$  power is lower in the vHPC than in the  
 743 dHPC, and vHPC cells are less  $\theta$ -modulated than dorsal ones: their firing is more dispersed across  
 744 different  $\theta$  phases [27].  $\theta$  power correlates with speed in dHPC but not vHPC [29]. Ripple amplitude  
 745 is lower in vHPC than in the dHPC, and vHPC cells are less ripple-modulated than dHPC ones [142]. It  
 746 is yet unknown whether the reactivation described in the dHPC also occurs in the vHPC.



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749 **Figure 2. Anatomical-functional characteristics throughout the hippocampus during sleep.** A. The  
 750 hippocampus is involved in emotional processing during sleep. During NREM or quiet wakefulness,  
 751 and preferentially during ripples (SWR), following reward/aversive learning, there are coordinated  
 752 reactivations between the dHPC and valence-processing structures: ventral striatum (vSTR), ventral  
 753 tegmental area (VTA), and basolateral amygdala (BLA);[128,135,136]. The vHPC was shown to

754 reactivate with the BLA and the medial prefrontal cortex (mPFC)[141]. During REM sleep following  
755 aversive learning, theta coherence increases between dHPC, BLA, and the medial prefrontal cortex  
756 (mPFC)[126] **B.** The observations summarized in (A) can only be partially explained by the anatomo-  
757 functional connectivity of the hippocampus along the dorso-ventral axis. Functional connections  
758 indicate that oscillatory or neuronal coordination between the hippocampus and the other  
759 structures represented in the graph have been described during sleep and correlated with memory  
760 formation. **C.** Oscillations propagating along the hippocampal dorso-ventral axis during sleep could  
761 mediate the transfer of contextual and emotional information along the longitudinal axis and  
762 towards the other structures of the emotional network. During NREM, dorso-ventral SWRs  
763 coordination decreases along the axis, and most vHPC SWRs are isolated from dorsal ones. During  
764 REM, theta oscillations travel across the dorso-ventral axis and their phase shifts [29,142].

## Highlights

- The rodent dorsal hippocampus displays spatial representations that can be biased by the positive or negative valence of the environment.
- The ventral hippocampus displays poorer spatial coding properties than dHPC but stronger valence-related processing.
- The reactivation of spatial representations in the dHPC that sustain spatial memory consolidation can occur conjointly with valence-processing structures despite limited direct anatomical connections.
- The vHPC has reciprocal connections with key structures of the valence-processing network such as the basolateral amygdala or medial prefrontal cortex.
- The vHPC has the potential to serve as a central hub for the integration of contextual information from the dorsal hippocampus and valence information from the rest of the network during sleep-dependent consolidation, through theta oscillations during REM sleep and sharp-wave ripples during Non-REM sleep.



## Outstanding questions

- It is now firmly established that dHPC ripples and the associated neural reactivation are necessary for spatial memory consolidation. Surprisingly, it is still unknown whether there is neural reactivation in the vHPC during sleep. If so, would vHPC reactivation also be associated with vHPC ripples? Would vHPC reactivation also sustain memory consolidation, and if so, which type of memory? We would expect vHPC ripples and reactivation to be more specifically involved in the consolidation of emotionally charged memories. A better characterization of ripple parameters and ripple-associated neural activity during consolidation in the vHPC is required.
- Ripples and theta oscillations are weakly coordinated along the dorso-ventral axis in the absence of consolidation requirements (i.e. previous learning or exploration). How is the dorso-ventral coordination during sleep affected by the valence of the preceding experience? What are the anatomical underpinnings of disconnection vs. coordination? Is the mechanism intra-hippocampal, or does it involve third-party coordinating structures?
- The physiological underpinnings of the role of REM sleep for emotional memory consolidation are still unclear. Could REM sleep be more important for vHPC-mediated emotional processing, as opposed to NREM for dHPC-mediated spatial processing?
- How does emotional valence during encoding influence sleep reactivation in the dorsal hippocampus? What are the mechanisms underlying these processes, and do they involve other structures like the BLA, known to mediate the potentiating effects of stress on memory formation?