Chapter 6
Reorganization of Hippocampal Place-Selective Patterns During Goal-Directed Learning and Their Reactivation During Sleep

David Dupret and Jozsef Csicsvari

Abstract Firing patterns of hippocampal principal cells are thought to participate in the formation of mnemonic representations of place, which ultimately can be used to guide the behavior of animals in space. Past studies have suggested that place-selective activity in the hippocampus can emphasize the representation of discrete locations associated with a strong behavioral salience. In the first part of this book chapter, we review work that has described how that hippocampal neuronal activity patterns reorganize during spatial learning. These studies revealed that new hippocampal maps emerge during spatial learning to represent the location of goal locations and demonstrated that, during recall, the reinstatement of these maps predicts successful memory performance. In the second part of this chapter, we discuss the role of sleep in memory consolidation in the context of goal-oriented spatial learning. We summarize work that has demonstrated the replay of goal-oriented neuronal assembly patterns that predict subsequent memory recall. Moreover, we argue that the initial strengthening of new maps may in fact take place during learning, triggered by waking sharp-wave/ripple patterns occurring at goal locations. These reviewed studies highlight that the reorganization and replay of place cell firing patterns might constitute a circuit signature for the expression of newly acquired hippocampal engrams.

Keywords Hippocampus • Place cells • Remapping • Sharp wave/ripple • Reactivation • Goal-directed learning

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Decades of research have lead to the widely accepted view that the hippocampus provides the brain with an allocentric representation of space, which is used to guide animals in their daily behavior. Numerous lesion studies have established that an intact hippocampus is required for learning the location of discrete places in reference to surrounding, external spatial cues. This was best documented by large body of experimental work on navigation in the Morris water maze [1–3]. Importantly, it has also been established that hippocampal principal neurons code for the location of the animal. These "place" cells selectively increase their activity when the animal moves through the cell's place field [4, 5]. Recording studies during exploration of open-field environments have shown that, once established, new place maps tend to be stable over time as the environment becomes familiar [6, 7]. This suggests that hippocampal place fields constitute the buildings blocks of spatial engrams and that their stability might signal the presence of memory patterns. In this regard, one needs to determine the extent to which the variability in place cell discharge relates to the ongoing changes/fluctuations of the real world in order to understand how hippocampal maps adapt to behavioral experience. Such adaptation of spatial maps has indeed been revealed; for example, it was shown that place cells can alter their firing patterns in response to changes in the layout of the environment [8, 9]. Moreover, their firing is influenced in an otherwise unchanged environment by additional factors such as speed, direction of movement, path stereotypy, and even behavioral task demands (e.g., [10–15]). In these conditions, a global (complete) remapping of place fields can be observed. That is, entirely new place fields appear and already existing place fields disappear or move to different locations. Alternatively, maps may reorganize through rate remapping during which the location of the place field is unchanged; however in-field firing rate of the cell is altered [9, 15–18].

Hippocampal remapping was traditionally studied in relation to the spatial exploration of different environments or when changes took place in the same environment. In these experiments, animals explored familiar or novel environments or a previously experienced environment in which some features such as shape or color were changed, while other features were kept constant. In these conditions, most place cells undergo the same type of remapping, suggesting that each environment is represented by a unique combination of place cell activity. However, in some instances, only a subset of place cells remaps their place fields in response to changes in certain environmental features or changes in behavioral task contingencies [19, 20]. This partial remapping could be due to the fact that different subsets of place cells anchor their place fields to different environmental features and hence use different reference frames. One possible reason for the coexistence of multiple maps associated with the same environment has been suggested to be the demand for the animal to keep track of different reference frames to solve spatial problems, particularly during reward-associated behavioral tasks [21]. Indeed, early studies have shown that the change of reward locations can trigger remapping. Here, place field remapping can be observed when animal's task is shifted from a foraging task in which the food is scattered randomly to a task in which they have to retrieve rewards from fixed locations [14]. Further support came from experiments in which

reward locations marked by cylindrical landmarks are moved across navigation trials [22]. In this task, the position of two landmarks moved from trial to trial with respect to fixed distal cues, while their relative positions were fixed. Moreover, the animal had to reach the rewards from a start box, the location of which was also moved across trials. In this condition, a subpopulation of place cells bound their place fields to goal location-related reference frames, while other place cells either fired in reference to the animal's physical position in the arena or relative to the start box.

Goal-oriented remapping is not exclusively anchored at appetitive reward locations [23–28], which suggests that hippocampal maps can represent the behavioral relevance of locations. When rats were trained to escape from water by finding a hidden fixed platform in an annular water maze, place fields tended to accumulate near the goal location of the escape platform [26]. This goal-oriented clustering of place fields has been observed after learning, in probe session in which the platform was however no longer present [26]. Importantly, no such preferred representation of the goal location was observed when the rats were instead trained to find variable goal locations in the same maze. Moreover, in the same spatial memory task, many place cells begun to increase their activity at a new goal location when the escape platform had been moved from a previously learned location to a new one [25]. A goal-related firing activity has also been observed in rats trained to a place preference task where the visit of an unmarked goal location triggered the release of a food pellet at a random location; in these experiments, many place cells selectively increased their activity at the goal location and, at the same time, maintained a place field outside the goal location [27].

Maps anchored to different reference frames can switch quickly, and different maps can even alternate rapidly when the behavior of the animal demands it. For example, such dynamic flickering of maps is seen in a two-frame place avoidance task in which animals have to keep track of two zones to avoid an electrical shock [29]. These experiments take place in a rotating arena, while animals foraging for food must keep away from the two zones, a stationary shock-zone and a zone rotating with the table. In this task, one map representation is linked to the external cues, while another one rotates with the arena, and because the animal has to keep track simultaneously of both reference frames, the maps flicker from one to the other rapidly.

As we summarized above, studies on place field remapping have emphasized the contribution of the hippocampus in the formation of brain representations of space. They also highlighted that multiple reference frames can exist, which enable behaviorally relevant locations to be represented by a subpopulation of place cells. Such goal-related maps could provide a more accurate code for salient locations to improve behavioral performance. It has been suggested that the formation of goal-related maps may highlight learning processes enabling the reliable association of a reward with a discrete location in space. Ultimately they can also serve as a code for spatial memory traces. However, an alternative explanation of these studies is also possible. One cannot exclude that the goal-oriented remapping is not caused by learning per se, but the findings may be better explained by associated changes in

behavioral patterns. That is, goal-related remapping might have been triggered by changes in the path stereotypy or related changes in the motor behavior. Excluding these possibilities requires systematic investigations using specially designed spatial learning paradigms.

Reorganization of Hippocampal Place Cells During Goal-Directed Spatial Learning

In order to test whether network activity in the hippocampus can code for a memory trace, one needs to track neuronal responses during the entire memory formation process including encoding, consolidation, and recall. In the context of spatial memory traces, one would expect that some place cells remap their place field during the acquisition of new spatial memories to represent the information that has to be learned and later remembered in relation to the task demand. During goal-directed learning, such reorganization of place cell activity should be, to some extent, oriented toward the learned goal locations to enable their mnemonic coding. If this is the case, one would need to show that such goal-oriented remapping is a consequence of learning and has not been merely triggered by alterations of motor behavior or locomotion path as seen when animals develop efficient navigation during the learning phase. Importantly, when such new memories are assessed later, the successful recall, as measured by good memory performance during recall, should correlate with the reinstatement of the newly acquired firing patterns such as the new goal-oriented maps acquired during learning. One would also expect that such learning-related neuronal patterns may also recur during the consolidation stage to facilitate the stabilization of memories, as we discuss later.

There have been several behavioral tasks developed as dry maze equivalents of the Morris water maze to assess place learning, including the Barnes maze or auditory avoidance task [30, 31]. We have chosen a task using the cheeseboard apparatus [32], which is a circular arena that contains many food wells in which food can be hidden in order to demonstrate the mnemonic contribution of hippocampal place cells [33]. Each day, rats have to learn a new set of three goal locations where food rewards were hidden and retrieve these rewards before returning to the start box to collect an additional reward (Fig. 6.1a). During this learning period, typically consisting of at least 40 trials, the task performance of the animals improves rapidly, reaching a nearly optimal performance within the first 5 trials (Fig. 6.1b). This shows that rats can rapidly encode reward locations and remember them across the remaining trials.

Work examining the stability of newly formed maps in novel environments suggested that NMDA-dependent plasticity is required for the stabilization of new maps when these maps are tested over longer periods [7]. This work also showed that such plasticity-associated map stabilization was needed even when the delay was as short as 2 h. Therefore, as we wanted to minimize the overall duration of our experiments to ensure stable neuronal recordings, we assessed the memory for the

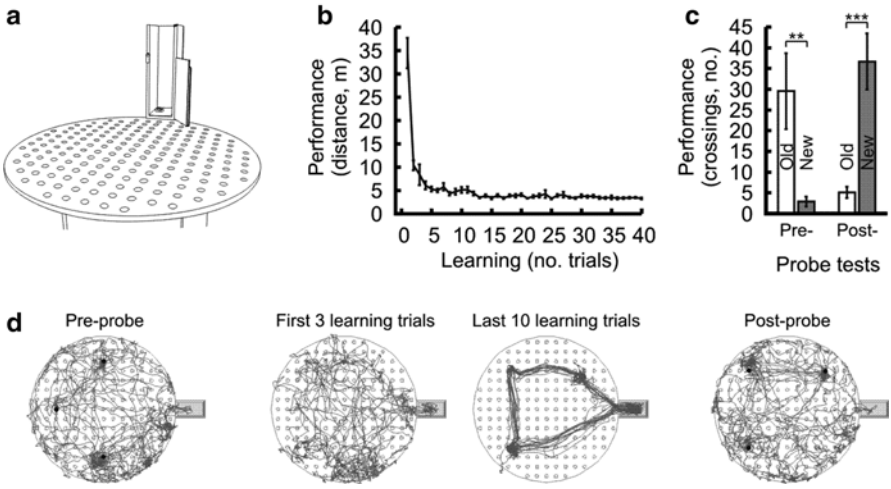

Fig. 6.1 Goal-directed learning paradigm on the cheeseboard maze. Rats were trained in a matching-to-multiple-places task to locate a new set of three hidden food rewards every day on a cheeseboard maze (**a**). Learning performance was estimated by the distance traveled to find all rewards per trial (**b**; means ± s.e.m). Memory performance (**c**, means ± s.e.m) was measured by the number of crossings at the goal locations learned the day before ("old") and the current day ("new"). Representative examples of animal's path (**d**); for clarity, only the first 10 min of each probe session are depicted (*black dots*: learned goal locations). Adapted from [33]

newly learned locations approximately 2 h after learning in subsequent probe trials. During the probe trials, food was no longer available, and recall performance was assessed by the number of crossings through the goal areas. As in the Morris water maze task where rats frequently cross the location of the removed escape platform, the previously learned reward locations were also crossed frequently by the rats trained on the cheeseboard maze (Fig. 6.1c, d). We also performed experiments under NMDA blockade (systemic administration of CPP). In these experiments, animals were able to learn goal locations under NMDA blockade, but they were no longer able to recall these goal locations after the 2 h delay. This confirmed that the newly learned spatial memories are needed to undergo some degree of NMDA-dependent stabilization for successful recall.

To reveal how spatial memories of new goal locations were represented in the hippocampus during our task, we recorded the activity of multiple place cells and oscillatory field potential patterns using multichannel extracellular techniques. As we mentioned above, previous work suggested that place cells can fire in reference to reward and associated goal locations [14, 22–24, 27, 28, 34, 35]. As with previous work, many place cells fire at the newly learned reward locations on the cheeseboard maze in our task as well (Fig. 6.2). However, in our case, we found that remapping was region specific. Here, goal-related remapping took place in the CA1 region of the hippocampus only, while CA3 place cells did not alter their spatial selectivity. Importantly, the reorganized CA1 place maps were reinstated in the

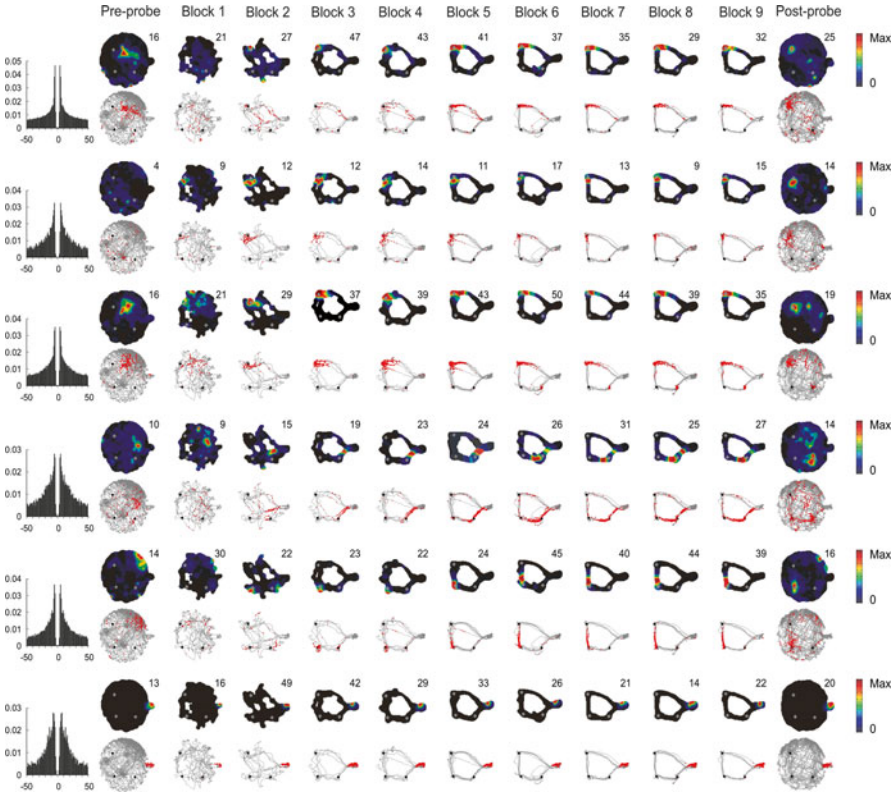

Fig. 6.2 Examples showing the activity of CA1 hippocampal place cells on the cheeseboard maze. Simultaneously recorded CA1 place cells are shown on alternating rows with their auto-correlogram, color-coded place rate maps, and individual spike locations superimposed on the animal's path. Both rate maps and raw spike data are depicted for each probe session ("pre-probe," "post-probe") and across successive learning trial blocks. The color code in the rate maps is from *blue* (low firing rate) to *red* (peak firing rate), with the maximum firing rate (Hz) of the color scale indicated on the *top right* of each map. High firing rate regions marked by warm colors indicate the "place field" of the cell and *gray dots* mark the goal locations. In the figures showing the movement path of the animal (*gray traces*), *red dots* mark action potential locations and black dots indicate the goal locations. Adapted from [33]

subsequent memory probe session where these new goal locations were recalled successfully. Moreover in the NMDA blockade experiments, while goal-oriented maps were formed during learning, these were not reinstated in the subsequent probe trials, mirroring the behavioral impairment of the animal.

Next we examined whether the alteration of motor patterns could cause the remapping of the CA1 cells in our task. To control for the effect of path stereotypy, we used a version of the task in which food locations were marked by visual intra-maze guide posts. In this paradigm, the animal did not need to use allocentric learning strategies to associate the food reward with discrete locations in space.

Consequently, we did not detect learning-related reorganization of hippocampal maps in this cued version of the task; the bait locations were no longer represented preferentially by CA1 place cells. Despite this, during this cued version of the task animals followed virtually identical stereotyped paths at similar speed as in the allocentric version of the task. Therefore, this control experiment excludes the possibility that alterations of motor behavior patterns underlie the remapping of place cells during the allocentric learning of goal locations. Further support for the notion that goal-oriented remapping relates to behavior during memory recall comes from the observation that the strength of hippocampal remapping established at the end of learning predicted recall performance. Specifically, the proportion of place cells that encoded a goal location correlated with the frequency at which animals returned to this location during the probe session. This suggests that the hippocampal maps may play a role in the recall of goal locations.

Our work on the cheeseboard maze provided additional support for the role of place maps in the representation of spatial memory traces. Yet, many questions are still unresolved and will require future work. The findings established on the cheeseboard maze need to be confirmed in other behavioral paradigms to test whether place cell remapping to newly learned goal locations always takes place during goal-directed behavior and especially to determine whether such remapping always takes place in the CA1 region only. Similarly it remains to be determined to which extent goal-related remapping occurs along the septo-temporal axis of the hippocampus. Further work is also needed to investigate how long this representation of a newly learned location is maintained, specifically whether such representations remain when familiarity increases. Ultimately, the role of hippocampal remapping during the learning process itself remains to be determined. To seek an answer to this question, we recently examined whether map formation dynamics during learning matches that of learning speed.

Dynamics of Hippocampal Place-Related Assembly Patterns During Spatial Learning

As a first level of investigation, we find that map formation dynamics lag behind learning speed in our cheeseboard task. Although the improvement in the behavioral performance we observed during learning reached asymptotic levels within few trials, the reorganization of hippocampal maps continued to evolve thereafter. To quantify the reorganization of hippocampal maps during the course of learning, in our earlier work we compared hippocampal maps that were calculated across successive trials during learning to those observed in the probe sessions before and after [33]. This type of analysis suggested a gradual reorganization of maps from the old to the new ones. These calculations, however, only examined the average temporal expression of the hippocampal maps over longer time windows consisting of entire trials. As we mentioned above, cell assembly firing patterns can flicker rapidly between the expression of distinct maps [21, 29, 36]. In our earlier work, we

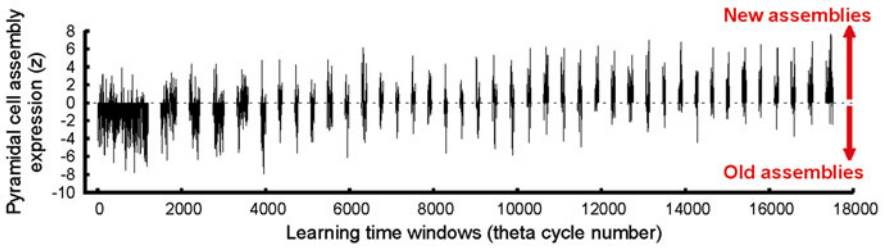

Fig. 6.3 Theta-paced flickering of hippocampal cell assemblies during spatial learning on the cheeseboard maze. In this analysis, the dynamic expression of pyramidal assemblies was quantified in theta cycles of each learning trials using a Fisher *z*-test. Positive *z* values indicate times when pyramidal firing patterns preferentially expressed the new cell assemblies ("new assemblies") while negative values indicate the expression of the old ones ("old assemblies"). Each block represents a learning trial spaced by intertrial intervals. Note the flickering between the old and the new assemblies in each trial. Adapted from [39]

may have missed such rapid switching between different maps; the rapid flickering of old and new maps may potentially explain why the neural dynamics related to map expression appears to occur at a slower time scale than learning speed. Accordingly, one possible explanation for this discrepancy could be that the new maps emerge early during learning, but they are initially competing against old maps. In this case, the old maps associated with previous learning episodes would still be temporarily expressed because in the initial phases of the task, the animal retains the old maps as well. However, as learning progresses, the new maps may undergo some additional refinement as they gain dominance over the old maps. Previous theoretical studies have indeed suggested that competitive network dynamics are an integral part of learning and cognitive processes (e.g., [37, 38]).

To test whether map switching can explain the discrepancy between the time course of both remapping and learning, we examined the temporal dynamics of map expression at short timescales during the course of learning [39]. We examined the possibility that flickering takes place between old and newly formed representations during goal-directed learning on the cheeseboard task. As in a recent study [36], we used theta oscillatory cycles during learning as time windows to evaluate whether the ongoing population activity was more similar to the assembly patterns representing the old maps (i.e., expressed before learning) or the new ones (i.e., recalled after learning). We found that, in the first learning trials, both the old and the new assemblies were expressed in nonoverlapping theta cycles, while later trials were dominated by the new maps (Fig. 6.3). Hence assemblies associated with new maps emerged early during the learning period, at the same time as the behavioral performance increased rapidly. However, initially new maps flickered with the old maps across nonoverlapping theta oscillatory periods.

These results could potentially be explained if map competition takes place during learning. As animals reliably locate rewards at new locations, newly formed maps gain influence because these can successfully predict the current goal locations

needed for the animal to solve the task. Animals may initially retain the old maps as it is uncertain whether the change of reward locations is transient or lasting. Our results also confirmed that the emergence of the new maps is correlated to the rapid improvement of behavioral performance. The mechanisms by which such a selection of the new maps over the old ones is achieved remain to be identified. One possibility lies in the involvement of the inhibitory circuit and its fine interplay with the activity of pyramidal cell assemblies [39]. Such a mechanism of map selection might then allow for the further refinement of new maps to aid efficient behavioral performance, provided that the newly acquired maps undergo a process of stabilization.

Sharp-Wave/Ripple Responses During Learning and Sleep

The memory for newly learned goal locations was stable following the completion of learning, suggesting that the newly acquired patterns might have undergone a process of consolidation. It is known that newly formed memories are labile and prone to interference with competing old memory traces. A consolidation process ensures the stability of the new memory traces allowing them to be reinstated to support later memory-related behavior [40–42]. Indeed, the role of the resting state, and particularly sleep, in memory consolidation has been demonstrated by several studies [43, 44]. Typically subjects do better in learning tasks if learning takes place in the evening and recall in the subsequent morning as compared to those in which learning took place in the morning and recall in the end of the day [45]. Moreover, memory recall could be facilitated by interventions during sleep. For example, reintroducing task-related sensory cues (i.e., odor, sound) during sleep that has been part of the context in which learning occurred has been shown to improve the subsequent memory recall [46, 47]. Certain stages of sleep are dominated by slow oscillatory patterns [48]. These slow-wave sleep periods are important for the consolidation of hippocampus-dependent declarative memories. Indeed, strengthening the power of slow oscillations by transcranial current stimulation improves the recall of declarative memories [49].

During slow-wave sleep, in the hippocampus, the most dominant oscillatory patterns are the intermittent sharp-wave/ripple events (SWRs, 150–250 Hz) [50–53]. During these events that are linked with 200 Hz ripple oscillations in the CA1 pyramidal layer and negative sharp waves in the stratum radiatum, a large number of CA3 and CA1 pyramidal cells fire action potentials together. These SWRs have been postulated to have a role in memory consolidation [42]. In support of this hypothesis, it was shown that hippocampal waking firing patterns are replayed during sleep SWRs, that is, SWR-related firing patterns resemble those observed in the previous active waking periods [54–56]. It has been suggested that SWRs might promote memory consolidation by promoting neuronal plasticity [57] and, through this, they could strengthen previously stored mnemonic patterns. It has been also proposed that SWRs may take part in systems-level memory consolidation by transmitting reactivated engrams to extra-hippocampal circuits [42].

In relation to place maps, SWRs and the associated reactivation of waking place cell patterns could represent a mechanism by which new hippocampal maps are stabilized [58]. As a consequence SWRs could facilitate the stabilization of new maps to promote the consolidation of related spatial memories. Indeed there is experimental support linking SWRs to spatial learning: the electrical stimulation-induced disruption of SWRs in sleep periods is associated with spatial learning impairments in mazes [59, 60]. These studies however could not link reactivation itself to spatial memory consolidation. Therefore, we set out to determine whether neuronal patterns during SWRs in sleep represent patterns that are related to learning and tested whether the reactivation of learning-related patterns can predict memory performance.

In the context of goal-directed learning on the cheeseboard maze, we hypothesized that goal location-related patterns will be emphasized during the following sleep period, reflecting what is subsequently remembered by the animal [33]. Therefore, in examining whether learning-related firing patterns are preferentially reactivated, we found that firing patterns observed at newly learned goal locations were reactivated stronger than patterns expressed by cells representing the start box (Fig. 6.4a). This result is in line with the finding that reward-related hippocampal waking patterns are enhanced during SWR events [61]. Importantly we went further by identifying the firing content of individual SWR in order to establish which location was best represented on the cheeseboard by each of the SWRs. We computed reactivation maps from each sleep SWR by measuring how similar the firing pattern of a SWR was to the waking patterns expected at the different location on the cheeseboard during waking periods (Fig. 6.4b). This analysis led to two results. Firstly, we observed that in many of the reactivation maps, only one location was preferentially represented which corresponded with one of the goal locations (Fig. 6.4c). This result suggests that places with a strong behavioral valence such as those predicting the presence of reward can be emphasized during sleep reactivation. Secondly, the occurrence frequency at which a given goal location was reactivated during SWRs predicted how well that particular location was remembered in the following probe session (Fig. 6.4d). This finding establishes a predictive value

Fig. 6.4 (continued) Place field similarity was calculated using place fields established at the end of learning while SWR cofiring was calculated in sleep periods before ("pre-") and after ("post-") learning. Correlation coefficients represent the partial correlations of place field similarity with the cofiring strength of one sleep session, each controlled by the cofiring strength of the other sleep session. (**b**) Illustration of the population vector-based procedure to compute SWR reactivation maps. For each map, the pixel color represents the correlation coefficient between assembly firing patterns that occurred during a single SWR and those representing that *x*–*y* location on the maze during the waking period. (**c**) Examples of individual sleep SWR reactivation maps (*black dots*: learned goal locations). Note that correlation coefficients are highest at one of the bait locations (color scale: correlation coefficient). (**d**) Scatter plot depicting post-probe memory performance (number of crossings at a given goal location) as a function of the proportion of SWRs in which assembly patterns represented the same goal location (in *gray*: regression line). Adapted from [33]

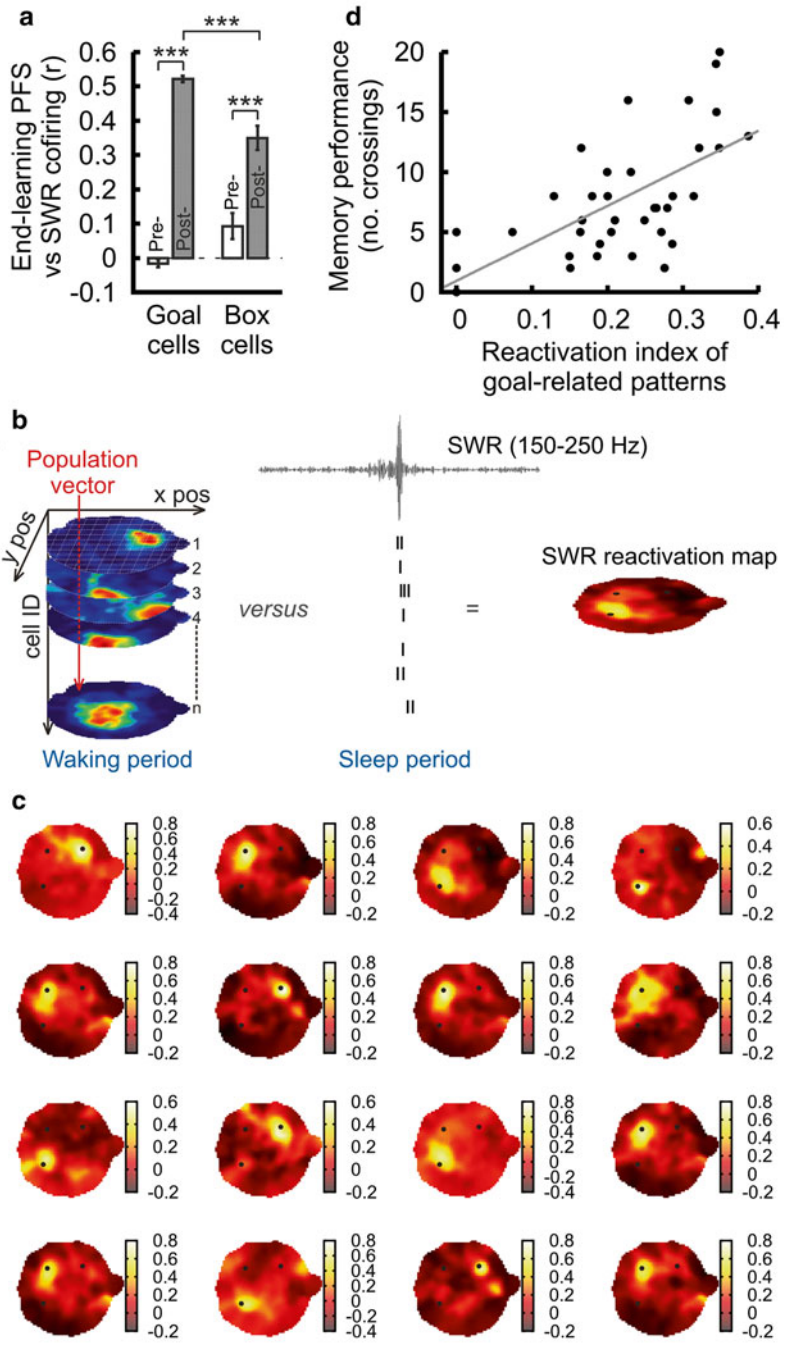

Fig. 6.4 Reactivation of CA1 place-related assembly patterns following goal-directed learning on the cheeseboard maze. (**a**) Correlation between place field similarity ("PFS") and sleep SWR cofiring strength calculated between pairs of "goal-centric" and "start-box" cells (means ± s.e.m).

for sleep reactivation in estimating memory performance and therefore highlights that it can represent a network mechanism for memory consolidation.

SWR-related activity is not only present during slow-wave sleep and in long periods of waking immobility but also during behavioral sessions in which animals are active. Waking neuronal patterns during SWRs occurring in these active waking periods have also been examined. This work revealed the reactivation of place cell firing patterns during these SWR as well and that these patterns could even represent entire movement sequences which may or may not have originated at the location where the SWR occurred [58, 62–69]. These waking SWRs have been suggested to play a role in the stabilization of new maps [62, 68] and to provide further time windows for memory consolidation during online periods. An interesting idea that has been put forward suggests that they may have a role in memory recall particularly in working memory tasks. As a confirmation for this latter hypothesis, spatial working memory deficits were detected when waking sharp waves were disrupted by electrical stimulation [70]. This study used a spatial alternation task on a W-maze that contained both working and reference memory components at different stages of the run. The on-the-fly electrical disruption of awake SWR resulted in deficits in the working memory component of the trials without affecting the spatial reference memory. As these animals were extensively trained beforehand to perform the task, the stability of the equally well-established maps was not expected to be affected by the electrical stimulation. Whether waking SWRs participate in the stabilization of new hippocampal maps and/or are incorporated into preexisting ones therefore remains to be tested.

Importantly, all waking SWRs are not identical as it is possible to differentiate two forms of them. Exploratory-related SWR (eSWR) events occur during brief (~2 s) pauses in locomotor activity, while other waking patterns (iSWR) can be detected during longer waking immobility [62]. iSWRs are similar to sleep SWRs in the sense that assembly patterns representing any locations of the animal's environment can be reactivated. In contrast, eSWRs are strongly influenced by the current location of the animal and mainly place cells with place fields that overlap with the location of the eSWR are active here. Nevertheless, place cells coding for the current location of the animal synchronize their activity during eSWRs much stronger than expected outside the SWRs during theta oscillations [62]. Such eSWR-related synchronization of place cell firing responses favors conditions for neuronal plasticity [57], specifically amongst cells representing the same location. This can help map stabilization and the initial strengthening of cell assemblies beyond their reactivation during sleep, therefore representing an online network mechanism to incorporate and stabilize new hippocampal maps.

We have specifically examined the expression of goal-associated patterns during eSWRs during learning on the cheeseboard maze. We have been able to detect both eSWR and iSWRs. Surprisingly the number of detected eSWRs at a particular goal location predicted the memory performance of that location, while iSWR numbers were not able to. This result highlights that one would need to differentiate eSWRs and iSWRs patterns in order to test for their behavioral role. Moreover we also

noticed that network synchronization was much stronger during eSWRs that occurred at the newly learned goal locations than in the start box. Such enhanced network synchronization of eSWRs is similar to those observed during the exploration of novel environments [68] and in relation to reward outcomes [61]. Hence, eSWRs tend to enhance the synchronization within those assemblies of cells that encoded newly learned goal locations. Furthermore, eSWR-related firing synchrony measured at different goal locations during learning also predicted the subsequent memory performance of the animal. Finally, the enhanced synchrony at goal locations during eSWRs could not be detected under NMDA blockade suggesting that the eSWRs may not have a role during the learning per se, but in the subsequent recall of these patterns, which was impaired under NMDA blockade. These findings point to a role of eSWRs in the stabilization of newly formed maps and in the concomitant stabilization of new spatial memory traces. Yet, establishing a causal evidence for the role of eSWRs in the stabilization of newly formed representations of discrete places and the related plasticity mechanism for their incorporation into preexisting maps is still lacking.

Conclusion

Here we have highlighted work supporting the notion that the reorganization and reactivation of hippocampal place cell firing patterns can contribute to goal-directed spatial learning. The data we reviewed demonstrated that spatial behavior involving learning a new set of goal locations is associated with the remapping of a subpopulation of place cells such that these cells encode the novel association between a discrete location and the reward. Such remapping cannot merely be explained by noncognitive factors such as changes in the motor behavior of the animal as such changes were observed only in conditions where allocentric learning of goal locations was required. Moreover, current data suggest a dual role in the CA3 and CA1 in these processes in which CA1 assemblies may be involved in the representation of particular discrete locations, while CA3 maps may hold a representation of the entire environment in which navigation has to be performed. More work is required however to confirm this complementary role of CA1 and CA3 regions, notably in other behavioral tasks. Furthermore, it would be essential to provide a causal link between hippocampal remapping and goal-directed learning.

Here we also reviewed a possible physiological mechanism for the stabilization of new maps and the resulting stabilization of memory traces coding goal locations. We highlighted the role of reactivated patterns that take place during SWRs. We also described that excitatory activity related to waking SWRs may play novel or complementary roles to those observed during sleep. Pinpointing the precise role of waking and sleep SWRs in learning and in the stabilization of memory traces will require systematic future work that could provide further insights to the inner working of the brain during memory formation.

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