Sleep enhances knowledge of routes and regions in spatial environments

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Sleep is thought to preferentially consolidate hippocampus-dependent memory, and as such, spatial navigation. Here, we investigated the effects of sleep on route knowledge and explicit and implicit semantic regions in a virtual environment. Sleep, compared with wakefulness, improved route knowledge and also enhanced awareness of the semantic regionalization within the environment, whereas signs of implicit regionalization remained unchanged. Results support the view that sleep specifically enhances explicit aspects of memory, also in the spatial domain. Enhanced region knowledge after sleep suggests that consolidation during sleep goes along with the formation of more abstract schema-like representations.

[Supplemental material is available for this article.]

Sleep supports memory consolidation in humans (Diekelmann and Born 2010; Rasch and Born 2013). Consolidation during sleep does not only strengthen memory traces but is also thought to help transform new detailed episodic representations into more generalized decontextualized semantic representations containing just the common invariant features shared by multiple experiences (Lewis and Durrant 2011; Inostroza and Born 2013; Dudai et al. 2015). Thus, compared with wakefulness, sleep after learning enhances the extraction of categories from objects sharing general features (Friedrich et al. 2015) and of statistical regularities and grammatical rules in complex stimulus patterns (Wagner et al. 2004; Durrant et al. 2011, 2013; Nieuwenhuis et al. 2013), such that participants after sleep were better able to explicitly express these regularities they had acquired implicitly before sleep (Fischer et al. 2006; Wilhelm et al. 2013). Indeed, sleep is thought to preferentially support the formation of explicit memory that crucially depends on hippocampal function (Robertson et al. 2004; Marshall and Born 2007, but see Weber et al. 2014).

Here, we examined whether the assumption of sleep preferentially supporting the formation of explicit memory in the hippocampus-dependent system also holds for the spatial domain. This is important, since the presumed memory function of sleep has been conceptualized based centrally on observations of activity of hippocampal place cells encoding spatial experience in rats. Patterns of activity in such place cell ensembles during encoding of a spatial maze have been consistently found to be reactivated during slow wave sleep after the encoding experience (Pavlides and Winson 1989; Wilson and McNaughton 1994; Skaggs and McNaughton 1996). This neural replay during sleep is considered to cause a strengthening and transformation of the spatial representation. Evidence showing an impact of sleep on spatial memory performance in humans is mixed, however, showing either beneficial (Ferrara et al. 2008; Wamsley et al. 2010; Nguyen et al. 2013) or no effects of sleep (Peigneux et al. 2004; Orban et al. 2006; Rauchs et al. 2008; Javadi et al. 2015).

In fact, rather than representing a unitary hippocampal function, spatial navigation in humans derives from a multitude of explicit and implicit processes and representations (e.g., Wolbers and Hergarty 2010), including, among others, knowledge about the semantic structure of space. Specifically, in this context, the term "regionalization" is used to refer to the observation that humans cluster spatial landmarks (hierarchically) on the basis of nonspatial attributes and that this clustering affects distance judgments (Stevens and Coupe 1978; Hirtle and Jonides 1985; McNamara 1986) and navigation (Wiener and Mallot 2003; Schick et al. 2015; Balaguer et al. 2016). In essence, these studies show that distances tend to be overestimated when routes cross regional barriers—both perceived and just imagined ones—compared with when they do not (Kosslyn et al. 1974; Newcombe and Liben 1982; Hirtle and Jonides 1985; Carbon and Leder 2005; Balaguer et al. 2016). Thus, to demonstrate regionalization, Wiener and Mallot (2003) asked participants to find the shortest path connecting three landmarks in a virtual maze (traveling-salesmen problem). Importantly, all landmarks within the maze pertained to one of three semantic categories (vehicles, animals, buildings) and were arranged such that landmarks of the same semantic category clustered together to form semantic regions. To investigate the effect of these regions on navigational planning, the authors constructed problems where two equidistant solutions to the navigation problem existed, which only differed in the number of—nonvisible—region boundaries between semantic regions that had to be crossed (Fig. 2A,B). As predicted, participants reliably preferred the routes passing fewer region boundaries to routes passing more boundaries (though both routes had the same length), with this bias indicating that the participants acquired an implicit knowledge of the regions (regionalization) that informed their navigation decisions.

Importantly, for the investigation of sleep's effect on spatial memory, the regularities among landmarks, which give rise to

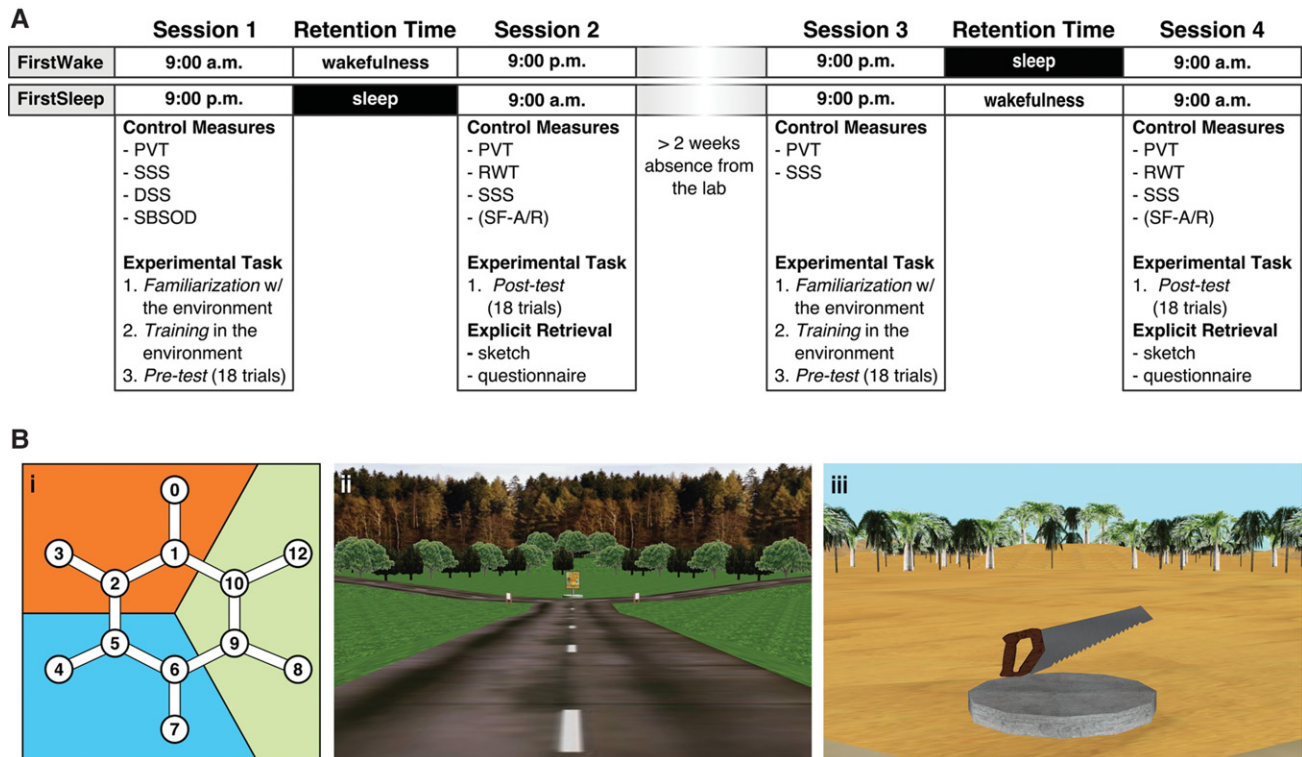Corresponding author: hannes.noack@uni-tuebingen.de

Figure 1. Study design (*A*). Sequence of experimental conditions (Sleep/Wake) for two groups: "FirstSleep" and "FirstWake." Participants were absent from the lab for more than two weeks between Session 2 and 3 (range: 14–45 d). Different control measures were assessed at each session. Measures in brackets were only administered in the Sleep condition: PVT, psychomotor vigilance test; SSS, Stanford sleepiness scale; DSS, digit-symbol-substitution; SBSOD, Santa-Barbara sense of direction scale; RWT, Regensburger wordfluency test; SF-A/R, sleep questionnaire (see Supplemtal Methods). Virtual environment (*B*): (i) Iterated y-maze structure of the virtual environment. Numbered circles refer to crossroads marked with a landmark. The three implicit regions correspond to clusters of landmarks belonging to the same semantic category. (ii) Example view at a decision point (crossroad) within the forest environment. (iii) Example view at one landmark (saw) within the desert environment. Both environments featured the same spatial layout but only differed in surface characteristics and landmarks.

semantic regions must be extracted from navigation experience, suggesting a beneficial role for sleep in the formation of these semantic regions. Here, we adapted this traveling-salesman paradigm to measure, apart from route memory (accuracy in finding the shortest path), implicit region memory (by the navigation bias for the route with fewer region crossings) and explicit region memory (by explicit recall of the semantic regions). We expected that sleep preferentially benefitted explicit memory for routes and regions, and we explored the effect of sleep on implicit regional bias.

Thirty-eight participants (20 female; mean age = 25 yr; range: 18–42 yr) performed on a virtual navigation task adapted from Wiener and Mallot (2003; see above) before (Pretest) and after (Post-test) a 12-h retention interval either filled with nighttime sleep (Sleep condition) or daytime wakefulness (Wake condition). All participants performed in both conditions but at different schedules with a minimum delay of 2 wk between conditions (range 14–45 d). Twenty participants slept during the first retention interval (FirstSleep group) and stayed awake during the second, and 18 other participants (FirstWake group) stayed awake during the first retention interval and slept during the second (see Fig. 1A; Supplemental Methods for a detailed description). Different environments (forest and desert) and different semantic categories (animals, artwork, and vehicles, or musical instruments, tools, and furniture) were used to minimize learning effects over repeated testing (see Fig. 1B).

After familiarization with the virtual maze at pretest, participants solved three types of traveling-salesmen problems (A, B,

and C; six trials each), where they were asked to find the shortest path connecting three landmarks in the virtual world. Problem type A and B were symmetric and, thus, offered two equidistant solutions of the problem (Fig. 2A,B). However, one solution would demand passage of more region boundaries than the other (A: one versus two boundaries; B: two versus three boundaries). The third problem type (C) was asymmetric and thus featured only one correct solution to the problem (see Fig. 2; Supplemental Methods).

Using four different measures, the performance results were as follows:

(1) Route memory (i.e., the number of correctly solved problems over the total number of problems) was based on data originating from all three problem types (A, B, and C). We found route knowledge generally improving over the 12-h retention interval ($F_{(1,34)} = 7.81$; $P = 0.008$, $\eta^2 = 0.01$, for Pretest/Post-test main effect). Importantly, this improvement was greater across the sleep than wake retention interval ($F_{(1,34)} = 6.92$, $P = 0.01$, $\eta^2 = 0.01$, for Pretest/Post-test × Sleep/Wake; Fig. 3A).

To further investigate potential time of day effects on navigation performance (i.e., differences between evening and morning sessions), we looked at performance during Pretest only. We found no Sleep/Wake (evening/morning) main effect in this analysis for navigation accuracy ($F_{(1,34)} = 0.02$) excluding a strong confounding circadian effect. Note there were also no accompanying differences in vigilance, word fluency, or self-reported sleepiness (see
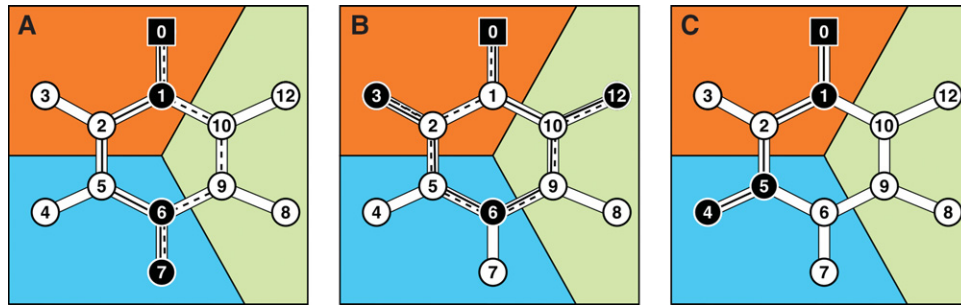
Figure 2. Problem types *A*, *B*, and *C* of the Test phases. On each trail, participants were asked to pass three landmarks (filled circles) taking the shortest possible route from the starting point (0). Problem types A and B are symmetric and allow for two equivalent solutions. Solid lines represent the solution with fewer boundary crossings (A1: 1,2,5,6,7; B1: 1,10,12,10,9,6,5,2,3) and dashed lines the solution with more boundary crossings (A2: 1,10,9,6,7; B2: 1,2,3,2,5,6,9,10,12). Importantly, the decision for one route or the other was always taken at decision point 1. Problem type C allows for only one correct solution. The starting point was rotated on a trial-by-trial basis, such that each dead-end road was the starting point once in every problem type and route decisions were independent of left–right decisions.

Supplemental Results) ruling out confounding influences from such nonspecific factors.

(2) Based on the assumption that regionalization biases navigation decisions toward routes with fewer boundaries, implicit memory of regions was assessed by the directional decision taken at the first decision point in problem types
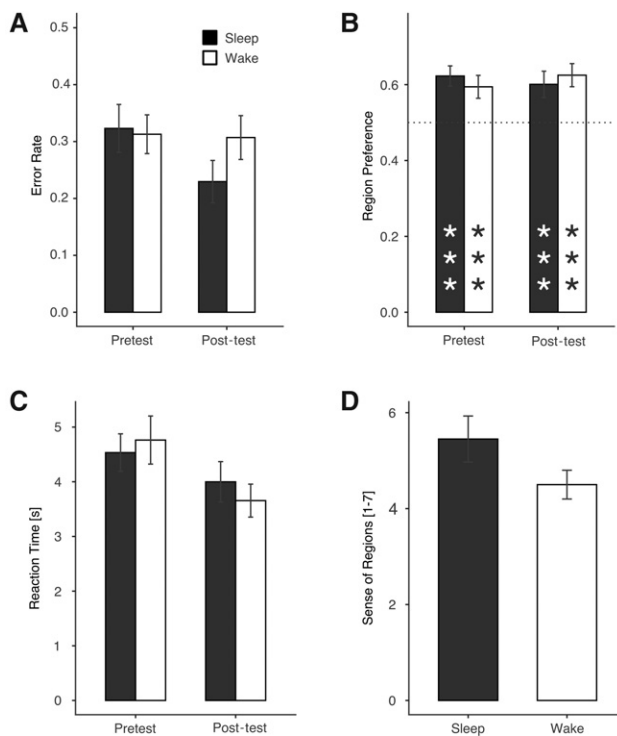

Figure 3. The effect of sleep on route memory and region preference. (*A*) Route knowledge assessed by error rates (number of trials where participants departed from the shortest path per total number of trials). (*B*) Region preference represents the decision to choose the route that crosses fewer region boundaries over route that crosses more. Chance level is denoted by the dotted line at a region preference of 0.5. Deviation from chance level was tested for each retention condition at Pretest and Post-test (***$p < 0.01$). (*C*) The effect of sleep on reaction time at the first decision point. (*D*) The effect of sleep on awareness of regionalization (by ratings between 1 and 7, no awareness vs. strong awareness).

A and B. The region preference index is the number of trials where the participants turned toward the route with fewer boundaries relative to the number of all trials of type A and B problems ($n = 12$), with an index of 1 indicating perfect preference for the routes crossing fewer region boundaries, and an index of 0.5 indicating random choices. In fact, we found a general preference for the routes crossing fewer region boundaries ($M = 0.61$; SEM $= 0.02$, $t_{(37)} = 5.54$, $P < 0.001$). However, at Post-test this preference did not depend on whether subjects had slept or stayed awake after learning ($F_{(1,34)} = 1.07$, $P > 0.250$, for Pretest/Post-test × Sleep/Wake; Fig. 3B).

(3) The reaction time at the first decision point in problem types A and B was taken as a measure of the fluency with which the decision was made. Reaction times (at the first decision point) generally decreased from Pretest ($M = 4660$ msec; SEM $= 350$ msec) to Post-test ($M = 3810$ msec; SEM $= 294$ msec; $F_{(1,34)} = 26.28$, $P < 0.001$, $\eta^2 = 0.04$) but were not modulated by sleep during the retention interval ($F_{(1,34)} = 1.68$, $P = 0.204$).

(4) After Post-test, we used an exit-questionnaire to assess explicit knowledge of the environment and its regionalized structure by asking the participants to draw a sketch and by asking them to answer two questions with a response scale ranging from 1 ("not at all") to 7 ("very strongly"): (1) "Did you mentally group the landmarks in the environment?" (2) "Did you have the feeling that the environment consists of different regions?" Of these items, question 2 was the only one allowing for differentiating sleep-related effects, because the sketch drawing task and question 1 revealed clear ceiling effects inasmuch as at least 74% of the participants in both the Sleep and Wake conditions drew correct sketches and recognized the semantic landmark categories (see Supplemental Results). For question 2, we found that participants in the Sleep condition expressed a distinctly stronger awareness of the regionalization ($M = 5.45$, SEM $= 0.48$) than in the Wake condition ($M = 4.50$, SEM $= 0.30$, $F_{(1,36)} = 5.98$, $P = 0.02$, $\eta^2 = 0.05$).

Here, we assessed the effect of sleep on two aspects of spatial memory, i.e., the memory for routes and for regions in a virtual environment. The regionalization of the environment has recently been revealed to be an important factor contributing to human spatial navigation behavior (Wiener and Mallot 2003; Schick et al. 2015; Balaguer et al. 2016). We found that sleep, compared with post-learning wakefulness, improved route memory, with

the participants committing fewer errors after sleep compared with wakefulness. Sleep also improved subjective awareness of the regionalized structure of the environment, as a measure of explicit region memory. However, the preference for routes that crossed fewer region boundaries, which we used as a measure of implicit region memory, remained unaffected by sleep. These results, therefore, support the notion that sleep preferentially enhances explicit over implicit memory representations. Additionally, that sleep enhanced the awareness of regions is consistent with the view of an active consolidation process during sleep that supports the abstraction of spatial structure from incidentally encoded landmarks.

The benefit from sleep in route-knowledge is in agreement with several previous studies, showing that sleep enhances spatial memory in virtual navigation tasks (e.g., Ferrara et al. 2008; Wamsley et al. 2010; Nguyen et al. 2013) but in disagreement with others that failed to reveal spatial performance benefits after sleep (Peigneux et al. 2004; Orban et al. 2006; Rauchs et al. 2008; Javadi et al. 2015). We have argued above that human spatial navigation is a highly complex behavior, which depends on a variety of different processes (Wolbers and Hegarty 2010), strategies (Hartley et al. 2003; Iaria et al. 2003), and representations of space (Hartley et al. 2014). The differentiation of strategies, e.g., whether subjects relied on a landmark-oriented stimulus–response strategy or on a survey strategy that takes the overall layout of the maze into account, is therefore necessary to pin-point the specific effects of sleep on spatial navigation. The complexity of our findings, which differentiate between route knowledge on the one hand and explicit and implicit regionalization on the other hand underline this view.

The finding of a sleep-induced increase in awareness of regionalization corresponds with the literature in several ways. To the extent that the regions within our environment are not a matter of direct experience but rather must be inferred from the continuous stream of episodic experience, the formation of representations of environmental regions constitutes a process of abstraction of superordinate (semantic) categories in a hierarchical spatial representation (Stevens and Coupe 1978; Wiener and Mallot 2003; Balaguer et al. 2016). Our findings are, thus, in line with current models of an active systems consolidation of memory, which posit that hippocampal representations of episodic memory become redistributed to neocortical sites, based on neural reactivation processes during sleep, thereby undergoing a transformation into less contextual and more abstract semantic representations (Lewis and Durrant 2011; Inostroza and Born 2013; Dudai et al. 2015). That sleep supports the formation of abstracted representations has been similarly shown in the nonspatial domain. Payne et al. (2009) showed, for example, that sleep favored false memory of words when these words pertained to the superordinate semantic categories of previously learned, semantically structured word lists (see also Diekelmann et al. 2010). Moreover, our finding of a sleep-induced increase in awareness of regionalization corresponds with findings showing that sleep supports the conversion of implicit into explicit sequence memory in serial reaction time tasks (Fischer et al. 2006; Wilhelm et al. 2013). Indeed, the conversion into explicit memory can be considered a kind of semantization of implicit task representations formed before sleep. Importantly, the interpretation of these results is limited to the degree that we found sleep-effects on only one question addressing the level of explicit regionalization. Assessment of multiple measures, addressing the same construct would be desirable for future studies.

At the implicit level, we replicated earlier findings showing a preference for routes that cross fewer region barriers (Wiener and Mallot 2003). The stronger awareness of regionalization of the environment in the sleep condition did not result in stronger route

preferences, however. Such a dissociation of sleep effects for explicit and implicit memory further suggests that sleep has a particular effect on the formation of explicit memory representations (Fischer et al. 2006; Wilhelm et al. 2013; T Zander, S Diekelmann, J Born, and KG Volz, in prep.). However, although indicating a sleep-dependent benefit for explicit memory formation, the present results do not exclude that sleep might also benefit implicit memory. First, the measure of route preference might not sensitively reflect implicit region memory. Specifically, our premise that the route preference scales with the strength of a unique region representation may not hold. In fact, correlations of route preference with explicit judgments of the regionalization across individuals were basically absent ($|r|$'s < 0.1).

Second, the influence of superordinate spatial categories may scale with the knowledge of the actual spatial relationships between the subordinate spatial items (McNamara 1986). That is, the better the spatial relationship between two locations is known, the lower the bias resulting from their respective superordinate categories should be. Our data do not support this hypothesis, however: to the contrary, we found that better navigation performance (i.e., committing fewer errors) was associated with stronger route preference across individuals ($r = -0.53$, 95% CI = [-0.72, -0.25]). Absent differences in implicit region memory may therefore not be explained by the sleep-related differences in route knowledge at post-test.

In summary, we showed that sleep supports consolidation of explicit spatial memory for routes and regions and strengthens subjective awareness of regions, whereas measures of implicit region memory remained unchanged. These findings further support the idea that sleep preferentially enhances the formation of hippocampus-dependent explicit memory. Our findings shed new light on the role of sleep in spatial memory consolidation by suggesting that abstraction processes during sleep favor the formation of nonspatially defined superordinate clusters. In combination with similar findings in other domains, the present data corroborate theories of sleep supporting an active systems consolidation process the formation of superordinate (abstract) categories of interrelated experience.

Acknowledgments

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