

Sleep-Dependent Consolidation of Contextual Learning

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Summary

Memory consolidation is facilitated by sleep [1–4]. Specifying the functional domain of sleep-dependent consolidation (SDC) is important for identifying the neural mechanisms underlying this phenomenon. Previous work indicates that SDC may be limited to conditions in which learning is explicit [5]. In the present study, we tested the hypothesis that SDC may also occur with implicit learning when learning benefits from the formation of contextual associations, a function associated with the hippocampus. Three versions of the serial-reaction-time task (SRTT) [6] were examined, and SDC was assessed by comparing performance after 12 hr breaks that included or did not include sleep. SDC was observed in the Explicit condition. Two implicit conditions were compared. In the Implicit Noncontextual condition, participants performed a concurrent tone-counting task with the pitch of each tone selected at random, precluding cross-dimensional associations. In the Implicit Contextual condition, participants responded to the color of the cues while the spatial location of the cues followed a correlated sequence. Whereas learning was observed in both implicit conditions, SDC was restricted to the contextual condition. Given that the formation of contextual associations is dependent on the hippocampus [7–9], we suggest that SDC is a hippocampus-mediated process.

Results and Discussion

We used three versions of the serial-reaction-time task (SRTT) [6], one in which learning was explicit and two in which learning was implicit. In the Explicit condition, responses were based on the location of the stimulus, and participants were told that the stimulus locations followed a repeating sequence. In the Implicit Noncontextual condition, the stimuli were the same; however, participants were not informed of the presence of the sequence. Moreover, to minimize awareness, a high- or low-pitched tone was presented in conjunction with each visual cue, and participants were instructed to covertly count the high-pitched tones. Because the pitch of each tone was randomly determined, it was not possible to form cross-dimensional, contextual associations between the stimulus locations and the tones. In

the Implicit Contextual condition, participants responded to the color of the stimulus that appeared in one of four locations. The location of the colored stimuli followed a sequence of the same length as the color sequence. Thus, the two stimulus features, color and location, were correlated even though only color was relevant for the response. Awareness of the color sequence was low, and participants were unaware of the incidental location sequence.

Two control groups were included in which the cues were presented randomly on all blocks. For the Explicit Control condition, participants were told that the stimulus locations would be randomly selected. For the Implicit Control condition, participants were not informed of the random presentation of the stimuli. These participants also performed the covert tone-counting task.

For the three sequence-learning groups, we included in each session blocks of trials in which the stimuli were randomized, and we compared reaction time (RT) on these blocks to neighboring blocks in which the stimuli followed the sequence. In the Implicit Contextual condition, we included a block in which the phase relationship between color and location sequences was altered. An increase in RT on this block provides a direct measure of contextual learning because the color sequence, and thus the response sequence, is unchanged; only the contextual associations are altered.

We evaluated sleep-dependent consolidation (SDC) by testing participants in three sessions and comparing changes in performance after 12 hr breaks with or without sleep.

Overall Reaction-Time Profile

Mean RTs for each group across blocks and sessions are presented in Figure 1. The two control groups provide a baseline performance indicator independent of learning.

As expected, participants in the Explicit group responded faster than in the other conditions. On sequence blocks, mean RTs for this group were below 300 ms by the end of session 1 and below 200 ms in session 3. Thus, these participants were clearly anticipating the stimuli [10]. The substantial increase in RT on each of the random probes further indicates that participants likely benefited from explicit sequence knowledge [$F(1,95) = 208.8, p < 0.001$].

Learning, as measured by the increase in RT on the random-probe blocks, is also evident in the functions for the two implicit-learning groups [Noncontextual: $F(1,95) = 24.5, p < 0.001$; Contextual: $F(1,131) = 47.1, p < 0.001$]. The degree of learning differed across the three sequence learning groups ($F(2,323) = 277.6, p < 0.001$). Post-hoc comparisons indicate that the increase on the random blocks is less for both implicit groups compared to the Explicit group [Explicit versus Implicit Noncontextual, $F(1,191) = 387.9, p < 0.001$; Explicit versus Implicit Contextual, $F(1,227) = 531.2, p < 0.001$] consistent with previous studies (e.g., [5, 11]). Importantly,

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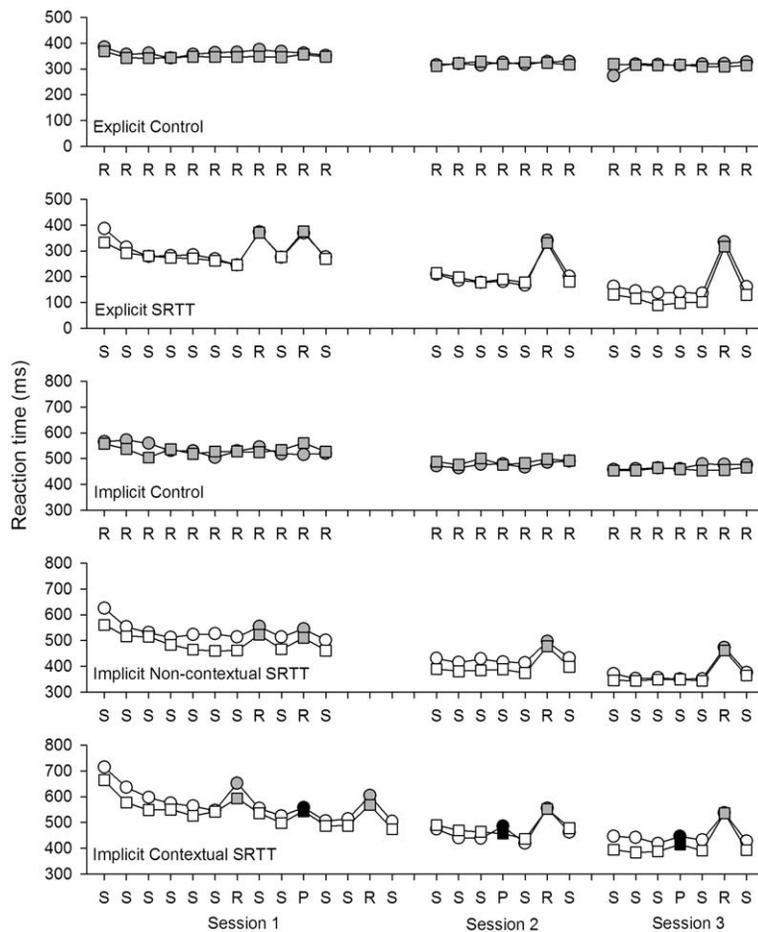


Figure 1. Mean RT for Each Group
White symbols are sequential blocks; gray symbols are random blocks; black symbols are phase-shift blocks (see text). Half of the participants within each group began testing in the morning (AM-PM-AM, squares), and half began testing in the evening (PM-AM-PM, circles). The initial learning functions did not differ between the AM-PM-AM and PM-AM-PM groups for any of the tasks, indicating that initial performance was not affected by the time of day at which training commenced. Note the difference in range on the y axes for explicit and implicit groups.

the RT functions indicate that cross-dimensional associations between the color and location sequences were learned because there was a modest increase in RT on the phase-shift blocks in each of the three sessions even though the color (and response) sequence was unchanged [$F(1,131) = 3.7, p = 0.05$]. Thus, the incidental position information has been incorporated into the representation of the sequence.

Sleep Benefit on Sequence Performance

Our primary interest was in how performance was affected by sleep. To assess this, we compared a normalized measure of the change in RT for sessions separated by a 12 hr break that included sleep relative to sessions separated by a 12 hr break in which the participants remained awake (Figure 2). With only one exception, the scores were positive, indicating that participants improved from one session to the next. The positive values for the two control groups indicate that there may be off-line improvements on the task in general or recovery from fatigue. However, if sleep has a specific benefit on the consolidation of sequence learning, these values should be larger after a break with sleep compared to a break without sleep. Moreover, this pattern should not be observed in the control groups. To test this hypothesis, we performed a 2×2 ANOVA with factors *sleep* (break with sleep [PM to AM] versus break without sleep [AM to PM]) and session *schedule* (AM-PM-AM versus PM-AM-PM) for each group.

The main effects of *sleep* and *schedule* were not significant for either the Explicit Control group [*sleep*: $F(1,23) < 1$; *schedule*: $F(1,23) = 1.8, p = 0.19$] or the Implicit Control group [*sleep*: $F(1,23) = 1.2, p = 0.30$; *schedule*: $F(1,23) < 1$]. The interaction term was not significant for the Explicit Control group [$F(1,23) < 1$] but was significant for the Implicit Control group [$F(1,23) = 4.7, p = 0.04$]. The latter is due to a time effect: Participants showed a greater improvement between the first and second sessions than between the second and third sessions, independent of whether the break included sleep or not.

An ANOVA of the performance of the Explicit Learn group revealed a significant benefit of sleep [$F(1,31) = 4.2, p = 0.05$]. The effect of order and the interaction terms were not significant [both $F(1,31) < 1$]. Participants exhibited considerable improvements in performance after each of the 12 hr breaks. Notably, this improvement was almost 100% larger after a break with sleep compared to a break without sleep. This profile is similar to that observed in a previous study of SDC in explicit sequence learning [3].

A similar analysis reveals a dissociation in the effects of sleep for the two implicit groups. For the Implicit Non-contextual group, neither the main effects [*sleep*: $F(1,31) < 1$; *schedule*: $F(1,31) < 1$] nor the interaction [$F(1,31) = 1.6, p = 0.22$] approached significance. Participants in this group tended to be faster at the start of each session compared to the end of the previous

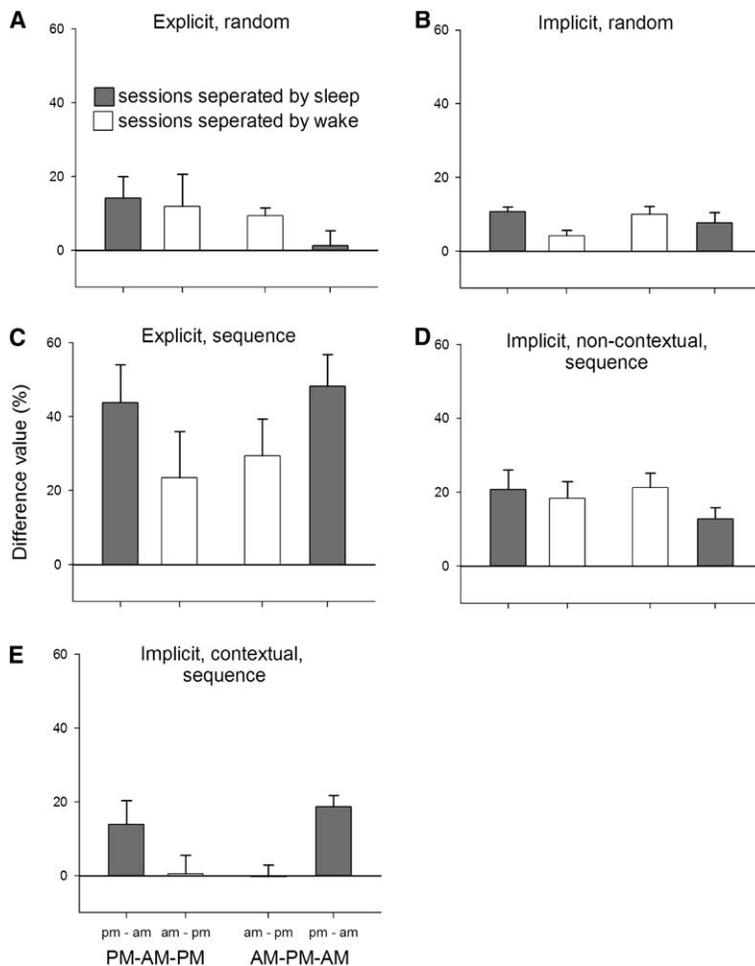


Figure 2. Difference Values across Groups (A–E) The difference value represents the difference in performance on the last two sequence blocks of session n minus the performance on the first two blocks of session $n+1$ as a percent of the performance on the first two blocks of session $n+1$ (see [3]). Positive numbers correspond to the situation in which the participant is faster after the break compared to before the break. Error bars represent the standard error (the variability in the mean cycle duration across subjects).

session, independent of whether the break included sleep. In contrast, the results for the Implicit Contextual group indicate the occurrence of SDC. Only the main effect of *sleep* was significant [$F(1,43) = 12.2, p = 0.001$; *schedule* and interaction terms: $F(1,43) < 1$]. Indeed, for this group, there was no improvement in performance after a 12 hr break without sleep. When the break included sleep, however, the mean RTs dropped by an average of 16%.

Another measure of learning is the slowing observed in RT for the random-probe blocks. To assess SDC in this regard, we compared the difference in RT for the random probe relative to the surrounding sequence blocks across sessions (Figure 3). The profiles were similar to that observed with the difference scores. Numerically, the increase in RT on the random probe was larger after sleep than after a 12 hr break without sleep for the Explicit and Implicit Contextual groups, but not for the Implicit Noncontextual group. However, these effects were not significant [Explicit and Implicit Noncontextual, $F(1,31) < 1$; Implicit Contextual, $F(1,43) = 2.2, p = 0.15$].

Awareness and SDC

The current results replicate previous findings showing that participants with explicit knowledge of the material to be learned exhibit SDC. Novel to the present work is evidence indicating that SDC also occurs under implicit

conditions when learning benefits from the formation of contextual associations. Given the methodological differences between the two implicit-learning tasks, it is important to consider whether there was a difference in sequence awareness for these two groups and whether this might account for the differential prevalence of SDC in the Contextual condition.

Participants were asked in a postexperimental survey to indicate whether they thought the stimuli appeared sequentially or were random. Interestingly, although never exposed to a sequence, 42% of the participants in the Implicit Control group judged that the stimuli followed a sequence, likely reflecting a bias to infer patterns even when none exists. Although the percentage was greater for both the Noncontextual (63%) and Contextual (64% for color location) groups, suggesting that some of the participants may have been aware of the presence of a sequence, the comparison of these values to that of the Implicit Control group was not significant [$\chi^2(2, N = 50) = 1.73, p > 0.05$]. The participants in the Contextual group were also asked if they thought the location of the stimuli had followed a sequence or were selected at random. Only 32% chose “sequence.” Participants in both implicit groups were, at best, only able to report limited portions of the stimulus/response sequence (see Supplemental Results in the Supplemental Data available online).

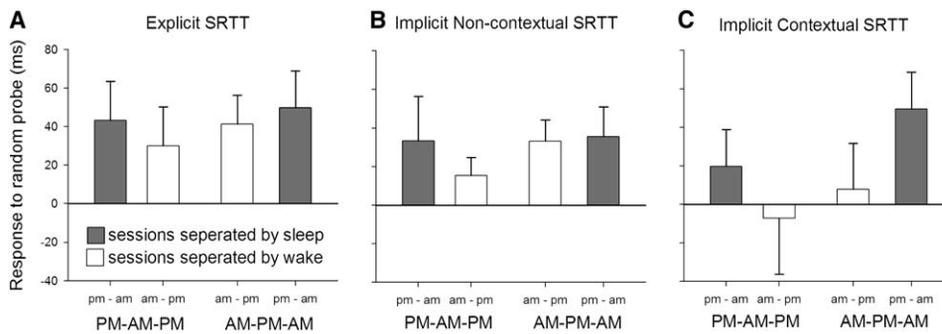


Figure 3. Difference in Response to the Random Probe across Sessions

Within each session, sequence learning was measured by the increase in RT on the random-probe block compared to surrounding sequence blocks (with the second random-probe block for session 1). The difference in these scores was then compared across sessions separated by sleep (dark bars) or without sleep (light bars).

The survey data do not point to a difference between the two implicit-learning conditions in terms of awareness. Nonetheless, given that participants in these groups were more likely to report that the stimuli followed a sequence than in the control condition, we performed two additional analyses to determine whether SDC in the Contextual group may be due to awareness. First, SDC was compared for participants who reported “sequence” and those who reported “random” in the assessment of awareness. The sleep-benefit scores did not differ between the two subgroups [$F(1,21) < 1$] (Figure 4A).

Second, we looked at the effect of sleep on the phase shift probe because this assay directly reflects contextual learning and participants had minimal, if any awareness that the stimulus locations followed a sequence. In a comparison of the phase-shift cost across sessions, the effect of *sleep* was reliable [$F(1,43) = 11.2, p = 0.002$] but not the effects of *schedule* or the interaction [$F(1,43) < 1$]. Thus, the pattern follows that associated with SDC: The phase-shift cost is larger after a 12 hr break with sleep than after a 12 hr break without sleep (Figure 4B).

The Hippocampus, Contextual Learning, and SDC

The present experiment was designed to evaluate two hypotheses concerning the requirements for SDC during sequence learning in humans. One hypothesis is derived from the taxonomic distinction that has been made

in the memory literature between explicit and implicit learning, with SDC limited to the former [5]. An alternative hypothesis is that SDC during sequence learning may be restricted to tasks in which the hippocampus plays a critical role in memory formation and consolidation [12]. Although there is certainly a strong correlation in the amnesia literature between explicit learning and the hippocampus, recent theoretical [13] and empirical work [7–9, 11] suggests that this structure, independent of awareness, is essential for learning contextual associations. On the basis of this hypothesis, we devised an implicit-sequence-learning task amenable to the formation of contextual associations. We observed SDC in this condition, despite the lack of awareness of the contextual associations.

The current interpretation is predicated on a proposed link between the hippocampus and context-dependent learning. Various lines of evidence demonstrate that contextual learning is impaired in people or animals with hippocampal lesions (e.g., [7–9, 14, 15]). Process models in which the hippocampus is hypothesized to be essential in the formation of associations between distributed cortical representations [16] offer a mechanism for contextual learning. With respect to sequence learning, this idea has been developed by Keele et al. [13], who propose a multiple-systems learning theory that makes a fundamental distinction between modules that form associations within a dimension and a system that is

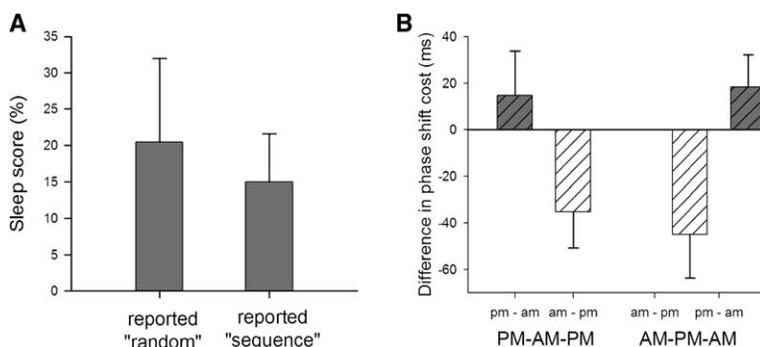


Figure 4. The Benefit of Sleep Relative to Awareness and Contextual-Learning Scores

(A) The effect of sleep in the Implicit Contextual group, calculated separately for those who reported “random” and those who reported “sequence” in the assessment of awareness. The sleep score for each participant was calculated as the difference value for the PM-AM interval minus the difference value for the AM-PM interval. Positive scores indicate that the improvement over the interval with sleep was greater than the improvement over the interval without sleep.

(B) The difference in the phase-shift cost across sessions. The phase-shift cost was calculated for each session as the difference in mean RT on the phase-shift probe minus the mean RT of the two surrounding sequence blocks.

capable of forming multidimensional associations. The latter is, in essence, a computational mechanism for context-dependent learning, a process we assume involves the hippocampus.

According to the theory, unidimensional and multidimensional associative processes operate in parallel. For all three versions of the SRTT used in the present study, learning would be expected to occur within the task-relevant modules (i.e., associations between successive stimulus locations for the Explicit and Implicit Noncontextual conditions, and between successive colors in the Implicit Contextual condition). The multidimensional system would also attempt to form associations, but the input to this system would incorporate all of the varying features of the display. For the Explicit condition, only the stimulus location varies, and thus learning would occur within the multidimensional system, as well as in the unidimensional system. For the Implicit Noncontextual condition, however, the random variation of the tones would interfere with, or add noise to, the associative process—that is, the location of a stimulus would not predict the next tone, and correspondingly, the tones would fail to support predictions regarding the forthcoming spatial location. As such, learning would be minimal within the multidimensional system. In contrast, the multidimensional system would be essential for forming associations between the correlated color and spatial sequences in the Implicit Contextual condition.

The multidimensional system should form predictive associations during single-task learning even when awareness is low (see [11]); as such, SDC is expected. Although this is true for our Implicit Contextual condition, the results of Robertson et al. [5] are at odds with this prediction. Notably, Robertson et al. do show a bigger decrease in RT after a 12 hr break that included sleep relative to a 12 hr break without sleep. The lack of SDC is based on the fact that there was a similar between-session change in RT on random blocks, suggesting that these were general changes in performance rather than ones specific to the benefits of sleep.

Future work is required to explore this issue in greater detail, as well as directly investigate the role of the hippocampus in SDC during contextual sequence learning. Focusing on computational principles such as the formation of contextual associations offers a useful avenue for developing neurobiological models that specify conditions that facilitate SDC as well as those in which SDC fails to occur.

Supplemental Data

Supplemental Data include Supplemental Experimental Procedures, Supplemental Results, and one table and are available with this article online at: <http://www.current-biology.com/cgi/content/full/16/10/1001/DC1/>.

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References

1. Karni, A., Tanne, D., Rubenstein, B.S., Askenasy, J.J.M., and Sagi, D. (1994). Dependence on REM sleep of overnight improvement of a perceptual skill. *Science* 265, 679–682.
2. Benson, K., and Feinberg, I. (1977). The beneficial effect of sleep in an extended Jenkins and Dallenbach paradigm. *Psychophysiology* 14, 375–384.
3. Walker, M.P., Brakefield, T., Morgan, A., Hobson, J.A., and Stickgold, R. (2002). Practice with sleep makes perfect: Sleep-dependent motor skill learning. *Neuron* 35, 205–211.
4. Stickgold, R., Hobson, J.A., Fosse, R., and Fosse, M. (2001). Sleep, learning, and dreams: Off-line memory reprocessing. *Science* 294, 1052–1057.
5. Robertson, E.M., Pascual-Leone, A., and Press, D.Z. (2004). Awareness modifies the skill-learning benefits of sleep. *Curr. Biol.* 14, 208–212.
6. Nissen, M.J., and Bullemer, P. (1987). Attentional requirements of learning: Evidence from performance measures. *Cognit. Psychol.* 19, 1–32.
7. Chun, M.M., and Phelps, E.A. (1999). Memory deficits for implicit contextual information in amnesic subjects with hippocampal damage. *Nat. Neurosci.* 2, 844–847.
8. Ryan, J.D., Althoff, R.R., Whitlow, S., and Cohen, N.J. (2000). Amnesia is a deficit in declarative relational memory. *Psychol. Sci.* 11, 454–461.
9. Ryan, J.D., and Cohen, N.J. (2004). Processing and short-term retention of relational information in amnesia. *Neuropsychologia* 42, 497–511.
10. Willingham, D.B., Nissen, M.J., and Bullemer, P. (1989). On the development of procedural knowledge. *Mem. Cognit.* 15, 1047–1060.
11. Schendan, H.E., Searl, M.M., Melrose, R.J., and Stern, C.E. (2003). An fMRI study of the role of the medial temporal lobe in implicit and explicit sequence learning. *Neuron* 37, 1013–1025.
12. Graves, L.A., Heller, E.A., Pack, A.I., and Abel, T. (2003). Sleep deprivation selectively impairs memory consolidation for contextual fear conditioning. *Learn. Mem.* 10, 168–176.
13. Keele, S.W., Ivry, R.B., Mayr, U., Hazeltine, E., and Heuer, H. (2003). The cognitive and neural architecture of sequence representation. *Psychol. Rev.* 110, 316–339.
14. Morris, R.G.M., Garrud, P., Rawlins, J.N.P., and O'Keefe, J. (1982). Place navigation is impaired in rats with hippocampal lesions. *Nature* 297, 681–683.
15. Burwell, R.D., Saddoris, M.P., Bucci, D.J., and Wiig, K.A. (2004). Corticohippocampal contributions to spatial and contextual learning. *J. Neurosci.* 24, 3826–3836.
16. Squire, L.R., and Alvarez, P. (1995). Retrograde amnesia and memory consolidation: A neurobiological perspective. *Curr. Opin. Neurobiol.* 5, 169–177.