Systems/Circuits

Sleep Consolidation Potentiates Sensorimotor Adaptation

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Contrary to its well-established role in declarative learning, the impact of sleep on motor memory consolidation remains a subject of debate. Current literature suggests that while motor skill learning benefits from sleep, consolidation of sensorimotor adaptation (SMA) depends solely on the passage of time. This has led to the proposal that SMA may be an exception to other types of memories. Here, we addressed this ongoing controversy in humans through three comprehensive experiments using the visuomotor adaptation paradigm ($N = 290$, 150 females). In Experiment 1, we investigated the impact of sleep on memory retention when the temporal gap between training and sleep was not controlled. In line with the previous literature, we found that memory consolidates with the passage of time. In Experiment 2, we used an anterograde interference protocol to determine the time window during which SMA memory is most fragile and, thus, potentially most sensitive to sleep intervention. Our results show that memory is most vulnerable during the initial hour post-training. Building on this insight, in Experiment 3, we investigated the impact of sleep when it coincided with the critical first hour of memory consolidation. This manipulation unveiled a benefit of sleep (30% memory enhancement) alongside an increase in spindle density and spindle–SO coupling during NREM sleep, two well-established neural markers of sleep consolidation. Our findings reconcile seemingly conflicting perspectives on the active role of sleep in motor learning and point to common mechanisms at the basis of memory formation.

Key words: consolidation; EEG; human; motor learning; sleep

Significance Statement

While there is compelling evidence that sleep improves declarative memory, its role in the consolidation of motor memories remains a long-standing debate. For example, it is currently established that sensorimotor adaptation (SMA) consolidates with the passage of time, irrespective of sleep. This has led to the proposal that SMA may be an exception to other types of memories. Our findings indicate that SMA memories may indeed consolidate with both the passage of time and sleep, depending on the proximity between training and bedtime. Our work sheds light on this controversy and points to the existence of common mechanisms supporting consolidation across memory domains. Furthermore, it may impact rehabilitation programs, expediting motor injury recovery by aligning training sessions with sleep.

Introduction

Sleep consistently enhances memory retention across various declarative learning paradigms such as face recognition, free recall, paired associates, and others (Tucker et al., 2006; Wagner et al., 2007; Talamini et al., 2008; Payne et al., 2012). In contrast, the contribution of sleep to procedural motor learning is more equivocal and, at first sight, appears to vary remarkably with the experimental paradigm.

Motor learning encompasses skill acquisition, the incorporation of new motor programs for precise movement execution, and sensorimotor adaptation, the ability to recalibrate pre-existing motor programs under changing environmental or internal conditions (Krakauer et al., 2019). One of the most popular experimental paradigms to study motor skill learning (MSL) in the laboratory is the motor sequence learning task, which involves performing a five-item sequence of movements on a keyboard using four fingers of the nondominant hand (Karni et al., 1998; Doyon et al., 2009; Albouy et al., 2015; Jacobacci et al., 2020). Sensorimotor adaptation (SMA), on the other hand, has been

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studied by imposing visual or proprioceptive perturbations that alter the sensorimotor coordination while the subject reaches targets (Shadmehr and Mussa-Ivaldi, 1994; Pine et al., 1996; Krakauer et al., 1999, 2000; Smith and Shadmehr, 2005; Gonzalez Castro et al., 2014; Villalta et al., 2015; Lerner et al., 2020). Substantial evidence underscores the significance of non-rapid eye movement (NREM) sleep in the stabilization of motor sequence learning (Rickard et al., 2008; Brawn et al., 2010; Nettersheim et al., 2015) or in the emergence of overnight offline gains when the sequence is encoded explicitly (Robertson et al., 2004; Nishida and Walker, 2007; Doyon et al., 2009; Diekelmann and Born, 2010; Albouy et al., 2013; Breton and Robertson, 2017). In contrast, the available evidence on SMA paradigms suggests that the consolidation of this type of motor memory is independent of sleep. Specifically, Donchin et al. (2002) have demonstrated that sleep deprivation after force-field adaptation spares memory retention, while Thürer et al., (2018) found no differences in overnight memory retention after a period of wake or sleep. Likewise, Doyon et al. (2009) and Debas et al. (2010) have shown similar levels of memory retention when visuomotor adaptation is followed by an equivalent period of sleep or wakefulness. Based on these findings, it has been argued that, unlike MSL, the consolidation of SMA relies exclusively on the passage of time (Brodt et al., 2023).

At first sight, this discrepancy between declarative learning and MSL, on one side, and SMA, on the other side, suggests the presence of different mechanisms supporting memory consolidation depending on the memory system and/or the experimental paradigm. It is noteworthy, however, that the majority of the studies reviewed above focused on tracking memory retention after a time interval that includes—or not—a period of sleep but tended to overlook the temporal gap between training and bedtime as a relevant factor. The close proximity between these events is indeed a strong modulator of declarative and motor sequence memories (Barrett and Ekstrand, 1972; Benson and Feinberg, 1977; Gais et al., 2006; Talamini et al., 2008; Doyon et al., 2009; Van Der Werf et al., 2009; Holz et al., 2012; Payne et al., 2012; Truong et al., 2023). Thus, it is possible that SMA also benefits from sleep when it occurs closely after training, while the memory trace is still in a fragile state.

To test this hypothesis, we conducted a series of experiments (Fig. 1) using a well-established SMA paradigm involving adaptation to an optical rotation, known as visuomotor adaptation (Villalta et al., 2015; Lerner et al., 2020; Albert et al., 2022). In Experiment 1, we investigated the impact of sleep on SMA when the time interval elapsed between training and bedtime is not experimentally controlled, consistent with the approach implemented by previous studies (Donchin et al., 2002; Doyon et al., 2009; Debas et al., 2010; Thürer et al., 2018). We predicted that sleep would not benefit SMA under these conditions. Next, in Experiment 2, we used an anterograde interference approach to determine the time window during which SMA memory would be most vulnerable and, thus, potentially most sensitive to sleep intervention in a controlled experimental setting. Based on the results of Experiment 2, in Experiment 3, we investigated the impact of sleep on SMA when the time interval elapsed between training and bedtime was experimentally controlled to either coincide with this sensitive time window or fall outside of it. Furthermore, to ascertain whether sleep operates through an active mechanism—as opposed to merely protecting against interference—we used EEG to quantify neural markers of consolidation well-established in the declarative and MSL literature, namely, the density of fast sleep spindles and their coupling with slow oscillations (Barakat et al., 2011; Ramanathan et al., 2015; Maingret et al., 2016; Ladenbauer et al., 2017; Boutin et al., 2018; Helfrich et al., 2018; Muehlroth et al., 2019; Navarro-Lobato and Genzel, 2019; Silversmith et al., 2020). We predicted that NREM sleep would benefit SMA through an active mechanism only when it overlaps with the sensitive time window during which memory remains in a fragile state.

Materials and Methods

Participants

A total of 290 human participants (150 females; mean ± SD = 24.3 ± 4 years old) with no known history of neurological or psychiatric disorders were recruited from the School of Medicine of the University of Buenos Aires. Subjects were right-handed as assessed by the Edinburgh Handedness Questionnaire (Oldfield, 1971) and were asked to maintain a regular sleep schedule before and during the study. This was monitored through self-recorded spreadsheets provided by the researcher

All volunteers signed the informed consent approved by the Ethics Committee of the Hospital de Clínicas (University of Buenos Aires), which complies with the Declaration of Helsinki in its latest version, and with the national law on the protection of personal data.

Experimental paradigm

Sensorimotor adaptation was studied using a visuomotor adaptation task (VMA), which has been previously described in detail elsewhere (Lerner et al., 2020; Solano et al., 2022a) and is briefly summarized here. As illustrated in Figure 1*a*, participants performed a center-out task involving moving a cursor from a starting point at the center of a computer screen to one of eight visual targets arranged concentrically, using a joystick controlled with the thumb and index finger of the right dominant hand. The vision of the hand was occluded throughout the task. Visual feedback for the cursor was continuously provided from the onset of each trial until the cursor crossed the virtual circle containing the targets, where it remained for 200 ms. Afterward, both the cursor and target disappeared for 1,500–2,000 ms (with temporal jitter) before a new target appeared. Participants were instructed to execute a shooting movement toward one of the eight targets as soon as it appeared on the screen. Each cycle consisted of eight trials, one per target, presented in a pseudorandomized order. In turn, 11 cycles composed one block. To prevent online corrections that would lead to submovements, the joystick's gain was set to 1.4, such that a 1 cm displacement of the joystick tip resulted in a 1.4 cm movement of the cursor on the screen (Villalta et al., 2015).

Three types of trials were presented throughout the study, which varied depending on the experiment (Experiment 1 through 3), the group (experimental or control), and the session (training or test). During null trials, in which no perturbations were applied, the movement of the cursor directly mapped onto the joystick's movement. During perturbed trials, a counterclockwise (CCW) or a clockwise (CW) optical rotation of 30° (in 14/15 groups of Experiments 1 through 3) or 45° (in one control group of Experiment 3) was applied to the cursor, deviating its trajectory. During error-clamp trials (EC), the cursor trajectory was manipulated to provide fake "straight" paths to the target that mimicked those generated during correct trials. The latter was accomplished by projecting the actual movement of the cursor to the straight line between the start point and the target, with some controlled variability (10° standard deviation). These trials allowed us to measure memory retention without the confound of learning from error (Criscimagna-Hemminger and Shadmehr, 2008). The SMA task was implemented in MATLAB (The MathWorks) using the Psychophysics Toolbox v3 (Brainard, 1997).

Experimental design

Experiment 1: determine the effect of sleep on SMA when the temporal gap between training and bedtime is not controlled. To investigate the impact of sleep on SMA when the gap between training and bedtime was not fixed, we first characterized the time course of memory decay based on the temporal evolution of memory retention throughout wakefulness (Fig. 1*b*, top panel). This time course allowed us to determine an asymptotic measure of retention without intermediate sleep, which

served as an unbiased reference to establish whether a night of sleep enhanced, stabilized, or rather impaired motor memory.

To characterize the memory decay, 111 participants were randomly assigned to five groups defined by the time elapsed between the end of training and the test session: 15 min ($n = 22$), 1 h ($n = 25$), 3 h ($n = 22$), 5.5 h ($n = 22$), and 9 h ($n = 20$). All participants underwent one block of null trials (baseline) and were then exposed to six blocks of a 30° CCW rotation. Memory decay was estimated based on the time course of memory retention assessed at the test session through two cycles of EC trials. To determine the effect of sleep on SMA under conditions where the temporal gap between training and bedtime was not controlled, the asymptotic level of memory retention derived from the decay curve was contrasted to the memory retention observed in a group of participants undergoing a full night of sleep ($n = 23$) and tested 24 h post-learning. Critically, all participants trained at different times throughout the day (Table 1), thereby eliminating any consistency in the training schedule.

Experiment 2: determine the optimal time window for sleep intervention in a controlled experimental setting. To determine the time window during which SMA memory would be most vulnerable and, thus, potentially most sensitive to sleep intervention, in Experiment 2, we examined the time course of memory consolidation during wake using an anterograde interference protocol (Lerner et al., 2020). This information was critical to assess the effect of sleep on SMA when the temporal gap between training and bedtime was experimentally controlled (Experiment 3).

To this aim, we analyzed unpublished data acquired as part of a larger study aimed at characterizing the effect of anterograde interference on SMA, some of which we reported recently (Lerner et al., 2020). In our previous work, we showed that adaptation to an optical rotation hinders the ability to adapt to the opposite rotation within a 6 h window. Unlike retrograde interference protocols, which have mostly failed at unveiling the time course of memory consolidation in sensorimotor adaptation (although see Brashers-Krug et al., 1996; Shadmehr and Brashers-Krug, 1997 for exceptions), we showed that the use of an anterograde interference protocol yielded a gradual pattern of release from interference. This suggests that our approach may be a good alternative to track memory consolidation in SMA and, thus, address the aim of Experiment 2.

To track memory consolidation during wake, we implemented an anterograde interference protocol consisting of sequentially adapting to two opposing optical rotations (A and B) separated by different time intervals from 5 min to 24 h; memory retention was assessed 24 h post-learning (Fig. 1*b*, middle panel). Specifically, after performing one block of baseline without perturbation, four groups of participants were sequentially exposed to six blocks of a 30-degree CCW optical rotation (A) followed by 6 blocks of a 30° CW optical rotation (B) separated by either 5 min ($n = 15$), 1 h ($n = 20$), 6 h ($n = 19$), or 24 h ($n = 18$). A fifth group, which acted as control ($n = 20$), trained only on rotation B. All volunteers returned 24 h after adaptation to B for the test session, during which they were exposed to two EC cycles to quantify long-term memory retention. Participants were instructed not to nap between adaptation sessions. Table 1 depicts the time of day at which training took place for each group. The variation in the time interval between perturbations A and B allowed us to assess how learning on A impacted the consolidation of B, and thus, infer the level of fragility/vulnerability of the memory trace.

Control experiment. In our prior study (Lerner et al., 2020), we demonstrated that the 5 min and 1 h groups exhibited slower learning rates due to anterograde interference, resulting in less time spent training at the asymptote compared with the other groups. To address the possibility that this lesser amount of "overlearning" (Krakauer et al., 2005; Shibata et al., 2017; Mooney et al., 2021) may influence long-term memory retention and, thus, act as a potential confound, we included an additional group of participants ($n = 20$) who trained at the asymptote for a duration similar to the average between the 5 min and 1 h groups and was also tested 24 h post-training. For practicality, we refer to this group as the "overlearning" group. To establish the training protocol for the overlearning group, we first quantified the amount of overlearning on B for the 5 min, the 1 h, and the control groups as the number of training cycles completed after reaching 95% of asymptotic performance. This estimation was based on $3 * \tau$ (τ = the time constant), derived from a single exponential fit applied to the pointing angle, where $\tau = 1/b$ and b represents the learning rate (see below, Data analysis). Note that the units of τ are training cycles. The number of cycles spent training at the asymptote was then computed by subtracting $3 * \tau$ from the total amount of training cycles. Then, the average amount of overlearning across the 5 min and 1 h groups was subtracted from the overlearning of the control group. Finally, this difference in cycles was in turn subtracted from the 66 cycles of the standard training protocol. This adjustment ensured that the amount of overlearning of the additional group matched that of the 5 min and 1 h groups.

Experiment 3: determine the effect of sleep on SMA when the temporal gap between training and bedtime is controlled. In Experiment 3, we investigated the impact of sleep on SMA when the time interval elapsed between training and bedtime was experimentally controlled to either coincide with the time window during which SMA memory is most vulnerable (determined in Experiment 2) or fall outside of it. We hypothesized that sleep intervention would be most effective when the memory trace is still in a fragile state.

Two different groups of participants were trained on the VMA task (Fig. 1*b*, bottom panel). One group trained in the morning ($n = 23$) and thus slept outside the optimal time window, while the other group trained at night ($n = 21$) and went to sleep during the optimal time window. Memory retention in both groups was assessed 24 h after training. We will refer to the former group as AM/AM because volunteers underwent training and testing in the morning and to the latter as PM/PM because participants in this group were trained and tested at night (see Table 1 for details on training time).

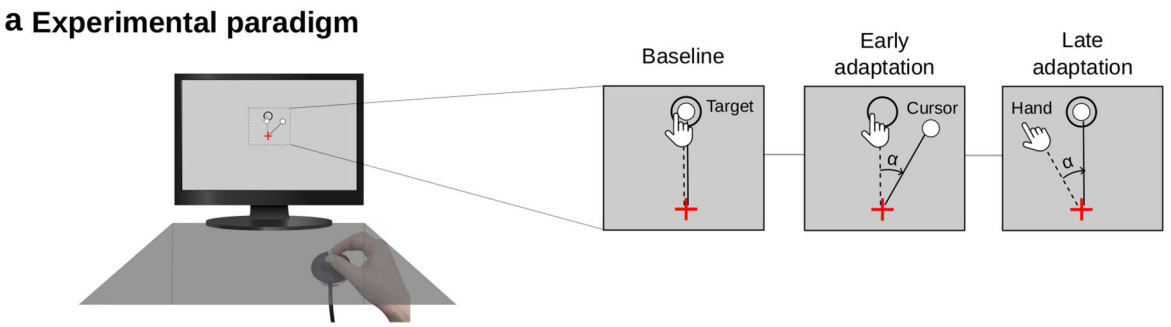
All participants were explicitly instructed to refrain from daytime napping. The VMA training session consisted of one baseline block of null trials followed by six blocks of perturbed trials in which a 30° CW optical rotation was imposed on the cursor. During the test session, participants were exposed to two cycles of EC trials to assess memory retention. In addition, participants from both the AM/AM and PM/PM groups underwent a polysomnographic (PSG) recording through the full night of sleep (see detailed description below). Only subjects fulfilling the criteria for good sleep quality based on the Pittsburgh Sleep Quality Questionnaire (Buysse et al., 1989) and the Epworth Drowsiness Scale (Johns, 1991) were included in the experiment.

To control for a potential circadian modulation associated with the time of the test, two additional groups of participants were included in the statistical analysis. An AM/PM group ($n = 20$) was trained in the morning on a 30° CW rotation and tested the same night (~9 h later) without intermediate sleep, whereas a PM/AM group ($n = 10$) was trained at night and tested the next morning (~9 h later), after a night of sleep. Data from the PM/AM group are part of a previously published

Table 1. VMA training time

Experiment 1	Mean	SD	Min	Max
15 min	01:53 P.M.	02:28	09:46 A.M.	05:58 P.M.
1 h	01:53 P.M.	02:03	11:06 A.M.	05:02 P.M.
3 h	12:05 P.M.	01:25	09:45 A.M.	02:49 P.M.
5.5 h	11:06 A.M.	01:35	08:39 A.M.	02:43 P.M.
9 h	08:21 A.M.	01:06	06:59 A.M.	10:46 A.M.
24 h	02:10 P.M.	02:20	09:38 A.M.	05:56 P.M.
Experiment 2				
5 min	03:25 P.M.	02:24	11:34 A.M.	07:29 P.M.
1 h	03:40 P.M.	02:16	10:31 A.M.	07:20 P.M.
6 h	11:38 A.M.	02:06	07:45 A.M.	03:05 P.M.
24 h	02:27 P.M.	02:55	09:53 A.M.	07:34 P.M.
Control	02:44 P.M.	02:29	10:32 A.M.	06:49 P.M.
Experiment 3				
PM/PM	10:48 P.M.	00:14	10:30 P.M.	11:18 P.M.
PM/AM	09:48 P.M.	00:16	09:28 P.M.	10:28 P.M.
AM/AM	09:14 A.M.	00:41	08:31 A.M.	11:16 A.M.
AM/PM	08:21 A.M.	01:06	06:59 A.M.	10:46 A.M.

Shown are the mean, standard deviation (SD), and earliest and latest time of day expressed in the format hh:mm, corresponding to the initiation of VMA learning for each group and each experiment.



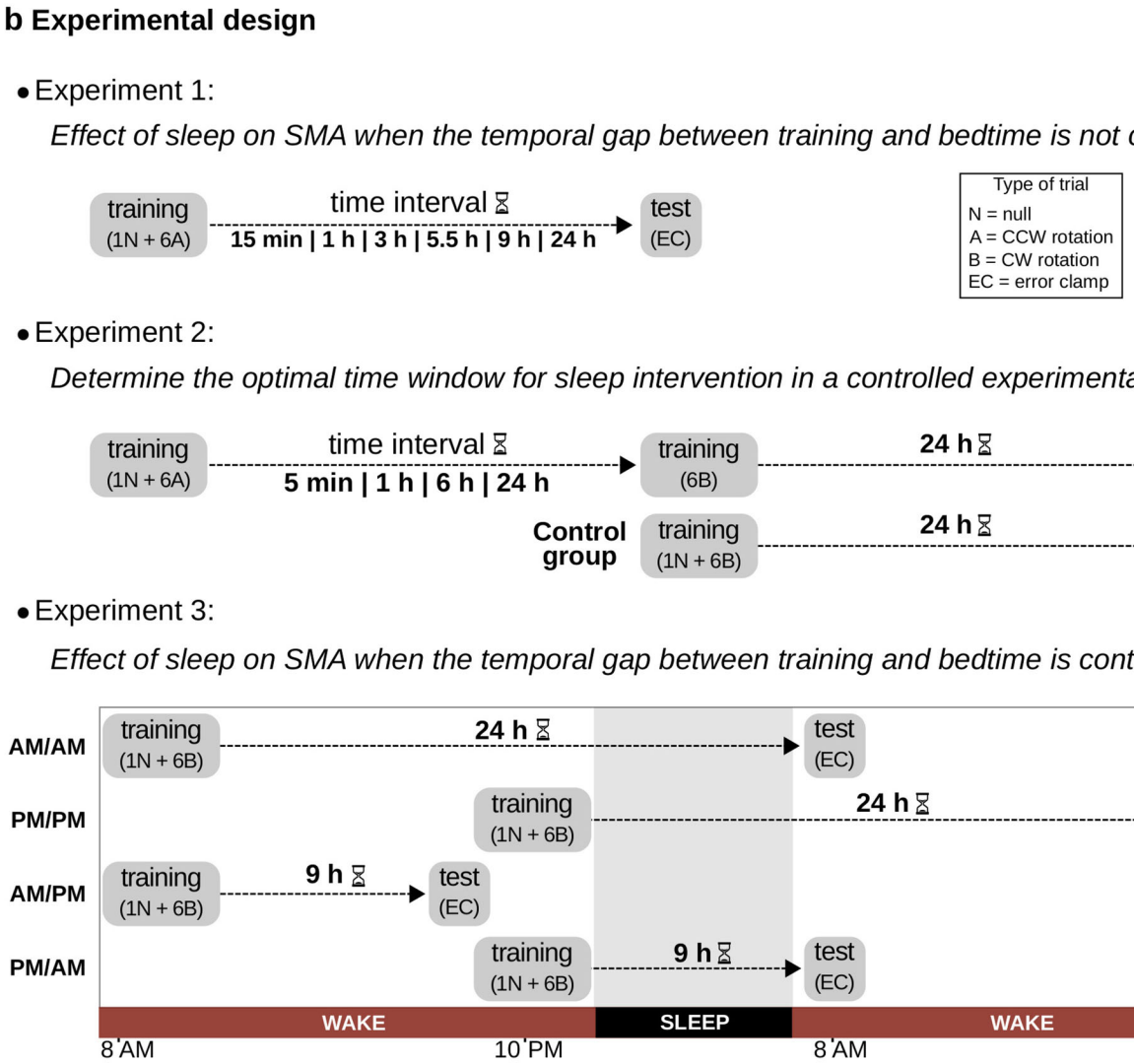


Figure 1. Experimental paradigm and experimental design. ***a***, VMA experimental paradigm. Subjects sat on a chair and performed center-out movements to one of eight visual targets displayed concentrically around the start point, using a cursor controlled with a joystick operated with their right dominant hand. One cycle was composed of eight trials (one per target), and one block was composed of 11 cycles. The vision of the hand was occluded. The inset depicts the visual display of the computer screen, illustrating the relationship between the hand manipulating the joystick (unseen) and the trajectory of the cursor (seen) during null trials (Baseline) and during early and late phases of adaptation to an optical CW rotation (α). ***b***, Experimental design. Three experiments were conducted to address the aims of the study in which different sets of subjects trained on the VMA paradigm, and adapted to a CCW (A) and/or a CW (B) rotation. In Experiment 1, we assessed the effect of sleep when the temporal gap between training and bedtime was not controlled. Six different groups of participants trained on A (one block of null trials followed by six blocks of A) at different time points throughout the daytime (between 7 A.M. and 6 P.M.), and their memory retention was tested after a variable time interval post-learning: 15 min, 1 h, 3 h, 5.5 h, 9 h, or 24 h (note that only the 24 h group underwent a full night of sleep). In Experiment 2, we determined the optimal time window for sleep intervention in a controlled experimental setting. Four groups of participants underwent an anterograde interference protocol to determine the time course of memory consolidation and, thus, the time point at which the motor memory was most fragile. Subjects adapted sequentially to A and B, separated by either 5 min, 1 h, 6 h, or 24 h, and memory retention was assessed 24 h after training on B. A control group trained only on B. In Experiment 3, we assessed the effect of sleep when the temporal gap between training and bedtime was controlled based on the results of Experiment 2. Two groups of volunteers trained on B and polysomnographic EEG recordings were performed overnight. One group trained in the morning and thus slept outside the optimal time window (AM/AM), while the other group trained at night and went to sleep during the optimal time window (PM/PM). Memory retention in both groups was assessed 24 h after training. To control for a possible circadian effect due to the time of test, two additional groups were tested at the opposite circadian time (AM/PM and PM/AM).

study in which subjects were exposed to a 45° optical rotation (Solano et al., 2022a).

PSG recording

Eleven surface EEG electrodes were placed over the prefrontal, motor, and parietal areas (FC1, FC2, FC5, FC6, C3, C4, P3, and P4) and over the midline (Fz, Cz, and Pz). Electrodes were mounted following the standard 10–20 arrangement (modified combinatorial nomenclature; Oostenveld and Praamstra, 2001). Both mastoids were used as references. In addition to EEG electrodes, two electrodes were placed over the periorbital area of both eyes and two additional electrodes over the chin to measure electrooculography (EOG) and electromyography (EMG), respectively. All signals were acquired at 200 Hz, using the Alice 5 (Philips Respironics) or BWMini (Neurovirtual) devices.

EEG processing

EEG, EOG, and EMG signals were bandpass-filtered to facilitate sleep scoring (EEG, 0.5–30 Hz; EOG, 0.5–15 Hz; EMG, 20–99 Hz). All PSG recordings were sleep-staged manually, according to standard criteria (Iber, 2004). Namely, 30 s epochs were classified as either wake (W), non-rapid eye movement (NREM1, NREM2, and NREM3), or rapid eye movement (REM) stage. After stage classification, sleep architecture was determined based on the following measures, expressed in minutes: total sleep time, sleep latency (latency to NREM1), REM latency, total wake time, wake after sleep onset (WASO), and time in NREM1, NREM2, NREM3, and REM. Sleep efficiency was also computed as the percentage of total sleep time relative to the time interval between lights off and lights on (%). Movement artifacts on the filtered EEG signal were detected by visual inspection and manually rejected.

Slow oscillations (SOs, 0.5–1.25 Hz) and sleep spindles (10–16 Hz) were automatically identified from the EEG signal corresponding to the stages NREM2 and NREM3 by using previously reported algorithms (see below).

Detection of SOs. The algorithm implemented to detect SOs was based on that reported by Mölle et al. (2011) and Antony and Paller (2017), and it is the same that we used in previous works (Solano et al., 2022a,b). The EEG signal was bandpass-filtered between 0.5 and 1.25 Hz. To quantify SOs, we first identified zero crossings of the EEG signal and labeled them as positive-to-negative (PN) or negative-to-positive (NP). Those EEG segments between two NP zero crossings were considered SOs if they lasted between 0.8 and 2 s. Next, we computed the peak-to-peak (P-P) amplitude as the difference between the positive peak and the negative peak. Finally, we determined the median of the P-P amplitudes for each channel and each subject and retained those SOs with a P-P amplitude greater than the median value (Mizrahi-Kliger et al., 2018).

Sleep spindle detection. The algorithm implemented to detect sleep spindles was based on that reported by Ferrarelli et al. (2007) and Mölle et al. (2011), and it is the same that we used in previous works (Solano et al., 2022a,b). The algorithm was run for each channel and each subject. First, the EEG signal was bandpass-filtered between 10 and 16 Hz before calculating the instantaneous amplitude (IA) and instantaneous frequency by applying the Hilbert transform (Tort et al., 2010). The IA was used as a new time series and was smoothed with a 350 ms moving average window. Next, those segments of the IA signal that exceeded an upper magnitude threshold (90th percentile of all IA points) were labeled as potential spindles. The beginning and end of potential spindles were defined as the time points at which the signal dropped below a lower threshold (70th percentile of all IA points). Putative spindles with a duration between 0.5 and 3 s were labeled as true spindles. Finally, only fast spindles with a mean frequency ≥12 Hz (Mölle et al., 2011; Cox et al., 2017) were included in further analysis, as they have been linked to memory consolidation during sleep (Barakat et al., 2011; Ladenbauer et al., 2017, Helfrich et al., 2018; Muehlroth et al., 2019; Navarro-Lobato and Genzel, 2019; Solano et al., 2022a,b).

Coupling between SOs and spindles. After identifying spindles and SOs, we looked for spindles that occurred during a SO. We quantified spindle–SO couplings according to the following criterion: if a spindle had its maximum P-P amplitude within ±1.2 s around the trough of a SO, it was counted as a spindle–SO coupling (Muehlroth et al., 2019; Kurz et al., 2021; Solano et al., 2022a). This algorithm was applied to each channel of each session.

Data analysis

Behavior. Behavioral performance was assessed based on the pointing angle, which was computed for each trial as the angle of motion of the joystick relative to the line segment connecting the start point and target position (Lerner et al., 2020; Solano et al., 2022a). Trials in which the pointing angle exceeded 120° or deviated by more than 45° from each cycle's median were excluded from further analysis. Trial-by-trial data was next converted to cycle-by-cycle time series by computing the median pointing angle across the eight trials of a cycle, for each subject. For graphical representation, the pointing angle was normalized when required. We empirically quantified each subject's learning rate by fitting a single exponential function ($y(t) = a * \exp(-b * t) + c$) to the sequence of pointing angles, where $y(t)$ represents the pointing angle on cycle t; a and c the initial bias and the asymptote of the exponential, respectively; and parameter b represents the learning rate.

To assess memory retention, the median pointing angle corresponding to each EC cycle was computed and expressed for each subject as a percentage of the asymptotic pointing angle, calculated based on the median of the last block of learning. Finally, the percentage measure was averaged across EC cycles.

Memory decay. To characterize the memory decay of VMA as a function of time, we fitted a single exponential function ($y(t) = a * \exp(-b * t) + c$) to the memory retention values across individual subjects from the five groups of Experiment 1 trained and tested without intermediate sleep. Here, $y(t)$ represents memory retention at minute t. Parameter a represents the initial retention value, b *is* the rate of memory decay, and c is the asymptote of the function. Exponential functions have been previously used to characterize forgetting in force-field adaptation (Criscimagna-Hemminger and Shadmehr, 2008) and also in declarative tasks (Wixted, 2004).

Electroencephalographic signal. As described above, SOs and spindles were automatically identified from the EEG signal previously classified as NREM2 and NREM3, corresponding to the first cycle of sleep. We computed the density of fast spindles during NREM sleep (number of fast spindles per minute of NREM sleep) and the density of fast spindles coupled with an SO (number of spindle–SO couplings per minute of NREM sleep).

In our previous work (Solano et al., 2022a), we found that visuomotor adaptation increased the overall density of fast spindles and fast spindles coupled with an SO rather locally, over the hemisphere contralateral to the trained hand (left hemisphere in our experiment). In that work, all volunteers underwent two PSG recordings, one after a control session in which subjects performed the VMA task in the absence of the optical rotation and another after a VMA learning session in which an optical rotation was applied. The strong interhemispheric modulation of the sleep metrics mentioned above was revealed after computing the percent change of these metrics in the experimental session relative to the control session. In the present study, however, participants in the PM/PM and AM/AM groups underwent a unique PSG recording after a VMA learning session. Thus, to assess the effect of learning on the density of sleep spindles and the spindle–SO coupling for the PM/PM and AM/AM groups, we computed their interhemispheric percent change according to the function (left hemisphere − right hemisphere) / right hemisphere * 100. This function was applied for each subject across corresponding EEG electrodes (FC1–FC2, FC5–FC6, C3–C4, and P3–P4). To illustrate the spatial distribution of the percentage difference between hemispheres, we report the results in topographic maps (MNE-Python; Gramfort 2013).

Statistical analysis

Parametric statistics were used to analyze all metrics of interest. Analyses were carried out using R (version 3.6.3; R Core Team, 2017) in RStudio (RStudio Team, 2020). Statistical differences were assessed at the 95% level of confidence ($\alpha = 0.05$).

For between-subjects statistical comparisons, we used one-way or two-way ANOVA. The variables of interest were either memory retention, the rate of learning (b parameter of the exponential function fitted to the pointing angle), or the median pointing angle from the last block of adaptation. The fixed factors were the group and the condition associated with the proximity between learning and sleep.

For the sleep metrics, we fitted a linear mixed model (LMM) in which random intercepts were estimated for each subject to take into account the repeated measures. The variable of interest was the interhemispheric percent change of the sleep metrics computed for all corresponding EEG electrodes (FC1–FC2, FC5–FC6, C3–C4, and P3–P4), and the fixed factor was the group. To assess the statistical significance of the fixed factor, we used F tests with Kenward–Roger's approximation of the degrees of freedom to obtain p-values (Halekoh and Højsgaard, 2014).

We used Dunnett's test or t tests corrected for multiple comparisons using Bonferroni, for post hoc assessment.

Results

Sleep does not benefit sensorimotor adaptation when the temporal gap between training and bedtime is not controlled

In contrast to declarative and motor sequence learning, the consolidation of SMA memory has consistently been shown to depend exclusively on the passage of time (Donchin et al., 2002; Doyon et al., 2009; Debas et al., 2010; Thürer et al., 2018). In this study, we hypothesized that the apparent lack of a sleep benefit found in the literature can be attributed to the considerable temporal gap elapsed between training and bedtime.

To this aim, we compared the asymptotic level of VMA memory retention attained during wake (derived from the five groups trained and tested without intermediate sleep) with that of a group undergoing a full night of sleep (Fig. 1*b*, top panel). Critically, training in all groups occurred throughout the day without any consistency in the training schedule. We found that all volunteers learned to compensate for the optical rotation by the end of training as depicted in Figure 2*a*. Learning was similar across groups as indicated by the rate of adaptation ($F_{(5,128)} = 0.85$, $p = 0.52$) and the level of performance attained during the last block of training ($F_{(5,128)} = 1.22$, $p = 0.30$). As depicted by Figure 2*b*, memory retention during wake declined progressively over time ($F_{(4,106)} = 13.51$, $p < 0.001$; mean ± SEM, 15 min = 79.6 ± 3.1%; 1 h = 66.8 ± 3.9%; 3 h = 53.6 ± 4.7%; 5.5 h = 44.1 ± 4.2%; 9 h = 42.0 ± 5.6%). This pattern of forgetting conformed to a single exponential function $y(t) = a * \exp(-b * t) + c$ (Fig. 2*c*), typically observed in declarative and force-field adaptation tasks (Criscimagna-Hemminger and Shadmehr, 2008; Murre and Dros, 2015). Specifically, VMA memory decayed with a time constant of 2.25 h ($b = 0.44\ \mathrm{h}^{-1}$) and reached an asymptote ($c = 40.97\%$) at approximately 5.5 h post-learning (retention at 5.5 h vs c, $t_{(21)} = 0.74$, $p = 0.94$, whereas retention at 3 h vs c, $t_{(21)} = 2.68$, $p = 0.028$, adjusted for multiple comparisons based on Bonferroni).

A direct comparison between the asymptotic level of VMA memory retention attained during wakefulness, as identified by the exponential fit, and that of the group undergoing a full night of sleep (24 h group) yielded no statistical difference (Fig. 2*d*; mean ± SEM, 24 h = 40.5 ± %4.1%; retention at 24 h vs c, $t_{(22)} = -0.122$, $p = 0.90$), suggesting no benefit of sleep in this context.

Altogether, these findings show that sensorimotor adaptation does not benefit from a full night of sleep when the temporal proximity between training and bedtime is not controlled for. Note that, under these experimental conditions, our results are in line with the prevailing literature supporting the notion that SMA memory consolidates with the passage of time (Donchin et al., 2002; Doyon et al., 2009; Debas et al., 2010; Thürer et al., 2018).

The optimal time window for sleep intervention in a controlled experimental setting is ∼1 h

In Experiment 1, we showed that sleep is ineffective when the temporal gap between training and bedtime is not taken into account. To determine the optimal time window for sleep intervention in a controlled experimental setting, in Experiment 2, we used an anterograde interference protocol to track the integrity of VMA memory through wake consolidation and, thus, estimate the level of vulnerability of the memory trace (Wigmore et al., 2002; Tong and Flanagan, 2003; Sing and Smith, 2010; Leow et al., 2014).

Four groups of participants ($n = 15$–20 per group) adapted sequentially to two 30° opposing optical rotations (A = CCW followed by B = CW) separated by one of four possible time intervals: 5 min, 1 h, 6 h, or 24 h (Fig. 1*b*, middle panel). In addition, a control group ($n = 20$) only adapted to B. Long-term memory for all groups was assessed 24 h after training on B. Visual inspection of the learning curves depicted in Figure 3*a* suggests that all participants learned to compensate for perturbation A to a similar extent (refer to Lerner et al., 2020, for corresponding statistics regarding the rate of adaptation and achieved level of asymptote). In contrast, anterograde interference significantly affected adaptation to B; while all groups reached asymptotic performance, the 5 min and 1 h groups were significantly slower than the control group (refer to Lerner et al., 2020 for corresponding statistics).

Memory consolidation during wake was inferred based on the pattern of retention after anterograde interference. As depicted by Figure 3*b*, we found that memory retention was significantly hindered by anterograde interference ($F_{(4,87)} = 7.61$, $p < 0.001$; mean ± SEM, 5 min = 18.0 ± 4.3%; 1 h = 19.1 ± 4.5%; 6 h = 38.6 ± 5.9%; 24 h = 41.0 ± 4.8; control = 48.3 ± 4.5%). Specifically, a strong deficit in memory retention was observed at 5 min and 1 h (Dunnett's test; 5 min vs control, $p < 0.001$; 1 h vs control, $p < 0.001$), which dissipated by 6 h (Dunnett's test; 6 h vs control, $p = 0.41$; 24 h vs control, $p = 0.65$). This temporal pattern, which resembles that observed for memory encoding, is consistent with a release from interference (Brashers-Krug et al., 1996; Shadmehr and Brashers-Krug, 1997).

In sum, Experiment 2 revealed that sensorimotor adaptation memories consolidate through wakefulness within a 6-hour window. Furthermore, and critical to the aim of Experiment 2, we found that memory remained most vulnerable during the initial hour post-training, providing relevant information to guide sleep intervention under the controlled experimental setting of Experiment 3.

Sleep benefits sensorimotor adaptation when the temporal gap between training and bedtime is controlled

Building on the findings of Experiment 2, in Experiment 3, we investigated the impact of manipulating the temporal gap between training and sleep on long-term memory and the neurophysiological markers of sleep consolidation. Our working hypothesis posited that sleeping early within the memory consolidation window, while the memory remains fragile, would enhance memory retention through an active mechanism.

To test this hypothesis, two groups of volunteers ($n = 21$ and $n = 23$) trained on the VMA task and slept either within the optimal time window identified in Experiment 2 (<1 h) or way outside the 6 h consolidation window (∼14 h). We refer to the first group, trained and tested at night (∼10 P.M.), as PM/PM, and to the second group, trained and tested in the morning, as AM/AM. Polysomnography recordings were acquired during sleep for these two groups. Two additional control groups were included to control for a potential circadian effect at the time of testing,

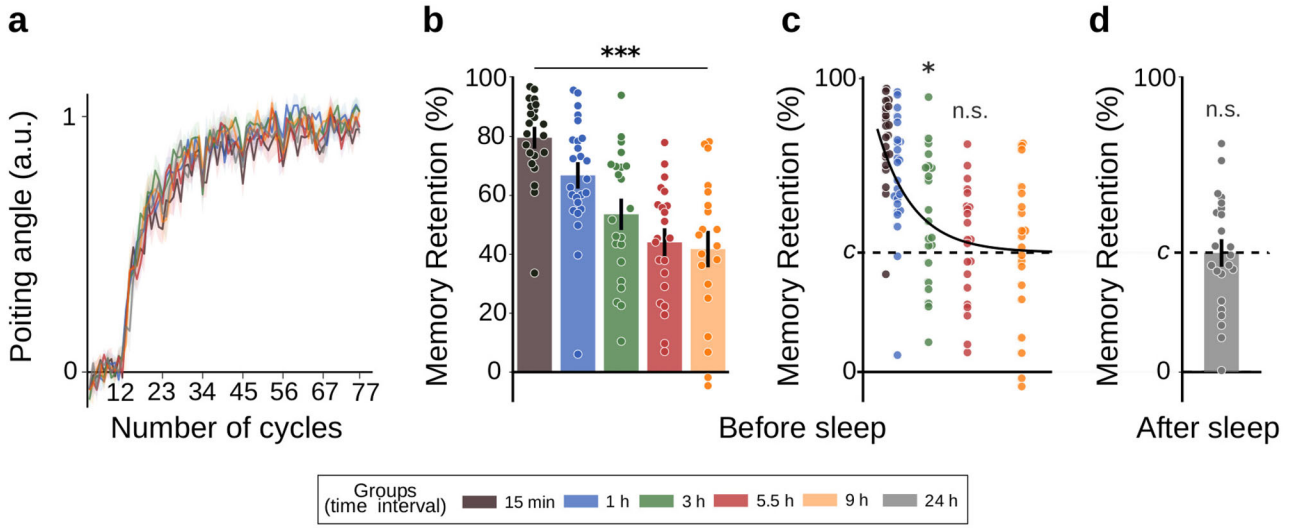


Figure 2. Experiment 1. Sleep does not benefit SMA when the temporal gap between training and bedtime is not controlled. ***a***, Learning curves. Shown are the median ± SEM of the normalized pointing angle (in arbitrary units) during visuomotor adaptation for all six groups. ***b***, Time course of memory retention. Memory retention was evaluated during the test session and expressed as % of learning. Shown are the mean ± SEM for each group and the individual data superimposed as dots. ***$p < 0.001$ indicates the result of the one-way ANOVA test across groups. ***c***, Characterization of VMA memory decay. Shown is the individual level of memory retention displayed on ***b***, where the abscissa scale represents the true time interval elapsed between the end of training and test (15 min through 9 h). Superimposed is the curve resulting from fitting a single exponential function: $y(t) = a * \exp(-b * t) + c$, with $a = 42.30\%$, $b = 0.44\ h^{-1}$, and $c = 40.97\%$. The dotted line represents the asymptote *c*. Memory decay stabilized ∼6 h after training. *$p < 0.05$; n.s., nonsignificance indicates the result of the *t* test between the 3 h and 5.5 h groups versus *c* adjusted for multiple comparisons based on Bonferroni. ***d***, Effect of sleep on VMA memory retention. Shown is the mean ± SEM of memory retention for the group that underwent a full night of sleep (24 h group). The dashed line represents the asymptote of memory decay during wakefulness (*c*). No significant difference was observed between the level of retention attained after a night of sleep and *c*.

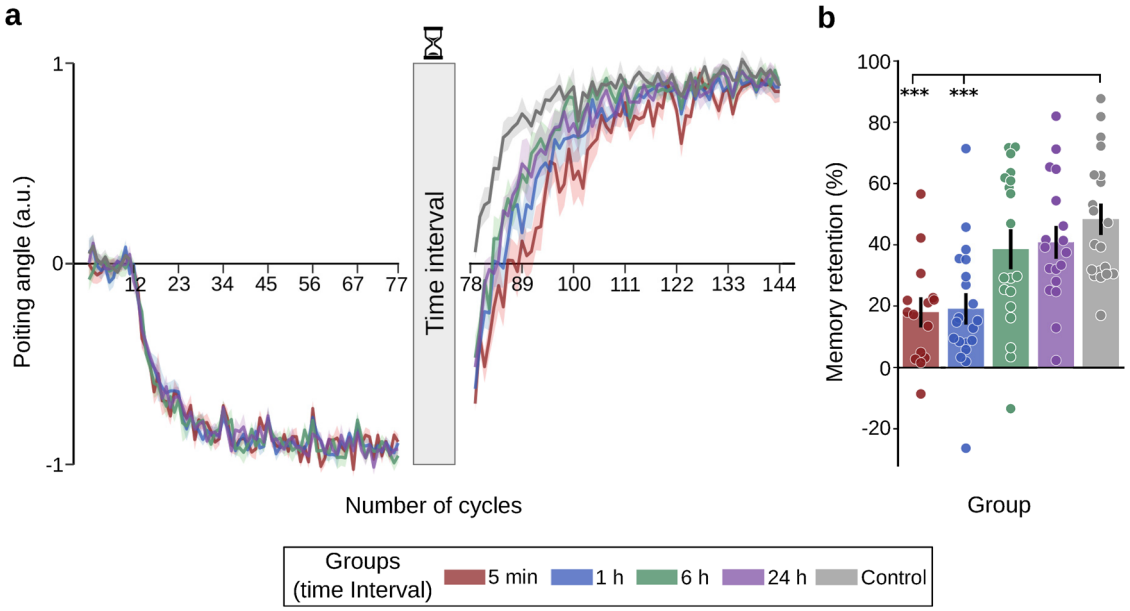


Figure 3. Experiment 2. Time course of SMA memory consolidates during wake. ***a***, Learning curves. Shown are the median ± SEM of the normalized pointing angle (in arbitrary units) for all groups as a function of the training session in which participants adapted sequentially to two opposing optical rotations (A followed by B) separated by one of four possible time intervals. In addition, a control group only adapted to B. ***b***, Time course of memory retention. Memory retention was evaluated during the test session by quantifying the pointing angle through two error-clamp cycles, expressed as a percentage of the asymptotic performance on B. Shown are the mean ± SEM of memory retention for each group, with individual data superimposed as dots. ***$p < 0.001$ indicates those groups that differed significantly from the control group according to Dunnett's test.

a PM/AM group that trained in the evening but was tested in the morning (with an intermediate sleep period) and an AM/PM group that trained in the morning but was tested in the evening (without an intermediate sleep period) (Fig. 1*b*, bottom panel).

All four groups adapted similarly to the optical rotation regardless of the time of training (Fig. 4*a*), as determined based on the rate of learning ($F_{(3,70)} = 1.46$, $p = 0.23$) and the achieved asymptotic performance ($F_{(3,70)} = 0.860$, $p = 0.461$). Critical to our manipulation, and in alignment with our hypothesis, we observed a 31% increase in memory retention (Fig. 4*b*) in the groups that trained immediately before sleep (PM/PM and PM/AM) compared with the groups that trained distant from sleep (AM/AM

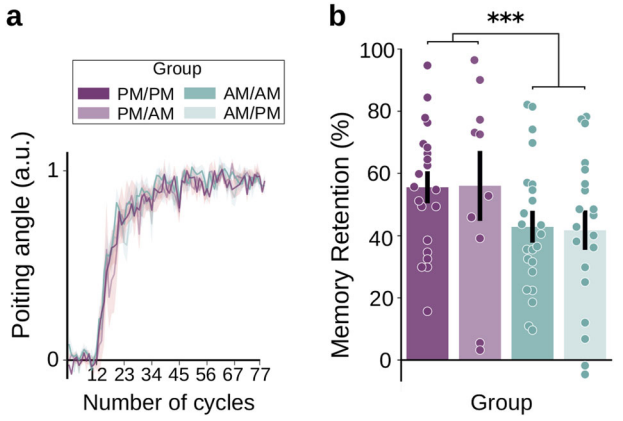


Figure 4. Experiment 3. Sleep potentiates SMA when it overlaps with the time window during which memory remains fragile. ***a***, Learning curves. Shown are the median ± SEM of the normalized pointing angle (in arbitrary units) corresponding to the AM/AM and PM/PM groups and their circadian controls (AM/PM and PM/AM). ***b***, Memory retention. Memory retention was evaluated during the test session by quantifying the pointing angle through two error-clamp cycles, which was expressed as a percentage of the asymptotic performance level. Shown are the mean ± SEM of the memory retention attained by each group; individual data are superimposed as dots. ***$p < 0.001$ indicates the result of the two-way ANOVA for the main effect of time of training on memory retention.

and AM/PM) (two-way ANOVA; significant main effect of training time: $F_{(1,70)} = 5.52$, $p = 0.02$; mean ± SEM: PM/PM = 55.5 ± 4.4%; PM/AM = 55.9 ± 10.5%; AM/AM = 42.9 ± 4.3%; AM/PM = 41.8 ± 5.6%). EEG analysis based on the onset of NREM 1 confirmed that volunteers in the PM/PM and PM/AM groups fell asleep within ∼20 min post-training (mean ± SEM = 21.9 ± 2.8 min), confirming a good overlap between sleep and the optimal time window. Critical to the specificity of our results, memory enhancement observed in the groups that trained close to bedtime cannot be explained by the time of test (two-way ANOVA; nonsignificant effect of time of test: $F_{(1,70)} = 0.18$, $p = 0.67$), ruling out a circadian modulation at the level of retrieval.

Notably, the level of memory retention achieved by the AM/AM group was comparable to that of the 24 h group from Experiment 1 (Fig. 2*d*), which trained sparsely during wakefulness without controlling the temporal gap between training and sleep (memory retention, mean ± SEM, AM/AM = 42.9 ± 4.3%; 24 h group from Experiment 1 = 40.5 ± 4.1%; $t_{(43.8)} = 0.40$, $p = 0.3$). This finding confirms that the observed benefit of sleep in memory retention represents a net enhancement of long-term memory.

Our findings indicate that sleeping early during the stabilization window potentiates SMA memory. We hypothesized that this effect reflects, at least in part, an active role of sleep in the consolidation of newly acquired information. To test this hypothesis, we assessed the effect of our manipulation on two well-established neural markers of sleep consolidation, which have been consistently observed across species and learning paradigms (Maingret et al., 2016; Ladenbauer et al., 2017; Helfrich et al., 2018; Muehlroth et al., 2019; Navarro-Lobato and Genzel, 2019). We and others have shown that motor learning increases the density of fast spindles and the SO–spindle coupling during NREM sleep (Kim et al., 2019; Silversmith et al., 2020; Hahn et al., 2022; Solano et al., 2022a,b). In our previous studies (Solano et al., 2022a,b), we found that this modulation predominantly occurs over the left hemisphere, contralateral to the trained hand, and predicts overnight long-term memory. Here we analyzed the EEG recordings from the AM/AM and PM/PM groups obtained during the night following SMA learning and contrasted these sleep metrics. We predicted that if sleep actively contributes to the consolidation of newly acquired SMA memory, it should increase the density of sleep spindles and SO–spindle couplings specifically over the contralateral hemisphere only in the PM/PM group.

As illustrated in Figure 5*a*, we found that training close to bedtime increased the spindle density over the left contralateral hemisphere (left/right hemisphere % change of fast spindle density, mean ± SEM, PM/PM = 12.1 ± 1.6%, AM/AM = 1.6 ± 1.5%; $F_{(1,38.87)} = 6.48$, $p = 0.015$, followed by t test vs zero; PM/PM, $t_{(20.36)} = 4.1$, $p = 0.001$; AM/AM, $t_{(18.8)} = 0.53$, $p = 1$). Likewise, Figure 5*b* shows that our manipulation also enhanced the spindle–SO coupling over the left hemisphere (left/right hemisphere % change of fast spindle–SO density, mean ± SEM, PM/PM = 14.8 ± 1.6%, AM/AM = 1.6 ± 1.1%; $F_{(1,37.74)} = 6.02$, $p = 0.019$, followed by t test vs zero; PM/PM, $t_{(19.8)} = 3.5$, $p = 0.004$; AM/AM, $t_{(19.2)} = 0.52$, $p = 1$). No significant differences were found in sleep architecture across groups suggesting that our results may not be attributed to differences in the quality or duration of sleep (Table 2).

In sum, Experiment 3 indicates that sleep potentiates long-term memory when it occurs early during the window of memory stabilization. The fact that the observed behavioral gain cannot be attributed to circadian effects, along with the specific contralateral modulation in spindle density and spindle–SO coupling in the group that trained close to bedtime, strongly suggests that sensorimotor adaptation undergoes consolidation during sleep.

Control experiment: overlearning does not impact memory retention

A potential confound to our findings from Experiment 2 is the possibility that the amount of training at the asymptote (aka overlearning) may have impacted memory retention, confounding the results from Experiment 2. This is because despite reaching the same level of asymptotic performance by the end of training on B, the two groups undergoing the strongest anterograde interference (5 min and 1 h groups) exhibited a slower rate of learning and, thus, spent relatively less amount of time training at the asymptote than the 6 h, 24 h, and the control (B only) groups. To explore the possibility that this lesser amount of "overlearning" (Krakauer et al., 2005; Shibata et al., 2017; Mooney et al., 2021) may explain the pattern of anterograde interference depicted in Figure 3*b*, we tested an additional group of subjects ($n = 20$) that trained a similar amount of time at the asymptote as the 5 min and 1 h groups. We hypothesized that if the observed decrease in memory retention was due to a lesser amount of overlearning rather than an impairment of the memory consolidation process, then the overlearning group should exhibit a similar level of retention as the 5 min and 1 h groups.

The amount of overlearning yielded by each group was as follows: (mean ± SEM) 5 min group = 28.2 ± 4.2 cycles; 1 h group = 27.4 ± 4.5 cycles; 6 h group = 36 ± 4.1 cycles; 24 h group = 31.3 ± 4.5 cycles; and control group = 43.33 ± 3.3. Given that all groups in Experiment 2 trained for six blocks on B (6 × 11 cycles = 66 cycles), and considering that the 5 min and 1 h groups spent approximately two fewer blocks than the control group (∼22 cycles) training at the asymptote, we exposed the new overlearning group to four blocks (44 cycles) of training on B. Figure 6*a* indicates that this manipulation was successful in matching the amount of overlearning of the 5 min and 1 h groups (mean ± SEM = 24.1 ± 2.4; $F_{(2,52)} = 0.326$, $p = 0.72$).

Note that, although the overlearning group spent less time training at the asymptote than the control group (Fig. 6*a*,

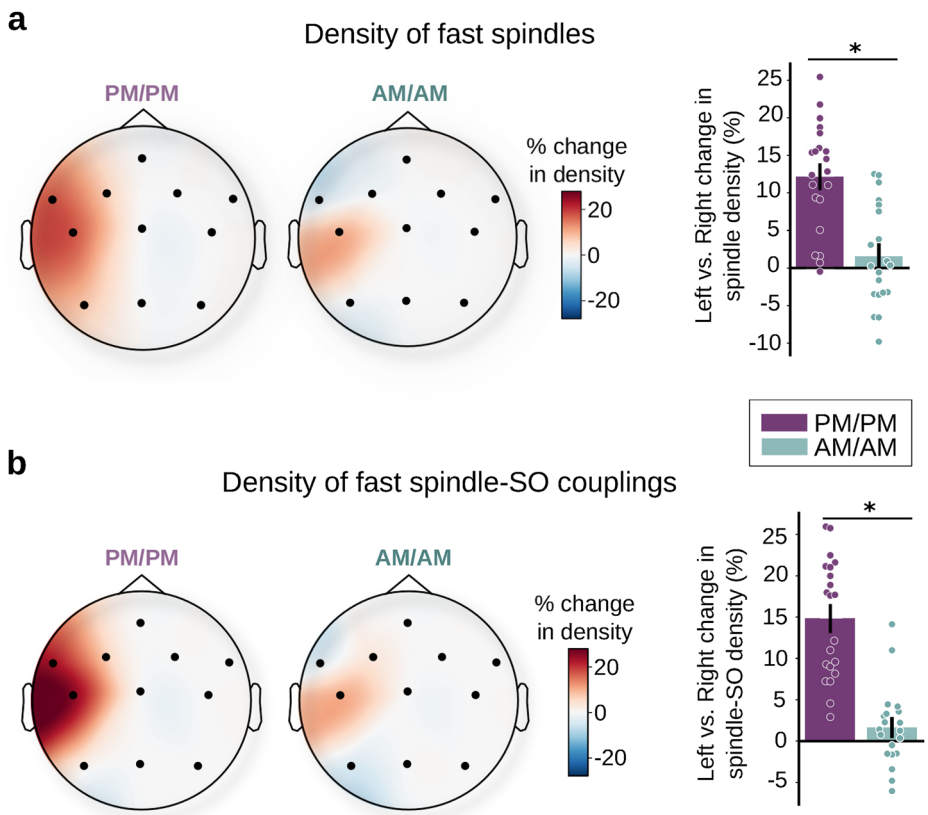


Figure 5. Sleep benefits SMA through an active mechanism. Shown are the topographic plots depicting the spatial distribution of the interhemispheric percent change of the density of fast spindles (***a***) and the fast spindle–SO couplings (***b***) during NREM of the first cycle of sleep for the PM/PM and the AM/AM groups. The interhemispheric change in these metrics was computed according to the function (left hemisphere − right hemisphere) / right hemisphere ∗ 100, applied across corresponding EEG electrodes. Barplots on the right depict the statistical quantification of these metrics across groups obtained based on LMMs. Superimposed on the bar plots is the estimated grand average for each subject (illustrated as dots). *$p < 0.05$ indicates the result of the *F* test across groups.

Table 2. Sleep architecture for AM/AM and PM/PM groups from Experiment 3

	AM/AM		PM/PM		*t* test	
Measure	Mean	SEM	Mean	SEM	*T*	*p*
Total Sleep Time (min)	433.07	7.01	434.59	4.44	0.10	0.92
Sleep Efficiency (%)	90.32	0.78	90.93	0.76	0.31	0.76
Sleep latency (min)	18.12	1.04	26.02	3.01	1.39	0.17
REM latency (min)	117.52	5.39	99.54	4.48	−1.41	0.17
Total Wake Time (min)	47.74	4.04	43.23	3.59	−0.46	0.65
Wake After Sleep Onset (min)	20.71	2.89	15.59	1.96	−0.80	0.43
NREM1 (min)	50.02	2.98	36.64	1.54	−1.76	0.09
NREM2 (min)	152.19	4.51	160.88	5.29	0.69	0.49
NREM3 (min)	117.95	3.89	127.23	3.71	0.95	0.35
REM (min)	112.90	4.69	109.83	3.47	−0.29	0.77

Shown are the mean and SEM corresponding to the sleep measures listed in the first column corresponding to the AM/AM and PM/PM groups from Experiment 3. The last columns depict the statistics and *p*-values yielded from comparing the two groups with *t* tests. All measures are depicted in minutes except for sleep efficiency, defined as the percentage of total sleep time relative to the time interval between lights off and lights on (%). As observed, no differences were observed in sleep architecture across groups.

$F_{(3,71)} = 5.78$, $p = 0.001$; followed by Dunnett's test, 5 min vs control, $p = 0.02$; 1 h vs control, $p = 0.006$; overlearning group vs control, $p < 0.001$), both groups attained a similar level of memory retention (Fig. 6*b*; $F_{(3,71)} = 20.04$, $p < 0.001$; followed by Dunnett's test, 5 min vs control, $p < 0.001$; 1 h vs control, $p < 0.001$; overlearning vs control, $p = 0.44$). Collectively, these results confirm that the temporal pattern of SMA memory consolidation unveiled in Experiment 2 is not confounded by the amount of time training at the asymptote.

Discussion

While there is compelling evidence that sleep improves different types of memories, its role in motor memory consolidation remains a topic of contention. Current work suggests that motor skill memory requires sleep to consolidate while sensorimotor adaptation is consolidated with the passage of time, irrespective of sleep. This evidence has led to the proposal that the latter may be an exception to other types of memories (Brodt et al., 2023). In the present study, we addressed this ongoing debate through a series of three meticulously designed experiments. In line with previous work, we show that SMA memory consolidates with the passage of time when training is distributed throughout the daytime. However, when the time interval between learning and bedtime is manipulated to ensure that sleep takes place while the memory trace is still in a fragile state, a significant memory enhancement becomes apparent. This marked improvement in long-term memory was accompanied by specific modulation of neural markers of sleep consolidation, including an increase in spindle density and spindle–SO coupling during NREM, thereby providing support for an active role of sleep behind the behavioral benefit.

Our work contributes to reconciling conflicting viewpoints regarding the mechanisms involved in the consolidation of motor memories, namely, MSL versus SMA. It is important to note that while numerous studies on SMA have provided supporting evidence for the hypothesis that both visuomotor and force-field adaptation memories consolidate over time (Donchin et al., 2002; Doyon et al., 2009; Debas et al., 2010;

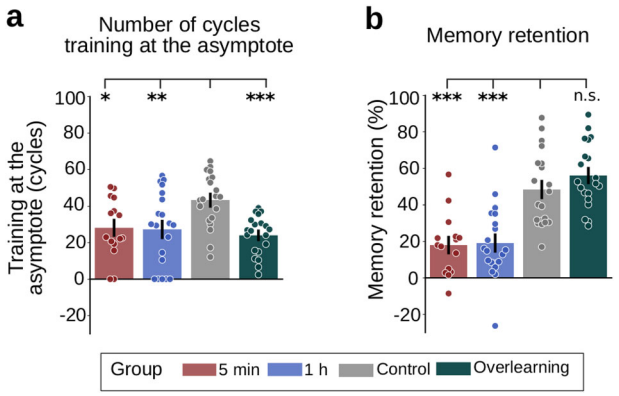


Figure 6. The time course of SMA memory retention is not explained by the time spent training at the asymptote. Shown are the mean ± SEM of the number of cycles training at the asymptote (***a***) and the level of memory retention (***b***) corresponding to the 5 min, 1 h, and control groups from Experiment 2 and to the overlearning group. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$; n.s., nonsignificance, indicates the result of the Dunnett's test for each group compared against the control.

Thürer et al., 2018), other research conducted by Tononi and colleagues has pointed to a distinct advantage of sleep in the context of visuomotor adaptation (Huber et al., 2004; Landsness et al., 2009). These apparent disparities can be resignified in light of our current results. While in the former set of studies, participants were trained sparsely throughout the daytime, in Tononi's work volunteers learned the motor task immediately before bedtime. Notably, in none of these studies, the temporal gap between learning and sleep was deliberately considered. By systematically manipulating this gap here, we demonstrate a net benefit of sleep on motor memory of approximately 30%. Our findings help settle the above controversy and suggest that, like motor skill learning and declarative learning, sensorimotor adaptation undergoes sleep consolidation.

Is the sleep-related memory benefit we observe herein the outcome of a passive or an active mechanism? There are currently two main hypotheses supporting an active role of NREM sleep in memory consolidation. According to the systems consolidation hypothesis, newly encoded memories, initially stored in hippocampal networks, are reactivated during slow-wave sleep and gradually integrated with existing memory traces at the level of the neocortex. This process is thought to depend on the close synchrony between slow oscillations, sleep spindles, and hippocampal ripples (Rasch and Born, 2007; Diekelmann and Born, 2010; Buzsáki, 2015; Maingret et al., 2016; Ladenbauer et al., 2017; Latchoumane et al., 2017; Helfrich et al., 2018; Muehlroth et al., 2019; Navarro-Lobato and Genzel, 2019). Another—not mutually exclusive—account of memory consolidation is the synaptic homeostasis hypothesis (SHY), according to which synaptic weights potentiated during learning are downscaled by sleep, improving their signal-to-noise ratio (Tononi and Cirelli, 2003, 2006). In line with the systems consolidation hypothesis, here we show that training specifically increased the spindle–SO coupling over the contralateral hemisphere, solely when it occurs immediately before bedtime, supporting an active role of sleep in SMA memory consolidation. Nevertheless, it remains plausible that sleep actively promotes consolidation while also providing passive protection from interference. Although our study was not aimed at testing this possibility, it is a topic of relevance worth future investigation. Note that our experimental design precluded us from directly examining whether our findings align with SHY (but refer to Solano et al., 2022a, for prior evidence from our laboratory supporting both theoretical accounts).

Our findings from Experiment 2 build upon our earlier work, showing that anterograde interference impairs the ability to learn within a 6-hour window (Lerner et al., 2020). Here we show further that anterograde interference also hinders long-term memory retention following a similar time course, suggesting that the same biological substrates may support both learning and memory stabilization (Della-Maggiore et al., 2015), a hypothesis in line with the modern concept of an engram (Josselyn and Tonegawa, 2020). Interestingly, SMA memory decay unveiled by Experiment 1, followed a similar temporal evolution to memory stabilization, leveling off ~6 h post-learning, a finding that is in line with work from force-field adaptation (Criscimagna-Hemminger and Shadmehr, 2008). This temporal alignment opens the possibility that the amount of forgetting may depend on the stability of the motor memory trace (Frankland et al., 2013; Davis and Zhong, 2017) so that more stable memories are less likely to undergo forgetting. Further studies in which these behavioral metrics could be tracked in the same participants would be needed to explore this interplay.

Why might the temporal proximity between learning and sleep play a crucial role in the overnight consolidation of SMA memory? While many studies from the declarative and nondeclarative memory fields have reported the beneficial effects of aligning learning with sleep (Gais et al., 2006; Talamini et al., 2008; Doyon et al., 2009; Van Der Werf et al., 2009; Holz et al., 2012; Payne et al., 2012; Inostroza et al., 2013; Sawangjit et al., 2018, 2020; Truong et al., 2023), the precise mechanism/s underlying this phenomenon remain/s elusive. Emerging evidence suggests that the coupling between sleep spindles and slow oscillations (SOs) observed during NREM sleep may promote the occurrence of hippocampal sharp-wave ripples (SWRs), a high-frequency oscillation (~90 Hz) directly implicated in memory reactivation (Ngo et al., 2020; Brodt et al., 2023; Staresina et al., 2023). Notably, this triad (SO–spindle–SWR) has been observed in rodents during the early phases of motor skill learning (Kim et al., 2023). Converging evidence from our lab underscores the involvement of the human hippocampus during the initial phase of MSL and SMA up to 30 min post-training (Jacobacci et al., 2020; Deleglise et al., 2022; Della-Maggiore et al., 2023). One possibility is that, like declarative learning, the hippocampus enables sleep-dependent motor memory consolidation. However, this process may be initiated only when sleep closely follows learning, ensuring the hippocampus remains actively engaged. Alternatively—but not exclusively—the neurochemical and/or neuromodulatory milieu of sleep may favor the activation of mechanisms associated with memory consolidation (Diekelmann and Born, 2010; Rasch and Born, 2013), such as synaptic homeostasis (Tononi and Cirelli, 2003, 2006, 2014) or de novo protein synthesis and gene expression, key for synaptic plasticity (Ramm and Smith, 1990; Nakanishi et al., 1997; Ribeiro et al., 1999; Mackiewicz et al., 2007; Seibt et al., 2012). Rigorous biological interventions would be essential to empirically test these hypotheses that at this stage remain speculative.

In conclusion, our findings indicate that consolidation of SMA depends both on the passage of time and sleep. Specifically, we showed that when training is distributed throughout the daytime and the temporal proximity between learning and sleep is not guaranteed, consolidation proceeds independently of sleep. Conversely, when sleep is strategically scheduled to overlap with the memory stabilization window while the memory trace is still in a fragile state, SMA memory is enhanced along with a distinct modulation

of the neural markers of sleep consolidation. Our work advances research at the basic and translational levels. At the basic level, it contributes to resolving a long-standing debate concerning the role of sleep in SMA memory consolidation. Furthermore, it opens the possibility of common mechanisms supporting consolidation across different memory domains. Finally, at the translational level, it may impact rehabilitation programs, potentially expediting motor injury recovery by aligning training sessions with the sleep cycle or incorporating strategic nap interventions.

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