Sleep preferentially enhances memory for a cognitive strategy but not the implicit motor skills used to acquire it

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ABSTRACT

Sleep is known to be beneficial to the strengthening of two distinct forms of procedural memory: memory for novel, cognitively simple series of motor movements, and memory for novel, cognitively complex strategies required to solve problems. However, these two types of memory are intertwined, since learning a new cognitive procedural strategy occurs through practice, and thereby also requires the execution of a series of simple motor movements. As a result, it is unclear whether the benefit of sleep results from the enhancement of the cognitive strategy, or the motor skills required to execute the solution. To disentangle the role of sleep in these aspects of procedural memory, we employed two tasks: (**1**) the Tower of Hanoi (**ToH**), and, (**2**) a modified version of the ToH, akin to an implicit Motor Sequence Learning (**MSL**) task. The MSL task involved the identical series of motor movements as the ToH, but without access to the information necessary to execute the task according to the underlying cognitive procedural strategy. Participants (n = 28) were trained on the 3-disk ToH, then retested on 5-disk versions of both ToH and MSL tasks. Half (n = 15) were trained and immediately tested at 8 PM and retested at 8 AM after a night of sleep. They were retested again at 8 PM after a day of wake (**PM-AM-PM** condition). The other half (n = 13) were trained and immediately tested at 8 AM, retested at 8 PM after a day of wake, and retested again at 8 AM after a night of sleep (**AM-PM-AM** condition). ToH performance only improved following a period of sleep. There was no benefit of sleep to implicit MSL. Our results show that sleep, but not wake, allowed individuals to extrapolate what was learned on a simpler 3-disk version of the task to the larger 5-disk problem, which included new elements to which they had not yet been exposed. Here, we isolate the specific role sleep plays for cognitive procedural memory: sleep benefits the cognitive strategy, rather than strengthening implicitly acquired motor sequences required to learn and execute the underlying strategy itself.

1. Introduction

Is sleep the mother of invention? New discoveries rely on the realization of the solution to a problem. One form of human memory requires novel cognitive strategies to be acquired in order to solve the problem at hand. The information must be stored and integrated into existing knowledge to be of future use. Sleep is thought to be an optimal time for these processes to unfold unfettered by waking life.

When novel cognitive strategies and their related motor skills are acquired, they are initially in a labile state, and undergo a process of consolidation; ultimately being transformed into a strengthened, integrated, and more easily retrieved form. This transformation is called "*memory consolidation*" and occurs preferentially during sleep, and is thought to occur from memory trace reactivation and replay (Lewis, Knoblich, & Poe, 2018). The relationship between procedural memory consolidation and sleep is well-established (Albouy et al., 2015; Barakat et al., 2013; Doyon et al., 2009; Fischer, Hallschmid, Elsner, & Born, 2002; Fogel et al., 2014; Fogel, Ray, Binnie, & Owen, 2015; Fogel et al., 2017; King, Fogel, Albouy, & Doyon, 2013; Kuriyama, Stickgold, & Walker, 2004; Laventure et al., 2016; Peters, Smith, & Smith, 2007; Plihal & Born, 1997; Rasch & Born, 2013; Schönauer, Geisler, & Gais, 2013; Sio, Monaghan, & Ormerod, 2013; Smith, 2001; Smith & MacNeill, 1994; Stickgold, 2005; Vahdat, Fogel, Benali, & Doyon, 2017; Vien et al., 2016; Walker, Brakefield, Morgan, Hobson, & Stickgold,

2002). However, it is not well-understood what specific aspects of this multifaceted relationship that are sleep-dependent *per se*. One issue contributing to this complexity is the heterogeneous nature of procedural memory. For example, procedural memory can be subdivided into several distinct subtypes, including motor sequence learning (**MSL**), and also, procedural skills that are cognitively complex. The latter involves the acquisition of novel cognitive strategies which are required in order to improve performance. It is unclear whether sleep contributes to the consolidation of these newly acquired cognitive strategies, or whether it provides a boost to performance via enhancement of motor skills required to execute the task.

There is a substantial body of evidence suggesting that sleep consolidates explicitly learned *motor skills*. A classic example of one of the tasks used to investigate cognitively simple and explicit motor sequence learning is the "Sequential Finger Tapping Task", adapted from Karni et al. (1995). The sequence of movements is normally uncued (*i.e.*, unguided), explicitly known to the participant prior to performing the task, and is typically short, comprised of only about 5 elements (*e.g.*, 4-1-3-2-4), and does not require the acquisition of a novel cognitive strategy to perform the sequence. Evidence from several sources has shown that sleep is beneficial to the offline consolidation of motor sequence memory: (**1**) sleep deprivation impairs performance on this task, as compared to a normal night of sleep (Smith & MacNeill, 1994), (**2**) an interval filled with sleep *vs.* an equivalent period of wake enhances simple motor sequence consolidation (Maier et al., 2017; Nettersheim, Hallschmid, Born, & Diekelmann, 2015; Walker et al., 2002; Walker, Stickgold, Alsop, Gaab, & Schlaug, 2005; Witt, Margraf, Bieber, Born, & Deuschl, 2010), (**3**) Stage 2 sleep and sleep spindles are increased following MSL (Barakat et al., 2011; Boutin et al., 2018; Fogel & Smith, 2006; Fogel, Smith, & Cote, 2007; Holz et al., 2012; Morin et al., 2008; Nishida & Walker, 2007; Peters et al., 2007), (**4**) targeted memory reactivation during sleep enhances consolidation (Antony, Gobel, O'Hare, Reber, & Paller, 2012; Cousins, El-Deredy, Parkes, Hennies, & Lewis, 2016; Diekelmann, Born, & Rasch, 2016; Laventure et al., 2016; Schönauer et al., 2013), and most recently, (**5**) the memory trace is strengthened and transformed during sleep (Vahdat et al., 2017), through the process of reactivation, associated with spindle events (Boutin et al., 2018; Fogel et al., 2017).

Despite this wealth of evidence for explicitly learned motor sequences, inconsistent findings have led to controversy over whether sleep-dependent memory consolidation occurs for procedural MSL that is acquired without conscious knowledge (*i.e.*, "implicit" learning). A classic example of one of the cognitively simple procedural tasks used to investigate implicit MSL is the "Serial Reaction Time Task". The locations of finger movements in this task are normally cued (*i.e.*, guided), and unbeknownst to the participant, there is an underlying sequence governing the order of the cues, which is typically long in duration (*e.g.*, 20-elements or more) in order to avoid acquiring explicit knowledge of the sequence. Unlike its explicit counterpart, there is mounting evidence that sleep *does not* appear to enhance implicit procedural memory consolidation (Conte & Ficca, 2013; Hallgató, Gyori-Dani, Pekár, Janacsek, & Nemeth, 2013; Keisler, Ashe, & Willingham, 2007; Meier & Cock, 2014; Nemeth et al., 2010; Pan & Rickard, 2015; Song, Howard, & Howard, 2007; Viczko, Sergeeva, Ray, Owen, & Fogel, 2018).

In addition, there is a long history of evidence suggesting that sleep affords optimal consolidation for other forms of procedural memory. In particular, for tasks that require the acquisition of a novel cognitive strategy, and may involve problem solving and rule-based learning (Fogel et al., 2007, 2015; Mandai, Guerrien, Sockeel, Dujardin, & Leconte, 1989; Nielsen et al., 2015; Plihal & Born, 1997; Smith & Smith, 2003; Smith & Weeden, 1990; Smith & Wong, 1991; Smith, 1995, 1996, 2001). For example, reduced rapid eye movement (**REM**) sleep impairs procedural memory consolidation for cognitive procedural strategies, but not procedural memory for cognitively simple motor skills and MSL (Conway & Smith, 1994; Karni, Tanne, Rubenstein, Askenasy, & Sagi,

1994; Sandys-Wunsch & Smith, 1991; Smith & MacNeill, 1994; Smith, 1993). In addition, sleep can provide insight into an underlying rule, either unconsciously (Lewicki, Czyzewska, & Hoffman, 1987), or lead to conscious knowledge and insight into a novel cognitive strategy (Wagner, Gais, Haider, Verleger, & Born, 2004). Sleep has also been shown to enhance statistical learning (Durrant, Taylor, Cairney, & Lewis, 2011), and induce creative problem solving (Lewis et al., 2018). Thus, sleep not only stabilizes procedural memory which requires the acquisition of a new cognitive strategy, but also actively reprocesses the newly acquired and intertwined skills and strategies required to perform these procedures. Sleep affords an even greater benefit as the complexity of a motor skill task increases (Kuriyama et al., 2004), and preferentially aids arriving at the solution to harder problems as compared to easier problems after an interval of sleep *vs.* wake (Sio et al., 2013). This further suggests that sleep preferentially favours the consolidation of cognitively complex strategies.

One classic example of a task used to investigate the role of sleep for procedural memory that requires the acquisition of novel cognitive strategies, is the Tower of Hanoi (**ToH;** Édouard Lucas first marketed the task in 1883 as "Dots and Boxes"). Improved performance on the ToH has been attributed to a consolidation interval containing sleep *vs.* wake (Brand, Opwis, Hatzinger, & Holsboer-Trachsler, 2010; Fogel et al., 2015; Nielsen et al., 2015; Smith, Nixon, & Nader, 2004). The ToH consists of three vertical pegs, equally spaced apart, and comprises a variable number of disks (typically three or five) of ascending size that can be moved from one peg to another. The task begins with all disks located in a stack, in increasing size from top to bottom, on the furthest left-most peg. The objective of the task is to move the stack of disks to the furthest right-most peg, obeying the following rules: (**1**) only one disk can be moved at a time, (**2**) each move can consist of taking the upper-most disk from one of the stacks and placing it on another peg, and, (**3**) only a smaller disk can be placed on top of a larger disk. These rules constrain the possible moves such that the ToH requires the acquisition of a new strategy needed to improve performance and complete the task according to the optimal strategy.

In the present study, we adapted the ToH in order to assess MSL performance that involves the same series of movements as the ToH, but without access to the information necessary to execute the underlying cognitive strategy. In this way, we could separate and compare the acquisition and sleep-dependent consolidation of a novel cognitive strategy to the performance of the execution of the exact same series of movements. Two computerized versions of the ToH task were employed: (**1**) a version of the "classic" ToH in which participants executed movements to solve the task by learning the underlying cognitive strategy, and, (**2**) a modified version of the task in which the guided motor movements were identical to those used in the classic ToH, but where the information necessary to use the underlying cognitive strategy to guide behaviour was not available, thereby making it similar to a classic implicit MSL task. This approach allowed for a differential comparison of the impact of sleep *vs.* an equivalent period of wake on the distinct cognitive and motor procedural components of the ToH.

It was hypothesized that following sleep: (**1**) performance on the ToH task will benefit from sleep *vs.* wake, and, (**2**) performance on the MSL task (*i.e.,* the adapted version of the ToH) will show no benefit of sleep *vs.* an equivalent period of wake

2. Materials and methods

2.1. Participants

Twenty-eight healthy young adults (16 female; mean age = 20.96 ± 2.66 years; age range: 19–29 years) participated in this study. All potential participants underwent an initial screening interview and were excluded if they reported that they were left-handed, considered themselves poor sleepers, had irregular sleep schedules (regular bedtime before 10 p.m. or wake time after 9 a.m.), had a body

mass index > 30, did not subjectively consider themselves to be in good health, or were diagnosed with a sleep disorder, were shift workers, took medications known to interfere with sleep, had a history of depression, anxiety, chronic pain, seizures, head injury or had mobility problems with their hands or fingers. Participants had to report normal, or corrected-to-normal vision. To be included, interested participants had to score < 10 on the Beck Depression (Beck & Beamesderfer, 1974) and the Beck Anxiety (Beck, Epstein, Brown, & Steer, 1988) inventories, have no signs of sleep disorders indicated by the Sleep Disorders Questionnaire, based on scores of < 32 (for females) or < 36 (for males) for the sleep apnea sub-scale, < 21 (for males and females) for the periodic leg movement sub-scale, or scored < 21 (for females) or < 19 (for males) for the psychiatric sleep disorder sub-scales (Douglass et al., 1994). Participants were not allowed to participate if they had previous experience with the ToH task, or any task that resembles it. Participants were asked to wear an 'Actiwatch' (Philips Respironics Inc., Andover, MA, U.S.A.), a wrist-worn accelerometer which measures sleep-wake-related limb movements, and to complete a log of their daily activities and sleep habits, to verify that they maintained a regular sleep schedule for the length of their participation in the study. Participants were excluded from further participation in the study if the results of their Actiwatch or sleep diary identified variability in their sleep schedule outside of the aforementioned criteria, or non-compliance with the study protocol. There were no significant differences between experimental conditions in demographic and subjective measures of sleep, or objective measured derived from actimetry. See Supplemental Table 1 for a summary of the sample demographics, including mean scores on the Stanford Sleepiness Scale, used to assess subjective sleepiness (Hoddes, Zarcone, & Dement, 1972; administered at Screening, and before Training, Retest 1 and Retest 2).

2.2. Ethics statement

All participants provided informed written consent prior to participation and were financially compensated $40 for their participation. This research was approved by the Western University Health Science Research Ethics Board (London, Ontario, Canada).

2.3. Behavioural testing

Two variants of the ToH task (Fig. 1) were used to test cognitive procedural and simple procedural learning. Both versions of the task were computerized and coded in Matlab 2014a (Mathworks Inc, Natick, MA, USA) using The Psychophysics Toolbox extension (Brainard, 1997; Kleiner, Brainard, & Pelli, 2007; Pelli, 1997).

2.3.1. Classic ToH task

In the classic version of the ToH task, participants were instructed to move the stack of disks, to the furthest right-most peg. The disks could be moved from one peg location to another by pressing the corresponding keypad buttons for each source and goal location for each move, while obeying the following rules: (**1**) they could only move one disk at a time, (**2**) each move could consist of taking an upper-most disk from one of the stacks and placing it on another peg, and, (**3**) only a smaller disk could be placed on top of a larger disk. These rules thus require the task to be solved according to a prescribed strategy. The optimal number of moves to complete the Tower of Hanoi is determined algebraically by $2^N - 1$, where N is the number of disks.

In the present study, two variants of the ToH task were used: (**1**) an uncued 3-disk version used only during the Training session, and, (**2**) a cued 5-disk version, where participants are guided on which move to make, used at the Immediate Test session, at Retest 1 and Retest 2 (see below for details of the experimental protocol). The uncued version of the ToH has been used in previous studies (Brand et al., 2010; Fogel et al., 2015; Nielsen et al., 2015; Smith et al., 2004), and has been shown to improve following sleep compared to wake. Immediate Test and Retest sessions were cued in order to be able to compare ToH performance to cued MSL performance. Importantly, whether cued or uncued, the strategy required to solve the ToH remains the same.

2.3.2. MSL task

An adapted version of the ToH task was used to assess motor skill learning (**MSL**). The MSL task was identical to the ToH with the exception that the disks were not visible. Unbeknownst to the participant, the exact same series of movements used to solve the classic ToH task were executed in the MSL task. Given that the disks were not visible, the information necessary for the participants to apply the underlying strategy was not available to them. One variant of the MSL task was used; a cued 5-disk version used at Retest 1 and Retest 2, administered in counterbalanced order with the cued 5-disk version of the ToH (see below for details of the experimental protocol).

2.3.3. Experimental protocol

To investigate the relative contribution of a retention interval filled with either sleep or wake to the consolidation of a newly acquired cognitive procedural *vs.* motor procedural memory, two experimental conditions were used. Using an established protocol to test for the effect of sleep *vs.* wake on memory consolidation (Fig. 1), participants were assigned to either the "sleep-first group" (**PM-AM-PM**) that were trained in the evening and retested in the morning, or the "wake-first group" (**AM-PM-AM**) that were trained in the morning and retested in the evening.

All participants were trained for 20 trials on the classic 3-disk uncued version of the ToH task. Immediately following training, participants were tested on 2 trials of the cued version of the ToH. This Immediate Testing session was used in order to: (**1**) ensure that all participants had learned the series of movements needed to solve the task during the Training session, and, (**2**) test their performance when the moves were cued, so that it would be comparable to the subsequent cued Retest sessions (Retest 1 and Retest 2). Twelve hours after the
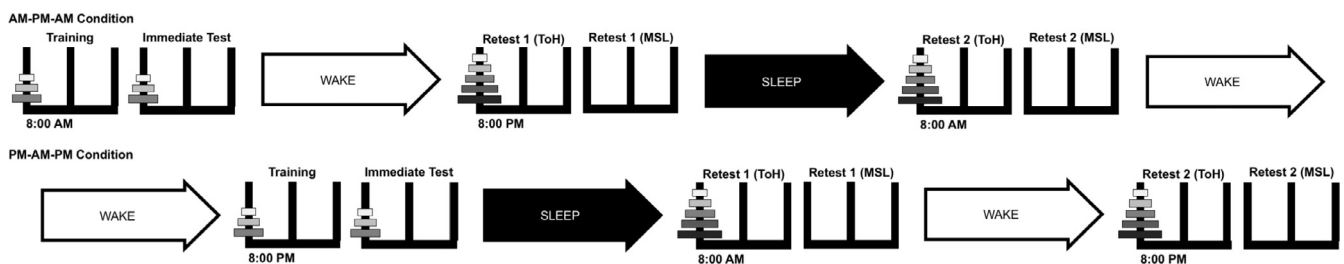

Fig. 1. Study Design. At the Training session, participants were trained for 20 trials on the uncued, 3-disk ToH task. Immediately after, at the Immediate Test session, they performed the cued 3-disk ToH task. Both Retest 1 and Retest 2 consisted of both 5-disk cued ToH and cued MSL tasks (in counterbalanced order across participants). The AM-PM-AM condition was trained and tested at 8 AM, retested at 8 PM after a day of wake, and retested again at 8 AM after a night of sleep. The PM-AM-PM condition underwent the same procedure with the exception that they were initially trained and tested at 8 PM, retested at 8 AM after a retention period of sleep, and retested again at 8 PM after a retention period of wake.

Immediate Test session, all participants were retested twice with a 12-hour interval in between retest sessions. Each retest session comprised 2 trials of a cued version of the ToH (disks visible), and 2 trials of a cued version of the MSL task (disks not visible). All retest sessions employed 5-disk versions of the tasks. The 5-disk version of the task can be solved, in part, by non-consecutively performing the pattern of movements needed to solve the simpler 3-disk ToH, three times.

In all cases, participants were instructed to complete the tasks as quickly and as accurately as possible. Participants were shown that the three buttons on the response pad corresponded to the three pegs displayed onscreen. They were instructed to always use their index, middle and ring finger to operate the same 3 buttons. Participants were then explained the rules of the task (see above). Participants were informed that they would complete 20 trials at training, followed by a brief 2-trial Immediate Test, where the moves would be cued. No additional instructions or feedback was given. Prior to the Retest sessions, participants were informed that they would be asked to perform two trials each of two different cued versions of the task. One where the disks were visible, and another version with no disks. They were also informed that the two sets of trials would occur in a randomized order. No additional instructions or feedback was given.

For the Sleep-first group (PM-AM-PM), on Day 1 at 8 PM, the participants (n = 15) were trained on the classic, uncued 3-disk version of the ToH for 20 trials. Immediately following training, participants were tested on the same task, though now cued, for two trials each. Participants were then allowed to sleep overnight (~11 PM–7 AM) in their own homes. All participants were instructed to abstain from alcohol throughout the study, and adhere to their regular sleep schedule, confirmed via sleep diary and Actigraphy. See Supplemental Table 1 for Actigraphy results. On Day 2, they were retested at 8 AM on 2 trials each of the 5-disk ToH and MSL tasks, in a randomized order. After an additional 12-h interval of wake, participants returned to the laboratory to be re-tested again at 8 PM on 2 trials of the 5-disk ToH and MSL tasks, again, in a randomized order (Fig. 1).

The procedure for the Wake-first group (AM-PM-AM) was identical, with the only difference being that participants (n = 13) were trained and tested at 8 AM, retested after 12-h of wake at 8 PM, then slept for the remainder of the night from 11 PM to 7 AM, and were finally retested again on Day 2 at 8 AM (Fig. 1).

2.4. Statistical analyses

The main variable of interest for each session was the time per move (*i.e.,* the total time divided by the total number of moves taken to complete the task). Accuracy was not of interest, given that each move included in the analyses at the Immediate Test and both Retest sessions for both ToH and MSL tasks, were cued (Supplemental Table 2).

First, independent samples t-tests were performed to ensure that initial training at different times of the day (*i.e.,* AM-trained *vs.* PM-trained) did not influence performance, and that the different sleep/wake groups did not differ at the outset. We also tested for differences in subjective sleepiness between conditions prior to the Immediate Test, Retest 1 and Retest 2.

In order to assess whether sleep preferentially enhanced consolidation of either ToH or MSL performance after a period of sleep *vs.* wake, a 2 (session) × 2 (sleep/wake condition) × 2 (ToH, MSL) ANCOVA was employed, controlling for initial performance at the Immediate Test session (entered as a covariate). This was followed-up by ANCOVAs to follow up how sleep/wake condition impacted performance across the sessions, for ToH and MSL performance. Specifically, two 2 (session) × 2 (sleep/wake condition) repeated measures ANCOVAs were used to follow-up the effects of session (Retest 1, Retest 2) and sleep/wake condition (AM-PM-AM *vs.* PM-AM-PM), controlling for initial performance at the Immediate Test session (entered as a covariate).

3. Results

3.1. Time-of-Day effects

Supplementary analyses were performed to determine whether training at different times of the day (*i.e.*, AM-trained *vs.* PM-trained) influenced ToH performance. An independent samples *t*-test on the Immediate Test session (at the end of the Training session) indicated that there was no difference between PM-trained (M = 1.35, SD = 0.87) and AM-trained (M = 1.27, SD = 0.49) groups (*t* (26) = 0.27, *p* = 0.79). In addition, there were no differences between sleep/wake condition (AM-PM-AM *vs.* PM-AM-PM) in terms of subjective sleepiness (Supplemental Table 1) as assessed by the Stanford Sleepiness Scale at Training (*t*(25) = 1.86, *p* = 0.08), Retest 1 (*t* (25) = 0.13, *p* = 0.90), or Retest 2 (*t*(25) = 1.17, *p* = 0.10), nor was there any significant correlations between subjective sleepiness scores and ToH or MSL performance at the Immediate Test, Retest 1 or Retest 2 (all *p* ≥ 0.12). Thus, as expected, time of training would not be expected to explain differences in performance.

3.2. Sleep/wake effects

A 2 (session) × 2 (sleep/wake condition) × 2 (task) ANCOVA tested for the interaction effect of session (Retest 1, Retest 2), sleep/wake condition (AM-PM-AM *vs.* PM-AM-PM) and task (ToH, MSL), controlling for initial performance at the Immediate Test session. As predicted, this analysis revealed a significant 3-way session by sleep/wake condition by task interaction ($F(1, 25) = 4.10$, $p = 0.05$, $\eta p^2 = 0.14$). This interaction was followed up by additional ANCOVAs for both the ToH task (Section 3.2.1 below) and the MSL task (Section 3.2.2 below), to formally characterize this interaction.

3.2.1. ToH retest

A 2 (session) × 2 (sleep/wake condition) within-participants ANCOVA tested the effect of session (Retest 1, Retest 2) and sleep/wake condition (AM-PM-AM *vs.* PM-AM-PM) on ToH task performance, controlling for initial performance at the Immediate Test session. As expected, there was no significant main effect of session (F $(1,25) = 0.22$, $p = 0.64$), or sleep/wake condition ($F(1,25) = 3.33$, $p = 0.08$), although there was a tendency towards statistical significance. Importantly, a significant session by condition interaction (F $(1,25) = 4.25$, $p = 0.05$, $\eta p^2 = 0.15$) was observed, whereby task performance on the ToH changed from Retest 1 to Retest 2 differently as a function of sleep/wake condition. This was followed up by testing for the difference between PM-AM-PM and AM-PM-AM condition at Retest 1 ($t(26) = 4.68$, $p < 0.0001$) and Retest 2 ($t(28) = 0.68$, $p = 51$), after controlling for initial performance at Immediate Test. These analyses revealed that an improvement in ToH overall performance was observed once the AM-PM-AM condition experienced a period of sleep from Retest 1 to Retest 2 as compared to the PM-AM-PM condition, where performance had already improved at Retest 1, and remained so at Retest 2. These results support our hypothesis that sleep, and only sleep, permitted enhanced consolidation on the ToH task, regardless of the initial training time (Fig. 2**A**).

3.2.2. MSL retest

To examine the impact of sleep *vs.* wake on MSL, a similar 2 (session) × 2 (sleep/wake condition) within-participants ANCOVA compared the effect of session (Retest 1, Retest 2) and sleep/wake condition (AM-PM-AM *vs.* PM-AM-PM) on MSL task performance, controlling for initial performance at the Immediate Test session. In contrast to the ToH, this analysis did not reveal a significant session by sleep/wake condition interaction ($F(1, 25) = 0.00$, $p = 0.96$) (Fig. 2**B**). There was no main effect of session ($F(1, 25) = 3.61$, $p = 0.07$), or sleep/wake condition ($F(1, 25) = 0.36$, $p = 0.55$). In line with our hypothesis, these results suggest that MSL performance was unchanged from Retest 1 to
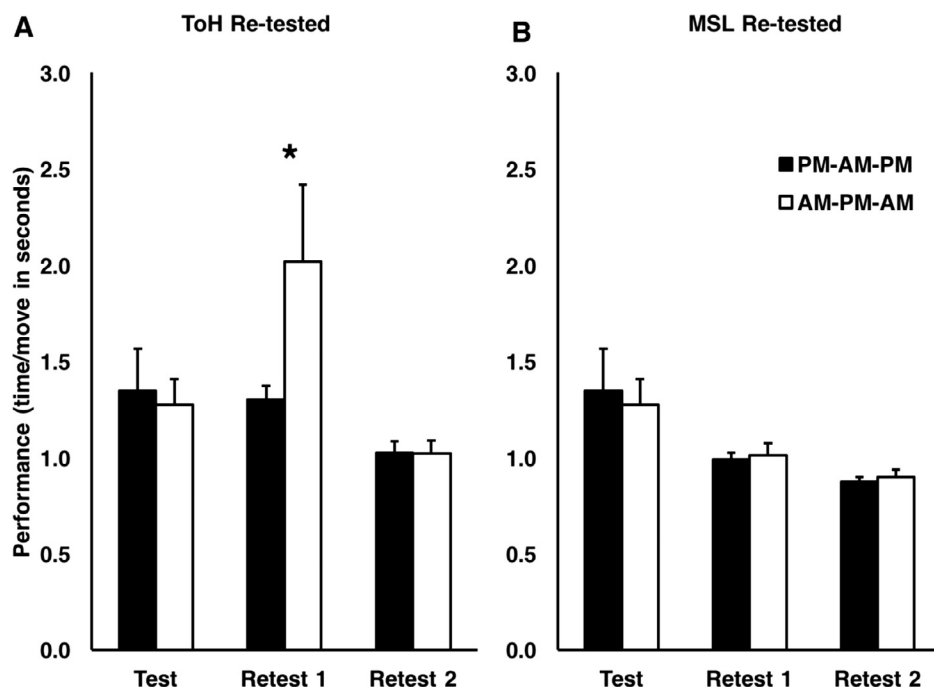
A **ToH Re-tested**

B **MSL Re-tested**

■ PM-AM-PM
□ AM-PM-AM

Fig. 2. The average time per move for the ToH trained condition at Immediate Test, Retest 1 and Retest 2. (**A**) **ToH-retested condition**: As would be expected, performance in the AM-PM-AM condition worsened from Immediate Test to Retest 1 following a period of wake, but then, remarkably, improved significantly from Retest 1 to Retest 2 following an equivalent period of sleep. By contrast, performance in the PM-AM-PM condition showed savings from Immediate Test to Retest 1 following a period of sleep. (**B**) **MSL-retested condition**: Despite executing the exact same series of movements, unlike the ToH, there was no sleep-wake condition by session interaction effect when trained on the ToH and retested on the MSL. * indicates significant difference between AM-PM-AM *vs.* PM-AM-PM condition at Retest 1, controlling for initial performance at Immediate Test at $p < 0.0001$.

Retest 2, and was not preferentially enhanced by sleep or wake.

4. Discussion

Procedural memory encompasses a wide variety of skills and knowledge. One form that procedural knowledge can take involves the acquisition of a new cognitive strategy or rule that is required in order to improve task performance. However, these cognitive strategies normally involve the execution of a sequence of motor movements in order to learn the new underlying strategy, *i.e.,* motor performance akin to motor sequence learning. The multifaceted nature of this type of motor skill precludes any clear conclusions that sleep-related performance enhancement is solely attributable to the acquisition of the new cognitive strategy, *per se*. As a result, the possibility remains that sleep is actually in part, or entirely, enhancing aspects other than the underlying cognitive strategy, and may in fact not be involved in the realization of novel ways of doing things and solving problems. Thus, it has remained unclear what contribution sleep makes to these two, intertwined, aspects of procedural memory that involve problem solving. The current study utilized a method which allowed us to disentangle the cognitive aspects from the motor aspects by comparing performance on the "classic" ToH task to a modified version of the ToH, *i.e.*, the MSL task. The MSL task employed the exact same series of movements as the ToH, but the information that would inform performance of the underlying strategy was not available (*i.e.*, the disks were not visible).

The results of the current investigation revealed that, as hypothesized: (**1**) cognitive procedural memory performance on the ToH task benefitted from a period of sleep, and only sleep, permitting enhanced consolidation, regardless of the initial training time, by contrast, and, (**2**) there was no differential benefit to performance from sleep *vs.* wake on the exact same series of movements executed in the MSL task. Taken together, our results extend upon previous findings by showing that sleep preferentially enhances procedural memory when a new cognitive strategy is required in order to improve performance (Fogel et al., 2015; Kuriyama et al., 2004; Peters et al., 2007; Smith et al., 2004), but not the series of implicitly learned movements required to perform the task. This may help to explain why implicit MSL is consolidated regardless of sleep or wake, but cognitively complex implicit procedural consolidation is specifically enhanced by sleep.

As would be expected, a significant decline in performance was observed from Immediate Test to the Retest session following a period of wake when trained and immediately tested on the 3-disk version of the ToH, and then retested on the more difficult 5-disk ToH. By contrast, no change in performance (*i.e.*, savings) was observed from Immediate Test to the Retest session following an equivalent period of sleep. This pattern of results suggest that sleep might allow for individuals to apply what they learned to more complex scenarios, as remarkably, participants extrapolated the relatively simple 3-disk strategy to the larger 5-disk problem. ToH performance at Retest 2 further strengthens the support for our hypothesis: once participants who only had a retention period of wake had the opportunity to sleep, their performance improved to a comparable level to those who received the benefit of sleep immediately after training. This benefit of sleep was task-specific, as there was no similar pattern of results for the MSL task, despite the fact that they executed the same set of motor movements. It is important to note that we did not observe differences between the AM-PM-AM and PM-AM-PM groups at initial testing (*i.e.*, Immediate Test session), or in terms of subjective sleepiness. This suggests that movement speed was similar regardless of the time tested, and it is unlikely that any circadian effects might have confounded the results. Taken together, these results suggest that sleep benefitted ToH performance by stabilizing performance across a period of sleep *vs.* an equivalent period of wake, specifically, via preferential enhancement of the underlying cognitive strategy required to optimally solve the puzzle.

Selective sleep deprivation paradigms and overnight polysomnography might also provide further insights into the types of sleep and the nature of learning-dependent changes in sleep electrophysiology that support cognitive aspects of procedural memory. Studies have revealed post-learning increases in REM sleep for cognitive procedural tasks (Peters et al., 2007; Smith et al., 2004). In addition, targeted memory reactivation during REM sleep enhances cognitive procedural memory consolidation (Smith & Weeden, 1990). Most recently, our research and others' (Fogel et al., 2015; Nielsen et al., 2015) have shown associations between increases in REM sleep following learning on strategy-based tasks. More specifically, on the night that participants became experts on the task, they experience increased REM sleep duration. Re-exposure to the task one-week after it has already been mastered resulted in increased Stage 2 sleep and sleep spindles (Fogel et al., 2015). Evidence therefore suggests an interplay

between both Stage 2 and REM sleep for cognitively complex procedural memory consolidation (Nielsen et al., 2015), whereby Stage 2 sleep might refine skills for cognitive strategies that are consolidated during REM sleep (Fogel et al., 2015). However, see Lewis et al. (2018) for a recent review on the complimentary role of non-REM and REM sleep for problem solving.

In addition to the need for electrophysiological support for the present findings (*e.g.,* involvement of spindle-related, or REM-related brain activity), it is recommended that future studies examine the functional brain anatomy involved in the process of sleep-dependent consolidation of cognitive strategies using *e.g.,* functional magnetic resonance imaging. Very little is known about the neurobiological substrates involved in the acquisition and subsequent consolidation of cognitively complex procedural memory. However, previous work on motor sequence learning suggests that activation of a motor memory trace is transformed as a function of practice (Doyon et al., 2002; Ungerleider, Doyon, & Karni, 2002) and subsequently with time (Lehericy et al., 2005). Brain regions such as the putamen appear crucial for the acquisition and consolidation of these motor skills. This work has identified a neuroanatomical-functional shift over the course of consolidation whereby activation of the more anterior dorsal (associative) part of the putamen decreases with practice, whereas activation of the more posterior ventrolateral (sensorimotor) part of the putamen increases with practice and remains that way for a period of at least several days (Lehericy et al., 2005). A recent neuroimaging study by our group suggests that sleep spindles are involved in the reactivation and related transformation of this memory trace (Fogel et al., 2017). We also observed post-training-related increases in sleep spindles following learning on the ToH (Fogel et al., 2015). Thus, suggesting that a similar phenomenon might support consolidation and sleep-related enhancement of cognitively complex procedural memory. In addition, animal studies have shown that the ventral striatal neurons fire during reward learning (Lansink, Goltstein, Lankelma, McNaughton, & Pennartz, 2009). This circuit is reactivated during subsequent non-REM sleep (Lansink et al., 2009; Valdés, McNaughton, & Fellous, 2015). Moreover, correlated firing between the ventral striatum and the hippocampus takes place following reward-related behavior (such as in the ToH task). Notably, an increase in neuronal firing in the ventral striatum is associated with hippocampal ripples (Pennartz et al., 2004), which are time-locked to sleep spindles (Clemens, Zvyagintsev, Sack, Heinecke, Willmes, & Sturm, 2011). This has been suggested as a possible mechanism for sleep-dependent memory consolidation (Girardeau, Benchenane, Wiener, Buzsáki, & Zugaro, 2009). Indeed, an extended network of brain structures including the hippocampus, prefrontal cortex motor cortical regions, parietal cortex, cerebellum and the ventral striatum are involved in goal-directed, on-line choice, action control and learning (Pezzulo, van der Meer, Lansink, & Pennartz, 2014). These regions are specifically recruited during ToH performance (Dagher, Owen, Boecker, & Brooks, 1999; Doyon, Owen, Petrides, Sziklas, & Evans, 1996; Owen, Doyon, Petrides, & Evans, 1996; Rowe, Owen, Johnsrude, & Passingham, 2001; Unterrainer & Owen, 2006; Van Den Heuvel et al., 2003). However, the role of sleep in the reactivation of cognitively complex procedural memory, and any role for spindles in this process remains to be explored.

We have by-and-large framed this research in the context of the role of sleep in the offline processing of newly acquired memories, as it applies to knowledge for problem solving (for an interesting recent review on the topic see: Lewis et al., 2018). Alternative explanations may also help guide future research in this area. Previous studies (Durrant et al., 2011; Lewicki et al., 1987; Lewis et al., 2018; Wagner et al., 2004) suggest that sleep might facilitate problem solving or rule acquisition, rather than improve memory *per se*. It is therefore possible that the observed spontaneous performance improvement from the 3-disk to the more difficult 5-disk version of the ToH following sleep might not be an effect of memory strengthening, but rather of sleep facilitating the solution to the overall strategy. Indeed, it is difficult to

reconcile how sleep could support the realization to the solution to a problem for which an individual has not yet been exposed to solely in terms of memory consolidation. Interestingly, there are many famous anecdotal accounts of this phenomena. René Descartes realized how to represent relationships using Cartesian coordinates; Frederick Banting thought to isolate the hormone insulin; and Albert Einstein uncovered the principle of relativity – *all manifested after a period of sleep*. This notion that sleep unravels realizations and problem solving is backed by several studies (Brand et al., 2010; Lewicki et al., 1987; Lewis et al., 2018; Wagner et al., 2004). Finally, it is important to note that there are several studies that did not find any benefit of sleep for the realization of cognitively complex strategies when compared to simple memory assessments (Mirkovic & Gaskell, 2016; Schönauer et al., 2018), or found that sleep enhanced but did not reorganize learning (Landmann et al., 2016), thus, highlighting the importance of further research on this topic to identify the precise role that sleep plays in facilitating the novel solutions to cognitively complex problems. Given the multi-faceted nature of the acquisition of novel cognitive strategies and more broadly, procedural memory, the current study might provide a means to resolve some of these inconsistencies, by isolating the features of human knowledge and performance that derive a benefit from sleep.

In conclusion, by separating the cognitive from simple aspects of procedural memory, we observed that sleep preferentially benefits the cognitively complex components of procedural memory, rather than strengthening the motor sequence performance required to learn the cognitive strategy itself.

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Declaration of interests

The authors declared that there is no conflict of interest.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.nlm.2019.04.005.

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