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Does Sleep Enhance the Consolidation of Implicitly Learned Visuo-Motor Sequence Learning?

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Graduate Program in Psychology
A thesis submitted in partial fulfillment of the requirements for the degree in Master of Science
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Abstract

Sleep has been shown to facilitate the consolidation (i.e., enhancement) of simple explicit (i.e., conscious) motor sequence learning (MSL). It remains unclear the degree to which this applies to implicit (i.e., unconscious) MSL. Employing reaction time and response generation tasks, we investigated the extent to which sleep is involved in consolidating implicit MSL, specifically whether the motor or the spatial cognitive representations of a learned sequence are enhanced by sleep, and whether these changes support the development of explicit sequence knowledge across sleep but not wake. Our results indicate that spatial and motor representations can be behaviourally dissociated for implicit MSL. However, neither representation was preferentially enhanced across sleep nor were developments of explicit awareness observed. These results suggest that like explicit MSL, implicit MSL has dissociable spatial and motor representations, but unlike explicit sequence learning, implicit motor and spatial memory consolidation is independent of sleep.

Keywords

Implicit learning, sleep, memory, consolidation, motor sequencing, serial reaction time task, motor skill, explicit awareness, recall, recognition.

Acknowledgments

First and foremost I would like to acknowledge and thank my supervisors Drs. Adrian Owen and Stuart Fogel, without whom I would not have had the opportunity to be a part of such an amazing research team, and whose thought, time, and mentorship have helped me become a stronger scientist across all aspects of research. I would also like to thank those who provided other important support helping me conduct this research, particularly Laura Ray who was instrumental in helping me solve all sorts of technical problems, help run data, and proofread on short notice when I was in a crunch. I would also like to thank the wonderful and eager volunteers, Juweiriya Ahmed and Orli Bogler, who bravely took on some of the overnight recording sessions for me throughout the lengthy data collection phase of this study.

Next, I would like to thank the special group of labmates and peers, who are now known better to me as some of the greatest of friends anyone could ask for. Without being able to share with you the laughs, adventures, and general feelings of crisis native to graduate-studies, I would not have been able to accomplish what I have. So to my "lab-sisters" Valya Sergeeva, Kathleen Lyons, and Avital Sternin, who embarked on the Masters journey in the Owen lab at the same time as me - I'm very glad to have had the pleasure and privilege of working with such inspirational and hardworking friends through it all, thank you. This does not just apply to those three incredible human beings, but to the rest of my friends across labs who also inhabited the graduate-students' Cubicle Town of the first floor Brain and Mind Institute (in no particular order); Dan Glizer, Rae Gibson, Brian Robertson, Tram Nguyen, Max Silverbrook, Evan Houlding, Aaron Gibbings …et al. (2015-2016)! I would like to send an extra special thank you to Natalie Osborne whose thoughtfulness and care kept me on point, and whose sushi-bearing, late-evening office visits saved me from an exclusively Veggie Straw™-based diet for the writing of this thesis.

Finally, I would like to thank my family, especially mom and dad, Audrey and Reg Viczko, whose love and support was a constant positive force felt even from across the country. They instilled in me great appreciation for opportunities to learn, educate, and work hard to give back to the world. These values have steered me well, serving to set me on the career path I have chosen. I know I have made them proud with my accomplishments so far and will continue to give my best. It is the best way I can think to reciprocate all they have done for me, and I am equally proud and grateful for such amazing parents.

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List of Abbreviations

ASRT	Alternating serial reaction time task
CN	Control session
EEG	Electroencephalography
EMG	Electromyogram
EOG	Electrooculogram
fMRI	Functional magnetic resonance imaging
HPC	Hippocampus
HPC-SWR	Hippocampal sharp-wave ripple
IM	Immediate post-training test
LT	Long-term retest session
MSL	Motor sequence learning
NREM	Non-rapid eye movement sleep
PI	Post-interval retest session
PRE	Pretraining test
PVT	Psychomotor vigilance task
REM	Rapid eye movement sleep
SDMC	Sleep-dependent memory consolidation
SHY	Synaptic Homeostasis Hypothesis
SLEEP	Sleep interval experimental condition
SRTT	Serial reaction time task
SWA	Slow-wave activity
SWS	Slow-wave sleep
TR	Training session
WAKE	Wake interval experimental condition

INTRODUCTION

"It is a common experience that a problem difficult at night is resolved in the morning after the committee of sleep has worked on it." -John Steinbeck, Sweet Thursday (1954)

Preface

About 1/3 of our life is spent asleep, yet we are only now uncovering the purpose and importance of sleep. While the benefits of sleep may go unnoticed during the bustle of our daily activities, it is in the absence of good sleep that its importance to optimal functioning is perhaps most appreciated. Acutely, sleep disruption has detrimental effects on mood (Garavan et al. 2001), vigilance (Carrier and Monk 2000), and cognitive function (Killgore, 2010; Walker, 2008). Chronic sleep disruption has been associated with increased risk and symptomology of psychiatric disorders (Alvaro, Roberts, & Harris, 2013), cancer (Kakizaki et al., 2008; Thompson et al., 2011), as well as metabolic (Knutson & Van Cauter, 2008), cardiovascular (Buxton & Marcelli, 2010), and degenerative disease (Pace-Schott & Spencer, 2011; Xie et al., 2013). On the other hand, adequate sleep is associated with mood regulation, increased vigilance, physical and mental restoration, and longevity (Tufik, Andersen, Bittencourt, & Mello, 2009).

However, one of the most important functions of sleep is for supporting learning and memory. A period of sleep, compared to wake, is known to enhance and transform labile memories into enduring long-term storage, enhances performance of newly learned skills, and can even promote conscious insight into otherwise unconscious knowledge. These enhancements in memory and skill performance after sleep are a phenomenon collectively referred to as sleep-dependent memory consolidation (SDMC). Sleep has been found to be particularly important for motor procedural SDMC, in particular when learned explicitly. Interestingly, sleep does not simply enhance all aspects of learning and memory equally. Rather, sleep preferentially supports the consolidation of dissociable memory representations (e.g., spatial aspects versus motor aspects) of a procedural motor skill (Albouy et al., 2015; Albouy, Fogel, et al., 2013; Cohen, Pascual-Leone, Press, & Robertson, 2005). However, it is not known whether this applies to motor skills that are learned without

conscious knowledge of the skill. This may help to elucidate whether sleep is involved in the consolidation of implicit MSL, for which there are unresolved inconsistencies in the literature.

The overall goal of the present study was to address the question - *does sleep enhance the explicit awareness and generalization of an implicitly learned motor sequence*? More specifically, this study aimed to dissociate the spatial- and motor-referent cognitive-behavioural representation of an implicitly learned motor sequence using a modified version of the serial reaction time task (a classic implicit motor learning task), and to explore whether sleep facilitates the development of explicit awareness in tandem with memory enhancement of the spatial, but not motor, representation of a sequence. Chapter 1 provides a description of the characteristics of sleep. This is followed by a discussion on the relevant learning, memory and sleep literature (Chapter 2). Chapter 3 outlines the role of sleep when memory is separated into various memory systems. And finally, Chapter 4 will present the focus of the present study.

Chapter 1 – The Characteristics of Sleep

Sleep is defined as a reversible state of reduced behavioural responsiveness accompanied by a reduction of conscious awareness of the external environment. However, sleep is not simply a quiescent state. Rather, sleep is more recently becoming regarded as a dynamic, altered state of consciousness that actively supports a wide variety of biological functions, physical and mental wellbeing, and, in particular, memory consolidation. However, the question of *why* we sleep remains a topic of hot debate. Modern theories account for sleep as process of restoration (Thomson & Oswald, 1977), thermoregulation (McGinty & Szymusiak, 1990), energy conservation (Berger & Phillips, 1995), immune-regulation (Bollinger et al., 2009), and also include developmental (Roffwarg, Musio & Dement, 1966) and learning theories (see Doyon, Korman, et al., 2009; Fogel & Smith, 2011; Maquet, 2001; Rasch & Born, 2013; Smith, 2001; Stickgold & Walker, 2013; Stickgold, 2013; Tononi & Cirelli, 2014 for reviews).

The following sections describe sleep in terms of behaviour and electroencephalography (EEG), the gold standard for categorizing sleep according to the characteristic and distinct neural oscillations of the sleeping brain. Although EEG techniques were originally pioneered by Hans Berger (1924) who is also credited with the discovery of alpha and beta frequency waves during waking rest, EEG was then first applied continuous sleep in 1950's (Aserinski & Kleitman, 1953) who alongside William Dement (Dement & Kleitman, 1957) and Michel & Jouvet (1959) are credited with the discovery of REM sleep.

Architecture of Sleep

At the broadest level, sleep is classified into non-rapid eye movement (NREM) and rapid eye movement sleep (REM). NREM is further subdivided into three stages; NREM stage 1 (NREM1), NREM stage 2 (NREM2), and NREM stage 3 (NREM3). At the macro-architectural level, across a full night sleep, brain activity transitions sequentially across NREM stages into

REM sleep. Figure 1 illustrates a typical time-course of sleep stage transitioning across a full night's sleep. Each ultradian sleep cycle lasts approximately 90 min. In infancy most of sleep is spent in REM, but into childhood, the proportion of REM is reduced as the amount of SWS increases, reaching maximal amounts before decreasing into puberty. With increasing age, the number of cycles, depth and efficiency of sleep decrease, accompanied by tendencies for earlier bed and rise times (for a review see Ohayon, Carskadon, Guilleminault, & Vitiello 2004).

NREM1. NREM1 is the first and "lightest" stage of sleep following wakefulness, marked by less than 50% alpha activity and its EEG features vertex sharp waves and low voltage, mixed frequency EEG marking the transition from wake to sleep. NREM1 accounts for approximately 5% of a total night's sleep. Vivid visual hypnogogic imagery occurs during NREM1, and there is evidence suggesting NREM1 dream mentation may be associated with memory processing (Lahl, Wispel, Willigens, & Pietrowsky, 2008; Stenstrom, Fox, Solomonova, & Nielsen, 2012; Wamsley, Perry, Djonlagic, Reaven, & Stickgold, 2010).

NREM2. As sleep progresses to more profound stages, as in NREM2, the EEG becomes more synchronized, electromyogram activity decreases and the arousal threshold for the external stimuli (e.g. external noise) rises. NREM2 typically occupies about 45% to 55% of the night's total sleep (Carskadon & Dement, 2011). Aminergic tone and cholinergic tone are reduced as compared to wake (Stickgold et al. 2001; Smith et al. 2004 for review). Positron emission tomography studies (Andersson et al. 1998; Braun et al. 1997; Hofle et al. 1997; Kajimura et al. 1999; Maquet et al. 1997) show that cerebral blood flow (CBF) significantly decreases during NREM as compared to wakefulness and REM across a variety of distributed cerebral networks, including the pontine, midbrain, thalamus, cerebellar, cingulate, basal ganglia, prefrontal, precuneate, and mesial temporal lobe cortices. Despite the comparative drop in overall metabolic rate NREM2 increases above waking levels of neural activity are observed during the events which characterize NREM sleep such as sleep spindles and slow waves.

The main physiological markers of NREM2 are sleep spindles and K-complexes. Sleep spindles, are short bursts of activity with a frequency of ~11-16 Hz, and last between ~0.25 and 3 seconds (Iber, Ancoli-Israel, Chesson Jr., & Quan, 2007). Classically, sleep spindles have been described to originate in the thalamus and are a result of rhythmic depolarizations of thalamocortical neurons (Steriade, 1995), modulated by thalamic GABAergic reticular interneurons (Bazhenov,

Timofeev, Steriade, & Sejnowski, 2000, 1999). Although, recent evidence suggests spindles are initiated cortically (Bonjean et al., 2011). Furthermore, it has been proposed that two types of sleep spindles exist: fast and slow spindle types (Schabus et al., 2007; Zeitlhofer et al., 1997). Slow spindles are distributed over the frontal regions and occur at a frequency of ~11-13.5Hz (Werth, Achermann, Dijk, & Borbély, 1997), while fast spindles are predominantly located over the central and parietal regions, recruit hippocampal activity (Schabus et al., 2007), and occur at a frequency of ~13.5-16Hz (De Gennaro, Ferrara, & Bertini, 2000).

In general, sleep spindles are thought to serve several functions, such as protection from external stimuli (Cote, Epps, & Campbell, 2000; Steriade, 1994), as well as optimal consolidation of procedural (e.g., skills, reasoning and rule-learning) and declarative (e.g., facts, figures and events) memory (Barakat et al., 2013; Fogel & Smith, 2006, 2011; Fogel et al., 2014; Lafortune et al., 2014; Mander et al., 2014). Sleep spindles, and in particular fast spindles, have also been suggested to play an active role in the sleep-dependent consolidation of new learning which is discussed in more detail throughout the following chapters (Bergmann et al., 2008; Rosanova & Ulrich, 2005; Steriade, 2005).

Another marker of NREM2, is the K-complex. K-complexes are slow frequency, large amplitude cortical events that consist of a negative sharp wave (> 100 μV), followed by a slower positive component (after ~350 to 550ms), and terminate with a final negative peak occurring around 900ms. Typically K-complexes last for ~ ≥0.5 seconds and are maximal at frontal derivations (Roth, Shaw, & Green, 1956) . They are thought to be generated in the thalamus, although their morphology and propagation across the scalp are influenced by cortical cells (Amzica & Massimini, 2002). While the functions of K-complexes are still unknown, some studies suggest that K-complexes appear as partial (i.e., subthreshold excitatory) phasic arousal events from endogenous information processing (Davis, Davis, Loomis, Harvey, & Hobart, 1937; Halász, Terzano, Parrino, & Bódizs, 2004; Roth et al., 1956), or from exogenous sensory processing (i.e.,external stimuli; Dang-Vu et al., 2011) breaching the tonic suppression of sleep. Alternatively others hypothesize the K-complex serves as an inhibitory process that protects sleep from arousal from external stimuli (Crowley, Trinder, Kim, Carrington, & Colrain, 2002; Nicholas, Trinder, & Colrain, 2002; Wauquier, Aloe, & Declerck, 1995).

NREM3. NREM3 or Slow Wave Sleep (SWS) typically occupies about 15% to 25% of total

sleep time, and predominates the first half of the night (Carskadadon & Dement, 2011). During this stage, electromyogram activity remains low. As well, awareness of external environment is at its lowest. Slow Wave Activity (SWA), or delta waves, are the most prominent markers of SWS and have a frequency of ~0.5-2 Hz and a large peak-to-peak amplitude of at least 75 μV (Iber et al., 2007). Delta waves are thought to reflect large-scale synchronous firing of thalamo-cortical networks (Steriade, 2006). At the cellular level, this corresponds to the synchronous fluctuation of membrane potentials from relatively hyperpolarized levels to suprathreshold levels (Steriade, McCormick, & Sejnowski, 1993). Progression of sleep cycles throughout a night results in decreases in SWS amplitude and duration, with slow waves typically propagating with an anterior-to-posterior areas (Greenberg & Dickson, 2013; Massimini, Huber, Ferrarelli, Hill, & Tononi, 2004). SWS also plays a critical role in SDMC of certain types of memories, in particular declarative and associative and memory (which is further discussed in Chapter 3 – Memory Systems and Sleep), and has also been implicated in the maintenance of neural synaptic homeostasis (detailed in Chapter 2 – Learning, Memory, and Sleep).

REM. REM occupies ~ 20% of total sleep with little change form young-to-late adulthood (Ohayon et al., 2004). Paradoxically, REM sleep EEG resembles that observed during conscious wakefulness (Chow et al., 2013). The wake-like EEG of REM sleep is characterized by mixed frequency, low amplitude desynchronized oscillations, including increases in alpha, beta, and gamma coupled to theta waves (Achermann & Borbély, 1998). The most prominent markers of REM sleep are the rapid, conjugate, horizontal eye movements, recorded by the electrooculogram (EOG). Animal (Callaway, Lydic, Baghdoyan, & Hobson, 1987) and human (Peigneux et al., 2001; Fernández-Mendoza et al., 2009) studies suggest that rapid eye movements are associated with the occurrence of phasic endogenous wave forms expressed in the pons (P), geniculate nuclei of the thalamus (G), and the occipital cortex (O). Such waves have been termed “PGO waves”. In turn PGO waves are thought to trigger cellular processes thought to favor brain plasticity during REM sleep (Datta, 1999).

Despite similarities in the EEG with wake, during REM sleep, cholinergic tone drops to that of about 60% of wake, with the exception of basal forebrain and hippocampal regions (Hasselmo, 1999; Vazquez & Baghdoyan, 2001). Neuroanatomical activation of the limbic system during REM sleep, particularly the modulation of the amygdala and occipo-temporal areas (Maquet and

Phillips, 1998), has been suggested to be a putative mechanism underlying dreaming activity and emotional memory processing (Schwartz & Maquet, 2002). A near silencing of the noradrenergic system during REM is accompanied by a significant muscle atonia of the major muscle groups (Chase & Morales, 1990; Vazquez & Baghdoyan, 2001). Despite this paralysis, phasic muscle twitches do occur throughout REM sleep. The muscle atonia of REM sleep has been proposed as an adaptive mechanism to protect against physically acting out dreams, which are characteristically vivid and narrative in nature, while dreaming mentation in NREM is typically briefer and more thought-like in nature (Llewellyn, 2013). The consequences of diminished REM atonia are observed in parasomnias, such as REM sleep behavior disorder, whereby individuals sometime violently act out their dreams. Like SWS, REM sleep has also been implicated in SDMC, particularly for complex procedural learning and processing emotionally salient memories (further discussed in Chapter 3).

Regulation of Sleep

Timing, initiation, onset and depth of sleep are widely thought to be determined by the interaction of two processes: homeostatic sleep pressure, termed Process S, and circadian rhythms, termed Process C (Borbély, 1982; Borbély, Daan, Wirz-Justice, & Deboer, 2016). Anatomically the suprachiasmatic nuclei of the hypothalamus is widely considered the 'master clock' orchestrating the circadian timing (the peaking and troughing) of important endogenous processes including core temperature regulation, metabolic activity, arousal, and relatedly, propensity for wake (Borbély et al., 2016; Saper, Fuller, Pedersen, Lu, & Scammell, 2010). Mammalian circadian rhythms demonstrate limited flexibility and in actuality a *near,* not exact*,* 24hr period. As such, the circadian biological rhythms are realigned daily according to external environmental cues, or "zeitgebers" (i.e., "time givers"), such as ambient light.

Whereas Process C follows a sinusoidal pattern across a 24hr period, Process S operates akin to an hourglass mechanism; which gradually fills up with increasing time awake (increasing pressure to sleep). During sleep, this pressure is released at an exponential rate. There is still debate on which biochemical substrate(s) accumulate during wake that reflect sleep pressure (for reviews see Krueger, 2008; Saper et al., 2010), and thus the only known indicator of process S is SWA in sleeping EEG activity, such that the amount of sleep pressure proportionally increases

the duration, and power of the SWA, and decreases latency to SWS onset (Borbély et al., 2016). Thus, with longer periods of wake, initial progression into SWS occurs faster and is emerges as a more intense and deeper sleep.

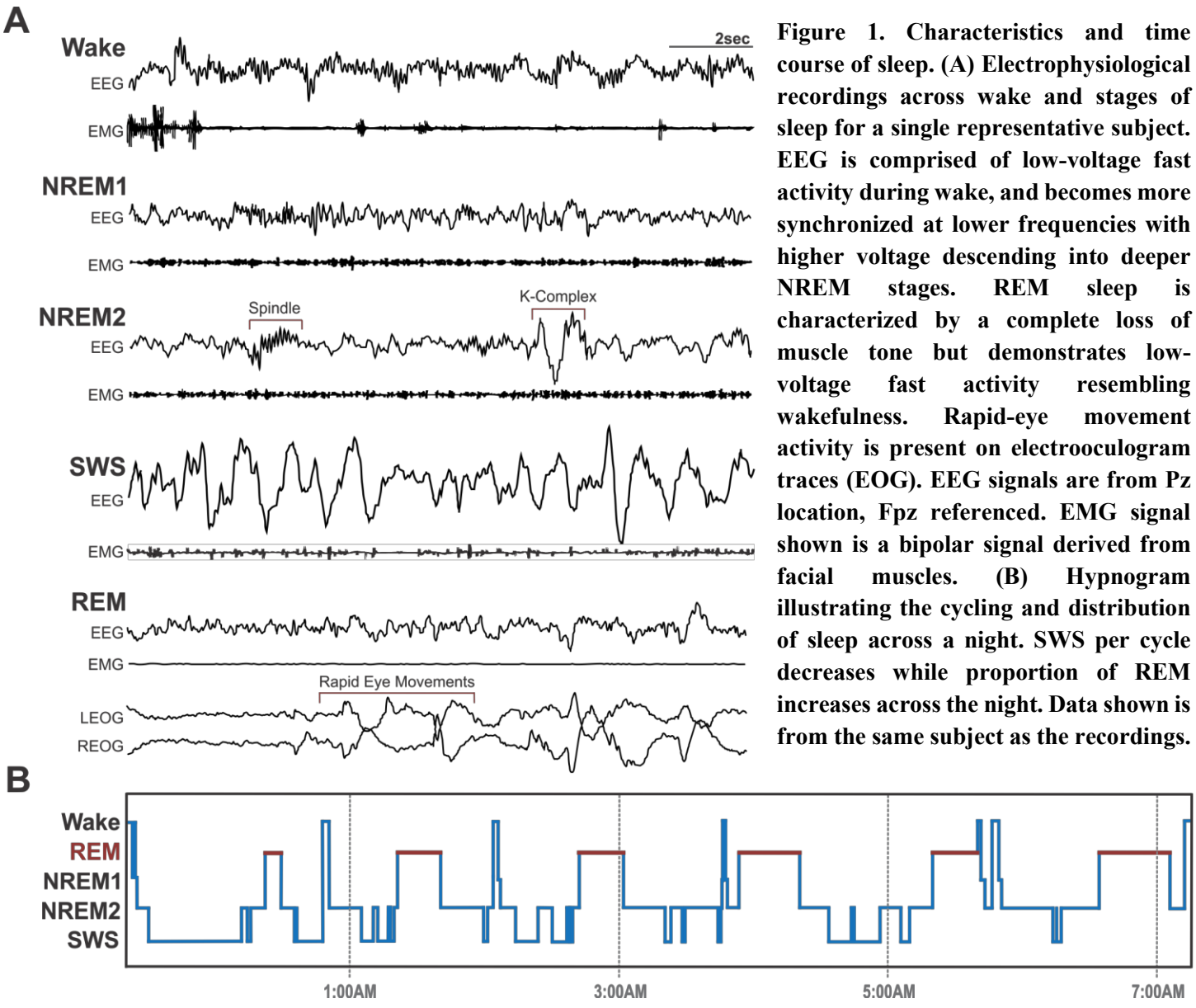


Figure 1. Characteristics and time course of sleep. (A) Electrophysiological recordings across wake and stages of sleep for a single representative subject. EEG is comprised of low-voltage fast activity during wake, and becomes more synchronized at lower frequencies with higher voltage descending into deeper NREM stages. REM sleep is characterized by a complete loss of muscle tone but demonstrates low-voltage fast activity resembling wakefulness. Rapid-eye movement activity is present on electrooculogram traces (EOG). EEG signals are from Pz location, Fpz referenced. EMG signal shown is a bipolar signal derived from facial muscles. (B) Hypnogram illustrating the cycling and distribution of sleep across a night. SWS per cycle decreases while proportion of REM increases across the night. Data shown is from the same subject as the recordings.

In terms of regulating sleep, circadian arousal is highest in the early evening maintaining wakefulness in the face of peaking sleep pressure accumulation. Sleep onset begins when the homeostatic sleep pressure has accumulated and circadian arousal begins to decline, typically in the mid-to-late evening, when zeitgebers such as dim light, trigger the release of melatonin to promote sleep. The first half of the night contains mostly SWA. The arousal system reaches a trough in the early morning hours, as sleep pressure non-linearly dissipates (reflected in less SWA and more REM per sleep cycle) across the sleeping period. At the time of sleep offset, mid-to-late morning, sleep pressure is diminished and the circadian arousal system starts to ascend. Thus, process S and process C work in opposition to maintain consolidated episodes of wake and sleep (Borbély et al., 2016; Dijk & von Schantz, 2005; Van Dongen & Dinges, 2003).

Notably this two-process model of sleep regulation has been robustly accurate in predicting cognitive, physiological, and neurobehavioral outcomes across times of, including fatigue and amount of SWA in naps or night's sleep after sleep deprivation manipulations (Achermann & Borbély, 2003; Borbély et al., 2016; Franken, Dijk, Tobler, & Borbély, 1991; Van Dongen & Dinges, 2003). Beyond this, the two-process model has provided an invaluable framework from which to understand the functions and physiology of sleep. In particular, the homeostatic nature of sleep has been associated with homeostatic support for memory function. This and other learning, memory, and sleep theory and research are expanded on in the next chapter.

Chapter 2 – Learning, Memory, and Sleep

Learning, Memory, and Neuroplasticity

The three basic stages in memory processing include encoding, consolidation, and retrieval (Abel & Lattal, 2001). Consolidation is considered to be an 'offline' process, meaning the memory continues to be gradually processed even after the 'online' encoding phase, in the absence of continued practice. Consolidation can be further subdivided into the processes of stabilization and integration. Stabilization occurs in a short window of time after encoding, on the order of minutes to hours, during which time the newly acquired memory becomes stable enough to resist interference (Brawn, Fenn, Nusbaum, & Margoliash, 2010; Diekelmann & Born, 2010b; Walker, 2005). Integration happens on the timescale of days to years and describes the processes of distributing or assimilating the short term memory into a longer-term memory where it is eventually stored in distributed neocortical networks for long-term memory retrieval (Giuditta, 2014; Marshall & Born, 2007; Rasch & Born, 2013; Sirota & Buzsáki, 2007; Squire, 2009; Takehara-Nishiuchi & McNaughton, 2008; Tononi & Cirelli, 2014). The processes of encoding and consolidation are presumed to be supported by a combination of complementary, independent and overlapping neuroanatomical structures including the hippocampus, striatum, and cortico-thalamic circuitry (detailed later in this section and the following chapter). Importantly, acquired memory traces may be stabilized, enhanced, strengthened, or transformed during the process of consolidation (Albouy et al., 2015; Diekelmann & Born, 2010b; Landsness et al., 2009; Stickgold & Walker, 2013). Furthermore, depending on the type of memory, this 'offline' consolidation can occur dependent, or independent of sleep (i.e., across post-learning periods of wake). However, when SDMC occurs it uniquely demonstrates rapid and robust memory enhancements, more-so than as compared to wake, or passage of time alone.

Neuroplasticity unfolds over the course of memory consolidation, marked by changes in anatomical, physiological, and functional neural connectivity. Neuroplasticity is supported by changes at the molecular, cellular, and neuronal level. Details on the mechanisms governing neuroplasticity are beyond the scope of this discussion (for review see; Cooke & Bliss, 2006).

Briefly, the process takes place as interaction between individual neurons. Importantly, for neurons to modify signalling connectivity with other neurons in proximal or distal networks, the neurons involved have to be significantly co-active within a short-time frame (within tens of milliseconds). Depending on the timing of pre and post-synaptic firing of neurons, the signal efficacy between neurons can either be potentiated (increased), or depressed (decreased). When these changes occur in a lasting way between neurons, these physiological processes are referred to as, respectively, long-term potentiation or long-term depression. In particular, long-term potentiation (Hebb, 1949) is widely thought to be the major cellular mechanism underlying learning and memory (Markram, Gerstner, & Sjöström, 2011). Thus, neuroplasticity, and memory processing, are thought to be activity-dependent processes.

The Synaptic Homeostasis Hypothesis: Sleep is for downscaling

The brain is comprised of very energy expensive tissue (Aiello, Wheeler, & Chivers, 1995; Hyder, Rothman, & Bennett, 2013). At a neurobehavioral level, repeatedly performing an action or repeated perceptual exposure to stimuli results in potentiation of large populations of neurons. This potentiation comes at a metabolic cost. The process of synaptic genesis, modification, maintenance, and, increased excitability of neurons results in significant energy demands. This, combined with limited inter-cranial space and cellular resources means that continuous potentiation is neither sustainable nor feasible to encode and sustain memory. One influential theory of the function of sleep is for the homeostatic regulation of the accumulated synaptic potentiation during episodes of prior wakefulness. This synaptic homeostasis hypothesis (SHY; Tononi & Cirelli, 2003, 2006, 2014), asserts that sleep is the price payed for plasticity. More specifically, SHY proposes that while wake results in net increases in synaptic strength, SWA uniformly downscales/depresses synaptic strength. With this global downscaling, the weakest synaptic connections are pruned, whereas the stronger connections, which are the result of learning, survive the downscaling process. SWS then is the process that increases the signal-to-noise ratio for the important (or at least statistically regular) network activity, and allows for new learning synaptic potentiation for the period of subsequent wakefulness.

Extensive research has been done evaluating SHY from molecular (Vyazovskiy, Cirelli, Pfister-

Genskow, Faraguna, & Tononi, 2008), cellular (Cirelli, Gutierrez, & Tononi, 2004), structural (Bushey, Tononi, & Cirelli, 2011; Maret, Faraguna, Nelson, Cirelli, & Tononi, 2011), and behavioral (Huber et al., 2006; Huber, Ghilardi, Massimini, & Tononi, 2004; Vyazovskiy & Tobler, 2008; Vyazovskiy, Borbély, & Tobler, 2000) approaches (for a review see Tononi & Cirelli, 2014). One of the most striking contributions of SHY research have been observations that homeostatic SWA activity occurs not just on a global cortical scale, but also emerges prominently over the local cortical regions (Krueger & Tononi, 2011; Vyazovskiy & Tobler, 2008b; Vyazovskiy et al., 2011, 2000). For example, Huber et al., (2004) demonstrated that after a motor adaption task involving the right partial cortex, subsequent increased SWA over that cortical region was observed, and was correlated with post-sleep improvement. By contrast, arm immobilization lead to a decrease in somatosensory and motor evoked potential in the contralateral sensorimotor cortices, and decreases SWA over those cortical regions (Huber et al. 2006).

Although SHY provides an elegant account for a variety of sleep and learning related phenomena, it is not without criticisms (Frank, 2015; Frank, 2012) including limited accounts for subcortical activity (such as in the hippocampus; Buzsaki et al. 2002), a role for REM sleep, and for contrary findings indicating that SWS has the capacity to potentiate synapses (Aton et al., 2013; Seibt et al., 2012; Steriade & Timofeev, 2003; Timofeev, 2011). The homeostatic hypothesis entails a mechanism of non-Hebbian plasticity, by which activity-dependent downscaling indirectly enhances memory processes. Other theories propose, conversely, that sleep is a time for increased Hebbian-plasticity in which cerebral activity *directly* contributes to memory consolidation, reviewed in the following section.

The Active System Consolidation Hypothesis: Sleep is for reactivation

The main tenet of reactivation-based hypotheses of sleep is the observation that certain brain systems, such as in the hippocampus, replay the activation dialogues of prior wake and learning experience to promote plasticity and potentiate memory engrams (Buzaki, 1996; Peigneux, Laureys, Delbeuck, & Maquet, 2001; Schwindel & McNaughton, 2011; Sirota & Buzsáki, 2007; Steriade & Timofeev, 2003; Wilson & Mcnaughton, 1994). The Active System Consolidation

Hypothesis (for review see: Rasch & Born, 2013) proposes that reactivations which occur during SWS potentiate memory representations, whereas REM sleep acts to integrate, or transform, acquired memories into a long-term storage system (i.e., actively, memory traces are transferred between short and long-term memory brain systems). The hippocampus (HPC) is thought to be the primary structure in the immediate acquisition and short-term storage of memories, whereas the neocortex is where long-term memories are integrated into, and stored across existing distributed networks.

Consistent with a previously proposed hypothesis ('the Sequential Hypothesis,' for a reviews see; Ambrosini & Giuditta, 2001; Giuditta, 2014) the Active System Consolidation Hypothesis implicates necessity of both NREM and REM, and specifically that their iterative, sequential nature is complementary and crucial in the process of SDMC. An extensive body of research supports this hypothesis (for other reviews see: Diekelmann & Born, 2010b; Ellenbogen, Hu, Payne, Titone, & Walker, 2007; Lewis & Durrant, 2011; Ribeiro & Nicolelis, 2004; Ribeiro, 2012). Some of the earliest evidence in support of this came from a study on texture discrimination learning in humans whereby performance was best predicted by the proportion of early night SWS *and* late night REM (as opposed to solely SWS or REM; Stickgold, Whidbee, Schirmer, Patel, & Hobson, 2000). As well, from rodents trained on a two-way avoidance task, where the sequencing order, and time spent in NREM-REM transitional states predicted performance improvements (Ambrosini & Giuditta, 2001).

Additionally, a primary characteristic of the Active System Consolidation model is that it stipulates that memories are discriminately, not globally, selected and tagged for sleep dependent consolidation, based on a variety of factors such as emotional salience (Hu, Stylos-Allan, & Walker, 2006; Nishida, Pearsall, Buckner, & Walker, 2009), task difficulty (Kuriyama, Stickgold, & Walker, 2004), the mass or arrangement of training (Brawn et al., 2010), motivation (Fischer & Born, 2009), self-relevance (Wilhelm et al., 2011), or how explicit (Robertson, Pascual-Leone, & Press, 2004) or intentional (Rauchs et al., 2011) the memory formation was. Thus, in contrast to SHY, sleep's role in memory consolidation is not viewed as a global phenomenon, encompassing all types of memory. Rather, the role of sleep is more nuanced, and appears to be based on the qualities of the memory representation itself rather than falling neatly into one memory category or another, defined by neuropsychological models (Graf

& Schacter, 1985; Squire & Zola, 1996; Tulving, 2002), a point which is further expanded on later (in Chapter 3 – Memory Systems and Sleep).

One of the primary mechanisms thought to promote reactivation consolidation are hippocampal sharp-wave ripples (HPC-SWRs; large amplitude negative EEG deflection, coupled with 100-200Hz oscillation, lasting 40-100ms, in HPC; Buzsáki, 2015). HPC-SWRs occur in phase together with NREM sleep spindles and SWS up-states and are believed to reflect HPC-neocortical communicative processing (Siapas & Wilson, 1998) in human (Bragin, Engel, Wilson, Fried, & Buzsáki, 1999; Le Van Quyen et al., 2010) and animal research (Buzaki, Pentfonen, Nadasdy, & Bragin, 1996; Sirota, Csicsvari, Buhl, & Buzsáki, 2003). Strong support for memory reactivation during sleep comes from *in vivo* rodent literature which has demonstrated ensembles of neurons replay the same patterns of activity as during laboratory training tasks in both NREM (Bendor & Wilson, 2012; Skaggs & McNaughton, 1995; Wilson & Mcnaughton, 1994) and REM (Louie & Wilson, 2001; Poe, Nitz, McNaughton, & Barnes, 2000) sleep.

Due to the depth of the HPC, HPC-SWRs are not visible on scalp-recorded EEG (although see Le Van Quyen et al., 2010, for a recent study investigating HPC-SWRs recorded from depth electrodes in patients with Epilepsy). While access to direct HPC recording is limited to deep probe implants (e.g., in the case of epileptic intervention), sleep spindle activity is easily recorded from surface EEG. Importantly, spindle activity is time-locked to HPC-SWRs (Siapas & Wilson, 1998; Sirota et al., 2003), and thus, spindles are also thought to be involved as mechanism of reactivation processing. Across multiple studies spindle activity has been associated with a wide array of sleep-dependent improvements in both declarative and procedural tasks (Barakat et al., 2013; Fogel & Smith, 2006, 2011; Fogel et al., 2014; Lafortune et al., 2014; Mander et al., 2014). For example, in one study (Saletin, Goldstein, & Walker, 2011), while memorizing a word list, words were cued either to be forgotten or remembered. Spindle density in this study was strongly correlated with better performance relative to the word cue directions (to either remember or forget). In support of Active System Consolidation Hypothesis, these results are taken to indicate that spindles in particular act to selectively tag important information for consolidation, as well as tag non-important information not to engage in consolidation (Saletin et al., 2011; Stickgold & Walker, 2013).

Finally, there is also evidence that SWA is implicated in memory reactivation and selection for consolidation process (Wilhelm et al., 2011). In a study exploring the causal relationship between sleep and memory (Rasch, Büchel, Gais, & Born, 2007), an odor cue was presented during a card matching game, and was re-presented during subsequent SWS or REM sleep. When the specific odor presented matched with the training odor was presented during SWS (but not REM sleep) gains in post-sleep memory performance were observed, with the odor cue thought to further enhance the underlying reactivation of the memory traces during sleep. Similar results have been obtained with auditory cueing (Rudoy, Voss, Westerberg, & Paller, 2009) and transcranial magnetic stimulation (Marshall, Helgadóttir, Mölle, & Born, 2006) during sleep. Thus, HPC-SWRs, spindles, and SWA have received support which, together, indicate NREM to be a state of reactivation, particular to networks recruited in the learning. This in in contrast to neurophysiological activity during REM sleep, where activity within-and-between networks activation is less constrained, possibly promoting a state of higher association and integration of information (Chow et al., 2013).

In summary, competing theories for sleep are not mutually exclusive, and likely characterize complementary memory functions ongoing during sleep, as evidenced by both selective potentiation (e.g., Chauvette, Seigneur, & Timofeev, 2012) and synaptic downscaling (e.g., Bushey, Tononi, & Cirelli, 2011; Gilestro, Tononi, & Cirelli, 2009) observed from sleep. Recent theories have sought to articulate the dual effects of reactivation potentiation and downscaling as previously discussed (e.g., The "Boom and Bust" model; Frank, 2015). However, no studies have provided evidence to support both processes taking place in parallel. While the investigation of how sleep supports different types of memory has led to many advances, it has also resulted in a fractured landscape of disparate results that are difficult to summarize in one unified theory. One way forward is to study the role of sleep in memory processing in terms of how sleep acts on both the neural representation and also the behavioural manifestation of these representations. For the final sections of this introduction we will turn the discussion to how previous research has focused on mapping distinct sleep states on dissociable memory systems and the developments beyond such a simplified perspective of sleep and memory. Thus, setting the necessary context to frame the questions and aims of the present study.

Chapter 3 – Memory Systems and Sleep

Declarative and Procedural Memory Systems

A traditional distinction in long-term memory from a neuropsychological perspective is between declarative and non-declarative memory systems (Graf & Schacter, 1985; Peigneux et al., 2001; Squire & Zola, 1996; Tulving, 2002). Declarative memory refers to both semantic (i.e., associations or facts) and episodic knowledge (i.e., events). Declarative memory can be thought of as the 'what/where' type of knowledge. A key feature of declarative memory, is that it is knowledge that can be articulated and recalled. It is therefore explicit in nature and is under conscious control and awareness. Classically, non-declarative memories are also referred to as procedural memories; and represent the 'how-to' type of knowledge. Procedural memories are memories for perceptual and motor skills, probabilities, as well as rule learning. Unlike declarative memories, procedural memory can be either explicitly or implicitly (i.e., unconsciously) acquired. Declarative memories are rapidly encoded (e.g., single-trial learning) and flexible whereas procedural memories are typically established gradually through repetition and are of a more rigid memory representation (e.g., 'practice makes perfect').

Both declarative and procedural memory, for the most part, rely on different neuroanatomical structures and appear to have different time-courses for consolidation. While both types of memories crucially involve thalamic and cortical connections for processing, declarative memories are dependent on the medial-temporal lobe structures, particularly the hippocampus (HPC), whereas procedural memories rely on striatal and cerebellar circuits and can be acquired without the medial temporal lobe (Doyon et al., 1997; Gilbert, 2001; Lehéricy et al., 2005; Rasch & Born, 2013). This memory system dissociation has been exemplified in amnesic and clinical neuropsychological populations (Knowlton, Mangels, & Squire, 1996; Knowlton, Squire, Paulsen, Swerdlow, & Swenson, 1996), as well as across a variety experimental and imaging studies (McDonald & White, 1993; Squire & Zola, 1996). However, recent evidence suggests that procedural and declarative memory systems are not as distinct as once thought, which is reviewed in the following sections.

The Dual-Process Hypothesis

The Dual-Process Hypothesis proposed that SWS sleep serves to support declarative memories and REM sleep supports the consolidation of procedural memory (Steffen Gais & Born, 2004; Peigneux, Laureys, Delbeuck, & Maquet, 2001; Plihal & Born, 1997; Smith, 2001). Much of the initial support for this theory came from studies evaluating the effects on pre-and post-interval memory retrieval after selectively depriving SWS or REM with awakenings during the early or later half of the night (called the 'night-half paradigm'), as well as from brain imaging studies recording (with EEG or fMRI) intervening periods sleep versus wake. Below, some classic neuroimaging and behavioural research results are briefly summarized, and serve to provide an initial overview of the relationship between sleep stages and types of learning, before moving towards a more nuanced and perhaps more powerfully predictive models of sleep and memory systems, and ultimately towards the focus of the present study.

Declarative memory and SWS. Some of the first evidence linking SWS to the processing of declarative memory came from single and multiple neuron recordings in rodents performing hippocampal-dependent spatial learning tasks. This series of studies demonstrated that hippocampal activity observed during learning was replayed during post-task sleep (Kudrimoti, Barnes, & McNaughton, 1999; Pavlides & Winson, 1989; Wilson & Mcnaughton, 1994). This finding was replicated in human studies employing fMRI and virtual reality route-learning, in which the overnight activation of the HPC also correlated with navigation performance post-sleep (Peigneux et al., 2004). In addition to spatial learning, (Peigneux et al., 2004; Plihal & Born, 1999) other forms of declarative learning have implicated SWS in SDMC, including word-pair list memorization and paired-stimuli association tasks (Plihal & Born, 1997; Yaroush, Sullivan, & Ekstrand, 1971). The relationship between SWA in SWS was found to be a causal one. In a study by Marshall et al. (2006) they were able to potentiate SWS SWA with oscillating slow frequency (.75 Hz) direct current stimulation, which resulted in a boost in word-pair memory recall, but for not a procedural finger sequencing task. Taken together this, and much of the replay/reactivation evidence previously cited (see Chapter 2- The Active System Consolidation Hypothesis: Sleep is for reactivation), have served to establish SWS as a state

essential for supporting the consolidation of declarative memories.

Procedural memory and REM. With regards to fine motor or sensorimotor skill learning, classical procedural learning paradigms that have been associated with increases in REM include motor adaption tasks such as mirror tracing (Plihal & Born, 1997; Smith, Nixon, & Nader, 2004), rotary pursuit, and finger tap sequencing (Fischer, Hallschmid, Elsner, & Born, 2002). REM-recruiting perceptual tasks include the visual discrimination task (Karni, Tanne, Rubenstein, Askenasy, & Sagi, 1994; Stickgold et al., 2000) and visual adaptation with prism glasses (De Koninck & Prévost, 1991, although cf.; Allen, Oswald, Lewis, & Tagney, 1972; Zimmerman, Stoyva, & Reite, 1978). Reasoning and complex rule learning have also been associated with REM sleep, in tasks such as the Tower of Hanoi (Smith et al., 2004). Finally, probabilistic learning represents another form of procedural learning, where sets of associations are complex, not completely deterministic, and as such, information must be accrued across many trails. The weather prediction task (Djonlagic et al., 2009; Knowlton, Squire, & Gluck, 1994) and artificial grammar learning (Gómez, Bootzin, & Nadel, 2006) are examples of probabilistic learning and have been associated with recruiting REM sleep activity, leading to hypotheses that REM sleep serves to integrate and extract rules from these structures and types of learned information.

Of particular relevance to this study are some of the early imaging studies of the serial reaction time task (SRTT). The SRTT is a classic and extensively used visual-motor sequencing task which has been employed to explore the acquisition and processing of implicit procedural memory (Cleeremans & McClelland, 1991; Destrebecqz & Cleeremans, 2001; Destrebecqz et al., 2005; Fischer, Drosopoulos, Tsen, & Born, 2006; Fu, Bin, Dienes, Fu, & Gao, 2013; Fu, Fu, & Dienes, 2008; Jiménez & Vázquez, 2005; Knopman & Nissen, 1987; Maquet et al., 2000; Schwarb & Schumacher, 2012; Wilkinson & Shanks, 2004). For the SRTT, a visual cue can appear at any one of four positions arranged horizontally on a computer screen. Participants have a key to press spatially corresponding to each cue location, with a designated finger assigned for each key. Participants must press the correct key as quickly and accurately as possible corresponding to where the cue appears, which across many trials results in a sequence of stimulus-response movements. Reaction time between cue onsets and keypress responses are the primary measure of the SRTT. Unbeknownst to the participant, the succession of cues follows a

pattern of either probabilistic grammar rules or a repetitive, complex and deterministic sequence. Over repeated blocks of practice, reaction times decrease as the participant unknowingly learns the pattern of sequencing. A transfer block is then administered in which the practice sequence is slightly modified, or a new sequence is presented, resulting in reaction times increases. The transfer block is followed a by re-administration of the learned sequence, in which reaction times recover to quicker speeds. This demonstrates learning specificity over general task improvements. Finally, the participants are probed for awareness, with the gold-standard of explicit sequence awareness being a verbal report. Alternatively, or in combination with the gold-standard, are behavioural tests such as cued and free generation tests, whereby the participants are asked to finish or recreate the previously learned sequence. Increasing the stimulus interval between cues (<250ms) has been shown to increase development of explicit sequence awareness, however the SRTT is typically very successful in training sequences below the level of conscious awareness (Destrebecqz & Cleeremans, 2001; Fu et al., 2008). In a series of imaging studies using positron emission tomography (Destrebecqz et al., 2005; Maquet et al., 2000; Peigneux et al., 2000, 2003), training of the SRTT with probabilistic grammar, in contrast to random sequences, was found to activate the prefrontal cortex, striatum and cuneus regions of the brain, with the striatum and cuneus areas also significantly active during REM stage of the post-learning sleep scans. Furthermore, the reactivation of learning areas in REM predicted reaction time improvements post-sleep. Thus, these studies provided initial evidence suggesting that sleep, particularly REM sleep, may play an important role in the consolidation of implicit motor sequence learning.

Reappraisal of Sleep and Memory Systems

While the results reviewed to this point lend support for the Dual Process Model, with many of these findings replicated since, as research has continued to examine different tasks and different aspects of how sleep supports consolidation in these memory systems, many results have accumulated that this explanation cannot entirely account for. A more complex understanding beyond the simple dichotic mapping of SWS-for-declarative, REM-for-procedural memory has begun to emerge, as described by the Active System Consolidation Hypothesis for example (see

Chapter 2 - The Active System Consolidation Hypothesis: Sleep is for reactivation), which take into account the nature of the memory representation and the processes supporting memory performance. Below, more recent neuroimaging and behavioural research results are briefly reviewed, re-painting over the earlier hypotheses of sleep stage and memory mapping, and illustrating the lay of contemporary sleep and memory landscape.

NREM. Largely the association between SWS, declarative memory, and hippocampal-dependent learning has held. In fact, now an impressive host of animal and human literature has arguably established SWA as necessary for the consolidation of many forms of declarative memory including verbal and non-verbal association (Alger, Lau, & Fishbein, 2012), and spatial learning as discussed throughout this work. Gaetan, Marie, Laure, & Karim (2013) recently and compelling demonstrated the tight relationship between SWA and spatial memory processing. In their study they used an *in vivo* method for online detection of HPC place-cell firing, in mice, to record and map place-cell firing during navigation of an open new environment. Firing of the mapped place-cells was then paired with stimulation of the medial forebrain bundle (a reward system in the rodent brain) during subsequent sleep. This intervention resulted in animals spending 4-5 times more time exploring the artificially created a place-preference memory post sleep, as compared to sham controls, which strongly demonstrates SWS role in spatial memory consolidation. Beyond the established role for declarative memory consolidation, currently SWS is also now believed to support synaptic homeostasis (see The Synaptic Homeostasis Hypothesis: Sleep is for downscaling) and prospective memory function (Dickson, 2010; Diekelmann & Born, 2010a; Marshall & Born, 2007; Tononi & Cirelli, 2006, 2014; Wilhelm et al., 2011).

While earlier evidence largely focused on SWS or REM, strong evidence now suggests a role for NREM2 and sleep spindles as candidate mechanisms for SDMC (see Chapter 2- The Active System Consolidation Hypothesis: Sleep is for reactivation). Contrary to the Dual-Process Model, increases in NREM2 duration and spindle density have correlated with performance improvements across a wide variety of procedural motor learning tasks. Tasks such as rotary pursuit, sequential finger tapping, and even fine-motor skill games like 'Operation' or Ball-in-cup (Fogel & Smith, 2006), have revealed performance improvements coupled increases in NREM2 and spindle activity as opposed to REM or SWS (Albouy et al., 2013; Fogel & Smith, 2006; Morin et al., 2008). Thus, more recent evidence suggests NREM2 and spindles play a role

in the consolidation of procedural memory.

However, behavioural and neuroimaging research have also emerged implicating NREM2 spindles in the SDMC of declarative memory (Fogel & Smith, 2011; Mander et al., 2014; Mander, Santhanam, Saletin, & Walker, 2011; Saletin et al., 2011; Tamminen, Payne, Stickgold, Wamsley, & Gaskell, 2010). Particularly, spindles as a mechanism for HPC-neocortical dialogue are thought to promote SDMC. As an example, Bergman et al. (2012), in a combined EEG/fMRI study, trained participants on a face-scene pairing task. During the imaging of a subsequent nap, they observed reactivations during NREM sleep of the hippocampal and neocortical brain areas known to be involved in the task. These reactivations were time locked to spindles and the strength of the reactivation co-varied with the spindle amplitudes, providing compelling evidence that spindles are involved in HPC-neocortical reactivation for declarative SDMC. In summary, spindle activity and NREM2 are now appreciated as playing unique and crucial roles in SDMC of both procedural and declarative memory. The exact neuropsychological characteristics of learning that are required and underpin the involvement of spindles and NREM2 processing has yet to be determined, and is an area of intense ongoing investigation, present study included.

REM. The factors underlying REM-dependent SDMC are less clear, and there have been many mixed results across decades of research. While previous evidence favors a role for REM in procedural but not declarative memory consolidation, the relationship between types of learning and REM SDMC are also complex, and recruitment of REM appears to be heavily dependent on task demands and conditions (Diekelmann, Wilhelm, & Born, 2009; Fogel, Ray, Binnie, & Owen, 2015). For example REM is now thought to be significant in emotional memory processing, including for emotional declarative memories (Hu et al., 2006; Nishida et al., 2009; Wagner Ullrich & Born, 2001; Wagner, Fischer, & Born, 2002). This has raised the questions of whether emotionally-charged memories are different in nature or degree from other memories, as well as tentative speculations that NREM SDMC might be particular to emotionally neutral declarative memory. Neither of these questions has yet been resolved (Alger, Chambers, Cunningham, & Payne, 2015; Rasch & Born, 2013).

As previously noted, the idea that REM ubiquitously supports motor procedural learning is not supported in light of more recent research indicating that NREM2 and spindles may provide better predictive markers of memory consolidation (Albouy, Fogel, et al., 2013; Barakat et al., 2013; Fogel & Smith, 2006; Fogel et al., 2014; Lafortune et al., 2014; Mander et al., 2014; Nishida & Walker, 2007; Saletin et al., 2011). This disparity is still an area of ongoing research. Seemingly, what appears to account for recruitment of NREM or REM are the level of complexity of the procedural learning, and the level of skill mastery. Factors involved in the complexity of learning include the length and difficulty of skill (e.g. longer and more challenging motor sequences), and whether the learning occurs explicitly or implicitly (Robertson et al., 2004). The simpler the task, and the more explicitly the learning occurs, the more likely that NREM SDMC will occur (Fogel & Smith, 2006; Robertson et al., 2004; Smith, Aubrey, & Peters, 2004). The current understanding of this relationship is that the more explicit in nature the learning is, the more hippocampal activity is subtending to both the acquisition and subsequent enhancement of the memory during consolidation (Robertson et al., 2004; Yordanova et al., 2008). On the other-hand, when the procedural learning is more cognitively complex, REM sleep consolidation is hypothesized to primarily play an integrative (rather than direct enhancement *per se*) role for consolidation (Barsky, Tucker, & Stickgold, 2015; Fogel, Smith, & Cote, 2007; Peters, Smith, & Smith, 2007; Smith, Aubrey, et al., 2004; Smith, 2001). This is to say that recruitment of REM is related to the difficulty of a task, which may be task-dependent, related to initial skill level, or to (un)familiarity of task demands. Then, depending on the amount of prior experience, REM is involved in the reorganization and integration of schemas (i.e., pre-existing knowledge representations); such that if a new schema needs to be built for unfamiliar complex information, REM will be recruited (Lewis & Durrant, 2011; Peters et al., 2007).

Dynamics and Interactions of Memory Systems and Sleep Stages in Procedural Learning

To isolate learning in terms of single memory systems, or link a process of memory consolidation by a single stage of sleep is often difficult, if not impossible, to do even in tightly controlled laboratory settings. Learning and consolidation are both complex and dynamic

processes, and this seems particularly true for procedural memories, which may account for many discrepancies particular to the procedural learning and sleep literature over the years (Albouy, King, Maquet, & Doyon, 2013; Rickard, Cai, Rieth, Jones, & Ard, 2008; Song, Howard, & Howard, 2007). As an example, a recent study by Fogel, Ray, Binnie, and Owen (2015) demonstrated that across days of mastering the Tower of Hanoi, a classic procedural reasoning task, NREM and spindle activity was increased during the initial days of learning. Then at the end of training, after the sessions when the participants had peak performance and mastery of the task, significant increases where observed in overnight REM duration, and changes in the quality of NREM spindles were observed. These results suggest that the nature of a memory and SDMC change over time, and that likely both NREM and REM work together (as per Active System Consolidation Hypothesis) in a complementary sequential fashion over multiple nights to fully serve memory processing (Diekelmann, Wilhelm, Wagner, & Born, 2013; Lewis & Durrant, 2011). Furthermore, an understanding of learning and SDMC as dynamic, ongoing processes carries implications for the careful consideration of study design and interpretation. Factors such as baseline proficiency and acquisition rates of skills, or previous task-related experiences may alter the timeline and observations of sleep-dependent effects across different methodological approaches (such as single or multiple nights of training and recording).

At present, procedural learning in even the most classic laboratory procedural tasks, such as the sequential finger tap and SRTT, are understood to involve multiple memory systems encoding different aspects of information across both distinct and shared networks over the course of training (Schendan, Searl, Melrose, & Stern, 2003; Willingham, Salidis, & Gabrieli, 2002). A recent series of behavioural and imaging studies (Albouy, King, Maquet, & Doyon, 2013; Albouy et al., 2008, 2015; Albouy, 2013) have demonstrated that, during visuo-motor sequence learning, both striatal and hippocampal networks are recruited, and interact competitively across training sessions. Their results have revealed a competitive interaction, whereby the hippocampus is primarily active early in MSL, and across training, as performance becomes more automated, hippocampal activation is reduced in favor of striatal activation (Albouy, King, et al., 2013; Albouy et al., 2008). Thus, across learning, different neural substrates are differentially recruited.

Central to the present work, Albouy et al. (2013) behaviorally dissociated spatial and motor components from a learned simple motor sequence. The spatial representation, which is variously referred to as the "extrinsic", "effector-independent", or "allo-centric" representation (Albouy, et al., 2013; Cohen, Pascual-Leone, Press, & Robertson, 2005; Wiestler, Waters-Metenier, & Diedrichsen, 2014; Witt, Margraf, Bieber, Born, & Deuschl, 2010), refers to the sequence of events mapped in space and time, regardless of body part or orientation involved. On the other hand, the motor representation, also referred to as "intrinsic", "ego-centric", or "self-referent" representation, refers to the sequence as understood in terms of the series of muscle movements. In order to assess the strength of each representation participants were trained with a response pad on a short explicit finger tapping sequence (Albouy, Fogel, et al., 2013). After training on a particular sequence the response pad was turned upside-down, thus switching keypad and hand coordinates. Participants then performed a sequence that was the same finger motor movements as the training sequence, which resulted in different spatial sequencing of keypresses, or performed a sequence that preserved where, spatially, the sequence events occurred but which consequently resulted in a different sequence of movement finger movements, relative to the initial training sequence. They found that, after a nap, gains in performance were limited to the spatial representation performance, and that these gains were related to the amount of NREM2 and spindle activity during the nap. In contrast, the motor representation sequence performance was merely maintained, independent of an interval of sleep wake. Thus, this behavioural dissociation indicated that the acquisition and consolidation of motor sequence memory involves two distinct mechanisms for cognitive spatial and motor representations, which also rely differentially on distinct neural substrates and on sleep for consolidation.

To investigate the neural underpinnings supporting each cognitive representation, Albouy et al. (2015) conducted a follow-up study replicating their previous results but with the inclusion of fMRI imaging and functional connectivity analyses of task performance. In doing so they further characterized the competitive interaction between striato-cortical and HPC-cortical systems during initial sequence learning (Albouy, King, et al., 2013). They observed that the motor-referent performance was dependent on striatal-cortico recruitment, and the spatial-referent performance was dependent on the HPC-cortico network recruitment. Striatal activity was observed to be negatively related to offline gains in the spatial representation performance. In

contrast, HPC activity was related to performance improvements, but only after the post-training nap (as opposed to an equal period of quiet wake). Collectively, these results indicate that that the HPC and the striatum support, respectively, the spatial (allocentric) and motor (egocentric) representations of a motor sequence during the learning process, with hippocampal activity related to SDMC. This is in alignment with previous literature implicating hippocampal and associative cortical networks in spatial coordinate response learning (Bohbot, Lerch, Thorndycraft, Iaria, & Zijdenbos, 2007; Doeller, King, & Burgess, 2008; Iaria, Petrides, Dagher, Pike, & Bohbot, 2003) and sleep-dependent consolidation (Albouy et al.,2013; Cohen, Pascual-leone, Press, & Robertson, 2005; Ferrara et al., 2008; Witt et al., 2010). This is also consistent with literature implicating striatal and motor-cortical network recruitment for motoric aspects of skilled MSL, and a sleep-independent stabilization of motor memory traces over time (Doyon, Bellec, et al., 2009; Doyon, Korman, et al., 2009; Hikosaka, Nakamura, Sakai, & Nakahara, 2002; Nakahara, Doya, & Hikosaka, 2001; Nettersheim et al., 2015).

Importantly, these studies (Albouy et al., 2015; Albouy, Fogel, et al., 2013) explored simple procedural motor learning, and employed the Sequential Finger Tapping task to explore the brain and behaviour properties of this type of learning. The SRT, which is a classic motor sequence learning task, requires participants to tap out an explicitly known short (5-item) sequence. Whether these same dynamic interactions occur in more complex, implicitly learned sequences, is unclear and could resolve existing controversies in the literature concerning whether sleep actively consolidates implicit motor sequence learning (Cohen, Pascual-leone, et al., 2005; Destrebecqz et al., 2005; Fischer et al., 2006; Maquet et al., 2000; Peigneux et al., 2003) or not (Keisler, Ashe, & Willingham, 2011; Nemeth et al., 2010; Nemeth, Csabi, Janacsek, Varszegi, & Mari, 2012; Pan & Rickard, 2015; Song, Howard, & Howard, 2007; Song, Howard, Howard, et al., 2007). It is this question which brings us to the focus of the current investigation.

Chapter 4 – Focus of the Present Study

The previous chapters provide evidence suggesting that memory processes are dynamically subtended to by multiple neural systems and across multiple states, including wake, sleep, and particular stages and features of sleep. Depending on the type of information and conditions under which the learning occurs, factors such as the complexity of the information, whether the learning is conscious and intentional, levels of motivational or emotional salience, or whether there are spatial or motor aspects – determine the recruitment of different neuro-substrates during acquisition, memory consolidation, and memory retrieval. In summary, and with regard to MSL, when the motor skill is simple and explicitly known, a hippocampal-dependent spatial representation is behaviourally dissociable, as is a motor movement-based striatal-dependent representation. Enhancement of the spatial, but not the motor cognitive representation, is sleep-dependent, an effect which may also underlie and account for the considerable host of studies describing SDMC of MSL enhancement after a period of sleep. However, while there is a strong case for explicit MSL, the literature is far more disparate with regards to implicit MSL SDMC.

Does Sleep Consolidate Implicit Motor Sequence Learning?

At present, there is little consensus about whether newly learned implicit motor sequences are enhanced over a period of sleep as compared to wake. While some earlier studies using classical tasks, such as the SRTT, have provided evidence of SDMC for implicit motor learning, describing behavioural gains as well changes in sleep related activity via electrophysiology and neuro-imaging (Maquet et al., 2000; Peigneux et al., 2000, 2003), other studies question the extent to which sleep plays a role in the consolidation of implicit MSL (Meier & Cock, 2014; Nemeth et al., 2010, 2012; Pan & Rickard, 2015; Song, Howard, & Howard, 2007). In addition, other support for SDMC of implicit sequence learning comes from studies conducted by Cohen, Pascual-leone, et al. (2005) and Fischer, Drosopoulos, Tsen, and Born (2006).

Cohen, Pascual-leone, et al., (2005) trained participants on a deterministic sequence SRTT protocol, then tested SRTT performance on the untrained hand with either a spatially preserved sequence, or a motor movement preserved sequence across a period of sleep or wake. They observed that motor-preserved performance was enhanced over the course of the day, while spatially preserved performance was enhanced over a period of sleep. Also using the SRTT paradigm, Fischer et al. (2006) examined whether a period of sleep versus wake facilitates the development of awareness of implicitly learned motor sequences, as has been shown to occur for other types of implicit learning such as for rule (Wagner, Gais, Haider, Verleger, & Born, 2004; Yordanova et al., 2008), inferential (Ellenbogen et al., 2007), grammar learning (Gómez et al., 2006), and gist extraction (Payne et al., 2009). To measure changes in awareness of the trained sequence after an interval of sleep or wake, participants completed a generation task where they were asked to recreate the previously learned sequence (Fischer et al., 2006). No increase in SRTT performance (i.e., reduction in reaction times) was identified across either consolidation interval. However, a gain in explicit awareness was observed after sleep, but not wake, indicating a significant increase in the participants' ability to correctly generate the training sequence following sleep. In contrast, across an interval of wake, sequence generations remained at chance. This has been taken to indicate that SDMC operates on implicit MSL to the end that it develops explicit awareness of implicitly learned motor sequences.

Other studies using a modified version of the SRTT, the Alternating Serial Reaction Time Task (ASRT; Howard & Howard, 1997), have challenged whether SDMC occurs for implicit sequence learning (Meier & Cock, 2014; Nemeth et al., 2010; Song, Howard, & Howard, 2007). The ASRT employs a deterministic sequence interleaved with a randomly occurring stimulus cue, such that if the sequence were 1-2-3-4, the sequence of stimuli would be 1-R-2-R-3-R-4-R, where R represents a random element (1-4). The ASRT was designed to better control for the development of explicit awareness compared to purely deterministic sequences, and to separate out general skill learning from sequence-specific learning by examining response performance on random and sequence items. Across ASRT studies, gains in general skill but not sequence-specific skill were observed after an interval of wake. No improvements in general skill or sequence specific skill were observed across a night of sleep in young (Meier & Cock, 2014; Song, Howard, & Howard, 2007) or old adults (Nemeth et al., 2010). Thus, these results have suggested that implicit MSL is a process completely independent of sleep.

Here we propose that a potential underlying factor, which may elucidate whether sleep is involved in memory consolidation of implicit-learned motor sequences, is the level of engagement of hippocampal and striatal activity recruited across learning (Nemeth et al., 2010; Robertson et al., 2004; Spencer, Sunm, & Ivry, 2006); which, at the cognitive and behavioural level, would be indicated by performance differences of dissociated spatial and motor representations of an implicitly learned visual-motor sequence. Importantly, neuroimaging evidence indicates that implicit MSL, similar to explicit MSL, also initially recruits hippocampal activity in addition to the more established striatal network involvement (Albouy et al., 2008; Cohen et al., 2005; Poldrack et al., 2001; Schendan et al., 2003; Willingham & Goedert-Eschmann, 1999). The rationale building from this is that the same interactions between dissociable spatial and motor representations and sleep, as described by Albouy et al. (Albouy, King, et al., 2013; Albouy et al., 2008, 2015; Albouy, Sterpenich, et al., 2013), may likewise be characterised in the unconscious learning of more complex motor sequences. An evaluation of this proposition may help to better understand and account for the nature and extent of SDMC for implicit MSL.

Experimental Aims of the Study

The present work aimed to explore a specific interaction between implicit learning and sleep, and answer the question - *does sleep enhance the explicit awareness and generalization of an implicitly learned motor sequence*? More specifically, the overall aim of this study was to investigate whether sleep would differentially facilitate dissociable spatial and motor-referent cognitive representations of implicitly learned visual-motor sequences, as has been observed in the case of explicit visual-motor sequence learning. In this way, this would allow us to ascertain whether the SDMC of the spatial representation was associated with sleep-dependent development of conscious awareness and skill transfer across hands.

The current study employed a modified version of the SRTT, with a manipulation based on Albouy, Fogel, et al., (2013), whereby spatial and motor representations could be behaviourally dissociated from an initial training sequence. Awareness over time was assessed by a combination of self-report, sequence recognition, and sequence generation tasks, with the latter

also used to probe skill generalization across hands. To test sleep versus time-dependent effects of offline consolidation and awareness change, measurements were taken before and after either night of sleep or a across a day of wake, as well as one week after training. EEG recordings were taken during overnight intervals to characterise the learning-dependent changes in sleep, and sleep features associated with post-sleep changes in task performance. Following from this approach were six experimental hypotheses:

Hypothesis 1. Similar to explicit MSL, implicit sequence learning would demonstrate behaviourally dissociable spatial and motor components.

Hypothesis 2. Only the spatial representation would show sleep dependent gains in performance, while the motor representation would show gains across wake.

Hypothesis 3. As compared to a novel sequence, the implicitly learned sequence would be recognized as highly familiar, and if sleep is specifically involved in consolidating the spatial representation (e.g., Hypothesis 2), the spatial component of the sequence will be rated as more similar to the training sequence than the motor representation.

Hypothesis 4. The performance gains in the spatial component of the task will be associated with an increase in awareness of sequence knowledge, specific only across intervals containing sleep. This would be reflected in better sequence generation performance and increases in the similarity ratings for the both the training sequence and spatial-representation sequence across sleep but not wake.

Hypothesis 5. Sleep dependent gains in the spatial representation will generalize into spatial-referenced sequence generations when skill transfer is tested across hands.

Hypothesis 6. The increases in spatial representation performance and awareness post-sleep would be associated with increases in sleep spindle characteristics such as spindle density, duration, and amplitude.

METHOD

Ethics

All participants gave informed written consent. This research was approved by Western University's Research Ethics Board. Participants were compensated financially for study participation.

Participants

Participants between the ages of 20 to 35 were recruited through advertisements posted around the university campus. An initial telephone interview was used to exclude participants for left-handedness (Edinburgh Handedness Inventory, Oldfield, 1971), hand mobility problems, atypical sleep patterns (sleep time outside the approximate hours of 10:00PM to 9:00 AM), shift work, head injury, regular cigarette smoking, use of medications known to affect sleep, and history of chronic pain. In addition, participants with professional training as a musicians or typists were excluded. Participants were required to abstain from drug use, caffeine, nicotine, and alcohol at least three days prior to, and throughout the duration of the study. Participants were asked keep consistent sleep routines throughout the study duration, which was confirmed by Actiwatch and sleep diaries.

Participants who met the criteria of the telephone interview (see Appendix B) underwent a sleep disorder screening night, during which standard polysomnographic recordings (including electroencephalogram (EEG), electrooculogram (EOG) and electromyogram (EMG); see Physiological Recordings) were obtained and subsequently analysed for the presence of sleep disorders. Additionally, in order to ensure normal sleep-wake patterns and signs of conditions that might interfere with sleep (e.g., anxiety and depression), all participants were asked to fill out the Sleep Disorders Questionnaire, the Napping Behaviour Questionnaire, Beck Depression (Beck et al., 1974) and Anxiety Inventories (Beck et al., 1988), Epworth Sleepiness Scale (Johns, 1991), The Horne-Ostberg Morningness-Eveningness Questionnaire (Horne and Ostberg, 1976;

see Appendix A for questionnaire battery). For participants assigned to the experimental condition with multiple overnights in the lab, the screening night also served as an acclimatization night (see Experimental Design, Figure 3).

Fifty-one participants met the criteria for the study. Of this, seven participants dropped out after prior to completing the study. One participant was excluded for a history of depression (identified after screening), and another for failing to comply with directions throughout the study. Two participants did not complete the final retest session, but had completed the control and first experimental session. Their data was included for these sessions, with missing data from the final session generated with multiple imputation (see Results). Thus, data from 42 participants (female $n = 28$) between 20-35 years of age ($M = 22.9$, $SD = 3.3$) were included in the analyses. Of these, 20 were assigned into the overnight interval experimental condition (SLEEP condition), and 22 were assigned to the across-day, wake-interval, testing interval (WAKE condition).

Behavioural Tasks

Serial Reaction Time Task. The Serial Reaction Time Task (SRTT; Nissen & Buller, 1987) is considered a classic implicit sequence learning paradigm. In the present study, learning performance was assessed using a modified version of the SRTT coded in MATLAB 2014a (Mathworks) using Psychtoolbox-3 (Brainard, 1997; Kliener et al. 2007). The task (Figure 2, panel A) display consisted of four horizontally arranged boxes on a black screen. The keypad was programmed so that each key corresponded to the location of one of the squares onscreen, such that if the keypad was placed face up on top of the table and being handled with the left (non-dominant) hand: the pinky finger would be on Key 1 and correspond to the leftmost box and the index finger would be on Key 4 and correspond to the rightmost box. If the keypad was placed underneath the desk, oriented upside down and being handled with the right hand then the pinky finger would be remain on Key 1 but now correspond to the right-most box, and the index finger would be on Key 1 but correspond to the leftmost box. In this way, with regards to where the keypad was placed (upside or underneath the table) the leftmost key always corresponded to the leftmost box, and rightmost key rightmost box, maintaining spatial alignment between

buttons and screen cues. In a 25 sec rest interval before each block, directions were displayed onscreen instructing where to place the keypad and which hand to use (e.g., "Left Hand/Keypad Up"). Participants were given a wrist support to prevent fatigue when completing blocks with the keypad on the table underside. Participants were video monitored to ensure compliance with the task instructions.

For the SRTT participants were instructed to "respond as quickly and accurately as possible" to the appearance of a yellow '*' cue, by pressing the corresponding key to which square the cue appeared in (Figure 2, panel A). The cue remained until one of the four keys were pressed, after which, the cue would disappear and then reappear in one of the four squares after a 120ms inter-stimulus interval. Unbeknownst to the participants during SRTT training blocks there was a repetitive underlying pattern determining the location of the cue. Auditory feedback was only was given if the incorrect key was pressed, by the sounding of a short tone.

The position where the cue appeared, the identity of the participant keypress, whether the key pressed was correct or not, and the reaction time between cue onset and the keypress were recorded. Decreases in average reaction time across SRTT blocks of training on a repetitive sequence indicates the extent that sequence knowledge has been acquired. Reductions in reaction times considered to be indicative of improvements in sequence learning, rather general task improvement, by the presentation of an SRTT block containing a novel sequence which results in an increase-to-baseline of reaction time performance.

SRTT Sequences. Two second-order 12-item sequences (Seq1 = 3-4-2-3-1-2-1-4-3-2-4-1; Seq2 = 3-4-1-2-4-3-1-4-2-1-3-2), and their mirror equivalents (respectively; Seq3 = 2-1-3-2-4-3-4-1-2-3-1-4 ; Seq4 = 2-1-4-3-1-2-4-1-3-4-2-3) were selected as the four possible sequences that could be assigned to train on. Each participant was assigned to only one of these sequences for 13 training blocks, with the keypad either on or underneath the desk, for a total of 8 sequence training conditions that any participant could be assigned to (4 Seqs, 2 keypad training locations; total of 8 training assignment conditions). Every block of the SRTT was comprised of eight repetitions of the assigned 12-item Seq (96 cues per block), with the blocks starting at a random point within the given sequence. For these second-order sequences the location of where the cue appears were completely determined by the previous two locations. Sequences were balanced for frequency of cue location, frequency of transitions between locations, and did not contain back-

to-back location repeats (e.g., 3-3) or consecutive "rolls" across all four keys (E.g., 4-3-2-1). Seq1 and Seq2 only differ in the second-order conditional structure such that each triplet within the sequence ends on a different location (E.g. Seq1 = 3-4-1…, Seq2 = 3-4-2…). The sequences were selected for these qualities and their use in existing literature (Fu et al., 2008; Reed & Johnson, 1994). The SRTT control session (i.e., no-learning) blocks were created by ordering eight randomly shuffled 12-item sequences (96 cues per block), while controlling for back-to-back repeats, section repetitions, distribution of keypresses, and across-key rolls.

SRTT Representation Testing. The representation test sections of the experiment consisted of four different SRTT blocks (96 cues per block; 25 sec rest intervals between blocks), with each block repeating one of the following sequences: the one of the sequences assigned for repetitive training sequence (Trained), an unfamiliar sequence (Other) which was the other equivalent sequence not assigned for training (i.e., if Trained = Seq1, Other = Seq2), a spatially but not motor movement preserving sequence (Spatial) of the training sequence, and a motoric but not spatial preserving sequence (Motor) of the training sequence. Trained representation testing blocks utilized the same sequence as training with the keypad placed on same side of the table as during SRTT training blocks. Other blocks required the keypad to be in the same orientation as the assigned training condition, however the sequence throughout the block did not contain any of the same triplets as their assigned sequence. For Spatial and Motor blocks the keypad was placed on the opposite side of the desk surface as compared to training (i.e., if training had the keypad table upside, then Spatial/Motor would have the keypad placed table underside). For the Spatial block, the cues appeared the same spatial locations onscreen as the training sequence but the sequence of finger movements was now different, centrally inverted, because the key-to-location response contingencies were remapped to maintain spatial alignment (see Serial Reaction Time Task). For the Motor block, participants responded to a spatially inverted version of the sequence, which then preserved the pattern of sequential finger movements as the training sequence but not the same on screen spatial pattern (Figure 2, panel B).

The representation test blocks (Trained, Other, Spatial, Motor) isolate and probe the strength of different representations, with Spatial and Motor only preserving either the spatial or motor component relative to the training sequence, and Other sharing as few transferable components as possible with the training sequence (while controlling for length, frequency and distribution of

locations). In this manner, spatial and motor representations could be dissociated by performance with the same hand and evaluated across retention intervals of time relative to the performance of trained and untrained sequences. The blocks of the representation testing were pseudo-randomly assigned so that the Trained block was tested third. This was in order to demonstrate a drop, and then recovery in performance when retested on the training sequence, to demonstrate performance changes were specific to learning and not due to general task practice effects.

Awareness Report. Immediately following the training session of the SRTT participants were asked: "Do you believe there was an underlying rule or pattern determining the training series." Responses were made to the keyboard face up and with their right hand (Yes = 4, No = 3). Subsequently, on-screen their answer was re-iterated, either as; "Yes the training series was determined by a pattern/rule" or "No - the training series was random" depending on their previous selection. They were then asked, "How confident are you of this?" (4 = Not at all (0%), 3 = Unsure (25%), 2 = Fairly Certain (75%), 1 = Absolutely Certain (100%)). If a participant indicated "Yes" there is a pattern with either 75 or 100% certainty, they were asked to call in the experimenter who probed the participants for a verbal description of what they believed the sequence to be (see Appendix A for Explicit Awareness Report the responses are recorded on). Pending the awareness probe, all participants were then informed that there was indeed a repeating sequence throughout the entirety of the training blocks. They were not, however, informed as to what the repeating sequence was.

Generation Task. After participants were informed that they were trained on a repeating sequence, they were asked to generate a series of responses that were as similar as possible to the training sequences (i.e., 'inclusion generation'), as well as, generate a series of responses that were as explicitly different as possible to the training series (i.e., 'exclusion generation'). The generation blocks consisted of two initial cues that the participant had to respond to as in the typical SRTT, by pressing the corresponding key where the cue appeared, then from the two starter cues proceed to create a series of 13 subsequent responses congruent with the instructions of that block (inclusion vs exclusion) with the '*' now appearing in the locations corresponding to keypresses (Figure 2, panel C. Each block consisted of seven sets of these series generations, with a different cue pair starting off each set (13 responses per set, seven sets, 91 responses total for each of inclusion and exclusion). Notably, this block design differs somewhat from previous

versions of the free generation task. In other generation tasks, after a short cue subjects go on to complete a full series of 91 item presses. In this version the 91 responses are broken up across a series of subset each with different cued starts. The reason for incorporating this break-up was twofold. First, this method is more likely to prevent over-repetition of partial sequence knowledge, insofar as starting cues at different points in the training sequence is likely to reduce over-repetition of sequence fragments. Second, while still allowing for measures of free generation performance, cued recall memory performance can also be measured by examining the first few responses immediate after the set cues.

In both inclusion and exclusion generation blocks participants were explicitly told to avoid generating in the same location twice (or more) in a row, not to make rolling transitions across the keypad (I.e., 4-3-2-1, 1-2-3-4), to be as non-repetitive as possible within response sets (e.g. avoid making a response like 3-2-1-3-2-1), and encouraged to make choices that came most naturally to them. Participants were also informed that this section of the experiment was not timed. Inclusion and exclusion blocks were performed by both right and left hands, with the keypad in the same orientation is training (up versus under), for a total of four generation blocks (one inclusion and one exclusion block per hand) with the keypad placed in the same orientation (up or under) assigned for training blocks, in a randomly assigned order.

The inclusion and exclusion blocks performed by the trained (i.e., left) hand together are considered a process dissociation procedure (Destrebecqz & Cleeremans, 2001; Jacoby, 1991); a technique used to assess extent that learned sequence knowledge exists as conscious versus unconscious knowledge. Under inclusion instructions, the amount of sequence responses congruent with the assigned training sequence is taken to indicate the level of explicit awareness of the sequence. However, as Destrebecqz and Cleeremans (2001) have previously noted that this score does not purely measure explicit awareness of the sequence, as performance is contaminated by the influence of implicit knowledge. On the other hand, the exclusion block is thought to be a direct measure of implicit knowledge. If the participant generates sequence triplets congruent with sequence of training, despite directions not to, this indicates that they have acquired the knowledge but cannot exert conscious control over it. Thus, taken together the inclusion and exclusion tasks provide a more sensitive measure of how explicit the sequence

knowledge is at a given time point throughout the study than purely inclusion generation instructions.

The generation task for the control session consisted of only two blocks, one per hand, with the keypad in the same orientation as the preceding baseline session SRTT. Given the same set of rules to follow as during inclusion and exclusion blocks (no repeats, rolls…etc) the control session generation task only differed in that the participants were naive to the testing and training sequencing and were asked to generate their own novel sequence within the aforementioned constraints.

Similarity Report. For post-training SRTT representation tests, after each block participants were instructed to place the keypad on the top of the table, and with their right hand respond to "how similar did that last round feel compared to your training series?" by pressing the key which corresponded to their answer (4 = Nothing in common, 3 = Mostly Dissimilar, 2 = Very Similar, 1 = Identical). Following this, their decision was re-iterated onscreen and they were asked to rate the confidence level associated with their choice (4 = Not at all (0%), 3 = Unsure (25%), 2 = Fairly Certain (75%), 1 = Absolutely Certain (100%)). These similarity reports were taken as a measure of familiarity and recognition memory.

Psychomotor Vigilance Task. The Psychomotor Vigilance task (PVT) was used as an objective measure of sustained vigilance (Dinges & Powell, 1985). The PVT is a simple reaction time test, whereby participants must respond as quickly as possible to a visual cue presented at a random interval (between 2 and 10 seconds) with a keypress. Participants performed 60 trials, taking approximately 8 minutes to complete. The PVT is used in this study to indicate vigilance at different times during the day and across experimental sessions.

Physiological Recordings

Embla Titanium (Natus, San Carlos, CA, USA) PSG systems were used to perform in-laboratory sleep recordings. Physiological data were recorded at a sampling rate of 512 Hz, with a high pass filter = 0.1 Hz and low pass filter = 220 Hz. EEG, electrooculogram (EOG), and electromyogram (EMG) recordings were taken using gold-plated electrodes applied to the skin. EEG and EOG

(from the left and right outer canthus of the eye) were recorded and re-referenced offline to the contralateral mastoid derivations (M1 and M2). The EMG (submental chin muscles) channel was recorded as a bipolar derivation. Scalp EEG were placed according to the international 10-20 system. Sleep stages were scored in 30 seconds intervals accordance with standard criteria (Iber et al., 2007) using RemLogic analysis software (Natus, San Carlos, CA, USA).

Screening Night. The screening night recordings included EMG, EOG, and EEG electrodes on the face and scalp (locations: Fpz, Fz, Cz, Pz, Oz, M1, M2), as well as PSG measurements of respiration (via thorax and abdomen respiratory belts), electrocardiographic activity (via electrodes placed on the surface of the skin below each clavicle), leg muscle activity (via electrodes placed on the surface of the skin on the anterior tibialis muscle of each leg) and blood oxygen saturation (via a finger probe placed on the index finger of the left hand). Recordings were scored by an expert registered polysolmnographic technician (lab technician LR, see Acknowledgments) according to clinical scoring guidelines (Iber, Ancoli-Israel, Chesson, & Quan, 2007).

Overnight Experimental EEG. The montage included EMG, EOG, and EEG electrodes placed at Fpz**,** F3, Fz, F4, C3, Cz, C4, P3, Pz, P4, Oz, M1, and M2. Sleep stage scoring was performed offline by an experienced sleep EEG scorer (author JV), trained to >90% inter-rater reliability by resident expert scoring (LR). Scoring was in accordance with standard R&K sleep stage criteria (Rechtschaffen and Kales, 1968) which includes wake, nREM sleep stages 1,2,3,4, and REM sleep. NREM stages 3 and 4 were combined into the broader category of slow-wave sleep. Detection of sleep spindles was performed using in-house EEGlab (Delorme & Makeig, 2004) compatible software written for Matlab R2014a (Mathworks Inc, Natick, MA, USA). The spindle detection was performed at Cz with EEG data initially down-sampled to 128 Hz and extracted from movement artifact-free, NREM sleep epochs. The detection method (Fogel et al., 2014; Ray et al., 2015), used a complex demodulation transformation of the EEG signal with a bandwidth of 5 Hz centered about a carrier frequency of 13.5 Hz. Each data point was transformed into z-scores using the mean and the standard deviation derived from a 60 s sliding window. Events (spindle onsets, peaks and offsets) were then detected on the transformed signal with a z-score threshold of $z = 2.33$. The variables of interest extracted from this method include

spindle peak amplitude, spindle duration, peak frequency and spindle density (number of spindles per-minute of NREM sleep).

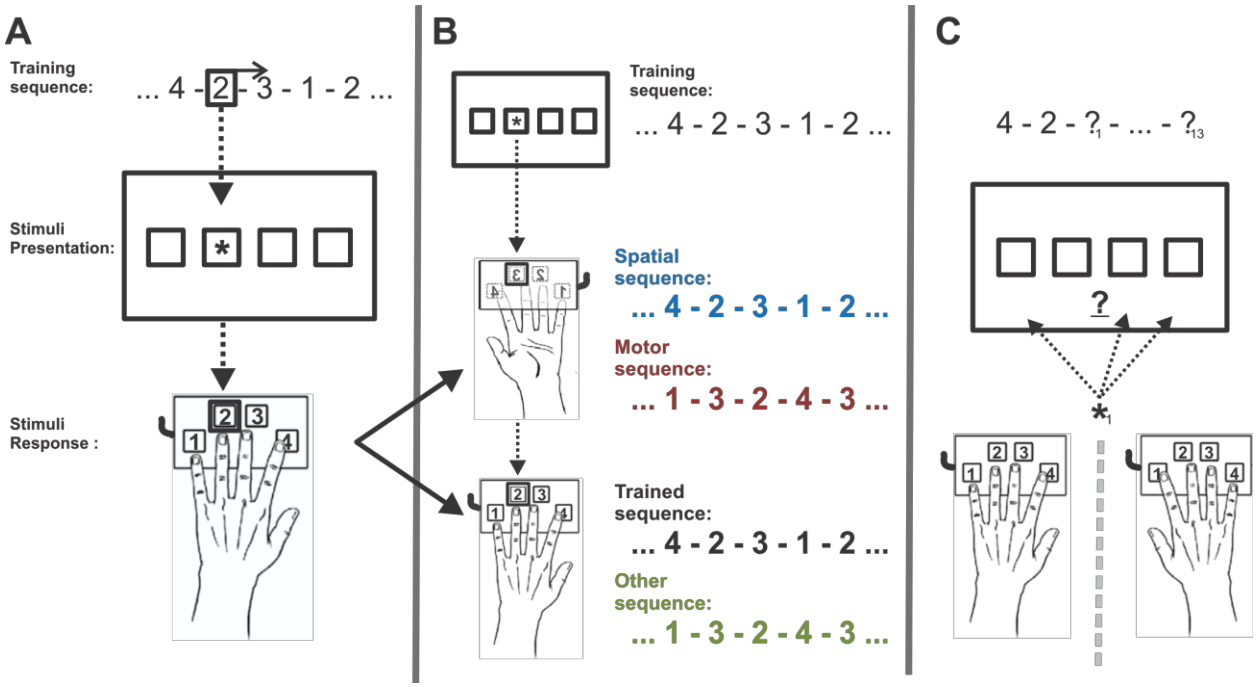


Figure 2. Behavioral tasks. (A) Serial Reaction Time Task (SRTT). A 12-item repeating pattern determines the series of locations an asterisk cue will appear in. Participants must click the corresponding key as quickly and accurately as possible but are not told there is a pattern guiding where the cue appears. Reaction times decrease across blocks of training without conscious awareness or appreciation, indicating implicit learning. (B) Representation testing. Relative to the training sequence, the SRTT was performed on each of four sequences. In two blocks the keypad was upside-down relative to training. In one block the sequence of stimuli the onscreen cues were identical to training, preserving the spatial aspect of the learned sequence, but not preserving the same motor contingency of finger presses as the training sequence. Conversely, in the other block a sequence was run which preserved the motor contingency of finger presses, by having the sequence cues appear in different (inverted) spatial order on-screen. Two blocks were also performed with the keypad in the same orientation as training. One block was the same sequence as training and the other block was a different sequence. Reaction times on these four blocks were used to interpret how well and what aspects of a sequence have been learned. (C) Generation task. After following two cues participants continued to create a sequence with 13 keypresses, according to inclusion or exclusion criteria, both

with trained and untrained hands. Ability to create (inclusion) or withhold (exclusion) creating responses congruent with the training sequence indicated the accessibility and level of conscious awareness of learned sequence knowledge.

Experimental Design

Participants first underwent the screening night prior to the experimental sessions (see Screening Night for details). At this time participants were given an actiwatch and a sleep diary to monitor sleep-wake patterns for the duration of the study. After the screening data had been analyzed and participants were confirmed as eligible, they were randomly assigned to one of eight sequence training conditions (keypad up or under; SOC1, 2, 3 or 4) and either to the across day (WAKE) or across night (SLEEP) experimental group.

Participants in both SLEEP and WAKE conditions completed the same set of experimental procedures over the course of four sessions as outlined in Figure 3: Control (CN), Training (TR), Post-interval (PI), and Long-Term Retest (LT). For those in the WAKE condition CN, TR, and LT sessions, were completed in the morning between 8-10am for WAKE, and in the evening between 8-10pm for SLEEP. The PI session occurred for WAKE around 8pm, and around 8am for SLEEP. Thus, for both conditions the interval between TR and PI was approximately 12 hours, the only difference being that the interval for SLEEP contained sleep and the interval for WAKE did not. The LT session was identical to PI session testing, only it occurred exactly one week after the PI session at the same time of day as TR. Participants in WAKE condition were told to continue with their normal daily activities before returning to the lab for the IR session, but to avoid napping or engaging in activities that rigorously used their hands and fingers (e.g., "avoid more than an hour of typing or video-gaming"). Participants in the SLEEP condition had EEG recordings taken for the duration of the night (see Overnight Experimental EEG for montage). Participants in the SLEEP group were allotted between 7 and 8.5 hours of sleep and were woken up shortly after transitions out of REM sleep, or naturally occurring arousals. Both groups were administered the PVT and sleepiness scales preceding sessions.

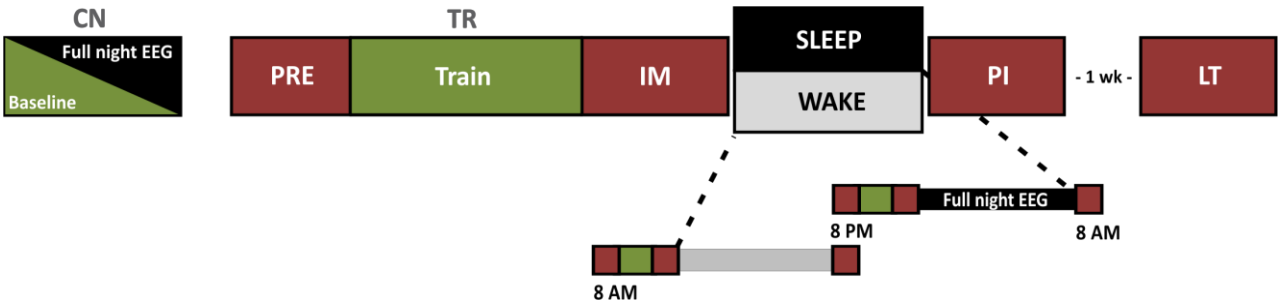


Figure 3. Experimental design. CN – Control session, PRE – Pretraining tests, TR – Training session, IM – Immediate post-training session, PI – Post-interval session, LT – Long-term session. CN consisted of SRTT with no-learning (random sequences) and a free generation task. Participants assigned to WAKE condition completed CN in the morning, whereas SLEEP completed CN in the late evening and had a baseline sleep EEG recorded. TR consisted of a SRTT representation pretest (PRE), then SRTT training of a sequence over many blocks. Participants were then probed for sequence awareness, and then informed that there was a repeating sequence but not told any further details. During IM post-testing the generation tasks were performed followed by another SRTT representation test with participants providing sequence familiarity ratings after each block. Likewise, both PI and LT consist of the generation tasks followed by SRTT representation tests and familiarity ratings. For the WAKE condition, TR and LT were performed in the morning, PI in the evening. For the SLEEP condition, TR and LT were performed in the evening, PI in the morning, with sleep EEG recorded between the TR and PI interval. LT occurred exactly one week after PI.

Control Session. The CN session was scheduled at least three days after the screening night. The CN-SRTT was identical to that of the experimental night only sequences did not contain statistical regularities or repetitive patterns (see SRTT Sequences) and served as a no-learning condition. Following the CN-SRTT, two blocks of the generation task, one per hand (7x13 cues; 182 cues total) in with the keypad in the same orientation (up versus under) as the previous CN-SRTT blocks (see Generation Task).

Training Session. The TR session was scheduled at least two days after CN. Participants first completed the four blocks of the SRTT representation test (Trained, Other, Spatial, Motor; see SRTT Representation Test) to assess pre-training performance. This was followed by SRTT training on an assigned sequence (see Serial Reaction Time Task and SRTT Sequences). After completing the training session, participants were probed for subjective awareness by an

Awareness Report (see Behavioural Tasks). Participants then performed the generation tasks (see Generation Task), and re-performed SRTT representation tests with similarity reports after each block (see Similarity Report).

Post-Interval and Long-term Retest Sessions. The PI and LT sessions were identical in task structure, with the only difference being that the PI session occurred approximately 12 hrs after TR, and the LT session occurred at the same time of day as the TR session only exactly one week later. Participants were reminded that they had previously been trained on a repeating sequence during the TR session the week before and were asked to complete the generation task, and the SRTT representation tests, providing similarity reports following each block.

Statistical Analyses

Analyses were performed using MATLAB 2015b (Mathworks Inc., Natick, MA, USA) to extracting and handle the raw behavioural data, REMlogic software (Natus, San Carlos, CA, USA) was used to sleep stage score overnight recordings, and statistical analyses were performed using SPSS Statistics (version 23, IBM Corp., Armonk, NY, USA).

Control Measures. Independent samples t-tests were performed on age and morning-ness evening-ness scores. Chi-squared tests were performed on gender and sequence assignment to evaluate homogeneity of demographic and experimental condition variables. Separate GROUP (Wake, Sleep) X SESSION (TR, PI, LT) mixed design 2 x 3 ANOVAs were conducted for Stanford Sleepiness Scale scores, Epworth Sleepiness Scale scores, and on mean PVT reaction times for each session to investigate time-of-day differences between groups for subjective sleepiness and vigilance.

Paired samples t-tests were run for sleep latency onset, morning rise time, total sleep time, and total wake after sleep to evaluate that the length and quality of sleep across CN and TR in the SLEEP group was comparable. Subjects who indicated that they were aware with 75-100% certainty during the explicit awareness probe had their verbal reports coded for accuracy based on the number of triplets and length of sequence response (see Appendix A – Explicit Awareness Report). Participants able to verbally report a sequence 9-15 items long and with at

least 75% of triplet transitions congruent with the training sequence, were deemed prematurely explicitly aware and not included in group analyses to ensure that sequence knowledge before experimental intervals was kept to be as purely implicit as possible. This control was necessary as previous research has indicated that the extent to which knowledge is implicit or explicit has consequences on the nature and time course (Cohen, Pascual-Leone, Press, & Robertson, 2005; Robertson et al., 2004; Yordanova et al., 2008).

SRTT. The first two keypresses beginning each SRTT block were removed from calculations as they alone do not contain sufficient or meaningful anticipatory information (Fu et al., 2008). Reaction times faster than 50ms (i.e., anticipatory responses) and higher than 1.1 seconds (i.e., lapses), and incorrect keypresses (i.e., errors), were removed from analyses (Schendan et al., 2003). Median reaction times were used as opposed to mean reaction times by block number because median scores are a better indicator of central tendency given positively skewed distributions, as is the case for reaction times. A SESSION (Control, Training) X GROUP (Wake, Sleep) X BLOCK (1-13blocks) mixed measures ANOVA was conducted to evaluate that improvements were particular to sequence learning and that learning achievement was comparable between groups. To evaluate the changes in cognitive representation of sequence knowledge, two-sets of mixed ANOVA's were conducted. The initial 2x2x4 mixed ANOVA was for GROUP (Wake, Sleep) X SESSION (PRE, IM) X BLOCKTYPE (Motor, Spatial, Trained, Other) to evaluate the changes in representations, and specificity of SRT learning as a result of training. A 2x3x4 mixed ANOVA, GROUP (Wake, Sleep) X SESSION (IM, PI, LT) X BLOCKTYPE (Motor, Spatial, Trained, Other), was conducted to evaluate how an interval of sleep or wake changed the strength of sequence knowledge over time.

Generation Task. Using a sliding 3-item window across generation blocks, sets of triplets were flagged as either matching: 1) the training sequence, 2) the other (non-training equivalent) sequence, as congruent with 3) the spatial, or, 4) motor components of the training sequence, or 5) none of those categories. The level of implicit versus explicit knowledge was first evaluated as per outlined in Fu et al. (2008), which is based on the process dissociation procedure (see Destrebecqz & Cleeremans, 2001) whereby a series of logical contrasts between number and type of triplets generated according to inclusion or exclusion instructions are compared. With this approach, the number of training-congruent triplets generated under the inclusion (I) was

compared to the mean number of training sequences generated under exclusion (E) conditions. The number of training sequence triplets generated was also compared to the number of other sequence triplets generated under inclusion instruction, which is considered a baseline comparison (B). If I = E and E > B, this indicates that sequence knowledge is implicit, because the sequence is being generated despite conditions. If, however, I > E and E = B, this indicates that subjects could refrain from producing the training sequence above baseline, which then is evidence of that the sequence knowledge is under conscious control and thus explicit in nature.

Implicit and Explicit Awareness. This inferential process was evaluated statistically in two ways. The first approach examined the mean number of triplets generated in the fashion described previously for trained hand performance. A 2x3x2 mixed ANOVA was conducted GROUP (Wake, Sleep) X SESSION (IM, PI, LT) X BLOCKTYPE (Inclusion, Exclusion) for mean training sequence triplets generated. This was followed by two 2x3x2 mixed ANOVAs, GROUP (Wake, Sleep) X SESSION (IM, PI, LT) X TRIPLET (Training, Other), for inclusion and exclusion block performance.

As a second approach, the difference between subjects' inclusion and exclusion performance was computed and used for analysis. This method was used primarily to explore the first three responses following the cueing as opposed to the full 13-item generation in the case that inclusion and exclusion ability was limited to the first few key presses after cuing. 2x3 repeated-measures ANOVA were ran for GROUP (Wake, Sleep) X SESSION (IM, PI, LT) on the difference of training triplets generated in inclusion and exclusion blocks. As well, these were followed by two 2x3x2 mixed ANOVAs for differences between triplet types, GROUP (Wake, Sleep) X SESSION (IM, PI, LT) X TRIPLET (Training, Other), for inclusion and exclusion block performance. These ANOVA's were run for the performance on first, second, and third responses following the set cueing, as well as for the full series of 13 responses for each block set.

Sequence representation transfer. To evaluate which representation (spatial or motor) was accessed in generalizing sequence knowledge in an across hand transfer, the mean number of spatial and motor triplets was first compared to mean number of other triplets, with 2x3x2 mixed ANOVAs, GROUP (Wake, Sleep) X Session (IM, PI, LT) X TRIPLET (Motor then Spatial, with Other), for both inclusion and exclusion instructions, and with the untrained (i.e., right) hand.

This was to determine if learned spatial or motor aspects of the trained sequenced generalized over as compared to that of an untrained sequence. Following this, 2x3x2 mixed model ANOVAs were run comparing spatial and motor triplet generation, as a GROUP (Wake, Sleep) X Session (IM, PI, LT) X TRIPLET (Motor, Spatial) analysis.

It is important to note that in other studies using the process dissociation procedure, participants are not as frequently exposed to the other sequence as in the current study, where subjects perform the other sequence across four SRT blocks over the course of sessions. The potential consequence here is that the difference between E and B is reduced as B is inflated by exposure and learning, resulting in a decreased chance of observing a significant difference. However, such an effect was not observed in the results (see Results).

Similarity Report. To assess familiarity and recognition memory of the training sequence, and explore whether the spatial or motor aspects would be more identifiable, a 2x3x4 mixed ANOVA, GROUP (Wake, Sleep) X SESSION (IM, PI, LT) X BLOCKTYPE (Motor, Spatial, Trained, Other), was conducted for similarity rating (relative to the training sequence) for each SRTT representation test block after training. The same ANOVA was used to assess the confidence rating corresponding to each similarity rating.

Sleep. Changes in the proportion of time spent in each sleep stage were evaluated with paired *t*-tests across CN and TR on the percentage of each stage of sleep across the each of the two nights. Spindles were categorized as slow spindles (11–13.5 Hz) at Fz, fast spindles (13.5–16 Hz) at Pz and total bandwidth spindles (11–16 Hz) at Cz. The variables of interest extracted for spindle analysis included peak amplitude, spindle duration, peak frequency and number of spindles during NREM2, at each central electrode derivation (Fz, Cz and Pz). Paired *t*-tests were run on these variables across recording nights. Because there was no sequence learning in the CN, and subjects had had a chance to acclimatize to the sleep laboratory environment, changes of sleep EEG on TR would be assumed to be due to sequence learning.

In general, normality of variables were tested for with Box's Test of Equality of Covariance Matrices and Levene's Tests of Homogeneity, where appropriate. Sphericity assumptions were tested with Mauchly's Tests of sphericity, and for significance below .05 with Hunh-Feldt adjustments made on degrees of freedom for sphericity violations where appropriate. When

variables were found to be not statistically different between groups or interact across sessions, sleep-wake group data where then combined to investigate effects for other factors, such as consolidation over time, irrespective of sleep or wake. Significant within-subject, between-subject, or interaction effects were followed up by specific ANOVA focused on the significant simple effect. Finally, significant differences between sessions and variables, were followed up with paired or independent sample *t*-tests ($\alpha = 0.05$), where appropriate and Bonferonni correction applied for multiple comparisons.

Sample

Remarkably, four out of forty participants across the experimental groups indicated that they were aware of a pattern to the SRTT and were able to verbally describe the sequence they had been assigned with greater than 75% accuracy. Their immediate explicit awareness was further confirmed by subsequent performance on tasks demonstrating the ability to respectively generate and withhold sequence knowledge via inclusion and exclusion instructions with the generation task, which is illustrated in Figure 8, and identify with certainty the training sequence from other block types during the SRT representation tests (data not shown). Because a central point of this study was evaluating changes from implicit to explicit awareness, and these subjects had already demonstrated developed explicit awareness before retention intervals, their data was excluded from the analyses. For two subjects (one per experimental group), missing LT data was imputed using SPSS monotone multiple imputation, with five iterations. All LT analyses were performed twice. First, with list-wise exclusion of participants with the missing values, then with imputed values. The imputations did not significantly alter the outcome of any analyses or result outcomes so were included to maximize data for analysis. The final analyses were performed on thirty-six subjects, with half in the WAKE (n = 18) condition and half in the SLEEP condition (n = 18; see Table 1).

RESULTS

Control Measures

Groups did not significantly differ on age, morning-ness-evening-ness, on assigned task conditions, or gender distribution (see Table 1). However, the sample was predominately female (F = 26, M = 10). There were no significant effect across session or between sleep or wake condition on sleepiness or vigilance, as indicated by Stanford Sleepiness Scores (Session; $F_{2,68}$ = 1.12, p = .33, Group; $F_{1,34}$ = 1.10, p = .30, SessionXGroup; $F_{2,68}$ = 1.75, p = .18), Epworth Sleepiness Scores (Session; $F_{2,68}$ = 2.65, p = .08, Group; $F_{1,34}$ = .002, p = .96, SessionXGroup; $F_{2,684}$ = .846, p = .43) or PVT mean reaction times (Session; $F_{2,68}$ = .286, p = .75, Group; $F_{1,34}$ = .012, p = .91, SessionXGroup; $F_{2,684}$ = 1.43, p = .25). Between CN and TR for SLEEP group, sleep latency onset (t_{17} = 1.87, p = .079), morning rise time (t_{17} = 1.67, p = .113), total sleep time (t_{17} = .75, p = .466), and total wake after sleep (t_{17} = 1.64, p = .119) were comparable (see Table 2).

Table 1

Demographic and experimental assignment distributions across groups

	WAKE	SLEEP	WAKE-SLEEP		COMBINED[1]	EXPLICIT[2]
	n=18	n=18	*diff*	*p*	n=36	n=4
Age[ŧ]	23.4*(3.3)*	21.8*(1.9)*	1.6	.087	22.6*(2.7)*	21.3*(1.9)*
Gender (Female)	12	14	2	.457	26	1
Circadian score[ŧ]	51.4*(6.8)*	51.3*(8.6)*	0.1	.966	51.3*(7.7)*	53.8*(8.1)*
Assigned training sequence:						
1	8	8	0	1	16	2
2	10	10	0	1	20	2
Keypad placement for training:						
Top	8	8	0	1	16	1
Under	10	10	0	1	20	3

Notes: [1] pooled WAKE and SLEEP groups who did not meet explicit awareness criteria.
[2] n=3 WAKE and 1 SLEEP who met explicit awareness exclusion criteria by indicating certainly aware and the capacity to immediately verbal report with >75% accuracy the 12item sequence they were trained on.
[ŧ]Independent samples t-test, all else χ^2 tests, *significance at $p < .05$

Table 2

Sleep measures between recording nights

	CN Mean*(SD)*	TR Mean*(SD)*	TR-CN *diff*	$t_{(17)}$	*p*
Sleep onset latency (min)	7.33*(7.53)*	4.46*(3.08)*	-2.87	1.87	.079
Rise time after midnight (hour)	7.45*(.56)*	7.70*(.64)*	0.25	1.67	.113
Total sleep time (min)	440.8*(41.1)*	447.9*(25.8)*	7.1	0.75	.466
Total wake after sleep (min)	29.7*(30.5)*	18.2*(16.3)*	-11.5	1.64	.119
% NREM 1	3.7(*2.2*)	3.6(*1.5*)	0.0	0.02	.987
% NREM 2	45.3(*8.6*)	41.4(*8.4*)	-3.9	1.62	.123
% NREM 3	30.0(*9.6*)	31.5*(7.1)*	1.4	0.56	.583
% REM	21.0(*5.0*)	23.5*(4.3)*	2.5	2.22	.041 *

Notes: * significance at $p < .05$, paired sample t-test

SRTT Training

Error rates for control and experimental sessions were low across SRTT sessions (< 5%). Means and standard deviations for reactions times across SRTT blocks for training are shown in Table 3. An omnibus SESSION (Control, Training) x GROUP (Sleep, Wake) x BLOCK(1-13) ANOVA yielded a significant SessionXBlock interaction, $F_{6.33,34} = 2.219$, $p = .039$, with no between-group effects, $F_{1,34} = .429$, $p = .517$, indicating equality between SLEEP and WAKE but differences between performance across blocks as a function of control or experimental training session. Significant differences across blocks were observed for control ($F_{4.64,157.89} = 8.31$, $p < .001$) and experimental training sessions ($F_{5.89,200.33} = 20.4$, $p < .001$). However, in the training session, reaction times consistently decreased across all but the final training block, whereas performance on the random SRTT fluctuated across the thirteen blocks. Pairwise comparison of marginal means between control ($M = .405 \pm .008$s) and training ($M = .325 \pm .008$s) sessions demonstrated superior reaction time performance in the training session ($p < .001$). Figure 4 illustrates the comparability of learning performance across the experimental WAKE and SLEEP SRTT sessions. It is worth noting that a potential fatigue effect was apparent

in the final block of the SRTT training session in both groups. However, between switching tasks this effect disappears, as is seen by the recovery of Trained performance at IM.

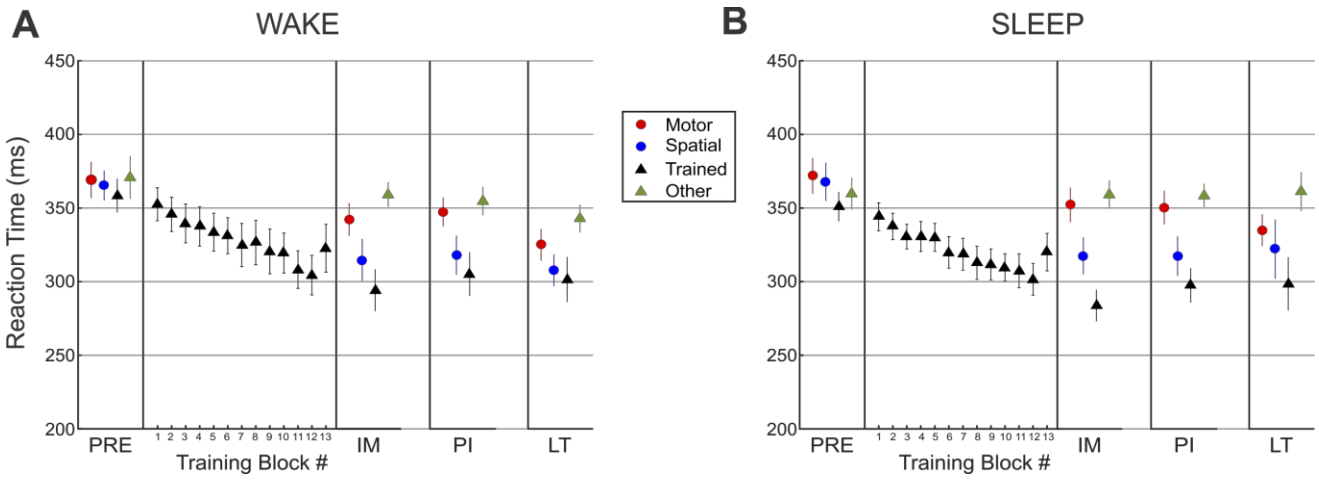


Figure 4. Overview of SRTT task performance across sessions for intervals of wake and sleep. Four representations of sequence knowledge were tested with a SRTT block across four time points, with a training period of 13 blocks on one sequence. For WAKE (A) the interval between IM and POST was morning-to-evening spent awake. For SLEEP (B) the interval was evening-morning filled with sleep. Reaction times are represented as the group averaged median response-times per block. Error bars indicate standard error of the mean. PRE – Pretraining test, IM - Immediate post-training test, PI - Post-interval retest, LT - Long-term retest .

Table 3

SRTT Training Reaction Times by Block

Block No.	1	2	3	4	5	6	7	8	9	10	11	12	13
	Mean *(SD)*												
WAKE	352.6*(47.6)*	*345.7 (49.3)*	339.6*(56.3)*	337.5*(38.0)*	333.6*(54.6)*	331.2*(51.8)*	324.9*(62.3)*	326.6*(64.1)*	320.5*(64.5)*	319.4*(57.7)*	308.1*(54.1)*	304.4*(57.0)*	322.7*(68.9)*
SLEEP	344.0*(40.4)*	337.5*(38.0)*	330.6*(35.2)*	330.7*(43.2)*	330.1*(40.2)*	319.9*(45.5)*	318.6*(45.8)*	312.8*(47.9)*	311.7*(44.8)*	309.6*(39.6)*	307.4*(48.9)*	301.6*(45.7)*	320.0*(54.0)*
COMBINED[1]	348.3*(43.7)*	341.6*(43.6)*	335.1*(46.5)*	334.1*(49.7)*	331.8*(47.3)*	325.5*(48.4)*	321.7*(54.0)*	319.7*(56.2)*	316.1*(54.9)*	314.5*(49.0)*	307.8*(50.8)*	303.0*(51.0)*	321.4*(61.0)*

Notes: Reaction times are in milliseconds. No significant difference were observed between WAKE and SLEEP with independent sample t-tests, $p < .05$.
[1] consists of pooled WAKE and SLEEP.

SRTT Representation Tests

Differences in block representation type performance (Motor, Spatial, Trained, Other) were evaluated before and after training (PRE, IM) and between conditions (SLEEP, WAKE). The reaction times for each representation type between groups and across sessions are displayed in Table 4. A significant interaction was observed for session and representation ($F_{3,102} = 33.74$, $p < .001$), but not for group ($F_{1,34} = .01$, $p = .925$) or for other interactions (SessionXGroup; $F_{1,34} = .33$, $p = .567$, SessionXBlockType; $F_{3,102} = 1.68$, $p = .177$, SessionXBlockTypeXGroup; $F_{3,102} = .47$, $p = .707$). Follow-up tests indicated that at pre-training (PRE), there was a difference between representation performance ($F_{3,105} = 1.68$, $p = .007$), whereby performance on the training sequence ($M_{\pm SE} = 355 \pm 7$ms) was significantly better than for the motor sequence ($M_{\pm SE} = 371 \pm 8$ms), by a margin of 160ms, $t_{35} = 3.41$, $p = .01$. However, this was the only difference at baseline, and although speculative, this could have resulted from having kept the training sequence third place in testing order (while other reps where randomized in the other slots) for PRE and IM sessions (see SRTT Representation Testing).

After training, at the IM test, performance across representation blocks was significantly different, $F_{3,35} = 66.11$, $p < .001$, as outlined in Table 5. While Motor ($t_{35} = 5.81$, $p < .001 = .01$), Spatial ($t_{35} = 8.87$, $p < .001$), and Trained ($t_{35} = 11.40$, $p < .001$) showed significant gains, only Other did not significantly improve after the training session ($t_{35} = 1.20$, $p = .240$). The difference in performance between Trained and Other after training is evidence that improvements are due to sequence specific knowledge as opposed to general task effects. These gains across session are outlined in Table 6 and illustrated in Figure 5 (panel A). Other performance after training was slowest ($M_{\pm SE} = 359 \pm 6$ms), followed by Motor ($M_{\pm SE} = 347 \pm 8$ms), Spatial ($M_{\pm SE} = 316 \pm 9$ms), and Trained ($M_{\pm SE} = 289 \pm 9$ms) as the fastest performed.

Table 4

SRTT representation test reaction times across sessions

		PRE	IM	PI	LT
WAKE		Mean*(SD)*	Mean*(SD)*	Mean*(SD)*	Mean*(SD)*
	Motor	369.1*(49.7)*	342.2*(46.1)*	347.4*(40.3)*	325.1*(44.7)*
	Spatial	365.3*(41.6)*	314.7*(59.3)*	318.1*(55.9)*	312.0*(45.4)*
	Trained	358.6*(47.8)*	294.1*(59.2)*	305.1*(61.7)*	301.4*(64.0)*
	Other	370.8*(60.7)*	359.2*(34.8)*	354.8*(39.8)*	343.0*(38.8)*
SLEEP					
	Motor	371.9*(50.4)*	352.2*(48.8)*	350.3*(47.6)*	335.0*(45.0)*
	Spatial	367.8*(54.5)*	317.5*(52.3)*	317.3*(55.7)*	322.0*(84.3)*
	Trained	351*(41.4)*	283.8*(44.4)*	297.4*(48.7)*	298.4*(75.9)*
	Other	359.7*(44.6)*	359.1*(39.1)*	358.7*(32.5)*	361.2*(54.6)*

Notes: Reaction times in milliseconds. PRE - Pretraining, IM - Immediate post-training, PI - Post-interval, LT - Long-term interval

Subsequent analysis aimed to compare changes in representation performance across post-training intervals (i.e., IM, PI, LT) and between experimental groups. Here, any performance changes between groups across sessions would be a result of the intervening sleep or wake on the memory representations. A significant interaction was observed between session and representation type ($F_{5.27,179.32} = 2.89$, $p < .014$), but not for sleep-wake group ($F_{1,34} = 0.05$, $p = .842$). Follow-up 1x3 repeated-measures ANOVA's were performed individually on each representation block across the three sessions in a BLOCKTYPE (Motor, Spatial, Trained, or Other) X SESSION(IM, PI, LT) set of analyses to dissect which representations were changing across time. Motor was found to have significant across-session change ($F_{2,70} = 9.66$, $p < .001$), but not Spatial ($F_{1.72,60.20} = 0.07$, $p = .915$), Trained ($F_{1.68,58.77} = 2.89$, $p = .155$), or Other ($F_{1.73,60.58} = 1.51$, $p = .229$). This gain in Motor was specific to the PI-to-LT interval ($t_{35} = 3.71$, $p = .001$) but not across the shorter IM-to-PI interval ($t_{35} = 0.34$, $p = .733$). This difference is observable in Figure 5 (panel A) which illustrates the time courses of representation block performance across sessions. Table 6 summarizes the difference in performance across sessions for each of the SRTT representation blocks.

Table 5

Pairwise comparisons between representation test reaction times across sessions

Comparison	PRE Mean*(SE)*	IM Mean*(SE)*	PI Mean*(SE)*	LT Mean*(SE)*
Other vs Motor	-5.3*(4.6)*	11.9*(4.0)* *	7.8*(3.7)*	22.1*(6.2)* *
Other vs Spatial	-1.3*(4.9)*	43.0*(5.8)* *	39.0*(6.7)* *	35.1*(6.8)* *
Other vs Trained	10.4*(3.8)*	70.2*(6.2)* *	55.4*(6.1)* *	52.2*(6.6)* *
Motor vs Spatial	3.9*(4.6)*	31.1*(5.6)* *	31.2*(6.8)* *	13.0*(8.7)*
Motor vs Trained	15.7*(4.6)* *	58.3*(5.8)* *	47.6*(6.2)* *	30.1*(7.8)* *
Spatial vs Trained	11.7*(3.8)*	27.2*(5.3)* *	16.4*(5.3)* *	-17.1*(5.2)* *

Notes: Reaction time differences are in milliseconds.
Data is from pooled WAKE and SLEEP conditions.
* denotes significance at $p < .05$, Bonferroni-corrected for multiple comparison.
PRE - Pretraining, IM - Immediate post-training, PI - Post-interval, LT - Long-term interval.

Table 6

Total representation test reaction times and pairwise comparisons across sessions

COMBINED[1]	PRE Mean*(SD)*	IM Mean*(SD)*	PI Mean*(SD)*	LT Mean*(SD)*	PRE-IM *diff (SE)*	IM-PI *diff (SE)*	PI-LT *diff (SE)*	IM-LT *diff (SE)*
Motor	370.5*(49.7)*	347.2*(47.1)*	348.9*(43.5)*	330.0*(44.5)*	23.3*(4.1)* *	-1.7*(4.9)*	18.9*(4.6)* *	17.2*(4.7)* *
Spatial	366.5*(47.8)*	316.1*(55.1)*	317.7*(55.0)*	317.0*(66.9)*	50.4*(5.7)* *	-1.6*(5.9)*	0.7*(7.7)*	-0.9*(8.9)*
Trained	354.8*(44.2)*	288.9*(51.8)*	301.3*(55.0)*	299.9*(69.2)*	65.8*(5.8)* *	-12.3*(4.9)*	1.4*(7.3)*	-11.0*(7.9)*
Other	365.3*(52.8)*	359.1*(36.4)*	356.7*(35.9)*	352.1*(47.6)*	6.1*(5.1)*	2.4*(3.9)*	4.6*(5.8)*	7.0*(6.1)*

Notes: Reaction times in milliseconds. PRE - Pretraining, IM - Immediate post-training, PI - Post-interval, LT - Long-term interval.
[1] consists of pooled WAKE and SLEEP conditions.
* significance at $p < .05$, Bonferroni-corrected for multiple comparison.

Table 7

Group similarity and confidence ratings across representation tests

	WAKE		SLEEP		COMBINED[1]	
Immediate	*Similarity*	*Confidence*	*Similarity*	*Confidence*	*Similarity*	*Confidence*
Motor	1.56*(0.71)*	1.39*(0.78)*	1.39*(0.78)*	1.72*(0.83)*	1.47*(0.74)*	1.56*(0.81)*
Spatial	2.22*(0.73)*	2.06*(0.80)*	1.83*(0.62)*	1.61*(0.85)*	2.03*(0.70)*	1.83*(0.85)*
Trained	2.28*(0.67)*	1.83*(0.92)*	2.00*(0.84)*	1.89*(0.90)*	2.14*(0.76)*	1.86*(0.90)*
Other	1.17*(0.86)*	1.89*(0.83)*	1.33*(0.91)*	1.94*(0.80)*	1.25*(0.87)*	1.92*(0.81)*
Post-Interval						
Motor	1.50*(0.71)*	1.56*(0.86)*	1.83*(0.62)*	1.78*(0.88)*	1.67*(0.68)*	1.67*(0.86)*
Spatial	1.78*(0.81)*	1.83*(1.04)*	1.72*(0.90)*	1.72*(0.83)*	1.75*(0.84)*	1.78*(0.93)*
Trained	2.22*(0.73)*	1.89*(0.90)*	1.94*(0.87)*	1.94*(0.94)*	2.08*(0.81)*	1.92*(0.91)*
Other	1.33*(1.03)*	1.67*(0.97)*	1.33*(1.03)*	1.72*(0.96)*	1.33*(1.01)*	1.69*(0.95)*
Long-term						
Motor	1.70*(0.87)*	2.05*(0.94)*	1.59*(0.73)*	1.74*(0.89)*	1.64*(0.79)*	1.89*(0.91)*
Spatial	1.87*(0.90)*	1.90*(0.89)*	1.69*(0.83)*	1.98*(0.77)*	1.78*(0.86)*	1.94*(0.82)*
Trained	2.17*(0.62)*	2.28*(0.67)*	2.06*(1.00)*	2.11*(0.90)*	2.11*(0.82)*	2.19*(0.79)*
Other	1.31*(0.83)*	1.91*(0.93)*	1.35*(0.97)*	1.93*(0.94)*	1.33*(0.89)*	1.92*(0.92)*

Notes. [1] consists of pooled WAKE and SLEEP. Mean*(SD)* reported.

Similarity ratings

Group means and standard deviations for similarity and confidence ratings are summarized in Table 7. No significant difference was observed between groups ($F_{1.,34} = 0.39$, $p = .54$) or across sessions effects ($F_{1.90,64.73} = 0.01$, $p = .99$) for the similarity ratings of SRTT representation blocks. However, there was a significant effect for representation type, $F_{1.81,61.52} = 15.85$, $p < .001$. Not surprisingly, Trained was rated the most similar ($M_{\pm SE} = 2.11 \pm .11$), followed by Spatial ($M_{\pm SE} = 1.85 \pm .10$), Motor ($M_{\pm SE} = 1.59 \pm .07$), and finally Other ($M_{\pm SE} = 1.31 \pm .11$). The pairwise comparisons are displayed in Table 8. The only pairwise difference not to reach significance was between Other and Motor, $t_{35} = 2.46$, $p = .113$. Regarding subjects' confidence on their similarity appraisals, subjects felt most confident about Trained ($M_{\pm SE} = 1.99 \pm .12$) ratings, followed by Spatial ($M_{\pm SE} = 1.85 \pm .11$), then Other ($M_{\pm SE} = 1.84 \pm .13$), and finally Motor ($M_{\pm SE} = 1.70 \pm .11$). The only significant difference for confidence rating was between Trained and Motor, $t_{35} = 3.75$, $p = .004$. Figure 5 (panel B) illustrates the differences in similarity and confidence ratings described, between representation SRTT blocks.

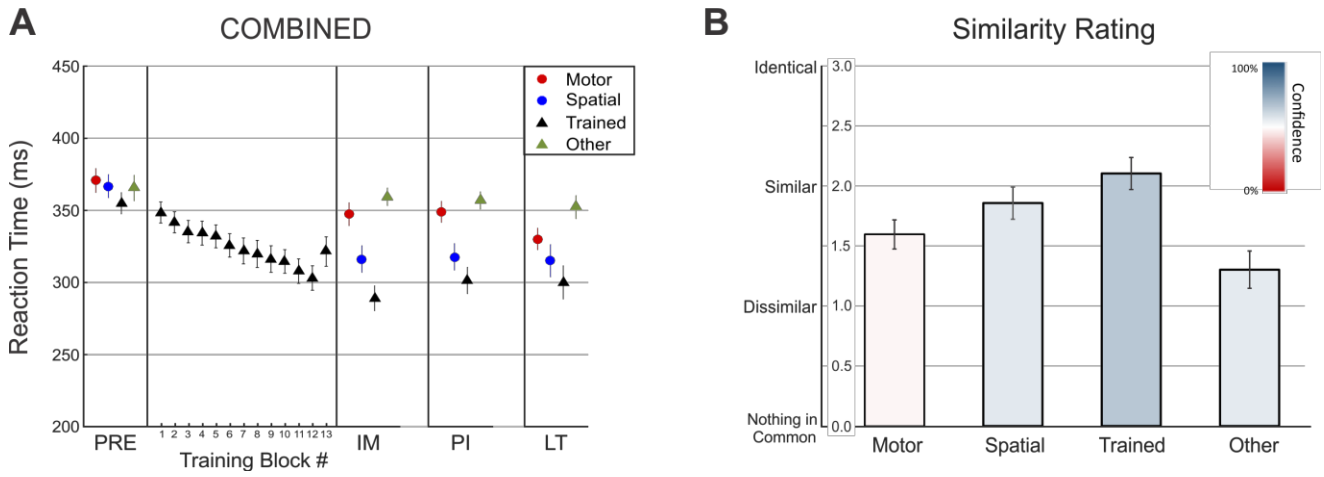


Figure 5. Combined group SRTT performance and representation similarity rating. (A) Overview of SRTT task performance across sessions for combined (WAKE+SLEEP) interval groups. Reaction times are block averaged median response-times. (B) Mean similarity ratings for representation blocks across sessions after training. The heat map (B) indicates the overall confidence rating corresponding to the similarity rating reported for each representation block. Error bars indicate standard error of the mean. . PRE – Pretraining test, IM - Immediate post-training test, PI - Post-interval retest, LT - Long-term retest.

Table 8

Pairwise comparisons between similarity ratings of representation tests and confidence ratings

Comparison	Similarity Diff (SE)		Confidence Diff (SE)	
Other vs Motor	-0.29*(.12)*		-0.14*(.08)*	
Other vs Spatial	-0.55*(.16)*	*	-0.01*(.08)*	
Other vs Trained	-0.81*(.17)*	*	-0.15*(.09)*	
Motor vs Spatial	-0.26*(.07)*	*	-0.15*(.07)*	
Motor vs Trained	-0.52*(.09)*	*	-0.29*(.08)*	*
Spatial vs Trained	-0.26*(.08)*	*	-0.14*(.08)*	

Notes: Data is for from combined SLEEP and WAKE groups.
* significance at $p < .05$, Bonferroni-corrected for multiple comparison.

Trained Hand Sequence Generation

The level of implicit versus explicit awareness of sequence knowledge was assessed immediately after training on a sequence (IM), and two more times across experimental intervals (PI, LT) by the testing subjects' ability to generate or withhold generating trained sequence responses with the trained (i.e., left) hand. After training, a significant effect for triplet type (Trained, Other) was observed for both inclusion ($F_{1,34} = 36.10$, $p < .001$) and exclusion instructions ($F_{1,34} = 19.38$, $p < .001$). More triplets were generated of the training sequence (i.e., Trained) than of the other untrained sequence (i.e., Other) across all sessions. Overall, across sessions, for inclusion the mean for Trained triplets generated was 37.00 (± 1.38_{SEM}) versus 27.30 (± 1.10_{SEM}) Other sequence triplets were generated ($p < .001$). For exclusion mean number of Trained triplets generated was 35.43 (± 1.16_{SEM}) versus 28.29 (± $.90_{SEM}$) Other ($p < .001$). Beyond this no significant effects were found between groups for inclusion ($F_{1,34} = 1.15$, $p = .292$) or exclusion instructions ($F_{1,34} = 2.37$, $p = .133$), or across session for inclusion ($F_{2,68} = 0.56$, $p = .555$) and exclusion instructions ($F_{2,68} = 1.99$, $p = .144$). This indicates that the sequence knowledge was acquired to the extent it was selectively generated more than other sequence they had been exposed to but not trained on. Furthermore, because of the comparative performance between inclusion and exclusion, this is indicative of sequence knowledge not being under explicit control. Following this, the analyses directly comparing mean Trained triplet generation across instruction type (Inclusion versus Exclusion; $F_{1,34} = 1.17$, $p = .287$), between group ($F_{1,34} = 2.37$, $p = .133$), and across session ($F_{2,68} = 1.93$, $p = .153$) did not yield any significant effects. This too indicates that sequence knowledge remained implicit, for both groups, and across the entirety of the study. The performance of inclusion and exclusion performance across sessions are displayed in Table 9.

In the event that training triplet generations occurred as limited to within in the first few keypresses after cueing in the generation sets, triplets were analyzed for the first, second, and third keypresses. Because the score ranges were lower for triplet generations with fewer responses, ratio scores were not a feasible approach (i.e., any 0 triplet score renders an un-interpretable ratio). Instead, the scores used for analysis were the difference of inclusion – exclusion mean Trained triplet generation. There were no significant effects when analyzing the up to the first (Group; $F_{1,34} = 0.27$, $p = .605$, Session; $F_{2,68} = 1.11$, $p = .336$; SessionXGroup;

$F_{2,68} = 1.33$, $p = .271$)., second (Group; $F_{1,34} = 0.03$, $p = .876$, Session; $F_{2,68} = 1.46$, $p = .239$; SessionXGroup; $F_{2,68} = 0.75$, $p = .478$), or third keypress after cueing (Group; $F_{1,34} = 0.02$, $p = .883$, Session; $F_{2,68} = 0.81$, $p = .450$; SessionXGroup; $F_{2,68} = 0.99$, $p = .376$). The difference score approach was also further verified the absence of change across time and between SLEEP and WAKE groups for the full extent of generation responses (Group; $F_{1,34} = 0.01$, $p = .929$, Session; $F_{2,68} = 1.65$, $p = .200$; SessionXGroup; $F_{2,68} = 0.04$, $p = .962$).

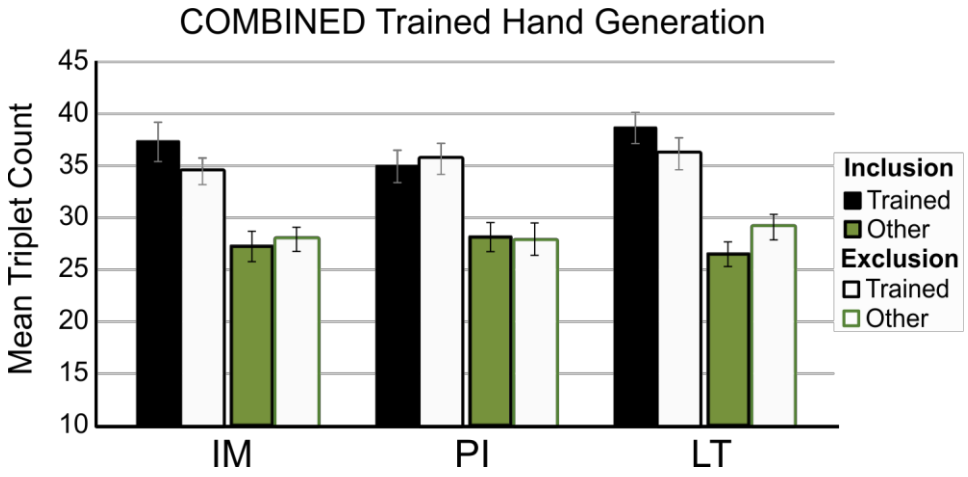


Figure 6. Trained hand performance of inclusion and exclusion generation task across testing sessions. Ability to produce trained triplets above untrained (Other) triplets indicates sequence learning. Ability to produce trained triplets under the inclusion instructions while withholding producing trained triplets (Trained) under exclusion instructions indicates explicit sequence knowledge. Across inclusion and exclusion instructions more training triplets were generated than other sequence triplets ($p < .05$). However, there were no differences between inclusion and exclusion performance generating training triplets within or across sessions ($p > .05$). Error bars indicate standard error of the mean. IM - Immediate post-training test, PI - Post-interval retest, LT - Long-term retest.

Untrained-hand Sequence Generation

A series of group by session by triplet type analyses were performed to test if sequence knowledge was accessible to the untrained hand, and which component of the representation (spatial or motor) was preferably selected in response generation. Comparing triplet type (Motor,

Other) showed a significant effect for triplet type generation, for inclusion ($F_{1,34} = 21.61$, $p < .001$) and exclusion ($F_{1,34} = 17.03$, $p < .001$) instructions. Whereas neither group nor session effect were significant for inclusion (Group; $F_{1,34} = 1.53$, $p = .225$ Session; $F_{2,68} = .26$, $p = .774$) or exclusion (Group; $F_{1,34} = 4.00$, $p = .053$, Session; $F_{2,68} = 2.24$, $p = .115$) instructions. Nearly the same pattern of results emerged comparing Spatial and Other triplet type, whereby significant effects for triplet generation for inclusion ($F_{1,34} = 22.76$, $p < .001$) and exclusion ($F_{1,34} = 14.61$, $p = .001$) instructions were observed, as well as no significant group or session effects for inclusion instructions (Group; $F_{1,34} = 1.67$, $p = .205$ Session; $F_{1.53,51.89} = 1.22$, $p = .295$). However, for the exclusion instructions, while the group effect was only trending (Group; $F_{1,34} = 3.36$, $p = .076$) there was a significant between session effect ($F_{2,68} = 6.81$, $p = .002$), but without a group interaction (GROUPxSESSION; $F_{2,68} = 0.46$, $p = .653$). Analyzing the main effect of session on Spatial and Motor triplets revealed a slight non-significant drop in mean between IM and PI (PI - IM = -1.38 ± .55, $p = 0.52$), then showed statistically significant increases between PI and LT (LT - PI = 2.20 ± .57, $p = 0.001$) comparable to initial, IM, scores (LT - IM = 0.82 ± .67, $p = 0.674$). Overall, these results indicate that spatial and motor components of training were accessed for sequence generation more-so than for untrained pattern of sequences.

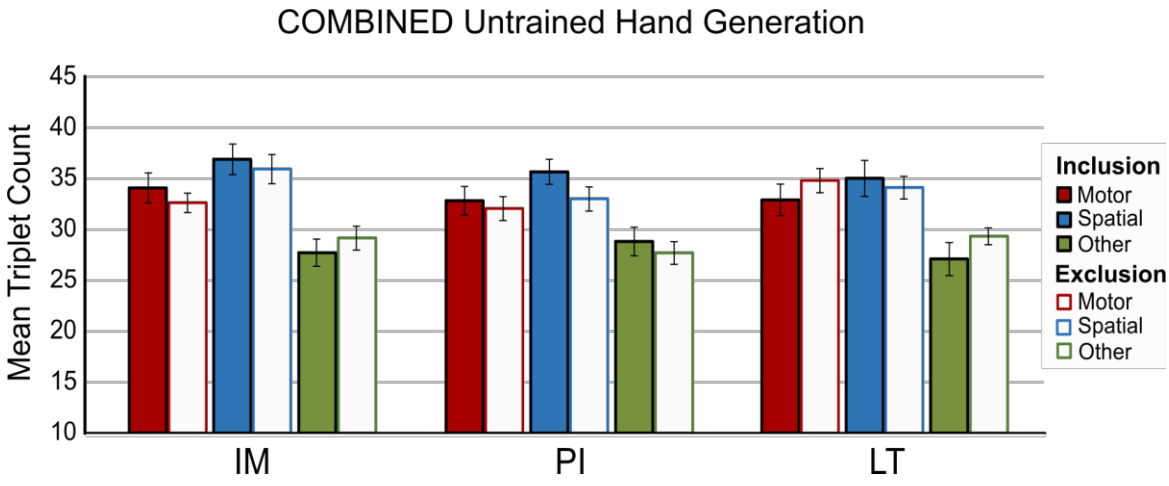


Figure 7. Untrained hand generation performance for each triplet type across inclusion and exclusion instructions for combined group data. Ability to produce more spatial and motor triplets of the trained sequence compared to un-trained (Other) triplets indicates training sequence representations were acquired and are inter-manually transferrable. Across inclusion and exclusion instructions

more spatial and motor triplets were generated than other sequence triplets ($p < .05$), with slightly more motor triplets generated under inclusion instructions than spatial ($p < .05$). Error bars indicate standard error of the mean. IM - Immediate post-training test, PI - Post-interval retest, LT - Long-term retest.

Following up from this, the mean number of Spatial and Motor triplets were compared to evaluate whether one trained representation component was predominantly generated over the other, between groups and across sessions, for inclusion and exclusion instructions. For the inclusion performance, a significant effect was observed for triplet type ($F_{1,34} = 4.50$, $p = .041$) but not for group ($F_{1,34} = 0.73$, $p = .400$) or session ($F_{2,68} = 1.29$, $p = .329$). More spatial ($M_{\pm SE}$ = 35.87 ± .12) than motor triplets ($M_{\pm SE} = 33.28 \pm 1.17$) were generated in the inclusion instructions overall, by an average of 2.56 ± 1.22 ($M_{\pm SE}$), $p = .041$. For exclusion performance, a significant effect was observed for session ($F_{2,68} = 3.12$, $p = .050$) but not for group ($F_{1,34} = 0.45$, $p = .509$) or triplet type ($F_{2,68} = 2.88$, $p = .099$). The difference between spatial ($M_{\pm SE} = 34.35 \pm 1.04$) and motor generation ($M_{\pm SE} = 33.16 \pm .82$) was 1.19 ± .69 ($M_{\pm SE}$), $p = .095$. Evaluating the session effect revealed a drop in mean number of generations between IM and PI (PI-IM; $M_{\pm SE}$ = 1.93 ± 0.84), followed by an increase from PI to LT (LT - PI; $M_{\pm SE} = 1.75 \pm 0.73$). However, pairwise comparisons of these changes did not achieve significance following Bonferroni correction (PI - IM; $p = .081$, LT-PI; $p = .065$). To summarize, more spatial than motor representations of the training sequence were produced for cross-hand generation, particularly when instructed to replicate the training sequence (i.e., inclusion instructions), irrespective of session or group.

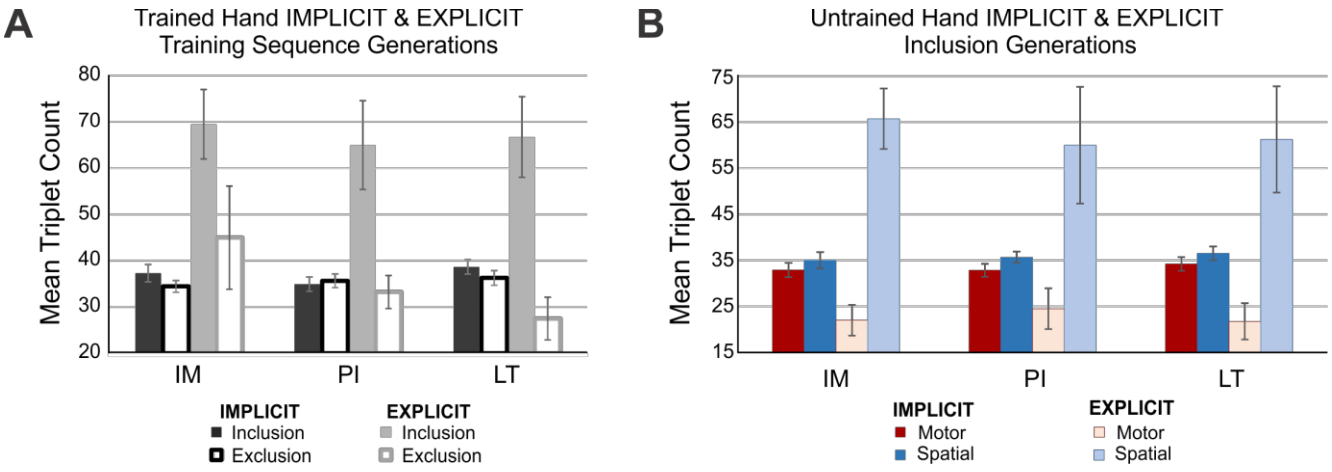


Figure 8. Performance of trained and untrained hand generations for implicit and explicitly aware groups of participants across sessions. (A) Trained hand generations of the training sequence for inclusion and exclusion instructions. Ability to produce trained triplets under the inclusion instructions while withholding producing trained triplets under exclusion instructions indicates explicit sequence knowledge. (B) Untrained hand generation performance for each triplet type across inclusion and exclusion instructions for implicitly and explicitly aware groups. Amount of motor versus spatial triplets of the trained sequence produced indicates which training sequence representations are preferred in the inter-manual transfer. Explicit awareness appears to result in a noticeably difference performance across tasks. IMPLICIT were combined SLEEP and WAKE group data ($n = 36$) for those not screened out as aware at IM. EXPLCIT ($n = 4$) are participants who met the criteria for explicit awareness at IM. Error bars indicate standard error of the mean. IM - Immediate post-training test, PI - Post-interval retest, LT - Long-term retest

Table 9

Triplet Generations across Session and Instruction Type for WAKE, SLEEP, COMBINED, and EXPLICIT Groups

		Immediate Post-training				Post-Interval				Long-term Re-test			
		Inclusion		Exclusion		Inclusion		Exclusion		Inclusion		Exclusion	
		Mean	*SD*	Mean	*SD*	Mean	*SD*	Mean	*SD*	Mean	*SD*	Mean	*SD*
WAKE													
Trained Hand													
	Trained	35.61	*12.67*	32.89	*8.59*	35.22	*9.14*	35.78	*10.61*	38.18	*10.02*	36.14	*10.82*
	Other	25.33	*9.07*	27.72	*8.17*	27.00	*6.88*	25.78	*7.05*	25.35	*7.34*	26.93	*7.04*
	None	21.83	*17.27*	21.89	*13.93*	19.72	*12.39*	21.39	*11.15*	17.76	*11.78*	18.90	*10.03*
Untrained Hand													
	Motor	32.28	*9.20*	33.94	*7.70*	31.89	*7.79*	31.39	*7.15*	32.71	*8.54*	31.92	*6.10*
	Spatial	35.94	*10.63*	33.89	*6.82*	33.83	*6.96*	33.56	*7.91*	35.50	*8.94*	34.32	*9.55*
	Other	25.44	*8.32*	27.61	*5.32*	27.61	*8.64*	25.61	*6.35*	26.03	*8.33*	28.11	*7.88*
	None	20.83	*15.71*	20.28	*8.73*	21.06	*12.55*	22.67	*9.87*	20.78	*12.18*	19.98	*9.21*
SLEEP													
Trained Hand													
	Trained	39.00	*9.95*	36.06	*6.44*	34.67	*9.74*	35.56	*7.24*	39.10	*8.10*	36.19	*7.67*
	Other	29.17	*8.28*	28.11	*5.81*	29.28	*9.84*	29.94	*5.22*	27.65	*6.84*	31.28	*7.27*
	None	16.78	*11.66*	18.83	*8.50*	19.61	*16.39*	18.28	*7.07*	17.42	*8.10*	15.79	*6.30*
Untrained Hand													
	Motor	33.56	*9.67*	35.67	*6.64*	33.78	*9.11*	32.72	*7.18*	35.46	*9.05*	33.32	*5.45*
	Spatial	34.11	*10.85*	34.33	*6.68*	37.50	*7.52*	32.44	*6.40*	38.31	*9.14*	37.55	*7.28*
	Other	28.78	*10.93*	31.06	*3.93*	30.06	*8.16*	29.78	*6.38*	29.43	*7.48*	30.21	*6.27*
	None	20.33	*16.11*	17.22	*5.62*	15.89	*11.04*	21.11	*8.56*	15.79	*7.85*	17.26	*8.36*
COMBINED[1]													
Trained Hand													
	Trained	37.31	*11.36*	34.47	*7.65*	34.94	*9.31*	35.67	*8.95*	38.64	*8.99*	36.16	*9.24*
	Other	27.25	*8.78*	27.92	*6.99*	28.14	*8.45*	27.86	*6.47*	26.50	*7.09*	29.11	*7.39*
	None	19.31	*14.75*	20.36	*11.48*	19.67	*14.32*	19.83	*9.34*	17.59	*9.96*	17.35	*8.40*
Untrained Hand													
	Motor	32.92	*9.32*	34.81	*7.14*	32.83	*8.41*	32.06	*7.10*	34.09	*8.78*	32.62	*5.75*
	Spatial	35.03	*10.63*	34.11	*6.66*	35.67	*7.38*	33.00	*7.12*	36.90	*9.03*	35.93	*8.53*
	Other	27.11	*9.72*	29.33	*4.93*	28.83	*8.38*	27.69	*6.62*	27.73	*7.99*	29.16	*7.10*
	None	20.58	*15.69*	18.75	*7.40*	18.47	*11.94*	21.89	*9.14*	18.29	*10.41*	18.62	*8.78*
EXPLICIT[2]													
Trained Hand													
	Trained	69.50	*7.51*	45.00	*11.14*	65.00	*9.60*	33.25	*3.57*	66.75	*8.73*	27.50	*4.63*
	Other	8.50	*5.14*	24.50	*8.06*	10.00	*5.49*	24.50	*2.63*	6.00	*3.67*	29.50	*1.85*
	None	10.50	*3.66*	15.50	*4.66*	13.50	*4.63*	27.00	*6.10*	15.00	*5.40*	24.00	*4.60*
Untrained Hand													
	Motor	22.00	*3.34*	33.00	*3.39*	24.50	*4.41*	36.25	*3.66*	21.75	*3.92*	35.75	*3.30*
	Spatial	65.75	*6.56*	34.50	*4.94*	60.00	*12.68*	33.50	*3.57*	61.25	*11.54*	36.25	*2.81*
	Other	8.50	*4.29*	26.25	*1.93*	12.00	*6.79*	30.25	*2.87*	6.75	*3.71*	29.75	*0.85*
	None	13.25	*2.84*	23.50	*4.29*	15.50	*5.58*	19.50	*3.97*	18.75	*7.23*	18.50	*1.50*

Notes: [1] pooled WAKE (n =18) and SLEEP (n = 18) groups.

[2] Participants who met explicit awareness exclusion criteria at immediate post-training (n = 4).

Sleep EEG

Analyses of post-training versus baseline sleep stage recruitment demonstrated a significant increase in the proportion of REM sleep observed from baseline compared to the post-training night, approximating an increase of 2.5% more REM sleep across the night ($t_{17} = 2.22$, $p = .041$). Comparisons for sleep stage proportions between baseline and post-training nights are depicted in Table 2. The percentage of NREM1 ($t_{17} = 0.02$, $p = .987$), NREM2 ($t_{17} = 1.62$, $p = .123$), and NREM3 ($t_{17} = 0.56$, $p = .583$) did not statistically differ between nights. Analysis of spindle variables such as duration, frequency, peak amplitude and density (number of spindles per-minute of NREM sleep) did not reveal any significant differences between control and experimental overnight sessions. Note: data for one participant was excluded from the spindle analysis due to a technical difficulty during recording. Descriptive statistics and paired sample t-test values from the spindle analysis are displayed in Table 10.

Table 10

NREM 2 sleep spindle characteristics between recording nights

Recording site		CN Mean*(SD)*	TR Mean*(SD)*	TR-CN *diff (SE)*	*t*(16)	*p*
Fz						
	Duration	515.5*(76.0)*	506.5*(72.5)*	-11.1*(5.2)*	0.73	0.476
	Frequency	12.86*(.11)*	12.87*(.10)*	0.04*(.01)*	1.23	0.237
	Amplitude	33.41*(9.96)*	31.43*(9.14)*	-1.76*(1.56)*	1.10	0.288
	Density	6.14*(1.31)*	6.37*(1.89)*	.61*(.49)*	0.85	0.409
Cz						
	Duration	298.3*(37.3)*	292.8*(39.2)*	-5.5*(7.0)*	0.78	0.444
	Frequency	13.50*(.12)*	13.51*(.16)*	0.01*(.03)*	-0.32	0.756
	Amplitude	32.98*(9.75)*	30.85*(9.81)*	-2.13*(1.57)*	1.35	0.195
	Density	10.19*(2.28)*	10.73*(2.92)*	0.54*(.58)*	0.94	0.361
Pz						
	Duration	591.6*(106.8)*	581.1*(142.4)*	-7.0*(4.1)*	0.59	0.566
	Frequency	14.02*(.13)*	14.02*(.09)*	0.00*(.02)*	0.16	0.877
	Amplitude	30.60*(8.82)*	30.14*(10.15)*	-0.76*(1.18)*	0.56	0.582
	Density	4.83*(1.30)*	5.02*(1.20)*	0.64*(.51)*	0.84	0.415

Notes: Units are duration *(ms)*, frequency *(Hz)*, amplitude *(mV)* and denisity *(mean number of spindles per minute).*
No significant differences, paired sample t-tests, $p < .05$.

DISCUSSION

While sleep is important for declarative and explicit procedural motor sequence memory consolidation, the role of sleep in implicit motor sequence memory consolidation remains unclear. The overall goal of the present study was to address the question - *does sleep enhance the explicit awareness and generalization of an implicitly learned motor sequence?* Given that sleep is involved in enhancing the consolidation of the spatial component of an explicitly learned motor sequence, in order to explore the role of sleep in implicit learning, we dissociated the spatial- and motor-referent representations from an implicitly learned motor sequence. It was hypothesized that sleep would preferentially enhance the spatial representation and support the development of explicit sequence awareness and inter-manual transfer of spatial-referent motor sequence skills.

Here, for the first time, we successfully dissociated the spatial and motor representations of an implicit motor sequence using with a within-hand transfer task. The importance of this is twofold. First, it was a necessary step required to test which aspects of the motor sequence were enhanced by sleep or wake. Second, perhaps more importantly, it supports the notion that, similar to explicit MSL, spatial and motoric aspects of a learned sequence are acquired in dissociable representations via implicit learning. Thus, we have established a method that opens up novel ways to investigate how the brain engages in and stores implicit MSL. However, contrary to our hypotheses, we did not find differences in offline gains for the spatial representation between the sleep and wake retention interval conditions. Thus, unlike explicit motor sequence learning, consolidation of an implicitly learned spatial representation of a motor sequence was found to be independent of sleep or wake, supporting the notion that sleep may not play a role in enhancing memory consolidation for implicit motor learning.

Implicit and Explicit Awareness at Training

Our results indicated the occurrence of implicit learning in the absence of explicit awareness. Across training blocks on the selected trained sequence, reaction times significantly decreased. Immediately after training, performance on the untrained sequence resulted in significantly slower reaction times as compared to the trained sequence. This demonstrates improvements were due to acquired sequence knowledge as opposed to general skill improvement, consistent with other studies employing the SRTT (e.g., Destrebecqz & Cleeremans, 2001). Stabilization of performance at the maximal trained sequence speed also indicated that task fatigue observed in the final training block was transient and alleviated by a brief rest and testing on the generation task. Performance results on the generation tasks immediately after training showed significant inclusion of the sequence specific to training, more-so than for the untrained sequence, for both inclusion and exclusion generation instructions. This indicates that sequence knowledge was acquired, but was not under conscious control, and was thus an implicit rather than explicit form of memory (Destrebecqz & Cleeremans, 2001). This was shown to be irrespective of the time of day, as training session performance did not differ between the sleep and wake conditions. Thus, taken together, these results suggest that at the end of training, the sequence knowledge had been implicitly acquired through practice with the absence of explicit sequence knowledge, independent of time-of-day.

Offline Memory Changes across Retention Intervals

Trained sequence. There is no consensus as of yet whether a newly learned implicit motor sequence is enhanced over a period of sleep as compared to wake. Here, no significant differences on the SRTT training sequences were observed between sleep-wake conditions or across the post-training testing sessions (IM, PI, LT). Reaction times were significantly and consistently fastest for the trained sequence compared to all other sequences tested, thus this pattern of results cannot be attributed to not having learned the sequence. Performance maintenance across post-training intervals suggest that the skill memory trace was stabilized, but not enhanced by an interval of sleep, wake, or even across a week's time (at LT). No

significant changes in the performance of the untrained sequence were observed across testing sessions, suggesting that performance stabilization following the initial training session was not due to non-sequence-specific motor skills for the task. Our results indicated that SRTT performance was stabilized independent of sleep or wake, which is congruent with previous studies (Meier & Cock, 2014; Nemeth et al., 2010; Song, Howard, & Howard, 2007). However, these studies reported gains in general skill performance across a day's interval of wake, which we did not observe as supported by maintained untrained sequence performance, at lower levels than the trained sequence between all testing intervals. Overall, our results indicated that implicit MSL was stabilized independent of sleep or wake, and was specific to the learned sequence. Thus, providing additional support for the extant literature which suggests that explicit, but not implicit motor sequence learning is enhanced by sleep as compared to wake.

Spatial and motor representations. Immediately after training (during the IM session), both the experimental groups demonstrated a significant dissociation of skill performance on the spatial and motor representation SRTT blocks, with the speeds for each block falling between mean reaction times for the trained and untrained sequence. Relative to the training sequence, spatial-referent sequence performance was next fastest, followed by the motor-referent sequence performance, and slowest reaction times were observed on the untrained sequence. Thus, our results show that both motor and spatial representations were acquired through implicit sequence learning, and groups were able to transfer both representations of sequence knowledge to skill performance, with the spatial representation demonstrating the most effective transfer, indicated by faster performance speed than motor-referent performance. This finding reflects dissociable spatial and motor representations are encoded during implicit MSL, and parallels the pattern of dissociation observed in explicit MSL (Albouy et al., 2015; Albouy, Fogel, et al., 2013).

When evaluating changes in spatial or motor-referent performance across post-learning interval (PI) of sleep or wake, there were no significant effects between groups or across intervals. Importantly, however, we did observe enhancement for the motor-representation one week later (LT), whereby the motor representation reaction times had decreased to the same level as the spatial-representation test. Thus suggesting that with the passage of enough

time, but independent of sleep or wake, the motor representation was slowly enhanced. This is consistent with previous studies suggesting that motor skill learning is consolidated over extended periods of time, lasting days or even weeks (Lehéricy et al., 2005; Press, Casement, Pascual-Leone, & Robertson, 2005; Robertson et al., 2004).

Spatial representation. The extant literature suggests that the implicit versus explicit distinction may not be sufficient to explain whether sleep is involved in the consolidation process. Research has demonstrated sleep dependent gains for the spatial but not the motor-referent representation of an explicit motor sequence (Albouy et al., 2015; Albouy, Fogel, et al., 2013). In the present study, we sought to determine whether implicit sequence learning could be separated into these distinct spatial and motor representations, and importantly whether this would help to resolve existing controversies about sleep-dependent implicit memory consolidation. Surprisingly, despite separating out the spatial and motor representation of implicitly learned sequences, there was no sign of improvement across a night of sleep on the spatial-referent performance. This is in contrast what has been observed in explicit MSL, where the performance of spatial-referent sequences are enhanced by a period of sleep as short as a nap. It is known that for explicit MSL, HPC activity is recruited during MSL learning, and the spatial-representation in particular is subtended to by HPC activation, which, is thought to underlie the sleep-dependent gains of the spatial-referent sequence knowledge (Albouy et al., 2008, 2012, 2015; Albouy, Fogel, et al., 2013). Like explicit MSL, there is also evidence that implicit learning, with the SRTT, also recruits HPC activation (Albouy et al., 2008; Schendan et al., 2003). Here, despite these similarities and the successful behavioural dissociation of these representations, we not observed sleep-dependent gains of the spatial representation of an implicitly learned motor sequence. These results suggest that like explicit MSL, implicit MSL has dissociable spatial and motor representations, but unlike explicit sequence learning, implicit spatial memory consolidation is independent of sleep.

One possibility, which may account for the absence of sleep-dependent gains on spatial performance is that research has shown that the hippocampus serves to "tag" the information for later sleep-dependent consolidation. Both implicit (Gheysen, Van Opstal, Roggeman, Van Waelvelde, & Fias, 2010; Schendan et al., 2003) and explicit MSL (Albouy

et al., 2008, 2015; Albouy, Fogel, et al., 2013; Schendan et al., 2003) imaging studies have revealed that medial temporal lobe activation, including hippocampo-cortico circuitry, is highest in the first block of MSL, and quickly decreases across the first few blocks of training, while inversely, striato-cortical networks increase recruitment across blocks. It may be that although the HPC is engaged in acquiring the spatial aspects of the sequence, as imaging studies of explicit learning and our behavioural results suggest, for implicitly learned motor sequences the HPC may not "tag" this information for enhancement. Thus, it is possible that this tagging does not occur in implicit learning, and thus subsequent sleep-dependent consolidation does not take place. Rather, as our delayed enhancement of the motor representation (at LT) would suggest, instead, consolidation of the trace relies on the slower process of striatal consolidation, which is independent of sleep or wake. Neuroimaging of the SRTT using the same paradigm employed here would help to elucidate the relative roles of the hippocampus and striatum in implicit learning and consolidation that may not manifest themselves at the behavioural level.

Motor representation. When tested across day or night intervals, performance on the motor-referent sequence was maintained but not enhanced. This result is in parallel with Albouy et al., (2013, 2015) who observed maintenance of the motor representation performance irrespective of sleep or wake for explicit MSL. However, our results differ from the work of Cohen et al.'s (2005). In their study, when the motor representation was tested by inter-manual transfer with an SRTT paradigm, an across day period of wake was found to enhance performance. This is in-line with the conceptualization of sleep-independent stabilization of the motor memory trace over time (Doyon, Bellec, et al., 2009; Doyon, Korman, et al., 2009; Hikosaka et al., 2002; Nakahara et al., 2001; Nemeth et al., 2010; Nettersheim et al., 2015) but in contrast to research proposing offline gains in MSL (Barakat et al., 2013; Fischer et al., 2002; Fogel et al., 2014; Morin et al., 2008; Press et al., 2005; Robertson et al., 2004; Tucker, McKinley, & Stickgold, 2011; Urbain et al., 2013).

Interestingly, we observed a significant increase of motor-representation performance when retested a week later. Very few studies have looked beyond an interval of a couple days for SRTT consolidation (Meier & Cock, 2014; Romano, Howard, & Howard, 2010), and none have looked specifically at motor representation transfer. Because both periods of sleep and

wake occupy the span of a week it is not possible for us to identify the processing contributions of one state over the other, or if these gains were the product of striatal, motor cortical, or cerebellar networks known to be involved in implicit memory (Doyon, Owen, Petrides, Sziklas, & Evans, 1996; Doyon, Bellec, et al., 2009; Lehéricy et al., 2005; Peigneux et al., 2000; Rauch et al., 1995, 1997; Schendan et al., 2003). Thus, it remains unclear why an enhancement in the motor representation would occur only after a week. As stipulated for the spatial-representation of this study, neuroimaging of performance during the motor-representation transfer blocks would be informative in understanding which cortical and subcortical regions are being engaged for the motor-referent sequence performance, and provide comparison to the motor-representations of explicit MSL.

Awareness. Our results did not indicate any increase in awareness between groups or across sessions. Components specific to the trained sequence were generated more than the untrained sequence across all inclusion and exclusion tests, indicating that the training sequence was learned and retained across intervals. However, the inability to produce or withhold generating components of the training sequence, as per inclusion and exclusion tasks, indicated that an awareness of the trained sequence content had not developed across intervals of post-sleep/wake or a after a week's duration. The absence of sleep-dependent awareness is in contrast to the results of Fischer et al. (2006) who found that sleep, but not wake, resulted in significantly better performance generation of the trained sequence after SRTT training. The increase in generation performance has widely been taken to indicate that sleep selectively promotes the development of explicit sequence knowledge from implicit motor sequence learning. Notably however, in their version of the generation task the correct cue location was displayed following each generated response whether the participants' responses were correct or not. This may have allowed the development of explicit sequence knowledge before sleep, which consequently may have resulted in sleep enhancing the explicit representation of the sequence, as opposed to the development of awareness from implicit sequence knowledge (Robertson, Pascual-Leone, & Press, 2004). Importantly, our results indicated that when awareness and performance are controlled for, the development of awareness for implicit motor sequence knowledge does not develop after a period of sleep or wake.

Familiarity. Accordingly, there were no significant changes in similarity ratings between groups or across sessions for the any post-performance ratings of the representation test blocks**.** Across sessions, the trained sequence was always rated as most similar to training, followed by the spatial-referent sequence, motor-referent sequence, and finally the untrained sequence was rated as least similar**.** This lack of change from an implicit baseline indicates familiarity but not full recognition memory of the training sequence, or its spatial or motor referent components. However, a significant difference was observed where the spatial-referent pattern was seen as more familiar than the motor-referent pattern. Whereas, overall, both the motor and untrained sequence were rated as comparably unfamiliar. While the ranking of the similarity ratings was as hypothesized, contrary to hypotheses, there was no increase in similarity ratings for the trained sequence or spatial-referent sequence. This is in agreement with other research indicating that familiarity memory may be a sleep-independent process (Darsaud et al., 2010). However, these familiarity ratings also paralleled performance outcomes on the SRTT representation blocks themselves which may mean that these ratings were also influenced by how well the participants performed each block which also did not change across session.

Generalization. Typically, speed-based performance of spatial or motor-referent sequences of a training sequence are used to explore the properties of skill transfer to the untrained hand (Cohen et al., 2005; Japikse, Negash, Howard, & Howard, 2003; Wiestler et al., 2014; Witt et al., 2010). Here, as opposed to testing skill fluency under task training conditions, we sought to assess whether spatial or motor representations are accessed when asked to freely and accurately generate the sequence with the other hand. Our analyses did not reveal any significant effects dependent on intervals of sleep or wake or when tested one week later. We did find that overall, both spatial and motor-referent triplets were generated significantly more than triplets congruent with the untrained, alternative SRTT sequence, which indicates that both representations were acquired and accessible above chance. Despite a close mix of both spatial and motor-referent triplets being generated, there was a significant preference for generating spatial sequence triplets. This suggests that when knowledge is implicit the spatial representation is preferentially accessed in producing sequences.

It was hypothesized, specifically, that there would be enhancement of the spatial representation over sleep, which would increase inter-manual transfer of the spatial-referent knowledge. However, this was not observed. Driving the assumption that the spatial aspects would be involved with skill generalizability comes from previous work evaluating how representations generalize across sleep, which have indicated the spatial referent representation is most closely involved in skill transfer and sleep dependent gains. In an explicit motor sequence learning task (Witt et al., 2010) inter-manual transfer of the spatial-referent sequence outperformed transfer of the motor-referent sequence immediately after learning. Across wake, the spatial performance was reduced to that of the motor-referent sequence. However, this deterioration of spatial performance was not seen if a period of sleep interleaved the transfer test, in which case, the advantage of the spatial performance was preserved. This suggests that sleep contributes to the generalization of skill, through the stabilizing sleep-dependent consolidation effects of the spatial representations of learned sequences. Using the SRTT task to explore whether the spatial or motor referent skill knowledge generalizes in implicit MSL, Cohen et al. (2005) found that the movement-referent sequence is enhanced across day while the spatial-referent sequence was enhanced over sleep. Taken together, these studies provide evidence that dissociable spatial and motor representations are both acquired across training, play different roles in the transfer of skill, and appear to have different consolidation processes. However, the measures of skill transfer in these studies were not free recall, but were cued or explicit motor sequence execution speeds. Here, when asking participants to generalize their sequence knowledge in the form of recall and generation we have observed an effect, where, although closely mixed, spatial-referent representations were produced more than motor. This is consistent with a more recent study (Wiestler et al., 2014) that has demonstrated wide-spread bilateral cortical activation is involved in encoding both spatial and motor-referent MSL knowledge. Their results indicated that inter-manual transfer involves encoding both spatial and motor representations across cerebral hemispheres during motor sequence training. Our findings also appear support this, given our evidence that both representations were accessed for generating triplets. Furthermore, our results suggest that when knowledge is implicit the spatial representation is preferentially accessed in producing sequences, regardless of intervening periods of time of day, or intervening sleep or wake between learning and recall.

Sleep Architecture and Implicit Memory Consolidation

To investigate whether implicit learning results in preferential recruitment of particular stages of sleep we compared EEG sleep architecture from a baseline night, after a control version of the SRTT, to sleep after implicit learning with the SRTT. We observed a significant increase in amount of REM, with no other significant change across any of the NREM stages. Reports for REM effects related to MSL tend to vary. To our knowledge, only one other study has found the amount of REM to be associated with SDMC of SRTT implicit learning, in which the presence of REM in naps across a forced routine protocol was associated with implicit learning improvement (Cajochen et al., 2004). Although the primary hypotheses predicted that increased spindle activity would be most implicated in SDMC for our study, this increase in REM is not completely out of context. Notably, increases in functional connectivity have been observed during REM sleep between the striatum and reactivated cortical areas after implicit probabilistic MSL with the SRTT which was suggested to be a process of skill memory reactivation for memory integration (Maquet et al., 2000; Peigneux et al., 2003). Furthermore, more recent neuroimaging studies have suggested that sleep is key for long-term functional reorganization in the neural circuits underlying implicit sequence learning (Debas et al., 2014) - even in the possible absence of detectable behavioral changes (Urbain et al., 2013). Thus, our results are consistent with this account in that we have observed and increase in REM, which is thought to be a state of motor memory stabilization and integration (Debas et al., 2014; Maquet et al., 2000; Peigneux et al., 2003; Urbain et al., 2013), without overt gains in SRTT training skill.

To further investigate the sleep-dependent mechanisms of consolidation, we sought to evaluate whether spindle activity in NREM2 sleep plays a role in the consolidation of implicit MSL, as it has been shown to do for explicit MSL (Albouy, Fogel, et al., 2013; Barakat et al., 2013; Fogel & Smith, 2006, 2011; Morin et al., 2008). However, we did not observe an increase in spindle recruitment as predicted, and spindle density, amplitude, duration and peak frequency was equivalent between the baseline and experimental recording across all center-line electrode derivations. Although these results came contrary to our hypotheses, they appear to fall in line

with the notion that implicit MSL may undergo a different process of consolidation than explicit MSL.

Conclusions

This study has contributed to the ongoing debate surrounding the processes involved in learning and memory consolidation for implicitly learned visual-motor learning, using a novel SRTT paradigm that allowed us to dissociate between spatial and motor representations. Our results indicated that similar to explicit motor sequence learning, behaviourally dissociable spatial and motor representations are acquired for implicitly learned visual-motor sequence learning. Similar to explicit memory, this likely reflects the involvement of distinct memory neurosubstrates. Contrary to our predictions, and unlike explicit memory, the spatial representation was not specifically enhanced by sleep and did not recruit spindle activity. However, post-training REM sleep duration increased as compared to a baseline, control night, suggesting that sleep may still play a role in the consolidation and stabilization of the memory trace that was observed.

Nevertheless, across both experimental groups, we did observe enhancement of the motor representation when re-tested a week after initial training which may reflect time-dependent offline consolidation of motor-referent sequence coordination. The exact mechanism underlying this change remains unresolved. Possibilities include a slower time-course of sleep dependent consolidation (i.e., across multiple nights), sleep-independent offline gains (i.e., the mere passage of time), the effects of practice across retests, or a combination these events. In conclusion, our results provide evidence that when MSL is implicit neither sleep nor wake contributes to the development of explicit awareness for implicitly learned visual-motor sequencing. Importantly, the results of this study suggest that like explicit sequence learning, implicit sequence learning is comprised of distinct spatial and motor representations. However, unlike explicit sequence learning, sleep does not preferentially enhance consolidation of the spatial representation. Thus, suggesting that implicit sequence consolidation takes place irrespective of sleep or wake, and importantly, that sleep is not recruited in all cases for the consolidation of spatial memory representations.

References

Abel, T., & Lattal, K. M. (2001). Molecular mechanisms of memory acquistion, consolidation and retrieval. *Current Opinion in Neurobiology*, *11*, 180–187.

Achermann, P., & Borbély, A. A. (1998). Coherence analysis of the human sleep electroencephalogram. *Neuroscience*, *85*(4), 1195–1208. http://doi.org/10.1016/S0306-4522(97)00692-1

Achermann, P., & Borbély, A. A. (2003). Mathematical models in sleep deprivation. *Frontiers in Bioscience*, *8*(13), s683–693. http://doi.org/10.2741/1064

Aiello, L. C., Wheeler, P., & Chivers, D. (1995). The Expensive-Tissue Hypothesis The Brain and the Digestive Evolution ’. *Current Anthropology*, *36*(2), 199–221. http://doi.org/10.1086/204350

Albouy, G., Fogel, S. M., King, B. R., Laventure, S., Benali, H., Karni, A., … Doyon, J. (2015). Maintaining vs. enhancing motor sequence memories: Respective roles of striatal and hippocampal systems. *NeuroImage*, *108*, 423–434. http://doi.org/10.1016/j.neuroimage.2014.12.049

Albouy, G., Fogel, S. M., Pottiez, H., Nguyen, V. A., Ray, L., Lungu, O., … Doyon, J. (2013). Daytime Sleep Enhances Consolidation of the Spatial but Not Motoric Representation of Motor Sequence Memory. *PLoS ONE*, *8*(1), 11–13. http://doi.org/10.1371/journal.pone.0052805

Albouy, G., King, B. R., Maquet, P., & Doyon, J. (2013). Hippocampus and striatum: dynamics and interaction during acquisition and sleep-related motor sequence memory consolidation. *Hippocampus*, *23*(11), 985–1004. http://doi.org/10.1002/hipo.22183

Albouy, G., Sterpenich, V., Balteau, E., Vandewalle, G., Desseilles, M., Dang-Vu, T. T., … Maquet, P. (2008). Both the hippocampus and striatum are involved in consolidation of motor sequence memory. *Neuron*, *58*(2), 261–72. http://doi.org/10.1016/j.neuron.2008.02.008

Albouy, G., Sterpenich, V., Vandewalle, G., Darsaud, A., Gais, S., Rauchs, G., … Maquet, P. (2012). Neural correlates of performance variability during motor sequence acquisition. *NeuroImage*, *60*(1), 324–331. http://doi.org/10.1016/j.neuroimage.2011.12.049

Albouy, G., Sterpenich, V., Vandewalle, G., Darsaud, A., Gais, S., Rauchs, G., … Maquet, P. (2013). Interaction between hippocampal and striatal systems predicts subsequent consolidation of motor sequence memory. *PloS One*, *8*(3), e59490. http://doi.org/10.1371/journal.pone.0059490

Alger, S. E., Chambers, A. M., Cunningham, T., & Payne, J. D. (2015). The Role of Sleep in Human Declarative Memory Consolidation. *Current Topics in Behavioral Neurosciences*,

25, 269–306. http://doi.org/10.1007/7854

Alger, S. E., Lau, H., & Fishbein, W. (2012). Slow wave sleep during a daytime nap is necessary for protection from subsequent interference and long-term retention. *Neurobiology of Learning and Memory*, *98*(2), 188–196. http://doi.org/10.1016/j.nlm.2012.06.003

Allen, S. R., Oswald, I., Lewis, S., & Tagney, J. (1972). The effects of distorted visual input on sleep. *Psychophsyiology*, *9*(5), 498–504.

Alvaro, P. K., Roberts, R. M., & Harris, J. K. (2013). A Systematic Review Assessing Bidirectionality between Sleep Disturbances, Anxiety, and Depression. *Sleep*, *36*(7), 1059–1068. http://doi.org/10.5665/sleep.2810

Ambrosini, M. V., & Giuditta, a. (2001). Learning and sleep: the sequential hypothesis. *Sleep Medicine Reviews*, *5*(6), 477–490. http://doi.org/10.1053/smrv.2001.0180

Amzica, F., & Massimini, M. (2002). Glial and Neuronal Interactions during Slow Wave and Paroxysmal Activities in the Neocortex. *Cerebral Cortex*, *12*(10), 1101–1113.

Aton, S. J., Broussard, C., Dumoulin, M. C., Seibt, J., Watson, A., Coleman, T., & Frank, M. G. (2013). Visual experience and subsequent sleep induce sequential plastic changes in putative inhibitory and excitatory cortical neurons. *Proceedings of the National Academy of Sciences of the United States of America*, *110*(8), 3101–6. http://doi.org/10.1073/pnas.1208093110

Barakat, M., Carrier, J., Debas, K., Lungu, O., Fogel, S. M., Vandewalle, G., … Doyon, J. (2013). Sleep spindles predict neural and behavioral changes in motor sequence consolidation. *Human Brain Mapping*, *34*(11), 2918–2928. http://doi.org/10.1002/hbm.22116

Barsky, M. M., Tucker, M. a., & Stickgold, R. (2015). REM sleep enhancement of probabilistic classification learning is sensitive to subsequent interference. *Neurobiology of Learning and Memory*, *122*, 63–68. http://doi.org/10.1016/j.nlm.2015.02.015

Bazhenov, M., Timofeev, I., Steriade, M., & Sejnowski, T. (2000). Spiking-Bursting Activity in the Thalamic Reticular Nucleus Initiates Sequences of Spindle Oscillations in Thalamic Networks. *J Neurophysiol*, *84*(2), 1076–1087.

Bazhenov, M., Timofeev, I., Steriade, M., & Sejnowski, T. J. (1999). Self-sustained rhythmic activity in the thalamic reticular nucleus mediated by depolarizing GABAA receptor potentials. *Nature Neuroscience*, *2*(2), 168–74. http://doi.org/10.1038/5729

Bendor, D., & Wilson, M. A. (2012). Biasing the content of hippocampal replay during sleep. *Nature Neuroscience*, *15*(10), 1439–1444. http://doi.org/10.1038/nn.3203

Berger, R. J., & Phillips, N. H. (1995). Energy conservation and sleep. *Behavioural Brain Research*, *69*(1-2), 65–73. http://doi.org/10.1016/0166-4328(95)00002-B

Bergmann, T. O., Mölle, M., Diedrichs, J., Born, J., & Siebner, H. R. (2012). Sleep spindle-related reactivation of category-specific cortical regions after learning face-scene

associations. *NeuroImage*, *59*(3), 2733–2742. http://doi.org/10.1016/j.neuroimage.2011.10.036

Bergmann, T. O., Mölle, M., Marshall, L., Kaya-Yildiz, L., Born, J., & Roman Siebner, H. (2008). A local signature of LTP- and LTD-like plasticity in human NREM sleep. *The European Journal of Neuroscience*, *27*(9), 2241–9. http://doi.org/10.1111/j.1460-9568.2008.06178.x

Bohbot, V. D., Lerch, J., Thorndycraft, B., Iaria, G., & Zijdenbos, A. P. (2007). Gray Matter Differences Correlate with Spontaneous Strategies in a Human Virtual Navigation Task. *Journal of Neuroscience*, *27*(38), 10078–10083. http://doi.org/10.1523/JNEUROSCI.1763-07.2007

Bollinger, T., Bollinger, A., Skrum, L., Dimitrov, S., Lange, T., & Solbach, W. (2009). Sleep-dependent activity of T cells and regulatory T cells. *Clinical and Experimental Immunology*, *155*(2), 231–238. http://doi.org/10.1111/j.1365-2249.2008.03822.x

Bonjean, M., Baker, T., Lemieux, M., Timofeev, I., Sejnowski, T., & Bazhenov, M. (2011). Corticothalamic feedback controls sleep spindle duration in vivo. *The Journal of Neuroscience*, *31*(25), 9124–34. http://doi.org/10.1523/JNEUROSCI.0077-11.2011

Borbély, A. A. (1982). A two process model of sleep regulation. *Human Neurobiology*, *1*(3), 195–204.

Borbély, A. A., Daan, S., Wirz-Justice, A., & Deboer, T. (2016). The two-process model of sleep regulation: a reappraisal. *Journal of Sleep Research*, (September 2014), 131–143. http://doi.org/10.1111/jsr.12371

Bragin, a, Engel, J., Wilson, C. L., Fried, I., & Buzsáki, G. (1999). High-frequency oscillations in human brain. *Hippocampus*, *9*(2), 137–142. http://doi.org/10.1002/(SICI)1098-1063(1999)9:2<137::AID-HIPO5>3.0.CO;2-0

Brawn, T. P., Fenn, K. M., Nusbaum, H. C., & Margoliash, D. (2010). Consolidating the effects of waking and sleep on motor-sequence learning. *Journal of Neuroscience*, *30*(42), 13977–82. http://doi.org/10.1523/JNEUROSCI.3295-10.2010

Bushey, D., Tononi, G., & Cirelli, C. (2011). Sleep and Synaptic Homeostasis: Structural Evidence in Drosophila. *Science*, *332*(June), 1576–1581.

Buxton, O. M., & Marcelli, E. (2010). Short and long sleep are positively associated with obesity, diabetes, hypertension, and cardiovascular disease among adults in the United States. *Social Science & Medicine (1982)*, *71*(5), 1027–36. http://doi.org/10.1016/j.socscimed.2010.05.041

Buzaki, G. (1996). The Hippocampo-Neocortical Dialogue. *Cerebral Cortex*, *6*, 81–92.

Buzaki, G., Pentfonen, M., Nadasdy, Z., & Bragin, A. (1996). Pattern and Inhibition-Dependent Invasion of Pyramidal Cell Dendrites by Fast Spikes in the Hippocampus in vivo. *Proceedings of the National Academy of Sciences of the United States of America*, *93*(18), 9921–9925.

Buzsáki, G. (2015). Hippocampal sharp wave-ripple: A cognitive biomarker for episodic memory and planning. *Hippocampus*, *25*(10), 1073–1188. http://doi.org/10.1002/hipo.22488

Cajochen, C., Knoblauch, V., Wirz-Justice, A., Kräuchi, K., Graw, P., & Wallach, D. (2004). Circadian modulation of sequence learning under high and low sleep pressure conditions. *Behavioural Brain Research*, *151*(1-2), 167–176. http://doi.org/10.1016/j.bbr.2003.08.013

Callaway, C. W., Lydic, R., Baghdoyan, H. A., & Hobson, J. A. (1987). Pontogeniculooccipital waves: spontaneous visual system activity during rapid eye movement sleep. *Cellular and Molecular Neurobiology*, *7*(2), 105–149. http://doi.org/10.1007/BF00711551

Carskadon, M. A., & Dement, W. C. (2011). Normal Human Sleep : An Overview. *Principles and Practice of Sleep Medicine*, 16–26. http://doi.org/10.1016/B978-1-4160-6645-3.00141-9

Chase, M. H., & Morales, F. R. (1990). The atonia and myoclonia of active (REM) sleep. *Annual Review of Psychology*, *41*, 557–84. http://doi.org/10.1146/annurev.ps.41.020190.003013

Chauvette, S., Seigneur, J., & Timofeev, I. (2012). Sleep Oscillations in the Thalamocortical System Induce Long-Term Neuronal Plasticity. *Neuron*, *75*(6), 1105–1113. http://doi.org/10.1016/j.neuron.2012.08.034

Chow, H. M., Horovitz, S. G., Carr, W. S., Picchioni, D., Coddington, N., Fukunaga, M., … Braun, A. R. (2013). Rhythmic alternating patterns of brain activity distinguish rapid eye movement sleep from other states of consciousness. *Proceedings of the National Academy of Sciences of the United States of America*, *110*(25), 10300–10305. http://doi.org/10.1073/pnas.

Cirelli, C., Gutierrez, C. M., & Tononi, G. (2004). Extensive and Divergent Effects of Sleep and Wakefulness on Brain Gene Expression. *Neuron*, *41*(1), 35–43. http://doi.org/10.1016/S0896-6273(03)00814-6

Cleeremans, A., & McClelland, J. L. (1991). Learning the structure of event sequence. *Journal of Experimental Psychology: General*, *120*(3), 235–253.

Cohen, D. A., Pascual-Leone, A., Press, D. Z., & Robertson, E. M. (2005). Off-Line Learning of Motor Skill Memory: A Double Dissociation of Goal and Movement. *Proc Natl Acad Sci U S A*, *102*(50), 18237–18241. http://doi.org/0506072102 [pii] 10.1073/pnas.0506072102

Cooke, S. F., & Bliss, T. V. P. (2006). Plasticity in the human central nervous system. *Brain*, *129*(7), 1659–1673. http://doi.org/10.1093/brain/awl082

Cote, K., Epps, T. M., & Campbell, K. B. (2000). The role of the spindle in human information processing of high-intensity stimuli during sleep. *Journal of Sleep Research*, *9*, 19–26.

Crowley, K., Trinder, J., Kim, Y., Carrington, M., & Colrain, I. M. (2002). The effects of normal aging on sleep spindle and K-complex production. *Clinical Neurophysiology*, *113*, 1615–1622. http://doi.org/10.1016/S1388-2457(02)00237-7

Dang-Vu, T. T., Bonjean, M., Schabus, M., Boly, M., Darsaud, A., Desseilles, M., … Maquet, P. (2011). Interplay between spontaneous and induced brain activity during human non-rapid eye movement sleep. *Proceedings of the National Academy of Sciences of the United States of America*, *108*(37), 15438–43. http://doi.org/10.1073/pnas.1112503108

Darsaud, A., Dehon, H., Lahl, O., Sterpenich, V., Boly, M., Dang-vu, T., … Collette, F. (2010). Does Sleep Promote False Memories ?, 26–40.

Datta, S. (1999). PGO wave generation: mechanism and functional significance. In B. N. Mallicl & S. Inoue (Eds.), *Rapid Eye Movement Sleep* (pp. 91–06). New Delhi, India: Narosa Publishing House. Retrieved from https://books.google.com/books?hl=en&lr=&id=r9k4CkerWLIC&pgis=1

Davis, H., Davis, P. A., Loomis, A. L., Harvey, E. N., & Hobart, G. (1937). Changes in human brain potentials during the onset of sleep. *Science (New York, N.Y.)*, *86*(2237), 448–50. http://doi.org/10.1126/science.86.2237.448

De Gennaro, L., Ferrara, M., & Bertini, M. (2000). Effect of slow-wave sleep deprivation on topographical distribution of spindles. *Behavioural Brain Research*, *116*(1), 55–9.

De Koninck, J., & Prévost, F. (1991). Paradoxical sleep and information processing: exploration by inversion of the visual field. *Canadian Journal of Psychology*, *45*(2), 125–39. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/1873752

Debas, K., Carrier, J., Barakat, M., Marrelec, G., Bellec, P., Tahar, A. H., … Doyon, J. (2014). Off-line consolidation of motor sequence learning results in greater integration within a cortico-striatal functional network. *NeuroImage*, *99*, 50–58. http://doi.org/10.1016/j.neuroimage.2014.05.022

Dement, W., & Kleitman, N. (1957). Cyclic variations in EEG during sleep and their relation to eye movements, body motility, and dreaming. *Electroencephalography and Clinical Neurophysiology*, *9*(4).

Destrebecqz, A., & Cleeremans, A. (2001). Can sequence learning be implicit? New evidence with the process dissociation procedure. *Psychonomic Bulletin & Review*, *8*(2), 343–350. http://doi.org/10.3758/BF03196171

Destrebecqz, A., Peigneux, P., Laureys, S., Degueldre, C., Del Fiore, G., Aerts, J., … Maquet, P. (2005). The neural correlates of implicit and explicit sequence learning: Interacting networks revealed by the process dissociation procedure. *Learning & Memory (Cold Spring Harbor, N.Y.)*, *12*(5), 480–90. http://doi.org/10.1101/lm.95605

Dickson, C. T. (2010). Ups and downs in the hippocampus: The influence of oscillatory sleep states on " neuroplasticity" at different time scales. *Behavioural Brain Research*, *214*(1), 35–41. http://doi.org/10.1016/j.bbr.2010.04.002

Diekelmann, S., & Born, J. (2010a). Slow-wave sleep takes the leading role in memory reorganization. *Nature Reviews. Neuroscience*, *11*(3), 218. http://doi.org/10.1038/nrn2762-c2

Diekelmann, S., & Born, J. (2010b). The memory function of sleep. *Nature Reviews Neuroscience*, *11*(2), 114–26. http://doi.org/10.1038/nrn2762

Diekelmann, S., Wilhelm, I., & Born, J. (2009). The whats and whens of sleep-dependent memory consolidation. *Sleep Medicine Reviews*, *13*(5), 309–21. http://doi.org/10.1016/j.smrv.2008.08.002

Diekelmann, S., Wilhelm, I., Wagner, U., & Born, J. (2013). Sleep Improves Prospective Remembering by Facilitating Spontaneous-Associative Retrieval Processes. *PLoS ONE*, *8*(10), 1–10. http://doi.org/10.1371/journal.pone.0077621

Dijk, D.-J., & von Schantz, M. (2005). Timing and Consolidation of Human Sleep, Wakefulness, and Performance by a Symphony of Oscillators. *Journal of Biological Rhythms*, *20*(4), 279–290. http://doi.org/10.1177/0748730405278292

Dinges, D. F., & Powell, J. W. (1985). Microcomputer analyses of performance on a portable, simple visual RT task during sustained operations. *Behavior Research Methods, Instruments, & Computers*, *17*(6), 652–655. http://doi.org/10.3758/BF03200977

Djonlagic, I., Rosenfeld, A., Shohamy, D., Myers, C., Gluck, M. A., & Stickgold, R. (2009). Sleep enhances category learning. *Learning & Memory (Cold Spring Harbor, N.Y.)*, *16*(12), 751–755. http://doi.org/10.1101/lm.1634509

Doeller, C. F., King, J. A., & Burgess, N. (2008). Parallel striatal and hippocampal systems for landmarks and boundaries in spatial memory. *Proc Natl Acad Sci U S A*, *105*(15), 5915–5920. http://doi.org/10.1073/pnas.0801489105

Doyon, J., Bellec, P., Amsel, R., Penhune, V., Monchi, O., Carrier, J., … Benali, H. (2009). Contributions of the basal ganglia and functionally related brain structures to motor learning. *Behavioural Brain Research*, *199*(1), 61–75. http://doi.org/10.1016/j.bbr.2008.11.012

Doyon, J., Gaudreau, D., Laforce, R. J., Castonguay, M., Bedard, P. J., Bedard, F., & Bouchard, J. P. (1997). Role of the striatum, cerebellum, and forntal lobes in the learning of a visuomotor sequence. *Brain and Cognition*, *34*(2), 218–245.

Doyon, J., Korman, M., Morin, A., Dostie, V., Hadj Tahar, A., Benali, H., … Carrier, J. (2009). Contribution of night and day sleep vs. simple passage of time to the consolidation of motor sequence and visuomotor adaptation learning. *Experimental Brain Research*, *195*(1), 15–26. http://doi.org/10.1007/s00221-009-1748-y

Doyon, J., Owen, a M., Petrides, M., Sziklas, V., & Evans, a C. (1996). Functional anatomy of visuomotor skill learning in human subjects examined with positron emission tomography. *The European Journal of Neuroscience*, *8*(4), 637–48. http://doi.org/10.1111/j.1460-9568.1996.tb01249.x

Ellenbogen, J. M., Hu, P. T., Payne, J. D., Titone, D., & Walker, M. P. (2007). Human relational memory requires time and sleep. *Proceedings of the National Academy of Sciences of the United States of America*, *104*(18), 7723–8. http://doi.org/10.1073/pnas.0700094104

Fernández-Mendoza, J., Lozano, B., Seijo, F., Santamarta-Liébana, E., Ramos-Platón, M. J., Vela-Bueno, A., & Fernández-González, F. (2009). Evidence of subthalamic PGO-like waves during REM sleep in humans: a deep brain polysomnographic study. *Sleep*, *32*, 1117–1126.

Ferrara, M., Iaria, G., Tempesta, D., Curcio, G., Moroni, F., Marzano, C., … Pacitti, C. (2008). Sleep to find your way: The role of sleep in the consolidation of memory for navigation in humans. *Hippocampus*, *18*(8), 844–851. http://doi.org/10.1002/hipo.20444

Fischer, S., & Born, J. (2009). Anticipated reward enhances offline learning during sleep. *Journal of Experimental Psychology. Learning, Memory, and Cognition*, *35*(6), 1586–1593. http://doi.org/10.1037/a0017256

Fischer, S., Drosopoulos, S., Tsen, J., & Born, J. (2006). Implicit Learning–Explicit Knowing: A Role for Sleep in Memory System Interaction. *Journal of Cognitive Neuroscience*, *18*(3), 311–319. http://doi.org/10.1162/jocn.2006.18.3.311

Fischer, S., Hallschmid, M., Elsner, A. L., & Born, J. (2002). Sleep forms memory for finger skills. *Proceedings of the National Academy of Sciences*, *99*(18).

Fogel, S. M., Albouy, G., Vien, C., Popovicci, R., King, B. R., Hoge, R., … Doyon, J. (2014). fMRI and sleep correlates of the age-related impairment in motor memory consolidation. *Human Brain Mapping*, *35*(8), 3625–3645. http://doi.org/10.1002/hbm.22426

Fogel, S. M., Ray, L., Binnie, L., & Owen, A. M. (2015). How to become an expert: A new perspective on the role of sleep in the mastery of procedural skills. *Neurobiology of Learning and Memory*, *125*, 236–248. http://doi.org/10.1016/j.nlm.2015.10.004

Fogel, S. M., & Smith, C. T. (2006). Learning-dependent changes in sleep spindles and Stage 2 sleep. *Journal of Sleep Research*, *15*(3), 250–255. http://doi.org/10.1111/j.1365-2869.2006.00522.x

Fogel, S. M., & Smith, C. T. (2011). The function of the sleep spindle: a physiological index of intelligence and a mechanism for sleep-dependent memory consolidation. *Neuroscience and Biobehavioral Reviews*, *35*(5), 1154–65. http://doi.org/10.1016/j.neubiorev.2010.12.003

Fogel, S. M., Smith, C. T., & Cote, K. A. (2007). Dissociable learning-dependent changes in REM and non-REM sleep in declarative and procedural memory systems. *Behavioural Brain Research*, *180*, 48–61. http://doi.org/10.1016/j.bbr.2007.02.037

Frank, M. G. (2012). Erasing synapses in sleep: is it time to be SHY? *Neural Plasticity*, *2012*, 264378. http://doi.org/10.1155/2012/264378

Frank, M. G. (2015). Sleep and Synaptic Plasticity in the Developing and Adult Brain. *Current Topics in Behavioral Neurosciences*, *25*, 123–149. http://doi.org/10.1007/7854

Franken, P., Dijk, D.-J., Tobler, I., & Borbély, a a. (1991). Sleep deprivation in rats: effects on EEG power spectra, vigilance states, and cortical temperature. *The American Journal of Physiology*, *261*, R198–R208.

Fu, Q., Bin, G., Dienes, Z., Fu, X., & Gao, X. (2013). Learning without consciously knowing: Evidence from event-related potentials in sequence learning. *Consciousness and Cognition*, *22*(1), 22–34. http://doi.org/10.1016/j.concog.2012.10.008

Fu, Q., Fu, X., & Dienes, Z. (2008). Implicit sequence learning and conscious awareness. *Consciousness and Cognition*, *17*(1), 185–202. http://doi.org/10.1016/j.concog.2007.01.007

Gaetan, D. L., Marie, L., Laure, R.-R., & Karim, B. (2013). Explicit memory creation during sleep: a causal role of place cell on navigation. *Nature Publishing Group*, *18*(4), 1–39. http://doi.org/10.1038/nn.3970

Gais, S., & Born, J. (2004). Declarative memory consolidation: Mechanisms acting during human sleep. *Learning & Memory*, *11*(6), 679–685. http://doi.org/10.1101/lm.80504

Gheysen, F., Van Opstal, F., Roggeman, C., Van Waelvelde, H., & Fias, W. (2010). Hippocampal contribution to early and later stages of implicit motor sequence learning. *Experimental Brain Research*, *202*(4), 795–807. http://doi.org/10.1007/s00221-010-2186-6

Gilbert, P. F. C. (2001). An outline of brain function. *Cognitive Brain Research*, *12*(1), 61–74. http://doi.org/10.1016/S0926-6410(01)00035-0

Gilestro, G. F., Tononi, G., & Cirelli, C. (2009). Widespread Changes in Synaptic Markers as a Function of Sleep and Wakefulness in Drosophila. *Science*, *324*(5923), 109–112. http://doi.org/10.1126/science.1166673

Giuditta, A. (2014). Sleep memory processing: the sequential hypothesis. *Frontiers in Systems Neuroscience*, *8*(December), 219. http://doi.org/10.3389/fnsys.2014.00219

Gómez, R. L., Bootzin, R. R., & Nadel, L. (2006). Naps promote abstraction in language learning infants. *Psychological Science*, *17*(8), 670–674.

Graf, P., & Schacter, D. L. (1985). Implicit and explicit memory for new associations in normal and amnesic subjects. *Journal of Experimental Psychology. Learning, Memory, and Cognition*, *11*(3), 501–518. http://doi.org/10.1037/0278-7393.11.3.501

Greenberg, A., & Dickson, C. T. (2013). Spontaneous and electrically modulated spatiotemporal dynamics of the neocortical slow oscillation and associated local fast activity. *NeuroImage*, *83*, 782–794. http://doi.org/10.1016/j.neuroimage.2013.07.034

Halász, P., Terzano, M., Parrino, L., & Bódizs, R. (2004). The nature of arousal in sleep. *Journal of Sleep Research*, *13*, 1–23. http://doi.org/10.1111/j.1365-2869.2004.00388.x

Hasselmo, M. E. (1999). Neuromodulation: Acetylcholine and memory consolidation. *Trends in Cognitive Sciences*, *3*(9), 351–359. http://doi.org/10.1016/S1364-6613(99)01365-0

Hikosaka, O., Nakamura, K., Sakai, K., & Nakahara, H. (2002). Central mechanisms of motor skill learning. *Current Opinion in Neurobiology*, *12*(2), 217–222. http://doi.org/10.1016/S0959-4388(02)00307-0

Howard, J. H., & Howard, D. V. (1997). Age differences in implicit learning of higher order

dependencies in serial patterns. *Psychology and Aging*, *12*(4), 634–656. http://doi.org/10.1037/0882-7974.12.4.634

Hu, P. T., Stylos-Allan, M., & Walker, M. P. (2006). Sleep facilitates consolidation of emotionally arousing declarative memory. *Psychological Science*, *17*(10), 891–898.

Huber, R., Ghilardi, M. F., Massimini, M., Ferrarelli, F., Riedner, B. a, Peterson, M. J., & Tononi, G. (2006). Arm immobilization causes cortical plastic changes and locally decreases sleep slow wave activity. *Nature Neuroscience*, *9*(9), 1169–76. http://doi.org/10.1038/nn1758

Huber, R., Ghilardi, M. F., Massimini, M., & Tononi, G. (2004). Local sleep and learning. *Nature*, *430*(6995), 78–81. http://doi.org/10.1038/nature02663

Hyder, F., Rothman, D. L., & Bennett, M. R. (2013). Cortical energy demands of signaling and nonsignaling components in brain are conserved across mammalian species and activity levels. *Proc Natl Acad Sci U S A*, *110*(9), 3549–3554. http://doi.org/10.1073/pnas.1214912110

Iaria, G., Petrides, M., Dagher, A., Pike, B., & Bohbot, V. D. (2003). Cognitive strategies dependent on the hippocampus and caudate nucleus in human navigation: variability and change with practice. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *23*(13), 5945–5952. http://doi.org/23/13/5945 [pii]

Iber, C., Ancoli-Israel, S., Chesson Jr., A. L., & Quan, S. F. (2007). The AASM Manual for the Scoring of Sleep and Associated Events: Rules Terminology and Technical Specifications 1st ed.

Jacoby, L. L. (1991). A process dissociation framework: Separating automatic from intentional uses of memory. *Journal of Memory and Language*, *30*(5), 513–541. http://doi.org/10.1016/0749-596X(91)90025-F

Japikse, K. C., Negash, S., Howard, J. H., & Howard, D. V. (2003). Intermanual transfer of procedural learning after extended practice of probabilistic sequences. *Experimental Brain Research*, *148*(1), 38–49. http://doi.org/10.1007/s00221-002-1264-9

Jiménez, L., & Vázquez, G. A. (2005). Sequence learning under dual-task conditions: Alternatives to a resource-based account. *Psychological Research*, *69*(5-6), 352–368. http://doi.org/10.1007/s00426-004-0210-9

Jouvet, M., & Michel, F. (1959). [Electromyographic correlations of sleep in the chronic decorticate & mesencephalic cat]. *Comptes Rendus Des Séances de La Société de Biologie et de Ses Filiales*, *153*(3), 422–5. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/13663472

Kakizaki, M., Inoue, K., Kuriyama, S., Sone, T., Matsuda-Ohmori, K., Nakaya, N., … Tsuji, I. (2008). Sleep duration and the risk of prostate cancer: the Ohsaki Cohort Study. *British Journal of Cancer*, *99*(1), 176–8. http://doi.org/10.1038/sj.bjc.6604425

Karni, A., Tanne, D., Rubenstein, B. S., Askenasy, J. J., & Sagi, D. (1994). Dependence on REM

sleep of overnight improvement of a perceptual skill. *Science*, *265*(5172), 679–682. http://doi.org/10.1126/science.8036518

Keisler, A., Ashe, J., & Willingham, D. T. (2011). learning Time of day accounts for overnight improvement in sequence Time of day accounts for overnight improvement in sequence learning. *Cold Spring Harbor Laboratory Press on October*, *7*(1), 669–672. http://doi.org/10.1101/lm.751807

Killgore, W. D. S. (2010). Effects of sleep deprivation on cognition. *Progress in Brain Research*, *185*(C), 105–129. http://doi.org/10.1016/B978-0-444-53702-7.00007-5

Knopman, D. S., & Nissen, M. J. (1987). Implicit learning in patients with probable Alzheimer's disease. *Neurology*, *37*(5), 784–784. http://doi.org/10.1212/WNL.37.5.784

Knowlton, B. J., Mangels, J. A., & Squire, L. R. (1996). A Neostriatal Habit Learning System in Humans. *Science*, *273*(5280), 1399–1402.

Knowlton, B. J., Squire, L. R., & Gluck, M. A. (1994). Probabilistic classification learning in amnesia. *Learn Mem*, *1*(2), 106–120. http://doi.org/10.1101/lm.1.2.106

Knowlton, B. J., Squire, L. R., Paulsen, J. S., Swerdlow, N. R., & Swenson, M. (1996). Dissociations within nondeclarative memory in Huntington's disease. *Neuropsychology*, *10*(4), 538–548. http://doi.org/10.1037/0894-4105.10.4.538

Knutson, K. L., & Van Cauter, E. (2008). Associations between sleep loss and increased risk of obesity and diabetes. *Annals of the New York Academy of Sciences*, *1129*, 287–304. http://doi.org/10.1196/annals.1417.033

Krueger, J. M. (2008). The role of cytokines in sleep regulation. *Current Pharmaceutical Design*, *14*(32), 3408–16. http://doi.org/10.2174/138161208786549281

Krueger, J. M., & Tononi, G. (2011). Local use-dependent sleep; synthesis of the new paradigm. *Current Topics in Medicinal Chemistry*, *11*(19), 2490–2. http://doi.org/10.2174/156802611797470330

Kudrimoti, H. S., Barnes, C. A., & McNaughton, B. L. (1999). Reactivation of hippocampal cell assemblies: effects of behavioral state, experience, and EEG dynamics. *The Journal of Neuroscience*, *19*(10), 4090–4101.

Kuriyama, K., Stickgold, R., & Walker, M. P. (2004). Sleep-dependent learning and motor-skill complexity. *Learning & Memory*, 705–713. http://doi.org/10.1101/lm.76304.appears

Lafortune, M., Gagnon, J.-F., Martin, N., Latreille, V., Dubé, J., Bouchard, M., … Carrier, J. (2014). Sleep spindles and rapid eye movement sleep as predictors of next morning cognitive performance in healthy middle-aged and older participants. *Journal of Sleep Research*, *23*(2), 159–67. http://doi.org/10.1111/jsr.12108

Lahl, O., Wispel, C., Willigens, B., & Pietrowsky, R. (2008). An ultra short episode of sleep is sufficient to promote declarative memory performance. *Journal of Sleep Research*, *17*(1), 3–10. http://doi.org/10.1111/j.1365-2869.2008.00622.x

Landsness, E. C., Crupi, D., Hulse, B. K., Peterson, M. J., Huber, R., Ansari, H., … Tononi, G. (2009). Sleep-dependent improvement in visuomotor learning: a causal role for slow waves. *Sleep*, *32*(10), 1273–84. Retrieved from http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2753806&tool=pmcentrez&rendertype=abstract

Le Van Quyen, M., Staba, R., Bragin, A., Dickson, C., Valderrama, M., Fried, I., & Engel, J. (2010). Large-Scale Microelectrode Recordings of High-Frequency Gamma Oscillations in Human Cortex during Sleep. *Journal of Neuroscience*, *30*(23), 7770–7782. http://doi.org/10.1523/JNEUROSCI.5049-09.2010

Lehéricy, S., Benali, H., Moortele, P. Van De, Waechter, T., Ugurbil, K., Doyon, J., … Peiegrini-issac, M. (2005). Distinct basal ganglia territories are engaged in early and advanced motor sequence learning. *Proceedings of the National Academy of Sciences of the United States of America*, *102*(35), 12566–12571. http://doi.org/129.100.246.217

Lewis, P. A., & Durrant, S. J. (2011). Overlapping memory replay during sleep builds cognitive schemata. *Trends in Cognitive Sciences*, *15*(8), 343–351. http://doi.org/10.1016/j.tics.2011.06.004

Llewellyn, S. (2013). Such stuff as dreams are made on? Elaborative encoding, the ancient art of memory, and the hippocampus. *Behavioral and Brain Sciences*, *36*(06), 589–607. http://doi.org/10.1017/S0140525X12003135

Louie, K., & Wilson, M. A. (2001). Temporally structured replay of awake hippocampal ensemble activity during rapid eye movement sleep. *Neuron*, *29*(1), 145–156. http://doi.org/10.1016/S0896-6273(01)00186-6

Mander, B. A., Rao, V., Lu, B., Saletin, J. M., Ancoli-Israel, S., Jagust, W. J., & Walker, M. P. (2014). Impaired prefrontal sleep spindle regulation of hippocampal-dependent learning in older adults. *Cerebral Cortex*, *24*(12), 3301–3309. http://doi.org/10.1093/cercor/bht188

Mander, B. A., Santhanam, S., Saletin, J. M., & Walker, M. P. (2011). Wake deterioration and sleep restoration of human learning. *Current Biology*, *21*(5), R183–R184. http://doi.org/10.1016/j.cub.2011.01.019

Maquet, P. (2001). The Role of Sleep in Learning and Memory, *294*(November), 1048–1052. http://doi.org/10.1126/science.1062856

Maquet, P., Laureys, S., Peigneux, P., Fuchs, S., Petiau, C., Phillips, C., … Cleeremans, A. (2000). Experience-dependent changes in cerebral activation during human REM sleep. *Nature Neuroscience*, *3*(8), 831–6. http://doi.org/10.1038/77744

Maret, S., Faraguna, U., Nelson, A. B., Cirelli, C., & Tononi, G. (2011). Sleep and waking modulate spine turnover in the adolescent mouse cortex. *Nature Neuroscience*, *14*(11), 1418–20. http://doi.org/10.1038/nn.2934

Markram, H., Gerstner, W., & Sjöström, P. J. (2011). A history of spike-timing-dependent plasticity. *Frontiers in Synaptic Neuroscience*, *3*(AUG), 1–24.

http://doi.org/10.3389/fnsyn.2011.00004

Marshall, L., & Born, J. (2007). The contribution of sleep to hippocampus-dependent memory consolidation. *Trends in Cognitive Sciences*, *11*(10), 442–450. http://doi.org/10.1016/j.tics.2007.09.001

Marshall, L., Helgadóttir, H., Mölle, M., & Born, J. (2006). Boosting slow oscillations during sleep potentiates memory. *Nature*, *444*(7119), 610–613. http://doi.org/10.1038/nature05278

Massimini, M., Huber, R., Ferrarelli, F., Hill, S., & Tononi, G. (2004). The Sleep Slow Oscillation as a Traveling Wave. *Journal of Neuroscience*, *24*(31), 6862–6870. http://doi.org/10.1523/JNEUROSCI.1318-04.2004

McDonald, R. J. J., & White, N. M. M. (1993). A triple dissociation of memory systems: hippocampus, amygdala, and dorsal striatum. *Behavioral Neuroscience*, *107*(1), 3. http://doi.org/10.1037/0735-7044.107.1.3

McGinty, D., & Szymusiak, R. (1990). Keeping cool: a hypothesis about the mechanisms and functions of slow-wave sleep. *Trends in Neurosciences*, *13*(12), 480–487. http://doi.org/10.1016/0166-2236(90)90081-K

Meier, B., & Cock, J. (2014). Offline consolidation in implicit sequence learning. *Cortex*, *57*, 156–66. http://doi.org/10.1016/j.cortex.2014.03.009

Morin, A., Doyon, J., Dostie, V., Barakat, M., Hadj Tahar, A., Korman, M., … Carrier, J. (2008). Motor sequence learning increases sleep spindles and fast frequencies in post-training sleep. *Sleep*, *31*(8), 1149–56.

Nakahara, H., Doya, K., & Hikosaka, O. (2001). Parallel cortico-basal ganglia mechanisms for acquisition and execution of visuomotor sequences - a computational approach. *Journal of Cognitive Neuroscience*, *13*(5), 626–47. http://doi.org/10.1162/089892901750363208

Nemeth, D., Csabi, E., Janacsek, K., Varszegi, M., & Mari, Z. (2012). Intact implicit probabilistic sequence learning in obstructive sleep apnea. *Journal of Sleep Research*, *21*(4), 396–401. http://doi.org/10.1111/j.1365-2869.2011.00983.x

Nemeth, D., Janacsek, K., Londe, Z., Ullman, M. T., Howard, D. V, & Howard, J. H. (2010). Sleep has no critical role in implicit motor sequence learning in young and old adults. *Experimental Brain Research*, *201*(2), 351–358. http://doi.org/10.1007/s00221-009-2024-x

Nettersheim, A., Hallschmid, M., Born, J., Diekelmann, S., Lu, D.-, Psychology, M., & Neurobiology, B. (2015). The Role of Sleep in Motor Sequence Consolidation : Stabilization Rather Than Enhancement, *35*(17), 6696–6702. http://doi.org/10.1523/JNEUROSCI.1236-14.2015

Nicholas, C. L., Trinder, J., & Colrain, I. M. (2002). Increased production of evoked and spontaneous K-complexes following a night of fragmented sleep. *Sleep*, *25*(8), 882–887.

Nishida, M., Pearsall, J., Buckner, R. L., & Walker, M. P. (2009). REM sleep, prefrontal theta, and the consolidation of human emotional memory. *Cerebral Cortex*, *19*(5), 1158–1166.

http://doi.org/10.1093/cercor/bhn155

Nishida, M., & Walker, M. P. (2007). Daytime naps, motor memory consolidation and regionally specific sleep spindles. *PloS One*, *2*(4), e341. http://doi.org/10.1371/journal.pone.0000341

Ohayon, M. M., Carskadon, M. a, Guilleminault, C., & Vitiello, M. V. (2004). Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. *Sleep*, *27*(2), 1255–1273.

Pace-Schott, E. F., & Spencer, R. M. (2011). Age-related changes in the cognitive function of sleep. *Progress in Brain Research*, *191*, 75–89. http://doi.org/10.1016/B978-0-444-53752-2.00012-6

Pan, S. C., & Rickard, T. C. (2015). Sleep and motor learning: is there room for consolidation? *Psychological Bulletin*, *141*(4), 812–34. http://doi.org/10.1037/bul0000009

Pavlides, C., & Winson, J. (1989). Influences of hippocampal place cell firing in the awake state on the activity of these cells during subsequent sleep episodes. *The Journal of Neuroscience*, *9*(8), 2907–2918.

Payne, J. D., Schacter, D. L., Propper, R. E., Huang, L. W., Wamsley, E. J., Tucker, M. A., … Stickgold, R. (2009). The role of sleep in false memory formation. *Neurobiology of Learning and Memory*, *92*(3), 327–334. http://doi.org/10.1016/j.nlm.2009.03.007

Peigneux, P., Laureys, S., Delbeuck, X., & Maquet, P. (2001). Sleeping brain, learning brain. The role of sleep for memory systems. *Neuroreport*, *12*(18), A111–A124. http://doi.org/10.1097/00001756-200112210-00001

Peigneux, P., Laureys, S., Fuchs, S., Collette, F., Perrin, F., Reggers, J., … Maquet, P. (2004). Are spatial memories strengthened in the human hippocampus during slow wave sleep? *Neuron*, *44*(3), 535–545. http://doi.org/10.1016/j.neuron.2004.10.007

Peigneux, P., Laureys, S., Fuchs, S., Destrebecqz, A., Collette, F., Delbeuck, X., … Maquet, P. (2003). Learned material content and acquisition level modulate cerebral reactivation during posttraining rapid-eye-movements sleep. *NeuroImage*, *20*(1), 125–134. http://doi.org/10.1016/S1053-8119(03)00278-7

Peigneux, P., Maquet, P., Meulemans, T., Destrebecqz, A., Laureys, S., Degueldre, C., … Cleeremans, A. (2000). Striatum forever, despite sequence learning variability: A random effect analysis of PET data. *Human Brain Mapping*, *10*(4), 179–194. http://doi.org/10.1002/1097-0193(200008)10:4

Peters, K. R., Smith, V., & Smith, C. T. (2007). Changes in sleep architecture following motor learning depend on initial skill level. *Journal of Cognitive Neuroscience*, *19*(5), 817–29. http://doi.org/10.1162/jocn.2007.19.5.817

Plihal, W., & Born, J. (1997). Effects of Early and Late Nocturnal Sleep on Declarative and Procedural Memory. *Journal of Cognitive Neuroscience*, *9*(4), 534–547. http://doi.org/10.1162/jocn.1997.9.4.534

Plihal, W., & Born, J. (1999). Effects of early and late nocturnal sleep on priming and spatial memory. *Psychophysiology*, *36*(5), 571–582. http://doi.org/10.1111/1469-8986.3650571

Poe, G. R., Nitz, D. a, McNaughton, B. L., & Barnes, C. a. (2000). Experience dependent phase reversal of hippocampal neuron firing during REM sleep. *Brain Res.*, *855*, 176–180. Retrieved from http://dx.doi.org/10.1016/S0006-8993(99)02310-0

Poldrack, R. A., Clark, J., Pare-Blagoev, E. J., Shohamy, D., Moyano, J. C., Meyers, C., & Gluck, M. A. (2001). Interactive memory systems in the human brain. *Nature*, *414*(November), 546–550. http://doi.org/10.1038/35107080

Press, D. Z., Casement, M. D., Pascual-Leone, A., & Robertson, E. M. (2005). The time course of off-line motor sequence learning. *Cognitive Brain Research*, *25*(1), 375–378. http://doi.org/10.1016/j.cogbrainres.2005.05.010

Rasch, B., & Born, J. (2013). About sleep's role in memory. *Physiological Reviews*, *93*(2), 681–766. http://doi.org/10.1152/physrev.00032.2012

Rasch, B., Büchel, C., Gais, S., & Born, J. (2007). Odor Cues During Slow-Wave Sleep Prompt Declarative Memory Condolidation. *Science*, *315*(March), 1426–1429. http://doi.org/10.1126/science.1138581

Rauch, S. L., Savage, C. R., Brown, H. D., Curran, T., Alpert, N. M., Kendrick, A., … Kosslyn, S. M. (1995). A PET investigation of implicit and explicit sequence learning. *Human Brain Mapping*, *3*, 271–286. http://doi.org/10.1002/hbm.460030403

Rauch, S. L., Whalen, P. J., Savage, C. R., Curran, T., Kendrick, A., Brown, H. D., … Rosen, B. R. (1997). Striatal recruitment during an implicit sequence learning task as measured by functional magnetic resonance imaging. *Human Brain Mapping*, *5*(2), 124–132. http://doi.org/10.1002/(SICI)1097-0193(1997)5:2<124::AID-HBM6>3.0.CO;2-5

Rauchs, G., Feyers, D., Landeau, B., Bastin, C., Luxen, A., Maquet, P., & Collette, F. (2011). Sleep contributes to the strengthening of some memories over others, depending on hippocampal activity at learning. *The Journal of Neuroscience*, *31*(7), 2563–8. http://doi.org/10.1523/JNEUROSCI.3972-10.2011

Ray, L., Sockeel, S., Soon, M., Bore, A., Myhr, A., Stojanoski, B., … Fogel, S. M. (2015). Expert and crowd-sourced validation of an individualized sleep spindle detection method employing complex demodulation and individualized normalization. *Frontiers in Human Neuroscience*, *9*(507), 1–16. http://doi.org/10.3389/fnhum.2015.00507

Reed, J., & Johnson, P. (1994). Assessing implicit learning with indirect tests: Determining what is learned about sequence structure. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *20*(3), 585–594. http://doi.org/10.1037/0278-7393.20.3.585

Ribeiro, S. T. (2012). Sleep and plasticity. *Pflugers Archiv European Journal of Physiology*, *463*(1), 111–120. http://doi.org/10.1007/s00424-011-1031-5

Ribeiro, S. T., & Nicolelis, M. A. L. (2004). Reverberation, storage, and postsynaptic propagation of memories during sleep. *Learning & Memory*, *11*(6), 686–96.

http://doi.org/10.1101/lm.75604

Rickard, T. C., Cai, D. J., Rieth, C. a, Jones, J., & Ard, M. C. (2008). Sleep does not enhance motor sequence learning. *J Exp Psychol Learn Mem Cogn*, *34*(4), 834–842. http://doi.org/2008-08549-010 [pii]\n10.1037/0278-7393.34.4.834 [doi]

Robertson, E. M., Pascual-Leone, A., & Press, D. Z. (2004). Awareness modifies the skill-learning benefits of sleep. *Current Biology : CB*, *14*(3), 208–12. http://doi.org/10.1016/j.cub.2004.01.027

Romano, J. C., Howard, J. H., & Howard, D. V. (2010). One-year retention of general and sequence-specific skills in a probabilistic, serial reaction time task. *Memory*, *18*(4), 427–441. http://doi.org/10.1080/09658211003742680

Rosanova, M., & Ulrich, D. (2005). Pattern-specific associative long-term potentiation induced by a sleep spindle-related spike train. *The Journal of Neuroscience*, *25*(41), 9398–405. http://doi.org/10.1523/JNEUROSCI.2149-05.2005

Roth, M., Shaw, J., & Green, J. (1956). The form voltage distribution and physiological significance of the K-complex. *Electroencephalography and Clinical Neurophysiology*, *8*(3), 385–402. http://doi.org/10.1016/0013-4694(56)90004-9

Rudoy, J. D., Voss, J. L., Westerberg, C. E., & Paller, K. A. (2009). Strengthening individual memories by reactivating them during sleep. *Science (New York, N.Y.)*, *326*(5956), 1079. http://doi.org/10.1126/science.1179013

Saletin, J. M., Goldstein, A. N., & Walker, M. P. (2011). The role of sleep in directed forgetting and remembering of human memories. *Cerebral Cortex*, *21*(11), 2534–2541. http://doi.org/10.1093/cercor/bhr034

Saper, C. B., Fuller, P. M., Pedersen, N. P., Lu, J., & Scammell, T. E. (2010). Sleep State Switching. *Neuron*, *68*(6), 1023–1042. http://doi.org/10.1016/j.neuron.2010.11.032

Schabus, M., Dang-Vu, T. T., Albouy, G., Balteau, E., Boly, M., Carrier, J., … Maquet, P. (2007). Hemodynamic cerebral correlates of sleep spindles during human non-rapid eye movement sleep. *Proceedings of the National Academy of Sciences of the United States of America*, *104*(32), 13164–13169. http://doi.org/10.1073/pnas.0703084104

Schendan, H. E., Searl, M. M., Melrose, R. J., & Stern, C. E. (2003). An fMRI study of the role of the medial temporal lobe in implicit and explicit sequence learning. *Neuron*, *37*(6), 1013–1025. http://doi.org/10.1016/S0896-6273(03)00123-5

Schwarb, H., & Schumacher, E. H. (2012). Generalized lessons about sequence learning from the study of the serial reaction time task. *Advances in Cognitive Psychology*, *8*(2), 165–178.

Schwartz, S., & Maquet, P. (2002). Sleep imaging and the neuropsychological assessment of dreams. *Trends in Cognitive Sciences*, *6*(1), 23–30. http://doi.org/10.1016/S1364-6613(00)01818-0

Schwindel, C. D., & McNaughton, B. L. (2011). Hippocampal-cortical interactions and the

dynamics of memory trace reactivation. *Progress in Brain Research*, *193*(May), 163–177. http://doi.org/10.1016/B978-0-444-53839-0.00011-9

Seibt, J., Dumoulin, M. C., Aton, S. J., Coleman, T., Watson, A., Naidoo, N., & Frank, M. G. (2012). Protein synthesis during sleep consolidates cortical plasticity in vivo. *Current Biology*, *22*(8), 676–682. http://doi.org/10.1016/j.cub.2012.02.016

Siapas, A. G., & Wilson, M. A. (1998). Coordinated interactions between hippocampal ripples and cortical spindles during slow-wave sleep. *Neuron*, *21*(5), 1123–1128. http://doi.org/10.1016/S0896-6273(00)80629-7

Sirota, A., & Buzsáki, G. (2007). Interaction between neocortical and hippocampal networks via slow oscillations. *Thalamus and Related Systems*, *3*(04), 245. http://doi.org/10.1017/S1472928807000258

Sirota, A., Csicsvari, J., Buhl, D., & Buzsáki, G. (2003). Communication between neocortex and hippocampus during sleep in rodents. *Proceedings of the National Academy of Sciences of the United States of America*, *100*(4), 2065–2069. http://doi.org/10.1073/pnas.0437938100

Skaggs, W. E., & McNaughton, B. L. (1995). Replay of Neuronal Firing Sequences in Rat Hippocampus During Sleep Following Spatial Experience. *Science*, *271*(5257), 3–6. http://doi.org/10.1126/science.271.5257.1870

Smith, C. T. (2001). Sleep states and memory processes in humans: Procedural versus declarative memory systems. *Sleep Medicine Reviews*, *5*(6), 491–506. http://doi.org/10.1053/smrv.2001.0164

Smith, C. T., Aubrey, J. B., & Peters, K. R. (2004). Different roles for REM and stage 2 sleep in motor learning: A proposed model. *Psychological Bulletin*, *44*, 79–102.

Smith, C. T., Nixon, M. R., & Nader, R. S. (2004). Posttraining increases in REM sleep intensity implicate REM sleep in memory processing and provide a biological marker of learning potential. *Learning & Memory*, *11*(6), 714–719. http://doi.org/10.1101/lm.74904

Song, S., Howard, J. H., & Howard, D. V. (2007). Sleep does not benefit probabilistic motor sequence learning. *The Journal of Neuroscience*, *27*(46), 12475–83. http://doi.org/10.1523/JNEUROSCI.2062-07.2007

Song, S., Howard, J. H., Howard, D. V, Nemeth, D., Janacsek, K., Londe, Z., & Ullman, M. T. (2007). Sleep Does Not Benefit Probabilistic Motor Sequence Learning. *Experimental Brain Research*, *201*(46), 12475–83. http://doi.org/10.1007/s00221-009-2024-x

Spencer, R. M., Sunm, M., & Ivry, R. B. (2006). Sleep-Dependent Consolidation of Contextual Learning. *Current Biology*, *16*(10), 1001–1005. http://doi.org/10.1016/j.cub.2006.03.094

Squire, L. R. (2009). Memory and Brain Systems: 1969 - 2009. *The Journal of Neuroscience*, *29*(41), 12711–12716. http://doi.org/10.1523/JNEUROSCI.3575-09.2009

Squire, L. R., & Zola, S. M. (1996). Structure and function of declarative and nondeclarative memory systems. *Proceedings of the National Academy of Sciences of the United States of*

America, *93*(24), 13515–13522. http://doi.org/10.1073/pnas.93.24.13515

Stenstrom, P., Fox, K., Solomonova, E., & Nielsen, T. (2012). Mentation during sleep onset theta bursts in a trained participant: A role for NREM stage 1 sleep in memory processing? *International Journal of Dream Research*, *5*(1), 37–46.

Steriade, M. (1994). Sleep Oscillations and Their Blockage by Activating Systems. *Journal of Psychiatry & Neuroscience*, *19*(5), 354–358.

Steriade, M. (1995). Thalamic origin of sleep spindles: Morison and Bassett (1945). *Journal of Neurophysiology*, *73*(3), 921–2.

Steriade, M. (2005). Sleep, epilepsy and thalamic reticular inhibitory neurons. *Trends in Neurosciences*, *28*(6), 317–24. http://doi.org/10.1016/j.tins.2005.03.007

Steriade, M. (2006). Grouping of brain rhythms in corticothalamic systems. *Neuroscience*, *137*, 1087–1106. http://doi.org/10.1016/j.neuroscience.2005.10.029

Steriade, M., McCormick, D. A., & Sejnowski, T. J. (1993). Thalamocortical oscillations in the sleeping and aroused brain. *Science*, *262*(5134), 679–85. http://doi.org/10.1126/science.8235588

Steriade, M., & Timofeev, I. (2003). Neuronal plasticity in thalamocortical networks during sleep and waking oscillations. *Neuron*, *37*(4), 563–576. http://doi.org/10.1016/S0896-6273(03)00065-5

Stickgold, R. (2013). Parsing the role of sleep in memory processing. *Current Opinion in Neurobiology*, *23*(5), 847–853. http://doi.org/10.1016/j.conb.2013.04.002

Stickgold, R., & Walker, M. P. (2013). Sleep-dependent memory triage: evolving generalization through selective processing. *Nature Neuroscience*, *16*(2), 139–45. http://doi.org/10.1038/nn.3303

Stickgold, R., Whidbee, D., Schirmer, B., Patel, V., & Hobson, J. A. (2000). Visual discrimination task improvement: A multi-step process occurring during sleep. *Journal of Cognitive Neuroscience*, *12*(2), 246–254. http://doi.org/10.1162/089892900562075

Takehara-Nishiuchi, K., & McNaughton, B. L. (2008). Spontaneous changes of neocortical code for associative memory during consolidation. *Science (New York, NY)*, *322*(5903), 960–963. http://doi.org/10.1126/science.1161299

Tamminen, J., Payne, J. D., Stickgold, R., Wamsley, E. J., & Gaskell, M. G. (2010). Sleep spindle activity is associated with the integration of new memories and existing knowledge. *The Journal of Neuroscience*, *30*(43), 14356–60. http://doi.org/10.1523/JNEUROSCI.3028-10.2010

Thompson, C. L., Larkin, E. K., Patel, S., Berger, N. A., Redline, S., & Li, L. (2011). Short duration of sleep increases risk of colorectal adenoma. *Cancer*, *117*(4), 841–7. http://doi.org/10.1002/cncr.25507

Thomson, J., & Oswald, I. (1977). Hormones and sleep. *Current Medical Research and Opinion*, *4*(3), 67–72. http://doi.org/10.1185/03007997709109386

Timofeev, I. (2011). Neuronal plasticity and thalamocortical sleep and waking oscillations. *Progress in Brain Research*, *193*, 121–144. http://doi.org/10.1016/B978-0-444-53839-0.00009-0.Neuronal

Tononi, G., & Cirelli, C. (2003). Sleep and synaptic homeostasis: a hypothesis. *Brain Research Bulletin*, *62*(August), 143–150. http://doi.org/10.1016/j.brainresbull.2003.09.004

Tononi, G., & Cirelli, C. (2006). Sleep function and synaptic homeostasis. *Sleep Medicine Reviews*. http://doi.org/10.1016/j.smrv.2005.05.002

Tononi, G., & Cirelli, C. (2014). Sleep and the price of plasticity: from synaptic and cellular homeostasis to memory consolidation and integration. *Neuron*, *81*(1), 12–34. http://doi.org/10.1016/j.neuron.2013.12.025

Tucker, M., McKinley, S., & Stickgold, R. (2011). Sleep optimizes motor skill in older adults. *Journal of the American Geriatrics Society*, *59*(4), 603–609. http://doi.org/10.1111/j.1532-5415.2011.03324.x

Tufik, S., Andersen, M. L., Bittencourt, L. R. A., & Mello, M. T. de. (2009). Paradoxical sleep deprivation: neurochemical, hormonal and behavioral alterations. Evidence from 30 years of research. *Anais Da Academia Brasileira de Ciências*, *81*(3), 521–38.

Tulving, E. (2002). Episodic Memory: From Mind to Brain. *Annual Review of Psychology*, *53*, 1–25.

Urbain, C., Schmitz, R., Schmidt, C., Cleeremans, A., Bogaert, P. Van, Maquet, P., & Peigneux, P. (2013). Sleep-dependent Neurophysiological Processes in Implicit Sequence Learning. *Journal of Cognitive Neuroscience*, *25*(11), 2003–2014. http://doi.org/10.1162/jocn_a_00439

Van Dongen, H. P. A., & Dinges, D. F. (2003). Investigating the interaction between the homeostatic and circadian processes of sleep-wake regulation for the prediction of waking neurobehavioural performance. *Journal of Sleep Research*, *12*(3), 181–187. http://doi.org/10.1046/j.1365-2869.2003.00357.x

Vazquez, J., & Baghdoyan, H. A. (2001). Basal forebrain acetylcholine release during REM sleep is significantly greater than during waking. *Am J Physiol Regulatory Integrative Comp Physiol*, *280*, 598–601. http://doi.org/10.1017/S0016756897007061

Vyazovskiy, V. V, Borbély, A. A., & Tobler, I. (2000). Unilateral vibrissae stimulation during waking induces interhemispheric EEG asymmetry during subsequent sleep in the rat. *Journal of Sleep Research*, *9*(4), 367–371. http://doi.org/10.1046/j.1365-2869.2000.00230.x

Vyazovskiy, V. V, Cirelli, C., Pfister-Genskow, M., Faraguna, U., & Tononi, G. (2008). Molecular and electrophysiological evidence for net synaptic potentiation in wake and depression in sleep. *Nature Neuroscience*, *11*(2), 200–8. http://doi.org/10.1038/nn2035

Vyazovskiy, V. V, Olcese, U., Hanlon, E. C., Nir, Y., Cirelli, C., & Tononi, G. (2011). Local sleep in awake rats. *Nature*, *472*(7344), 443–447. http://doi.org/10.1038/nature10009

Vyazovskiy, V. V, & Tobler, I. (2008). Handedness leads to interhemispheric EEG asymmetry during sleep in the rat. *Journal of Neurophysiology*, *99*(2), 969–75. http://doi.org/10.1152/jn.01154.2007

Wagner Ullrich, & Born, S. G. and J. (2001). Emotional Memory Formation Is Enhanced across Sleep Intervals with High Amounts of Rapid Eye Movement Sleep. *Learning & Memory*, *8*, 112–119. http://doi.org/10.1101/lm.36801

Wagner, U., Fischer, S., & Born, J. (2002). Changes in Emotional Responses to Aversive Pictures Across Periods Rich in Slow-Wave Sleep Versus Rapid Eye Movement Sleep. *Psychosomatic Medicine*, *64*(4), 627–634. http://doi.org/10.1097/01.PSY.0000021940.35402.51

Wagner, U., Gais, S., Haider, H., Verleger, R., & Born, J. (2004). Sleep inspires insight. *Nature*, *427*(6972), 352–5. http://doi.org/10.1038/nature02223

Walker, M. P. (2005). A refined model of sleep and the time course of memory formation. *The Behavioral and Brain Sciences*, *28*(1), 51–64; discussion 64–104. http://doi.org/10.1017/S0140525X05000026

Walker, M. P. (2008). Cognitive consequences of sleep and sleep loss. *Sleep Med*, *9*(Suppl.1), S29–34. http://doi.org/S1389-9457(08)70014-5 [pii]\r10.1016/S1389-9457(08)70014-5

Wamsley, E. J., Perry, K., Djonlagic, I., Reaven, L. B., & Stickgold, R. (2010). Cognitive replay of visuomotor learning at sleep onset: temporal dynamics and relationship to task performance. *Sleep*, *33*(1), 59–68. Retrieved from http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2802248&tool=pmcentrez&rendertype=abstract

Wauquier, A., Aloe, L., & Declerck, A. (1995). K-complexes: Are they signs of arousal or sleep protective? *Journal of Sleep Research*, *4*(3), 138–143.

Werth, E., Achermann, P., Dijk, D. J., & Borbély, A. A. (1997). Spindle frequency activity in the sleep EEG: Individual differences and topographic distribution. *Electroencephalography and Clinical Neurophysiology*, *103*(5), 535–542. http://doi.org/10.1016/S0013-4694(97)00070-9

Wiestler, T., Waters-Metenier, S., & Diedrichsen, J. (2014). Effector-Independent Motor Sequence Representations Exist in Extrinsic and Intrinsic Reference Frames. *Journal of Neuroscience*, *34*(14), 5054–5064. http://doi.org/10.1523/JNEUROSCI.5363-13.2014

Wilhelm, I., Diekelmann, S., Molzow, I., Ayoub, A., Mölle, M., & Born, J. (2011). Sleep Selectively Enhances Memory Expected to Be of Future Relevance. *The Journal of Neuroscience*, *31*(5), 1563–1569. http://doi.org/10.1523/JNEUROSCI.3575-10.2011

Wilkinson, L., & Shanks, D. R. (2004). Intentional control and implicit sequence learning. *Journal of Experimental Psychology. Learning, Memory, and Cognition*, *30*(2), 354–369.

http://doi.org/10.1037/0278-7393.30.2.354

Willingham, D. B., & Goedert-Eschmann, K. (1999). The Relation Between Implicit and Explicit Learning: Evidence for Parallel Development. *Psychological Science*, *10*(6), 531–534. http://doi.org/10.1111/1467-9280.00201

Willingham, D. B., Salidis, J., & Gabrieli, J. D. E. (2002). Direct comparison of neural systems mediating conscious and unconscious skill learning. *Journal of Neurophysiology*, *88*(3), 1451–1460.

Wilson, M. A., & Mcnaughton, B. L. (1994). Reactivation of Hippocampal Ensemble Memories During Sleep. *Science*, *265*, 676–679.

Witt, K., Margraf, N., Bieber, C., Born, J., & Deuschl, G. (2010). Sleep consolidates the effector-independent representation of a motor skill. *Neuroscience*, *171*(1), 227–34. http://doi.org/10.1016/j.neuroscience.2010.07.062

Xie, L., Kang, H., Xu, Q., Chen, M. J., Liao, Y., Thiyagarajan, M., … Nedergaard, M. (2013). Sleep drives metabolite clearance from the adult brain. *Science (New York, N.Y.)*, *342*(6156), 373–7. http://doi.org/10.1126/science.1241224

Yaroush, R., Sullivan, M. J., & Ekstrand, B. R. (1971). Effect of sleep on memory. II. Differential effect of the first and second half of the night. *Journal of Experimental Psychology*, *88*(3), 361–366. http://doi.org/10.1037/h0030914

Yordanova, J., Kolev, V., Verleger, R., Bataghva, Z., Born, J., & Wagner, U. (2008). Shifting from implicit to explicit knowledge: different roles of early- and late-night sleep. *Learning & Memory (Cold Spring Harbor, N.Y.)*, *15*(7), 508–15. http://doi.org/10.1101/lm.897908

Zeitlhofer, J., Gruber, G., Anderer, P., Asenbaum, S., Schimicek, P., & Saletu, B. (1997). Topographic distribution of sleep spindles in young healthy subjects. *Journal of Sleep Research*, *6*(3), 149–55.

Zimmerman, J. T., Stoyva, J. M., & Reite, M. L. (1978). Spatially rearranged vision and REM sleep: a lack of effect. *Biological Psychiatry*, *13*(3), 301–16. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/208666

APPENDIX A: Questionnaire Battery

The Epworth Sleepiness Scale

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to how you are feeling **today only**. Even if you have not done some of these things today, try to work out how they would have affected you.

Use the following scale to choose the most appropriate number for each situation:
0 = no chance of dozing
1 = slight chance of dozing
2 = moderate chance of dozing
3 = high chance of dozing

Situation	**Chance of Dozing**
Sitting and reading	_____
Watching TV	_____
Sitting inactive in a public place (e.g. a theater or a meeting)	_____
As a passenger in a car for an hour without a break	_____
Lying down to rest in the afternoon when circumstances permit	_____
Sitting and talking to someone	_____
Sitting quietly after a lunch without alcohol	_____
In a car, while stopped for a few minutes in traffic	_____

For administrative use only-

SubID: _____ Date: _____

TOTAL SCORE (add up scores for all items)**:** _____

APPENDIX A

The Stanford Sleepiness Scale

Last time asleep (hh:mm AM/PM): _____

Last time awoke (hh:mm AM/PM): _____

Instructions: Circle the scale rating that best describes how you feel **right now**.

Degree of Sleepiness	Scale Rating
Feeling active, vital, alert, or wide awake	1
Functioning at high levels, but not at peak; able to concentrate	2
Awake, but relaxed; responsive but not fully alert	3
Somewhat foggy, let down	4
Foggy; losing interest in remaining awake; slowed down	5
Sleepy, woozy, fighting sleep; prefer to lie down	6
No longer fighting sleep, sleep onset soon; having dream-like thoughts	7
Asleep	X

For administrative use only-

SubID: _____ Date: _____

APPENDIX A

SILRA Explicit Awareness Report

Participant ID: _____

Date: _____

Experimenter: _____

This sheet is used in follow up when a participant reports that they are 75%-100% certain that the sequence from training was determined by a rule or pattern.

1) **Did they train with Keyboard (Circle one):** UP / Down

2) **Ask what they believe the sequence to be and record the response in the space provided below:**

Verbal Accuracy Score: _____

3) **Did they have noticeable difficulty in trying to verbalize the sequence (Circle one):** Y / N

   Additional notes supplementary to response 3):

4) **Did they use finger movements to help explain the sequence (Circle one):** Y / N

5) **Ask if they used any particular strategy during training that helped identify the sequence. Record the response in the space provided below:**

Experimenter Signature: _____

APPENDIX A

Beck Anxiety Inventory

Instructions: Below is a list of common symptoms of anxiety. Please carefully read each item in the list. Indicate how much you have been bothered by that symptom **during the past month, including today**, by circling the number in the corresponding space in the column next to each symptom.

Rating scale:
Not At All
Mildly: "it didn't bother me much"
Moderately: "it wasn't pleasant at times"
Severely: "it bothered me a lot"

	Not At All	Mildly	Moderately	Severely
Numbness or tingling	0	1	2	3
Feeling hot	0	1	2	3
Wobbliness in legs	0	1	2	3
Unable to relax	0	1	2	3
Fear of worst happening	0	1	2	3
Dizzy or lightheaded	0	1	2	3
Heart pounding / racing	0	1	2	3
Unsteady	0	1	2	3
Terrified or afraid	0	1	2	3
Nervous	0	1	2	3
Feeling of choking	0	1	2	3
Hands trembling	0	1	2	3
Shaky / unsteady	0	1	2	3
Fear of losing control	0	1	2	3
Difficulty in breathing	0	1	2	3

APPENDIX A

2

	Not At All	Mildly	Moderately	Severely
Fear of dying	0	1	2	3
Scared	0	1	2	3
Indigestion	0	1	2	3
Faint / lightheaded	0	1	2	3
Face flushed	0	1	2	3
Hot / cold sweats	0	1	2	3

For administrative use only-

SubID: _____ Date: _____

TOTAL SCORE (add up scores for all items)**:** _____

APPENDIX A

Beck Depression Inventory II

Instructions: This questionnaire consists of 21 groups of statements. Please read each group of statements carefully, and then pick the **one statement** in each group that best describes the way you have been feeling during the past **two weeks**, including today. Circle the number beside the statement you picked. If several statements in the group seem top apply equally well, circle the highest number for that group. Be sure that you do not choose more than one statement for any group, including Item 16 (Changes in Sleeping Pattern) or Item 18 (Changes in Appetite).

1. **Sadness**
   - 0 I do not feel sad.
   - 1 I feel sad much of the time
   - 2 I am so sad all the time.
   - 3 I am so sad or unhappy that I cannot stand it.

2. **Pessimism**
   - 0 I am not discouraged about my future.
   - 1 I feel more discouraged about my future than I used to be.
   - 2 I do not expect things to work out for me.
   - 3 I feel my future is hopeless and will only get worse.

3. **Past Failure**
   - 0 I do not feel like a failure.
   - 1 I have failed more than I should have.
   - 2 As I look back, I see a lot of failures.
   - 3 I feel I am a total failure as a person.

4. **Loss of Pleasure**
   - 0 I get as much pleasure as I ever did from the things I enjoy.
   - 1 I don’t enjoy things as much as I used to.
   - 2 I get very little pleasure from the things I used to enjoy.
   - 3 I can’t get any pleasure from the things I used to enjoy.

5. **Guilty Feelings**
   - 0 I don't feel particularly guilty.
   - 1 I feel guilty over many things I have done or should have done.
   - 2 I feel quite guilty most of the time.
   - 3 I feel guilty all of the time.

6. **Punishment Feelings**
   - 0 I don't feel I am being punished.
   - 1 I feel I may be punished.
   - 2 I expect to be punished.
   - 3 I feel I am being punished.

7. **Self-Dislike**
   - 0 I feel the same about myself as ever.
   - 1 I have lost confidence in myself.
   - 2 I am disappointed in myself.
   - 3 I dislike myself.

8. **Self-Criticalness**
   - 0 I don't criticize or blame myself more than usual.
   - 1 I am more critical of myself then I used to be.
   - 2 I criticize myself for all of my faults.
   - 3 I blame myself for everything bad that happens.

9. **Suicidal Thoughts or Wishes**
   - 0 I don't have any thoughts of killing myself.
   - 1 I have thoughts of killing myself, but I would not carry them out.
   - 2 I would like to kill myself.
   - 3 I would kill myself if I had a chance.

10. **Crying**
   - 0 I don't cry any more than I used to.
   - 1 I cry more than I used to.
   - 2 I cry over every little thing.
   - 3 I feel like crying, but I can't.

11. **Agitation**
    - 0 I am no more restless or wound up than usual.
    - 1 I feel more restless or wound up than usual.
    - 2 I am so restless or agitated that it's hard to stay still.
    - 3 I am so restless or agitated that I have to keep moving or doing something.

12. **Loss of Interest**
    - 0 I have not lost interest in other people or activities.
    - 1 I am less interested in other people or things than before.
    - 2 I have lost most of my interest in other people or things.
    - 3 It's hard to get interested in anything.

13. **Indecisiveness**
    - 0 I make decisions about as well as ever.
    - 1 I find it more difficult to make decisions than usual.
    - 2 I have greater difficulty in making decisions than I used to.
    - 3 I have trouble making any decisions.

14. **Worthlessness**
    - 0 I do not feel I am worthless.
    - 1 I don't consider myself as worthwhile and useful as I used to be.
    - 2 I feel more worthless as compared to other people.
    - 3 I feel utterly worthless.

15. **Loss of Energy**
    - 0 I have as much energy as ever.
    - 1 I have less energy than I used to have.
    - 2 I don't have enough energy to do very much.
    - 3 I don't have enough energy to do anything.

16. **Changes in Sleeping Pattern**
    - 0 I have not experienced any change in my sleeping pattern.
    - 1a I sleep somewhat more than usual.
    - 1b I sleep somewhat less than usual.
    - 2a I sleep a lot more than usual.
    - 2b I sleep a lot less than usual.
    - 3a I sleep most of the day.
    - 3b I wake up 1-2 hours early and can't go back to sleep.

17. **Irritability**
    - 0 I am no more irritable than usual.
    - 1 I am more irritable than usual.
    - 2 I am much more irritable than usual.
    - 3 I am irritable all the time.

18. **Changes in Appetite**
    - 0 I have not experienced any change in my appetite.
    - 1a My appetite is somewhat less than usual.
    - 1b My appetite is somewhat greater than usual.
    - 2a My appetite is much less than usual.
    - 2b My appetite is much greater than usual.
    - 3a I have no appetite at all.
    - 3b I crave food all the time.

19. **Concentration Difficulty**
    - 0 I can concentrate as well as ever.
    - 1 I can't concentrate as well as usual.
    - 2 It's hard to keep my mind on anything for very long.
    - 3 I can't concentrate on anything.

20. **Tiredness or Fatigue**
    - 0 I am no more tired or fatigued than usual.
    - 1 I get more tired or fatigued more easily than usual.
    - 2 I am too tired or fatigued to do a lot of the things I used to.
    - 3 I am too tired or fatigued to do most of the things I used to.

21. **Loss of Interest in Sex**

0 I have not noticed any recent change in my interest in sex.
1 I am much less interested in sex than I used to be.
2 I am much less interested in sex now.
3 I have lost interest in sex completely.

For test administrator use-

SubID: _____ Date: _____

TOTAL SCORE (add up scores for all 21 items)**:** _____

APPENDIX A

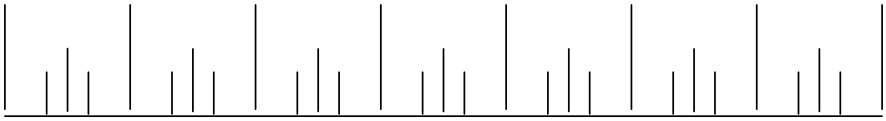
Circadian Rhythms Questionnaire

Instructions:

1. Please read each question very carefully before answering.
2. Answer ALL the questions.
3. Answer each question in numerical order.
4. Each question should be answered independently of others. Do NOT go back and check your answers.
5. All questions have a selection of answers. For each question, place and "X" alongside ONE answer only. Some questions have a scale instead of a selection of answers. Place an "X" at the appropriate point along the scale.
6. Please answer each question as honestly as possible. Both your answers and the results will be kept in strict confidence.
7. Please feel free to make any comments in the section provided below each question.

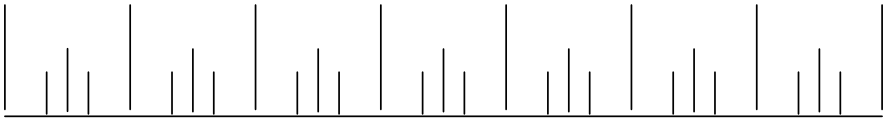
Questions:

1. Considering only your own "feeling best" rhythm, at what time would you get up if you were free to plan your day?



5 AM 6 7 8 9 10 11 12 PM

2. Considering only your own "feeling best" rhythm, at what time would you go to bed if you were entirely free to plan your evening?



8 PM 9 10 11 12 AM 1 2 3 AM

3. If there is a specific time at which you have to get up in the morning, to what extent are you dependent on being woken up by an alarm clock?

___ Not at all dependent
___ Slightly dependent
___ Fairly dependent
___ Very dependent

4. Assuming adequate environmental conditions, how easy do you find getting up in the morning?

___ Not at all easy
___ Not very easy
___ Fairly easy
___ Very easy

5. How alert do you feel during the first half hour after having woken in the morning?

___ Not at all alert
___ Not very alert
___ Fairly alert
___ Very alert

6. How is your appetite during the first half hour after having woken in the morning?

___ Very poor
___ Fairly poor
___ Fairly good
___ Very good

7. During the first half hour after having woken in the morning, how tired do you feel?

___ Very tired
___ Fairly tired
___ Fairly refreshed
___ Very refreshed

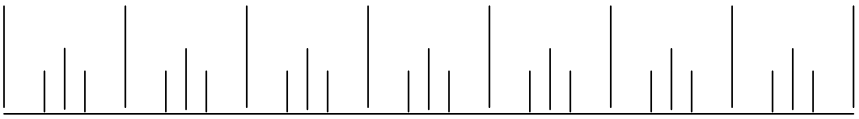
8. When you have no commitments the next day, at what time do you go to bed compared to your usual bedtime?

___ Seldom or never later
___ Less than one hour later
___ One to two hours later
___ More than two hours later

9. You have decided to engage in some physical exercise. A friend suggests that you do this one hour twice a week and the best time for him/her is between 7 and 8 AM. Bearing in mind nothing else but your own "feeling best" rhythm, how do you think you would perform?

___ Would be on good form
___ Would be on reasonable form
___ Would find it difficult
___ Would find it very difficult

10. At what time in the evening do you feel tired and, as a result, in need of sleep?



8 PM 9 10 11 12 AM 1 2 3 AM

11. You wish to be at peak performance for a test which you know is going to be mentally exhausting and lasting for two hours. You are entirely free to plan your day and considering your own "feeling best" rhythm, which ONE of the four testing times would you choose?

___ 8 to 10 AM
___ 11 AM to 1 PM
___ 3 to 5 PM
___ 7 to 9 PM

12. If you went to bed at 11 PM, at which level of tiredness would you be?

___ Not at all tired
___ A little tired
___ Fairly tired
___ Very tired

13. For some reason you have gone to bed several hours later than usual, but there is no need to get up at any particular time the next morning. Which ONE of the following events are you most likely to experience?

___ Will wake up at usual time and will NOT fall back to sleep
___ Will wake up at usual time and will doze thereafter
___ Will wake up at usual time but still fall asleep again
___ Will NOT wake up until later than usual

14. One night you have to remain awake between 4 and 6 AM in order to carry out a night watch. You have no commitments the next day. Which ONE of the following alternatives will suit you best?

___ Would NOT go to bed until watch was over
___ Would take a nap before and sleep after
___ Would take a good sleep before and nap after
___ Would take ALL sleep before watch

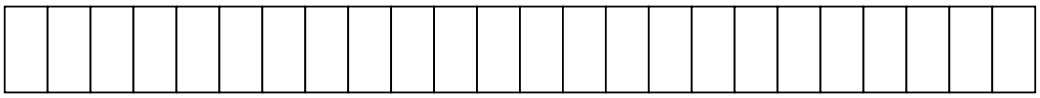
15. You have to do two hours of hard physical work. You are free to plan your day and considering only your own "feeling best" rhythm, which ONE of the following times would you choose?

___ 8 to 10 AM
___ 11 AM to 1 PM
___ 3 to 5 PM
___ 7 to 9 PM

16. You have decided to engage in hard physical exercise. A friend suggests that you do this for one hour twice a week and the best time for him/her is between 10 and 11 PM. Bearing in mind nothing else but your own "feeling best" rhythm, how well do you think you would perform?

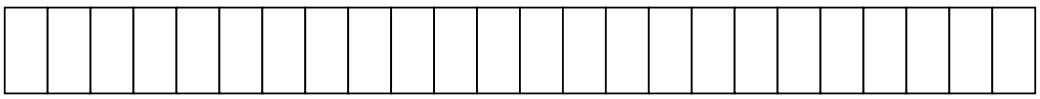
___ Would be on good form
___ Would be on reasonable form
___ Would find it difficult
___ Would find it very difficult

17. Suppose you can choose your own work hours. Assume that you work a FIVE hour day (including breaks) and that your job was interesting and paid by results. Which FIVE CONSECUTIVE HOURS would you select? (mark them in the scale below)



12 1 2 3 4 5 6 7 8 9 10 11 12 1 2 3 4 5 6 7 8 9 10 11 12
MIDNIGHT NOON MIDNIGHT

18. At what time of day do you think that you reach your "feeling best" peak? (Please choose one hour only)



12 1 2 3 4 5 6 7 8 9 10 11 12 1 2 3 4 5 6 7 8 9 10 11 12
MIDNIGHT NOON MIDNIGHT

19. One hears about “morning” and “evening” types of people. Which one of these types do you consider yourself to be?

___ Definitely a “morning” type
___ Rather more a “morning” type than an “evening” type
___ Rather more an “evening” type than a “morning” type
___ Definitely an “evening” type

For administrative use only-

SubID: _____ Date: _____

APPENDIX A

Edinburgh Handedness Inventory

Instructions: Please indicate your preferences in the use of hands in the following activities **by putting a check in the appropriate column**. Where the preference is so strong that you would never try to use the other hand, unless absolutely forced to, **put 2 checks**. If in any case you are really indifferent, **put a check in both columns**.

Some of the activities listed below require the use of both hands. In these cases, the part of the task, or object, for which hand preference is wanted is indicated in parentheses. Please try and answer all of the questions, and only leave a blank if you have no experience at all with the object or task.

Activity	Left	Right
1. Writing		
2. Drawing		
3. Throwing		
4. Scissors		
5. Toothbrush		
6. Knife (without fork)		
7. Spoon		
8. Broom (upper hand)		
9. Striking Match (match)		
10. Opening box (lid)		

For test administrator use only-

SubID: _____ Date: _____

TOTAL SCORE (add up all checks in each column)**:** _____

Cumulative total (left + right) _____

Difference (right – left) _____

Index [(difference/cumulative total)*100] _____

APPENDIX A

Napping Behaviour Survey 1

Instructions: For questions #1 to #7, check the **one** answer that **best** describes:

1. Given the opportunity to nap, would you take a daytime nap?
   ___ Yes
   ___ No

Instructions: If you responded 'yes' to #1, continue to answer questions #2 to #7. If you responded 'no' to #1, skip to question #8.

2. How often do you nap?
   ___ Every day
   ___ Once or twice a week
   ___ Once or twice a month
   ___ Less than once a month

3. How long do your naps usually last?
   ___ Less than 10 minutes
   ___ 10 - 20 minutes
   ___ 20 - 30 minutes
   ___ 30 - 60 minutes
   ___ More than 60 minutes

4. How long does it take you to fall asleep?
   ___ Less than 5 minutes
   ___ 5-10 minutes
   ___ 10-20 minutes
   ___ 20-60 minutes
   ___ More than 60 minutes

5. Do you ever fall asleep unintentionally during the day?
   ___ Yes
   ___ No

6. Do you nap because you:

___ Can no longer stay awake (e.g., due to a medical condition or excessive daytime sleepiness)?
___ Did not get enough sleep the night before?
___ Anticipate having to stay up late the following night?
___ Simply enjoy napping?

7. Upon awakening from a nap, do you feel:
___ Irritable
___ Groggy
___ Relaxed
___ Alert / Rested

Instructions: If you responded 'yes' to #1, do not respond to question #8.

8. You avoid taking daytime naps because:

For administrative use only-

SubID: _____ Date: _____

APPENDIX A

Sleep Disorders Questionnaire (SDQ)

Instructions: In answering the questions, consider each question as applying to the **past six months** of your life. In the next section, the questions are simple statements. You answer by circling a number from 1 to 5. If you strongly disagree with the statement, or if it never happens to you, answer "1". If the statement is always true in your case, or you agree strongly with it, answer "5". You may also choose "2; rarely", "3; sometimes", or "4; usually" as your answer. Notice that an "answer key" appears at the bottom of each page to remind you what is meant by the numbers. Please answer all of the questions.

1 NEVER (strongly disagree)	2 RARELY (disagree)	3 SOMETIMES (not sure)	4 USUALLY (agree)	5 ALWAYS (agree strongly)

3. I have trouble getting to sleep at night. 1 2 3 4 5

4. I wake up often during the night. 1 2 3 4 5

6. At bedtime, thoughts race through my mind. 1 2 3 4 5

7. At bedtime, I feel sad and depressed. 1 2 3 4 5

12. When falling asleep, I have "restless legs" (a feeling of crawling, aching, or inability to keep legs still) 1 2 3 4 5

21. I am told that I snore loudly and it bothers others. 1 2 3 4 5

22. I am told I stop breathing ("hold my breath") in sleep. 1 2 3 4 5

23. I awake suddenly gasping for breath, unable to breathe. 1 2 3 4 5

24. At night my heart pounds, beats rapidly, or beats irregularly ("palpitation"). 1 2 3 4 5

25. I sweat a great deal at night. 1 2 3 4 5

APPENDIX A

2

1 NEVER (strongly disagree)	2 RARELY (disagree)	3 SOMETIMES (not sure)	4 USUALLY (agree)	5 ALWAYS (agree strongly)

31. My sleep is disturbed by "restless legs" (a feeling of crawling, aching, or inability to keep legs still) 1 2 3 4 5

33. My sleep is disturbed by sadness or depression. 1 2 3 4 5

38. I have a lot of nightmares (frightening dreams). 1 2 3 4 5

43. I have been unable to sleep <u>at all</u> for several days. 1 2 3 4 5

45. I feel that I have insomnia. 1 2 3 4 5

71. I have high blood pressure (or once had it). 1 2 3 4 5

84. I am unhappy about loving relationships in my life. 1 2 3 4 5

89. I have considered or attempted suicide. 1 2 3 4 5

101. Someone in my family has been hospitalized for a psychiatric illness or "nervous breakdown". 1 2 3 4 5

108. I smoke tobacco within two hours of bedtime. 1 2 3 4 5

139. I have a problem with my nose blocking up when I am trying to sleep. 1 2 3 4 5

141. My snoring or my breathing problem is much worse if I sleep on my back. 1 2 3 4 5

142. My snoring or my breathing problem is much worse if I fall asleep right after drinking alcohol. 1 2 3 4 5

APPENDIX A

Instructions: In the next section, please circle the item (numbered 1 to 5) that best matches your answer.

154. How long is your longest wake period at night?

1) less than 5 minutes 2) 6 to 19 minutes 3) 20 to 59 minutes

4) 1 to 2 hours 5) more than 2 hours

155. How many times in a night do you get up to urinate?

1) None 2) one 3) two

4) three 5) four or more times

163. What is your current weight in lbs.?

1) 134 or less 2) 135 to 159 3) 160 to 183

4) 184 to 209 5) 210 or more

170. How many years were you a smoker?

1) None 2) one 3) 2 to 12

4) 13 to 25 5) 26 or more

173. How old are you now?

1) 25 or under 2) 26 to 35 3) 36 to 44

4) 45 to 50 5) 51 or older

For test administrator use only-

SubID: _____ Date: _____

*See separate page for scoring instructions

APPENDIX B – Recruitment Materials

The Brain & Mind Institute
Sleep Research Laboratory

The BMI Sleep Laboratory is looking for adults aged 20-35 years to participate in a research study investigating the relationship between sleep and visual and motor performance. Participants must be in good healthy and describe themselves as a "good" sleeper. Participants will be asked to complete some questionnaires to verify that they are eligible to participate. The participants that are chosen, will be asked to spend four non-consecutive days, staying up to 3 nights in the laboratory. During the sleep sessions, the brain activity of the participants will be recorded via electrodes placed on their scalp and face. For the second, third and fourth visits to in the laboratory, our participants will be asked to perform a simple visual-motor task. If you are interested, please send an email to the address below for further information: [redacted]

Western
The Brain and Mind Institute

Version Date: December 16, 2014

[redacted]

E-mail: E-mail: E-mail: E-mail: E-mail: E-mail: E-mail: E-mail: E-mail:

[redacted]

APPENDIX B

Brain & Mind Institute Sleep Research Laboratory

Telephone Recruitment Survey

I. Script

1) Hello, may I please speak with {insert the name of the potential participant}.

If the potential participant is not home ask if there is a better time to call. Do not leave a message as it may be a confidential matter you are calling about that may not be apparent to you

If they are home, continue with the conversation

2) Hi, {insert the name of the potential participant} this is {insert your name} calling from the Brain and Mind Sleep Research Laboratory.

I am calling today to ask if you are interested in a research study that we are conducting. The study is being conducted by Dr. Adrian Owen and will look at the relationship between sleep and learning. The study would involve you first completing a series of general questions to verify that you are eligible to participate. . If eligible, you will be asked to come into the sleep laboratory for four, non-consecutive experimental sessions. The first two experimental sessions will be overnight sleep sessions where your brain activity will be recorded via electrodes placed on the surface of your scalp and face. Before bed-time on the 2nd night, you will be asked to complete a simple, visual-motor task. The third experimental session will either be an in-lab, overnight sleep session where you will be asked to complete the simple, visual-motor task before going to bed and after awakening in the morning or a daytime wake session where you will be asked to complete the simple, visual-motor task in the morning, leave the lab for the day and return again in the evening to complete the task. The fourth experimental session will be a short, in-lab retest session where you will, again, be asked to complete the simple, visual-motor task. Would you be interested in hearing more about this study?

If no, thank them for their time and say good-bye

If yes, continue to explain the study details to them based on the letter of information

3) If you have a few minutes, I am now going to read you the letter of information.

At this point, read the letter to them

4) Do you have any questions?

If yes, answer their questions to the best of your ability

5) Are you still interested in participating in this study?

If yes, continue with the inclusion criteria questions

If no, thank them for their time and say good-bye

APPENDIX B

Brain & Mind Institute Sleep Research Laboratory

Telephone Recruitment Survey

6) I have a few questions for you to make sure you are eligible for the study. You are free to ask questions or discontinue at any time.

II. Pre-Screening Questions (Inclusion criteria noted in square brackets)

Subject ID: _____ Date (dd/mm/yy): _____ Time: _____ am / pm

General Questions

1. How old are you? [20-35]: _____
2. Are you a smoker or non-smoker? [non-smoker]: smoker / non-smoker
3. How many caffeinated drinks do you typically have in a day? [≤2]: _____
4. How many alcoholic drinks do you typically have in a week? [≤14]: _____
5. Are you right or left handed? [right]: left / right
6. Are you a trained, or professional musician? [no]: yes / no
7. Are you a trained, or professional typist? [no]: yes / no
8. Are you willing and able to abstain from caffeine, nicotine, drugs and alcohol, at least 3 days prior to and throughout participating in this study? [yes]: yes / no

Sleep Questions

1. What is your usual bedtime? [10pm to 1am]: _____
2. What is your usual wake time? [6am to 9am]: _____
3. Are you willing and able to go to bed between 10pm and midnight and wake between 7am and 9am, at least 3 days prior to and throughout participating in this study? [yes]: yes / no
4. Do you work nights or shift-work? [no, in past month]: yes / no
5. Have you taken a trans-meridian trip in the last month? [no]: yes / no
6. Do you have difficulty falling asleep at night? [no]: yes / no
7. Do you wake up often during the night and are unable to return to sleep? [no]: yes / no
8. Would you describe yourself as excessively tired during the day? [no]: yes / no
9. Have you ever been diagnosed with a sleep disorder? [no]: yes / no
10. Do you know, or has anyone ever told you that you stop breathing while asleep? [preferably no]: yes / no
11. Do you know, or has anyone ever told you that you snore? [preferably no]: yes / no

Health Questions

1. Are you presently in good health? [yes]: yes / no
2. Are you pregnant? [no]: yes / no
3. Are you presently taking any medications? [preferably no]: yes / no
4. Do you have a history of chronic pain? [no]: yes / no
5. Do you have a history of anxiety or depression? [no]: yes / no
6. Have you ever suffered any kind of head trauma? [no]: yes / no
7. Have you ever suffered any kind of seizure? [no]: yes / no
8. Have you ever been diagnosed with any neurological or psychiatric condition? [no]: yes / no
9. What is your weight? _____; and your height? _____
   BMI = (Weight in Pounds / (Height in inches x Height in inches)) x 703
   BMI = (Weight in Kilograms / (Height in Meters x Height in Meters))
   BMI [≤25]: _____
10. Do you have any mobility problems with your hands or fingers? [no]: yes / no

APPENDIX B

III. Contact Information

Name*: _____

Telephone number(s)*: _____

E-mail*: _____

Date of testing: _____

Subject ID: _____

*** IMPORTANT NOTE:** The subject's contact information (indicated by *) and ID are to be entered into a separate password-protected, name-ID key database, containing only their name, telephone number, email (i.e., information that could be used to identify the participant) and ID to prevent their identity from being linked to their data, without the key. The remaining information collected in **Section II and Section III**, is to be immediately entered into a password-protected database, using only the subject's unique ID (i.e., no name, telephone number or email) to identify each record. Once this information is entered into the database, the paper version of **Section III** is to be destroyed, and **Section II**, is to be filed in a secure location (e.g., locked filing cabinet, in a locked office).

APPENDIX C – Sleep Diary

Brain & Mind Sleep Diary

	To be completed in the morning...							To be completed at the end of the day...				
	I went to bed last night at:	I got out of bed this morning at:	Last night, I fell asleep in:	I woke up during the night:	When I woke up for the day, I felt:	Last night I slept a total of:	My sleep was disturbed by:	I consumed caffeinated drinks in the:	I exercised at least 20 minutes in the:	Approximately 2-3 hours before going to bed, I consumed:	Medication(s) I took during the day:	About 1 hour before going to sleep, I did the following activity:
DAY 1 _____ YY/MM/DD:	____:____ PM/AM	____:____ PM/AM	_____ Minutes	_____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	_____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		
DAY 2 _____ YY/MM/DD:	____:____ PM/AM	____:____ PM/AM	_____ Minutes	_____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	_____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		
DAY 3 _____ YY/MM/DD:	____:____ PM/AM	____:____ PM/AM	_____ Minutes	_____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	_____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		
DAY 4 _____ YY/MM/DD:	____:____ PM/AM	____:____ PM/AM	_____ Minutes	_____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	_____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		
DAY 5 _____ YY/MM/DD:	____:____ PM/AM	____:____ PM/AM	_____ Minutes	_____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	_____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		
DAY 6 _____ YY/MM/DD:	____:____ PM/AM	____:____ PM/AM	_____ Minutes	_____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	_____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		
DAY 7 _____ YY/MM/DD:	____:____ PM/AM	____:____ PM/AM	_____ Minutes	_____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	_____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		

	COMPLETE IN MORNING							COMPLETE AT END OF DAY				
	I went to bed last night at:	I got out of bed this morning at:	Last night, I fell asleep in:	I woke up during the night:	When I woke up for the day, I felt:	Last night I slept a total of:	My sleep was disturbed by:	I consumed caffeinated drinks in the:	I exercised at least 20 minutes in the:	Approximately 2-3 hours before going to bed, I consumed:	Medication(s) I took during the day:	About 1 hour before going to sleep, I did the following activity:
DAY 8 _____ YY/MM/DD:	____:____ PM/AM	____:____ PM/AM	_____ Minutes	_____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	_____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		
DAY 9 _____ YY/MM/DD:	____:____ PM/AM	____:____ PM/AM	_____ Minutes	_____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	_____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		
DAY 10 _____ YY/MM/DD:	____:____ PM/AM	____:____ PM/AM	_____ Minutes	_____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	_____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		
DAY 11 _____ YY/MM/DD:	____:____ PM/AM	____:____ PM/AM	_____ Minutes	_____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	_____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		
DAY 12 _____ YY/MM/DD:	____:____ PM/AM	____:____ PM/AM	_____ Minutes	_____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	_____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		
DAY 13 _____ YY/MM/DD:	____:____ PM/AM	____:____ PM/AM	_____ Minutes	_____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	_____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		
DAY 14 _____ YY/MM/DD:	____:____ PM/AM	____:____ PM/AM	_____ Minutes	_____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	_____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		

APPENDIX C

	COMPLETE IN MORNING							COMPLETE AT END OF DAY			
	I went to bed last night at:	I got out of bed this morning at:	Last night, I fell asleep in:	I woke up during the night:	When I woke up for the day, I felt:	Last night I slept a total of:	My sleep was disturbed by:	I consumed caffeinated drinks in the:	I exercised at least 20 minutes in the:	Approximately 2-3 hours before going to bed, I consumed:	Medication(s) I took during the day:	About 1 hour before going to sleep, I did the following activity:
DAY 15 YY/MM/DD:	___:___ PM/AM	___:___ PM/AM	____ Minutes	____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		
DAY 16 YY/MM/DD:	___:___ PM/AM	___:___ PM/AM	____ Minutes	____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		
DAY 17 YY/MM/DD:	___:___ PM/AM	___:___ PM/AM	____ Minutes	____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		
DAY 18 YY/MM/DD:	___:___ PM/AM	___:___ PM/AM	____ Minutes	____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		
DAY 19 YY/MM/DD:	___:___ PM/AM	___:___ PM/AM	____ Minutes	____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		
DAY 20 YY/MM/DD:	___:___ PM/AM	___:___ PM/AM	____ Minutes	____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		
DAY 21 YY/MM/DD:	___:___ PM/AM	___:___ PM/AM	____ Minutes	____ Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	____ Hours		☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Morning ☐ Afternoon ☐ Within 3 hours of going to bed ☐ None	☐ Alcohol ☐ A heavy meal ☐ None		

APPENDIX D – Letter of Information

Western
The Brain and Mind Institute

Project Title: Sleep and Visual-Motor Performance

Principal Investigator:
Adrian Owen, PhD
Department of Psychology, Brain & Mind Institute, Western University

Co-investigator:
Stuart Fogel, PhD
Department of Psychology, Brain & Mind Institute, Western University

Letter of Information

1. **Invitation to Participate**

   Because you meet the general selection criteria we have defined for healthy, young individuals, you are invited to participate in this research study that investigates the sleep of healthy, young adults as they learn a simple, visual-motor task.

2. **Purpose of the Letter**

   The purpose of this letter is to provide you with information required for you to make an informed decision regarding participation in this research.

3. **Purpose of this Study**

   The purpose of this study is to investigate the role of sleep in the learning of a visual-motor reaction time task. More specifically, we will examine whether practicing the task alters sleep brain waves and how the changes to sleep brain waves relate to changes in reaction time performance.

Western
The Brain and
Mind Institute

4. Inclusion Criteria

Individuals who are in good health, between 20 and 35 years of age, have a normal BMI (<25), are right-handed, are non-professional musician/typists, non-smokers, do not consume excessive caffeine (< 2 servings/day) or alcohol (< 14 servings/week), describe themselves as subjectively "good" sleepers, are non-shift-workers, keep regular sleep schedules (sleep between 10pm and 9am), have no history of sleep disorders, are non-diabetic, are relatively free from medication, have no history of chronic pain, seizures, head injury, depression, anxiety and have normal mobility of the hands and fingers are eligible to participate in this study.

5. Exclusion Criteria

Individuals who do not meet the inclusion criteria described above, who exhibit signs of disordered/disrupted sleep, or who are unable to adhere to a regular sleep schedule and abstain from excessive caffeine, nicotine, drugs or alcohol 3-days prior to and throughout participation are not eligible to participate in this study.

6. Study Procedures

If you agree to participate, and meet the inclusion and exclusion criteria, you will be asked to complete a series of screening questionnaires. The questionnaires include items about handedness, general psychological health, and sleep behaviors, which together typically take less than 20 minutes to complete. If eligible, you will be asked to wear a wristwatch that measures the movement of your arm to track your sleep-wake cycle, to complete an aptitude test and keep a daily log of your activity and sleepiness for the length of your participation in the study. You will

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The Brain and Mind Institute

also be asked to spend 3 nights maximum in the sleep lab where your brain waves will be recorded via electrodes placed on your scalp and face. After an overnight screening and an overnight baseline sleep recording, you will be randomly assigned (like flipping a coin) - either stay another night sleeping over in the lab, or come into the lab during a morning and return the subsequent evening. You will also be asked to perform a simple, visual-motor task during some of the visits to the laboratory. In total, you will be asked you to visit the laboratory on 4 separate, non-consecutive, days.
For the overnight sessions you will be asked to arrive at the lab each evening by 7:45 pm and you will leave the lab each morning around 9am. The evening visual-motor task session will be from 7:45-8:45pm and the morning visual-motor task session will be from 7:45-11am.The task will be conducted at the Brain & Mind Sleep Research Laboratory. There will be up to 3 total participants (including you) run per night, for a total study size of 40 participants.

7. Possible Risks and Harms

The only known possible risks or discomfort to you may experience, if you have sensitive skin include a temporary, slight skin irritation caused by the exfoliant used to gently clean the surface of the skin where the electrodes are applied.

8. Possible Benefits

Participants will be shown how valuable sleep is toward maximizing intellectual function and memory. The potential benefits to society would include that the results will emphasize the importance of sleep for learning, memory, visual and motor performance, and intellectual function.

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9. Compensation

You will be compensated $20 for the first night, $25 for the second night, $25 for the third day or night and $30 for the final daytime, re-test session. If you do not complete the entire study, you will be compensated on a per-night/day basis.

10. Voluntary Participation

Participation in this study is voluntary. You may refuse to participate, refuse to answer any questions or withdraw from the study at any time with no effect on your future academic status. Following withdrawal from the study you may also choose withdraw any of the data collected from you that was acquired up to the point of the withdrawal decision. You do not waive your legal rights by signing this form.

11. Confidentiality

All data collected will remain confidential and accessible only to the investigators of this study. The master list (identifying the individual - including name, phone number and email - and their corresponding unique ID) will be stored electronically in a password-protected database on a hard drive within the local network of the locked sleep laboratory, and backup copies in the PI's on-campus office, stored on local password-protected hard drives. Under no circumstances will a participant's data be stored with personal information that could be used to identify them. The data will be stored indefinitely and will be accessible only to the investigators of this study. Cambridge Brain Science test data is stored on a server in the United Kingdom, where different privacy and confidentiality rules may apply. This data is mirrored and protected on our server at the Brain and Mind Institute as

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per previously described. If the results are published, your name will not be used. Representatives of The University of Western Ontario Health Sciences Research Ethics Board may contact you or require access to your study-related records to monitor the conduct of the research.

12. Contacts for Further Information

Dr. Adrian Owen resides as this projects principle investor. If you require any further information regarding this research project or your participation in the study you may contact either the project Team Leader, Dr. Stuart Fogel, [redacted] or the project facilitator, Jeremy Viczko, [redacted]

If you have any questions about your rights as a research participant or the conduct of this study, you may contact The Office of Research Ethics [redacted]

13. Publication

If the results of the study are published, all data will be pooled and your name will not be used. If you would like to receive a copy of any potential study results, please contact: Dr. Stuart Fogel, [redacted]

This letter is yours to keep for future reference.

APPENDIX D

Western
The Brain and
Mind Institute

Consent Form

Project Title: Sleep and Visual-Motor Performance

Study Investigator's Name(s): Adrian Owen, PhD / Stuart Fogel, PhD

I have read the Letter of Information, have had the nature of the study explained to me and I agree to participate. All questions have been answered to my satisfaction.

Participant's Name (please print): _____

Participant's Signature: _____

Date: _____

Person Obtaining Informed Consent (please print): _____

Signature: _____

Date: _____

APPENDIX E – CER Ethics Approval

Western Research

Research Ethics

Western University Health Science Research Ethics Board
HSREB Annual Continuing Ethics Approval Notice

Date: May 02, 2016
Principal Investigator: Dr. Adrian Owen
Department & Institution: Social Science\Psychology,Western University

Review Type: Expedited
HSREB File Number: 106182
Study Title: Does sleep facilitate the awareness of the spatial-referent representation of an implicitly learned motor sequence?
Sponsor: Canadian Excellence Research Chair

HSREB Renewal Due Date & HSREB Expiry Date:
Renewal Due -2017/04/30
Expiry Date -2017/05/14

The Western University Health Science Research Ethics Board (HSREB) has reviewed the Continuing Ethics Review (CER) Form and is re-issuing approval for the above noted study.

The Western University HSREB operates in compliance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS2), the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Guideline for Good Clinical Practice (ICH E6 R1), the Ontario Freedom of Information and Protection of Privacy Act (FIPPA, 1990), the Ontario Personal Health Information Protection Act (PHIPA, 2004), Part 4 of the Natural Health Product Regulations, Health Canada Medical Device Regulations and Part C, Division 5, of the Food and Drug Regulations of Health Canada.

Members of the HSREB who are named as Investigators in research studies do not participate in discussions related to, nor vote on such studies when they are presented to the REB.

The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

[redacted]

Ethics Officer, on behalf of Dr. Joseph Gilbert, HSREB Chair

Ethics Officer to Contact for Further Information: Erika Basile ___ Katelyn Harris___ Nicole Kaniki___ Grace Kelly ___ Vikki Tran ✓

Curriculum Vitae

Name: Jeremy Viczko

Post-secondary Education and Degrees:

University of Western Ontario
London, ON, Canada
2014 – 2016 M.Sc (Psychology)

University of Alberta
Edmonton. AB, Canada
2010 – 2013 B.Sc. (Honours Psychology)

Red Deer College
London, Ontario, Canada
2009 – 2010 (General Sciences)

Honours and Awards:

Western Graduate Research Scholarship
2014 – 2015, 2015-2016

Ralph S Devereux Award in Psychology for Excellence at Masters Level
2015

Branch Out Neurological Foundation Summer Studentship
2013

Award for Academic Excellence
2013

Jason Lang Scholarship
2009, 2010, 2011, 2012

Related Work Experience

Teaching Assistant
University of Western Ontario
2014 – 2016

Research Assistant
University of Alberta
2013 – 2014

Publications:

(*In Review*) Fang, Z., Sergeeva, S., Ray, L.B., **Viczko, J**., Owen, A.M., & Fogel, S.M. Sleep spindles and intellectual ability: Epiphenomenon or intrinsically linked?. *J Cognitive Neurosci.*, Submission date: 25/01/2016.

(*In Press*) Sergeeva, V., **Viczko, J.**, Owen, A.M, & Fogel, S.M. Sleep Oscillations and Aging. In Dang-Vu, T., & Courtemanche, R. (Eds.). *Neuronal Oscillations of Wakefulness and Sleep.* New York, NY: Springer.

(2014) **Viczko, J**., Sharma, A., Pagliardini, S., Wolanksy, T., & Dickson, C.T. Lack of respiratory coupling with neocortical and hippocampal slow oscillations. *J Neurosci., 34*, 3937-46. doi: 10.1523/jneurosci.3581-13.2014.

Presentations:

Oral

(2015) **Viczko, J.**, Ray, L., Owen., A.M., & Fogel, S.M. "Rhythm, routine, and reason: Circadian markers relate to intellectual ability." *Canadian Sleep Society Conference*, Toronto, Ontario. September 25-27.

(2014) **Viczko, J**., Whitten, T., Greenberg, A., LeBlancq, S., McKinney, T., & Dickson, C.T. "Rhythm of the Light, Rhythm of the Night: The role of synchronized oscillatory brain activity for hippocampal function in both offline and online states." *Centre for Neuroscience Graduate Studies Seminar*, University of Alberta, Edmonton, AB.
January 14.

(2014) **Viczko, J**., Sharma, A., Pagliardini, S., Wolanksy, T., & Dickson, C.T. "No Nose in the Cerebral Slows: Lack of respiratory coupling in the neocortex and hippocampus." *Canadian Spring Conference on Behaviour and Brain*, Fernie, BC. February 20-23.

(2012) **Viczko, J**., & Dickson, C.T. "Neural Dynamics of Sleep Rhythms: Learning in the motor cortex." *Brian Harder Honors Day Conference*, University of Alberta, Edmonton, AB. April 13.

Poster

(2015) **Viczko, J.**, Ray, L., Owen., A.M., & Fogel, S. "Rhythm, routine, and reason: Circadian markers relate to intellectual ability." *Inaugural Brain and Mind Institute Symposium*, London, Ontario. September 20.

(2013) **Viczko, J**., Sharma, A., Pagliardini, S., Wolanksy, T., & Dickson, C.T. "Respiratory Coupling to Sleep and Sleep-like Slow EEG Waves: A cerebral no-show for the slow blows of the nose." *13th International Symposium on Sleep and Breathing*, Sofitel Mile End Hotel, Montreal, QC. October 16-19.

(2012) **Viczko, J**., Sharma, A., Pagliardini, S., Wolanksy, T., & Dickson, C.T. "A Cerebral No-Show for the Slow Blows of the Nose: No evidence for a respiratory component in neocortical and hippocampal oscillations." *The Joseph R. Royce Research Conference*, University of Alberta, Edmonton, AB. March 12.

Other

(2015) Adam, R. (Host), Moszczynski, A. (Host), & **Viczko, J.** (Guest). Sleep and Muscle Memory with Jeremy Viczko [Radio and Podcast]. In Johnson, T. (Producer), *Gradcast*. July 22. London, ON; CHRW.