Donders Graduate School for Cognitive Neuroscience
Master of Science Programme
MSc Thesis

Investigating the effect of sleep on different spatial learning paradigms and its underlying neural correlates

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Abstract

Sleep has been shown to enhance memory consolidation and improved performance in spatial navigation in virtual environment tasks. The processing of spatial memory can be further disentangled into allocentric (spatial) and egocentric (motor) representations. Not much research has been conducted to disentangle their differential effects on sleep using spatial navigation tasks. A preliminary study done in rats on the water-maze showed that sleep enhanced performance in the probe trial under allocentric training condition. We developed a human analogue of the study and conducted an fMRI investigation wherein participants had a locate a treasure box in virtual water maze environment. Group of participants were trained in either allocentric or egocentric conditions and took a nap or watched a movie between training and retrieval test period. Analogous to findings in the rats, we found sleep promoting an increased accuracy in marking the location of the treasure box under allocentric training condition. Performance in the egocentric condition remained independent of sleep effects. Our results were hence able to replicate the behavioral findings in rats showing that the underlying consolidation mechanisms might be conserved in both species.

Keywords: sleep, wake, memory, consolidation, allocentric, egocentric, spatial navigation, fMRI, EEG, hippocampus, striatum

Introduction

While awake, we are constantly surrounded by all kinds of stimuli – visual, auditory, olfactory and tactile. There is a vast amount of information presented to us which the brain is continuously processing. We are encountered with experiences – big or small, constantly learning new information and revisiting old ones. Specific regions of the brain are in constant interplay storing these experiences and information as memories. However how do all these memories get consolidated and stored?

More than over a century of research has established the fact that sleep plays a crucial role in memory consolidation. Diekelmann and Born (2010) showed sleep optimizes the consolidation of newly acquired information, depending on the specific conditions of learning and the timing of sleep. Consolidation during sleep has been shown to promote both quantitative and qualitative changes of memory representations. Consolidation involves reorganization of brain circuits at both synaptic and systems level. Synaptic level consolidation happens within hours of performing/learning a task and involves changes in synaptic connectivity in specific localized circuits. In contrast, systems consolidation is a longer process where memories initially dependent on the hippocampus, are reorganized as time passes. Starting at the time of learning, gradual changes occur in the neocortex, establishing stable long-term memory by increasing the distribution and connectivity among multiple cortical regions (Squire et al. 2015).

There exist several reports on models explaining the process of systems consolidation. According to the standard consolidation model (Frankland and Bontempi 2005) encoding of perceptual, motor and spatial information initially occurs in several specialized primary and associative cortical areas. The hippocampus integrates information from these distributed cortical modules and fuses them into a coherent memory trace. Successive reactivation of this hippocampal–cortical network leads to progressive strengthening of cortico-cortical connections (McClelland, McNaughton, and O’Reilly 1995; Squire and Alvarez 1995).

Increased strengthening of these connections eventually allows new memories to become independent of the hippocampus and to be gradually integrated with pre-existing cortical memories.

Multiple studies have investigated in detail the underlying mechanisms on how this process happen in the brain. One key phenomenon how this is accomplished is ‘neural replay’ which refers to the spontaneous recurrence of hippocampal activity that occurred originally during learning. Series of experiments by Wilson (2002) and Sutherland and McNaughton (2000) have demonstrated that coordinated replay occurs in the hippocampus and in both hippocampal-cortical and cortico-cortical networks (Qin et al. 1997). A key finding by Wilson and McNaughton (1994) shows that replay of ensemble of cells activated during learning of behavior tasks in rats happens during NREM sleep. On similar lines, a study conducted in humans (Peigneux et al. 2004) showed that hippocampal areas activated during route learning in a virtual town are subsequently activated during slow wave sleep and led to improved task performance.

A recent study (Maingret et al. 2016) has provided evidence on how hippocampal-cortical coupling mediates memory consolidation during sleep. It shows how reinforcing of endogenous coordination between hippocampal SWRs, cortical delta waves and spindles results in reorganization of PFC networks, leading to increased responsivity to the task and higher recall performance. Further studies have shown in humans, through participation in virtual navigation tasks, that sleep promotes consolidation of navigation memory and enhances the hippocampus dependent aspects of spatial memory (Nguyen et al. 2013; Ferrara et al. 2008; Ferrara et al. 2006). A behavioral study by Ferrara et al. (2006) wherein subjects were tested on a virtual route learning task showed that even though performance speed was the same in both sleep and wake groups, the accuracy in the task was significantly improved only in the sleep group. Adding on to the finding, research conducted by Nguyen et al. (2013), disentangled further whether sleep mediated improvements in spatial tasks was due to consolidation of cognitive maps or did it affect nonhippocampal aspects of navigation as well. Results revealed that sleep solely improved subjects’ performance in more accurate navigation to the goal. Overall these findings prove that sleep enhances the hippocampus dependent spatial information.

Further reports in this field have shown daytime naps to also have a significant effect on enhancing memory consolidation. A comparative study (van Schalkwijk et al. 2017) between daytime napping and full-night sleep on the consolidation of declarative and procedural information reveals the significant effect of a nap in consolidation of procedural memories. Another study (Backhaus and Junghanns 2006) investigating the effect of daytime naps in humans using a mirror-tracing task, reported it to enhance procedural motor learning. Parallel studies have shown the significant effects of naps in enhancement of declarative memory consolidation as well (Schabus et al. 2005; Schmidt et al. 2006; Lahl et al. 2008). Furthermore, these studies report the amount of slow wave sleep during the naps to be positively correlated with the task performance. Along with a few more examples (Lemos, Weissheimer, and Ribeiro 2014; Alger, Lau, and Fishbein 2012), naps seem to have a significant contribution to enhancement in memory consolidation. The effect of naps on spatial memory however still remain elusive.

The hippocampus has been shown to be the crucial region involved in spatial memory processing (Olton, Walker, and Gage 1978). It serves as the cognitive spatial map of the brain, containing specialized groups of hippocampal pyramidal cells called place fields which play a crucial role in spatial navigation abilities in both rodents and humans (O’Keefe et al. 1998). Additionally, it has been shown for some time that hippocampal neurons transiently display an increased firing rate during sleep (Olmstead, Best, and Mays 1973). Combining both facets, recent studies (Wilson 2002; Wilson and McNaughton 1994), have demonstrated that these place cells ensembles in the hippocampus fire while doing a task and also when the memory is reactivated during quiet wakefulness or sleep in the same sequence, implying reactivation of the previous wakeful experience. Importantly, the correlated cell firing activity was shown to be most pronounced during sharp wave ripples, reflecting the activity of the cells during earlier spatial exploration (Skaggs and McNaughton 1996). Several other studies (Girardeau et al. 2009; Ego-Stengel and Wilson 2010) have shown disruption of ripple associated hippocampal activity to impair spatial learning. Overall, in light of these findings, hippocampal replay during sleep is crucial in enhancing consolidation of spatial memories. The underlying mechanisms behind how specific representations of spatial memory are consolidated however still remain to be investigated in detail.

Spatial memory processing involves encoding of allocentric and egocentric representations. Allocentric representations are conditions in which information about the location of the object is encoded with respect to positions of other objects and is independent of the viewpoint of the self

(Sarkisyan and Hedlund 2009) and is shown to be hippocampal dependent (Holdstock et al. 2000). Egocentric representations, as the name suggests, on the other hand, are conditions where information about the location of the object is encoded relative to the body axes of the self (Sarkisyan and Hedlund 2009). The encoding thus happens from a stationary point of view. Parallel studies (Brasted et al. 1997) have shown egocentric representations to be striatal dependent. Both processes happen in parallel when encoding spatial memories. In light of hippocampal replay, hence it could be hypothesized that allocentric memory, being hippocampal dependent, would benefit more from sleep compared to the egocentric condition.

Several recent studies have to tried to disentangle the differential effects of sleep on allocentric and egocentric memory representations. A study by Cohen et al. (2005) showed that different components of any skill task are differentially processed during consolidation. The egocentric frame is enhanced over wake whereas the allocentric frame is enhanced over a night of sleep. Following up on this, another study (Cohen and Robertson 2007) showed that consolidation of both allocentric and egocentric frames of a skill task is constrained either by having a critical time window or competitive interaction between the two frames. Another study (Himmer et al. 2017) showed that sleep-mediated consolidation of memory depends on the level of integration at encoding. Explicit learning was shown to be enhanced by sleep but fast learning strategies where new information is added to pre-existing knowledge is independent of sleep effects. To go into further detail on the underlying mechanisms behind consolidation of allocentric and egocentric representations, a study (Albouy et al. 2013) investigated the effect of daytime sleep (nap) on spatial (allocentric) and motor (egocentric) representations of a finger sequence learning task. The allocentric (spatial) representation of the task had the same spatial sequence but different finger movements. The egocentric (motoric) representation on the other hand had the same finger movements but different spatial sequences. They reported enhancement in consolidation of spatial but not motoric representation of sequence memory. This suggested that certain aspects of motor sequence memory acquisition and consolidation involved distinct sleep related mechanisms and were dependent on whether the sequence was performed under allocentric or egocentric conditions. Another study (Albouy et al. 2015), investigated the functional role of hippocampal and striatal systems in humans using an explicit sequential finger-tapping task. Performance was shown to be enhanced after sleep for the hippocampal dependent memory trace. The performance for the striatal dependent memory trace however was maintained irrespective of the sleep condition. It is thus established that consolidation of allocentric memory is sleep dependent. However, knowledge on the underlying detailed mechanisms still remain elusive. Additionally, most of the studies so far have been conducted on motor sequence tasks. It would be interesting to study if the same effects are found while performing spatial tasks.

Study done in rats

A previous study was conducted on rats to study the differential effects of sleep on allocentric and egocentric memory representations. Rats were trained on the water-maze with two different training regimes – allocentric (rats always had to find the platform from a different starting point each trial) and egocentric (rats always had the same starting point to find the platform each trial) and tested on the same conditions. In between the training and testing conditions, a group of rats were allowed to sleep for 6 hours while another group of rats were sleep deprived by gentle handling. Performance analysis on the probe trial showed an improved performance in the allocentric condition post sleep. Performance in the egocentric condition was independent of sleep effects. Additionally, retrieval induced IEG expression studies in the hippocampus, PFC and striatum showed increased levels of c-fos,arc and zif in all three brain areas after retrieval for both allocentric and egocentric training in the sleep condition. Sleep deprived rats, however, showed increased expression solely in the hippocampus for allocentric condition and in striatum for egocentric condition. Both behavioral and molecular results thus indicate sleep playing a crucial role in mediating memory consolidation in the allocentric condition. Increased IEG levels in all three regions post sleep imply hippocampal-cortical and cortico-cortical interactions during sleep, leading to a systems level memory consolidation. In the allocentric (hippocampal dependent) training condition, sleep possibly promotes neural replay of the task and HPC-PFC coupling, leading to an improved performance in the probe trial. Below shown are the results from the behavior.

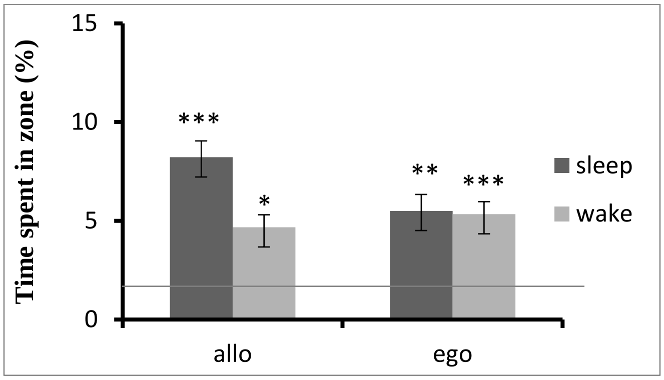


Figure 1. Average amount of time spent in zone during the probe trial after sleep and wake condition. The time spent in the target zone is significantly higher post sleep in the rats in the allocentric condition compared to wake. (p = 0.02)

Developing human analogue of the study

Taking the study a step further, this project involves developing a human analogue of the study. Previous studies (Albouy et al. 2015; Viczko et al. 2018) in humans show consolidation of allocentric and egocentric representations of memory could be differently regulated, depending on the nature of the task. Additionally, most studies done in humans to disentangle allocentric and egocentric representations so far have involved motor sequence tasks. It would be interesting to study the phenomenon in a spatial task and investigate the neural correlates in further detail. The aim of the project hence would be to study the effect of naps on egocentric vs. allocentric spatial memory training in virtual reality and investigate the underlying neural signatures. Analogous to findings in the rats, we except to find similar behavioral findings in humans. Neural replay in the hippocampus after tasks during sleep has been shown to occur in rats, along with evidence pointing to replay leading to enhanced memory consolidation and thus improved task performance. We hope to see a sleep dependent improved effect in the allocentric training condition and an increased coupling between between HPC-PFC circuits during retrieval.

Methods

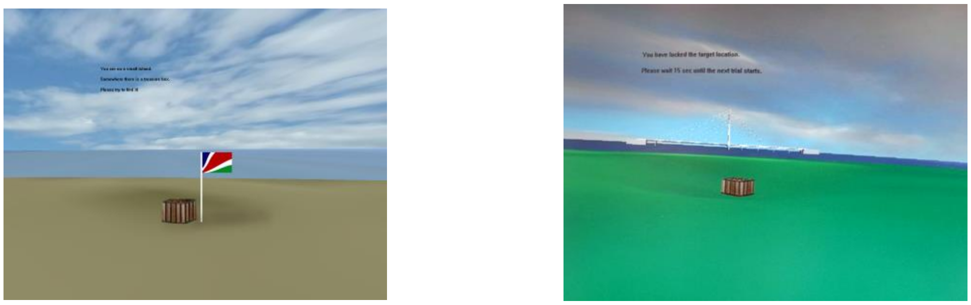
Participants

Sixty-two human male, right handed healthy subjects (age 18-30 years) participated in the experiment. Being a translational study, only males were chosen since only male rats were used in the previous experiment. Additionally, a study conducted by Genzel et al. (2012) showed that sex and menstrual cycle affected sleep dependent memory consolidation. Hence, only males were chosen for this study. Participants were recruited through the Radboud Research Participation System. All participants provided written informed consent prior to the start of the experiment. This study was approved by the local ethics committee (CMO Arnhem-Nijmegen, Radboud University Medical Center) under the general ethics approval (“Imaging Human Cognition”, CMO 2014/288), and the experiment was conducted in compliance with these guidelines. All participants were required to maintain a sleep diary one week prior to the experiment session. Exclusion criteria for the participants were taking sleep medications, regular naps and gamers. They were screened for these criteria before the start of the session. Additionally, their alertness levels and sleep quality was assessed for with the Stanford Sleepiness Scale (see results) and Pittsburgh Sleep Quality Index respectively during the experiment session. The PSQI values were <10 for all subjects.

Task

The participants performed the task in the MRI scanner. The overall objective of the task was to assess their spatial memory abilities based on specific training conditions and whether it was differentially affected by sleep. A virtual water maze environment was thus developed for the task. The environment setting consisted of two islands – cued and un-cued. The cued island was a plain brown island with a visible flag (cue) along with the treasure box. The location of the flag and treasure box was randomized and changed across all blocks. The un-cued island was a green one, surrounded by global cues and a hidden treasure box (in a depression valley on the island), which remained at the same location across all blocks. The box was kept in the depression valley so as to make it invisible from far (analogous to the hidden platform in the water-maze). The goal of the participants was to locate the treasure box in both settings. Additionally, they had to learn the location of the hidden treasure box in the un-cued island on which they would be tested later. The objective of the cued island was to control for the navigation abilities of all the participants and serve as a control block between the uncued (target) island.

The task design was a block design, with 8 alternating blocks each of the cued and un-cued island. Each trial was self-initialized and ended only when the participant marked the target location. They were given a MRI compatible joystick to navigate through the island. Additionally, the task was divided into two training conditions – allocentric and egocentric. Participants were randomly allocated into either of the two conditions. The cued island remained the same in both conditions. The visible flag was always at different locations, and the participants had to randomly navigate through the island and find it. The main difference lay in the un-cued island. In this island, the location of the hidden treasure box remained fixed across all trials and also across both conditions. The participants, hence, had to use the surrounding clues to orient themselves and learn the location of the hidden treasure box. Those in the allocentric condition, always had a different starting point at each block, thus needing to reorient themselves each time. Those in the egocentric condition, always had the same starting point across all blocks. This remained constant across both learning and test conditions. For the test condition, they were assessed with a retrieval trial, where the hidden treasure box in the un-cued island was removed. The participants were required to mark, to the best of their accuracy, where they thought the box was. Below are snapshots of the islands developed in the program.



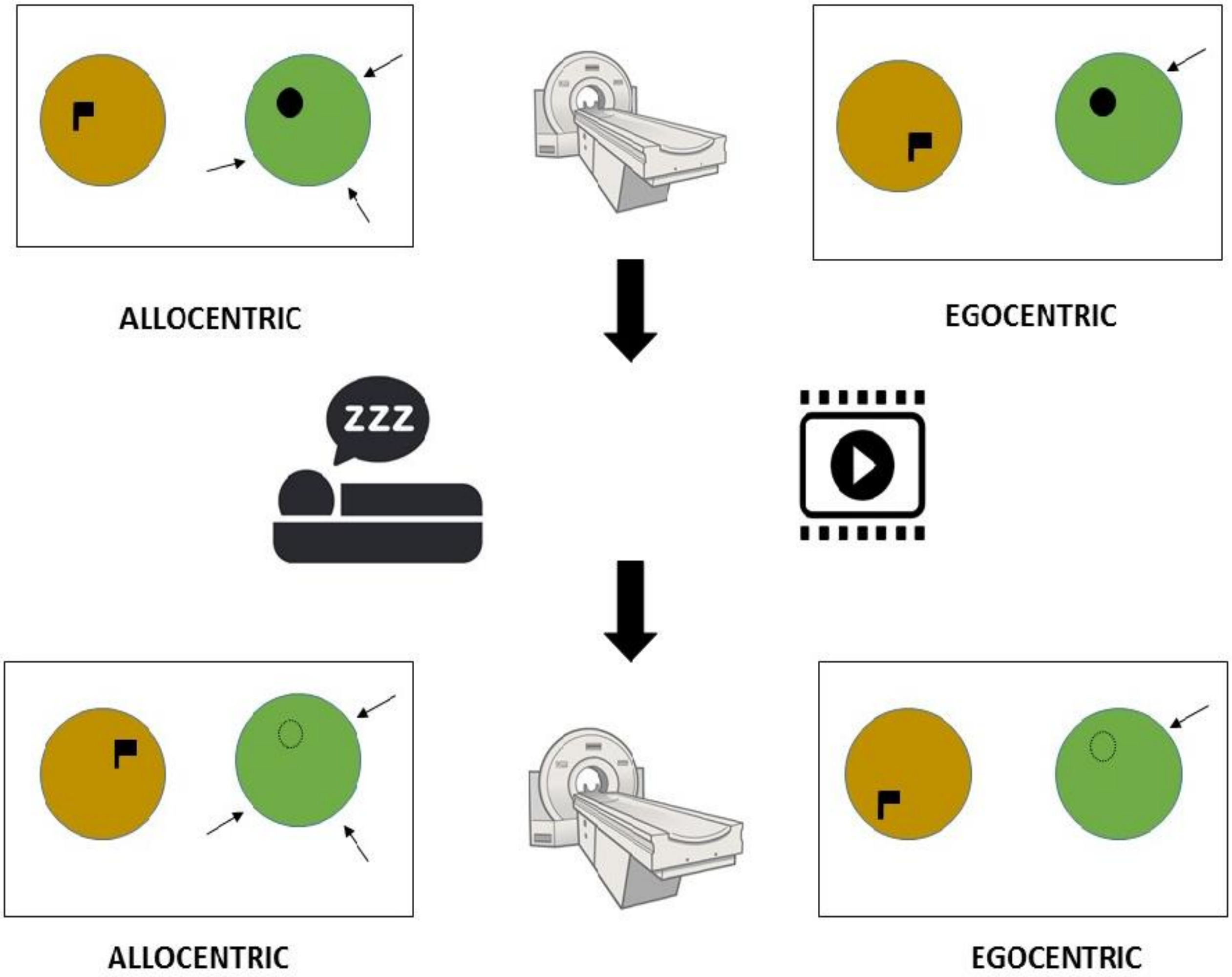
You are on a small island.
Somewhere there is a treasure box.
Please try to find it.

You have locked the target location.
Please wait 15 sec until the next trial starts.

Figure 2. On the left panel is a picture of the cued (brown) island with a visible flag (cue) along with a treasure box. On the right panel is a picture of the un-cued (green) island which has a

treasure box in a depression valley (can be seen above) in the island, in a fixed location next to one of the cues (bridge). The island contains more global cues on other sides.

Study Design



Procedures

All participants attended a minimum session which lasted approx. 6 hours. The whole session was split into three parts – training session in the MRI scanner, 2.5-3 hour interval involving either taking a nap with EEG or watching a movie, test session in the MRI scanner. Participants in the sleep group were asked to come another day for a second re-sleep session within 2-3 weeks of the first session. In the first part, participants were first asked to fill out the screening questionnaire and rate their awareness levels on the Stanford Sleepiness Scale. The MRI session started with a T1-weighted anatomical scan which lasted 5 mins. It was followed by a Resting State scan where the participants were asked to fixate on a cross projected on the screen. This scan lasted for 8 min 45 s. Next, they performed 16 blocks of the training task (allocentric or egocentric). The 16 blocks consisted of 8 alternating blocks each of the cued and un-cued island. The participants were required to find the flag each time in the cued island and learn the location of the hidden treasure box in the un-cued island across the 8 trials. The duration of this scan varied across all participants and ended when they successfully completed all the blocks. Following the task, the Resting State scan was repeated and then the session ended. At the end of the session, they were informed which condition (sleep/wake) were they in. This allocation was also made randomly. Overall the whole session lasted 75-80 mins including participant preparation. Next, the participants in the wake group were allowed to watch a movie of their choice for 2.5 hours. The movies chosen were neutral with no extreme arousal elements in them. The participants in the sleep group were first prepped with sleep EEG cap and then allowed to sleep in a dark room for approx. 1 hour 45 mins. At the end of either of the sessions, participants were asked to fill out the Pittsburgh Sleep Quality Index questionnaire and rate their awareness levels again on the Stanford Sleepiness Scale. Finally, following the movie/nap, they were tested on the task in the MRI scanner. This session started with the Resting State Scan which lasted 8 mins 45 s. This was followed by 16 blocks of task session (allocentric or egocentric), consisting of 8 alternating blocks each of cued and un-cued island. This was the probe trial session, so the treasure box was no longer present. The participants were required to remember the location of the fixed hidden treasure box in the un-cued island from the learning session and mark on where they thought the box was to the best of their accuracy. The cued island remained the same as the training session. The duration of this scan varied across all participants and ended when they successfully completed all the blocks. Following the task, the Resting State scan was repeated and then the session ended. Overall this session lasted 60-75 mins including participant preparation. Participants from the sleep condition were asked to come another day for a second session where they had to take a short nap again with EEG. The timing of the nap was almost similar to that of the previous one. The objective of the re-sleep session was to assess if there were any differences in sleep patterns when they slept immediately after learning a task and not.

MRI acquisition parameters

Functional images were acquired with a 3T Prisma MRI system (Siemens, Erlangen, Germany), using a T2*-weighted gradient-echo multiband EPI sequence (TR/TE = 1000/34 ms, 66 transversal slices, voxel size 2x2x2 mm, 60° flip angle). Anatomical images were acquired using a T1-weighted MP-RAGE sequence (TR/TE = 2300/3.03 ms, voxel size 1x1x1 mm, 8° flip angle).

Polysomnography

32 channels were recorded for the study, including EEG recordings from Fz, F3, F4, Cz, C3, C4, Pz, P3, P4, Oz, O1, O2 electrode sites, EMG on the chin (musculus mentalis), EOG (around the eyes) and ECG (in the upper left chest). Signals were amplified (BrainAmp, Brain Products, Gilching, Germany), digitized (sampling rate > 250 Hz) and filtered (EEG and EOG 0.3–35 Hz, EMG 10–100 Hz). The EEG signals were recorded using BrainVision Recorder software.

Analysis

Behavioral data analysis

Two parameters – proximity (distance between the marked and actual location of target) and latency (time taken to reach the target location) were calculated for both cued and un-cued islands to measure the performance of the participants in the test sessions. These measurements were done across both allocentric and egocentric group after sleep/wake interventions, for the retrieval trials a repeated measures ANOVA was used to test the main effects and the interaction effects of the islands for two factors - proximity and latency with the within subject levels test (cued and un-cued island) and the between subjects levels (Allocentric and egocentric, wake and sleep). Further, a two-way ANOVA was used to assess the proximity and latency in the un-cued island with the between subjects factors (Allocentric and egocentric, wake and sleep). The results were then further explored with unpaired t-tests to compare the proximity and latency with regard to the main group (wake and sleep). All statistical analyses were performed in IBM SPSS Statistics for Windows.

EEG Sleep analysis

Sleep scoring was done by a single rater visually using the SpiSOP (Weber,2016) software. The scoring was based on EEG recordings from F3, F4 C3, C4, O1, O2, EOG, and EMG for subsequent 30-s epochs according to standard scoring rules as mentioned in the AASM Manual for the Scoring of Sleep and Associated Events, Version 2.2. Total sleep time (TST), time spent in different sleep stages (wake; sleep stages 1, 2, 3, REM sleep) were determined for each participant. Individual values were then averaged for all participants.

Results

Stanford Sleepiness Scale

Participants had to rate their alertness levels on the scale in the morning before the training session and in the afternoon after the wake/nap interval. Results depicted no difference in SSS1 between the wake and sleep groups. The SSS2 values were higher for the wake group compared to the sleep group, but the difference was marginally significant (p = 0.063)

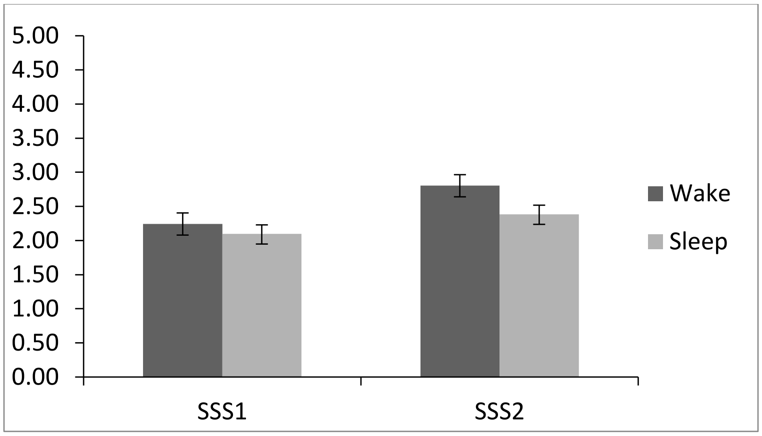


Figure 3. The SSS1 levels between wake and sleep groups and SSS2 levels between wake and sleep groups. There was no significant difference between any of the groups.

Sleep EEG Results

Total time spent in each sleep stage was calculated and averaged across individuals. Results show Stage 2 sleep to be the most dominant stage followed by Stage 3 (slow wave sleep). REM sleep was observed in 12 out of a total of 26 participants in the cohort.

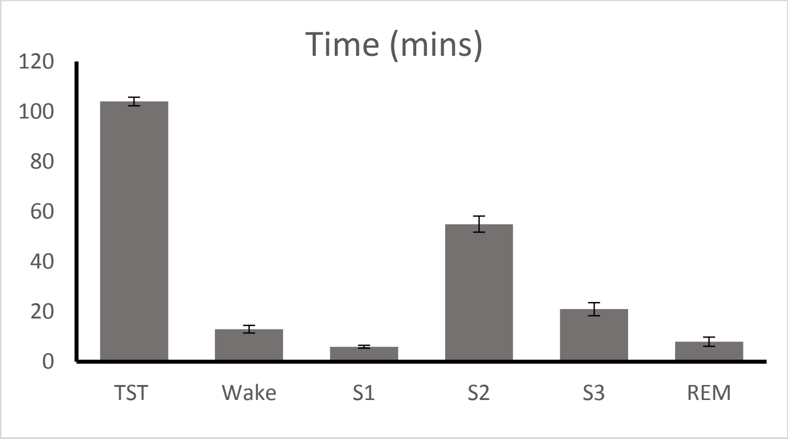


Figure 4. Average values of time (minutes) spent in each sleep stage.

Behavior results

A. Latency

Results revealed a highly significant difference in the main interaction effect between the cued and un-cued island ($F_{1,55} = 147.5$, $p < 0.0005$) and this difference persisted on interaction with the training conditions (islands x a_e ; $F_{1,55} = 5.98$, $p = 0.018$). Interaction with the intervention conditions (island x w_s ; $F_{1,55} = 1.09$, $p = 0.30$) was not significant. Interaction with the main islands and both of the between subjects factors (islands x a_e x w_s ; $F_{1,55} = 0.76$, $p = 0.38$) was also not significant. Interactions among the between subject factors in both islands were found to be significant for all (a_e - $F_{1,55} = 26.43$, $p < 0.005$; w_s - $F_{1,55} = 9.78$, $p < 0.005$; a_e x w_s - $F_{1,55} = 14.85$, $p < 0.005$).

Further on, focusing on the main effects in the un-cued island, there was a significant difference between the allocentric and egocentric conditions ($F_{1,55} = 31.07$, $p < 0.005$). Difference between the wake and sleep condition was also significant ($F_{1,55} = 9.93$, $p < 0.005$). Additionally, interaction between the allocentric/egocentric and wake/sleep conditions revealed a marginal significant difference ($F_{1,55} = 7.31$, $p =0.09$).

Lastly, as post-hoc contrast unpaired t-tests were run between sleep and wake participants for allocentric and egocentric conditions. Results showed significance in the allocentric condition ($t_{26} = 3.05$, $p = 0.005$) and no significant difference in the egocentric condition ($t_{26} = 0.561$, $p = .579$)

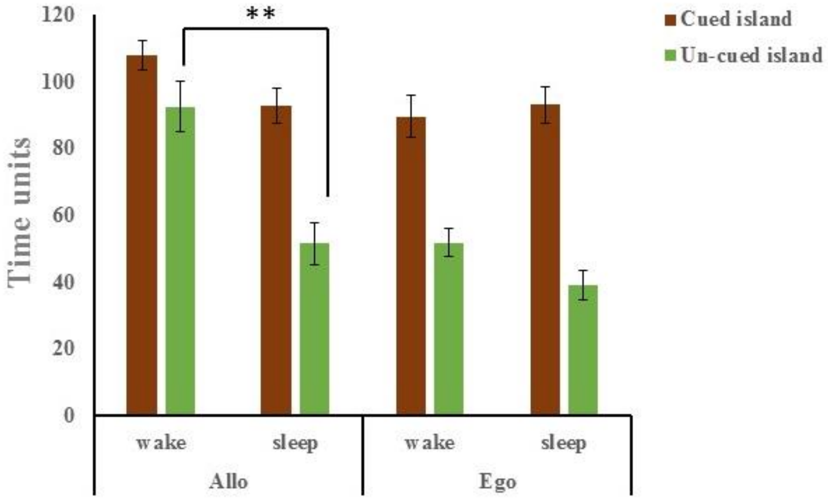


Figure 5. Latency values for both training conditions (allocentric and egocentric) after wake/sleep condition for the retrieval trials in both the islands. Results show a significant reduction in latency values after sleep in the allocentric condition.

B. Proximity

Results revealed a highly significant difference in the main effect between the cued and un-cued island ($F_{1,55} = 71.06$, $p = 0.0005$) and this difference persisted on interaction with the training conditions (islands x a_e ; $F_{1,55} = 7.26$, $p = 0.009$). Interaction with the intervention conditions (island x w_s ; $F_{1,55} = 1.67$, $p = .201$) was not significant. However interaction with the main islands and both of the between subjects factors (islands x a_e x w_s ; $F_{1,55} = 3.63$, $p = 0.062$) was marginally significant. Interactions among the between subject factors in both islands were found to be significant for all (a_e - $F_{1,55} = 7.20$, $p = 0.01$; w_s - $F_{1,55} = 4.10$, $p = 0.04$; a_e x w_s - $F_{1,55} = 3.87$, $p = 0.054$).

Further on, focusing on the main effects in our learning condition (the un-cued island), there was a significant difference between the allocentric and egocentric conditions ($F_{1,55} = 7.65$, $p = 0.008$). Additionally, mirroring the rodent results, interaction between the allocentric/egocentric and wake/sleep conditions revealed a significant difference ($F_{1,55} = 3.96$, $p = 0.05$).

Lastly, unpaired t-tests were run between sleep and wake participants for allocentric and egocentric conditions. Results showed a marginal significance in the allocentric condition ($t_{26} = 1.95$, $p = 0.062$) and no significant difference in the egocentric condition ($t_{26} = -.33$, $p = .737$)

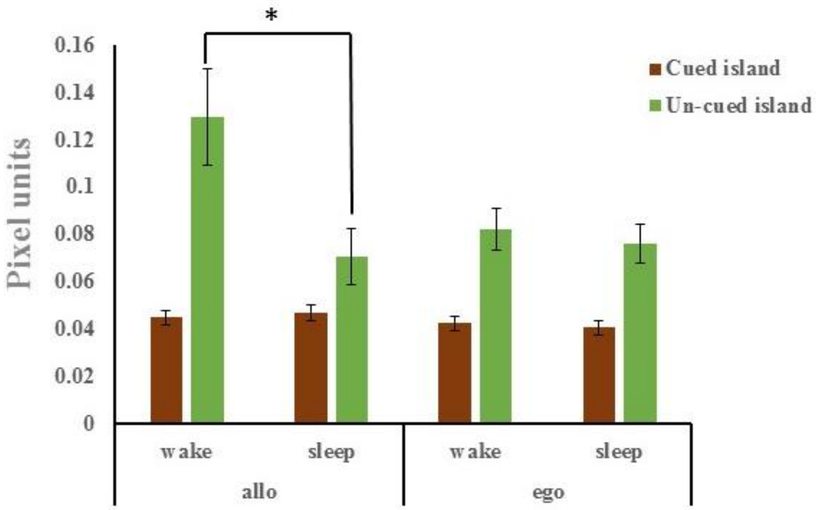


Figure 6. Proximity values for both training conditions (allocentric and egocentric) after wake/sleep condition for the retrieval trials in both the islands. Results show a significant reduction in proximity values (increase in accuracy) after sleep in the allocentric condition.

Discussion

The aim of the study was to study the differential effects of daytime nap on allocentric and egocentric memory training conditions in a virtual water maze environment. Participants were trained to navigate through an island and locate a hidden treasure box under either allocentric or egocentric training conditions. Post sleep/wake intervention, they did a retrieval test where they had to mark the location of the treasure box from the training session. Our results show that participants in the allocentric condition displayed increased accuracy in the retrieval test after sleep in contrast to wake. Performance of the participants in the egocentric condition remained independent of sleep effects. Additionally, the latency to mark the location of the box in the retrieval test was also significantly reduced in the participants in the allocentric condition post sleep. No such significant differences were found in the egocentric condition.

Our behavioral results are consistent with the findings in the rats. The underlying mechanisms behind the behavioral output might still differ across rats and humans, since rats had to physically navigate around the maze and make associations with the clues, whereas in humans, it was similar to a motor task and they used a joystick to navigate around the maze. We have hence developed a paradigm conceptually linked to rodent studies.

We didn’t find any significant difference in navigation abilities in the cued island across participants from both conditions. Additionally, similar latency levels in the cued island shows all participants had normalized navigation skills.

Previous studies conducted in virtual navigation environments (Ferrara et al. 2008; Ferrara et al. 2006) in humans showed that spatial accuracy in memory was enhanced only in the post sleep condition. Our results are consistent with these findings. However, in their findings, the performance speed of all participants remained the same before and after sleep. Our result contradicts that finding. However, this might be because of two reasons – firstly the previous studies were solely behavioral and were conducted in relaxed lab environments. In contrast, participants in this study were trained and tested in the MRI scanner, which might have been a more stressful environment. Secondly, the previous navigation studies had implicit allocentric and egocentric representations which according to a recent finding by Viczko et al. (2018), is independent of sleep effects. Our task, however, had explicit allocentric and egocentric representations. Learning in the allocentric condition involved starting from a different location every block, which could have been the reason of slowing down their performance. Another potential factor of difference could have been that the participants in the behavioral studies slept the whole night, in contrast to our participants, who took a 2-hour nap. Previous studies (van Schalkwijk et al. n.d.; Schabus et al. 2005; Lahl et al. 2008) however have shown naps to have a significant effect in improving procedural and declarative memory consolidation. Additionally, our results are in line with findings by Albouy et al. (2015), where they showed that naps mediated improvement solely in the allocentric representation of the task, whereas only maintaining the egocentric representation.

A sleep-dependent improvement in performance speed and accuracy was only seen for the allocentric training condition. No differences in the SSS1 values in the morning session show that all participants had similar alertness levels and showed no signs of sleep debt. SSS2 values were higher for the wake group in comparison to the nap group. This might be because naps have been shown to have a restorative effect on functioning levels of the brain and lead to increased vigilance and alertness afterwards (Mednick et al. 2002; Bonnet 1991) Given the sample sizes in each condition, a close inspection of results indicated that sleep-dependent gains in performance were consistent and robust across all subjects in the allocentric training condition. In contrast, gains in performance for the egocentric training condition was observed irrespective of the sleep or wake condition. The results thus suggest that naps specifically enhance the consolidation of allocentric (spatial) memory, whereas it only maintains, but doesn’t enhance the consolidation of egocentric (motor) memory. Thus the effect could not be solely caused by a decrease in fatigue.

Previous studies have reported that nocturnal sleep favors the consolidation of goal-based (spatial), but not of movement based (motor) representations of newly learned task sequences (Cohen et al. 2005). Sleep has been shown to facilitate transfer of the extrinsic (spatial) but not the intrinsic (motor) representation of motor learning tasks (Witt et al. 2010). The egocentric training condition in our task represents the motor component of spatial memory, and performance in this condition was shown to be independent of sleep effects. Our results hence, even though based on a different task, is in line with these findings.

It is known in rodents already that hippocampal replay during sleep is critical to the consolidation of spatial memories (Girardeau et al. 2009). Extending the finding to humans, it might be one of the potential underlying mechanisms behind the enhanced consolidation of allocentric memory. A study shows that wakeful rest period following learning the route of a virtual environment promoted the integration of spatial memories into accurate cognitive maps (Craig et al. 2016). The study does resonate with the evidence of hippocampal replay in rodents and could be associated with sleep.

Results from our sleep EEG analysis, reveal stage 2 sleep to be the most dominant of all states, which comprises of sleep spindles and k complexes (Genzel et al. 2014). It has been shown previously in human EEG that amount of sleep-spindle related activity is positively correlated with efficient cortical-subcortical connectivity and linked to improved memory abilities (Schabus et al. 2006). Additionally, another study has shown a strong interaction between spindle occurrence and hippocampal functional connectivity in sleep stage 2, with increased hippocampal/neocortical connectivity during spindles (Andrade et al. 2011). Increased connectivity might imply stage specific contribution to enhancing of memory consolidation. Lahl et al. (2008) has shown only 6 mins of light sleep to be sufficient for memory consolidation. Overall it is proposed that light sleep is the dominant stage for memory consolidation (Genzel et al. 2014). Clemens et al. (2007) shows in humans that ripple density is higher in NREM sleep and is coordinated with spindle activity and this temporal coupling has been suggested to serve as hippocampal-neocortical dialogue underlying memory consolidation. Allocentric memory representation, being hippocampal dependent (Holdstock et al. 2000), it could thus then be hypothesized that this temporal coupling contributes to enhanced memory consolidation over the egocentric representation.

Further on, detailed MRI and EEG analyses need to be conducted to shed more light on the underlying mechanisms. One future step would be to compare the EEG spectra in participants from when they took a nap immediately after learning to that after a couple of weeks without any learning event and check for spindle density, number and SO-spindle coupling differences. With MRI analyses, we would investigate the shifts in network connectivity before and after sleep and post retrieval. We expect there to be increased HPC-PFC coupling in the participants under allocentric training condition, following retrieval. Another idea in the long run would be asses for long term retention of allocentric vs. egocentric representation of memory. A behavioral study by Ferrara et al. (2008), shows improvement in spatial performance only when learning is followed by a period of sleep, irrespective of the retention interval length. Viczko et al. (2018), investigates the allocentric and egocentric representations of implicit motor sequence learning, shows the time course of consolidation to be differentially regulated. Schönauer, Grätsch, and Gais (2015) investigate the differential long term effects of sleep on declarative and procedural memory tasks. Their results show a short term performance gain post sleep or wakefulness which disappear after recovery sleep. However, long lasting sleep mediated benefits are shown in performance in hippocampal-independent motor learning tasks. This implies consolidation of memory of the two spatial representations – motor or spatial might be differentially regulated. It would be interesting to delineate the role in hippocampus in long term consolidation of both systems. It could be a possibility that spatial memories require reactivation of the memory traces and their strength depends on the hippocampal-cortical interactions whereas implicit motor memories only require overall strengthening of synaptic connections.

To conclude, with our findings, we have been able to bridge the gap between rat and human findings and consistent with previous findings, have shown that consolidation of allocentric memory representation is enhanced by sleep leading to improved retrieval and task performance. Further in depth EEG and MRI analyses would shed light on the underlying mechanisms and pave the way for more translational possibilities.

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