Aus dem

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Sleep and Navigation – Testing the effect of sleep on the consolidation of landmark- and boundary-based spatial memory representations

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Abbreviations

ANOVA	Analysis of variance
BND	Boundary
EEG	Electroencephalogram
EMG	Electromyography
EOG	Electrooculography
EPSP	Excitatory postsynaptic potential
Fig.	Figure
fMRI	functional magnetic resonance imaging
LM	Landmark
LTM	Long-term memory
LTP	Long-term potentiation
M	Mean
PET	Positron emission tomography
REM	Rapid eye movement
SEM	Standard error of the mean
STM	Short-term memory
SWS	Slow wave sleep
VR	Virtual reality

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1. Theoretical Background

1.1. Introduction

The present study investigated the effect of sleep on spatial memory formation based on landmark- and boundary-based spatial references.

To orient in a given environment, to find one's way – be it to the nearest source of food, to one's home or to retrace a path in unfamiliar surroundings is a vital skill for both animals and humans. Not surprisingly, spatial navigation and navigational skills have long been of interest in research. How do we find, learn and remember a certain path? How do we orient in a new environment? Numerous studies have sought and still seek the answer to these questions. From the first half of the 20th century a vast number of studies, such as behavioural experiments in both animals and humans (Hampton, Hampstead, & Murray, 2004; Maguire, Nannery, & Spiers, 2006; Morris, Garrud, Rawlins, & O'Keefe, 1982), invasive single-cell recordings (O'Keefe & Dostrovsky, 1971) or modern neuro-imaging studies employing fMRI (Hartley, Maguire, Spiers, & Burgess, 2003; Maguire et al., 1998) have identified the hippocampus as one of the key cerebral structures for navigation and spatial cognition. In the mid-nineties, Wilson and McNaughton (1994) found that hippocampal activity that was recorded during a spatial navigation task in the awake state is replayed during subsequent slow-wave sleep. According to recent models of memory consolidation during sleep, this replay both strengthens hippocampal memories and also promotes their distribution to extra-hippocampal regions, such as the neocortex where these memories are integrated into the existing network of long-term memory (Diekelmann & Born, 2010).

To date, numerous studies exist demonstrating the beneficial effect of sleep on memory consolidation. The consolidation of spatial memories has received particular interest because the hippocampus is relevant to both spatial cognition and memory consolidation during sleep.

Results of this research has been inconclusive, however. While some of these studies found a beneficial effect of sleep on the consolidation of spatial memories

for humans (Nguyen, Tucker, Stickgold, & Wamsley, 2013; Noack, Schick, Mallot, & Born, 2017; Peigneux et al., 2004), others did not (Orban et al., 2006; Rauchs et al., 2008). However, despite the absence of behavioural effects, Orban et al. (2006) found sleep-related changes in brain activity during a virtual navigation task. Besides a general decrease in hippocampal activity and a general increase in striatal activity, the authors report that striatal activity was higher after sleep as compared to after wakefulness.

The striatal and the hippocampal navigation system have been identified earlier in human (e.g. Doeller et al. (2008); Maguire et al. (1998)) and animal studies (Packard & McGaugh, 1996). It has been suggested that these systems form the foundations of different strategic approaches (see Table 1 for a detailed description) which are based on different spatial reference frames. The hippocampus is involved in processing spatial information related to local boundaries whereas the striatum processes information related to proximal landmarks. Importantly, the acquisition of both reference frames may occur in parallel (Doeller et al.2008).

Since there are different ways to handle spatial navigation problems, the role of sleep in spatial memory consolidations can only be understood, if these different systems are taken into account. Thus, several questions emerge: (1) How does sleep affect spatial memory formation with regard to these different cues? (2) Is there a difference between landmark- and boundary-based spatial representations concerning the impact of sleep?

Yet, there has been no study to specifically and comparatively investigate the effect of sleep on the consolidation of striatal and hippocampal spatial memory representations, respectively.

To answer these questions, we took advantage of the relationship between different spatial cue types (local boundaries and proximal landmarks) on the one hand and the different representational systems (striatal and hippocampal) on the other. We conducted an experiment using a virtual reality environment containing either a proximal landmark or a local boundary. Participants were asked to learn six object locations within the virtual environment. After an interval of a night of total sleep deprivation and a consecutive recovery night or two nights of

undisturbed nocturnal sleep, retrieval knowledge was tested. The study was devised according to a mixed randomized cross-over design study, containing both between- (participants were assigned to either landmark or boundary cue type group) and within-subjects (all participants performed in both sleep and wake condition) factors.

1.2. Spatial Cognition

Navigating in an environment or in our surroundings, one might employ two different strategies using either an allocentric or egocentric representation of space. Allocentric space representation is characterized by object to object relations in the environment, whereas an egocentric representation is characterized by the position of objects in relation to one's own position. They show some remarkable differences. For instance, they follow different learning rules (Doeller & Burgess, 2008; Doeller et al. 2008), are associated with different brain regions (Gramann et al., 2010; Jordan, Schadow, Wuestenberg, Heinze, & Jäncke, 2004; Zaehle et al., 2007) and are more or less prone to error, e.g. after disorientation (Waller & Hodgson, 2006). Whether we use one type of representation or the other to navigate might depend on a variety of factors, such as former experience or familiarity with the environment (Iaria, Petrides, Dagher, Pike, & Bohbot, 2003), size of the environment or number of objects that need to be remembered within the environment (Burgess, 2006). Burgess (2006) also suggested that both of these systems might work in parallel. Studies in both rodents and non-human primates came to the conclusion that allocentric spatial representation and allocentric spatial memory is clearly associated with the hippocampus (Feigenbaum & Rolls, 1991; Hampton et al., 2004; Packard & McGaugh, 1996; Pearce, Roberts, & Good, 1998). Case studies in humans with bilateral hippocampal lesions confirmed these findings: hippocampal dysfunction seems to impair allocentric spatial memory in particular (Guderian et al., 2015; Holdstock et al., 2000).

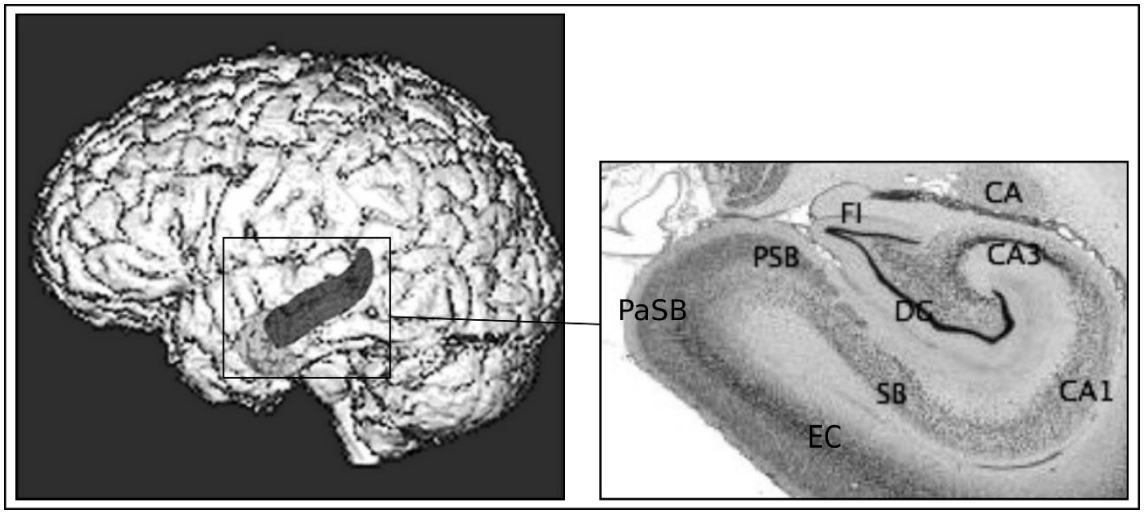

Figure 1: Anatomy of the hippocampal formation.
FI – Fornix, CA – Cornu ammonis, DG – Dentate gyrus, SB – Subiculum, PSB – Presubiculum, PaSB – Parasubiculum, EC – Entorhinal cortex. Picture on the left side from "The hippocampus book", p.44 (Andersen, 2007), picture on the right taken from BrainMaps.org Screenshots.

Knowledge about the hippocampal role on navigation and spatial memory did not only derive from lesion studies in animals or humans but also from electro-physiological experiments using single-neuron recordings within the hippocampus (for anatomy of the hippocampal formation see Figure 1 as well as Figure 2 for anatomy of the hippocampus and striatum). While recording firing patterns of hippocampal cells in rats that were exploring their surroundings, O'Keefe and Dostrovsky (1971) identified cells within the hippocampus that coded for an animal's specific location or place in an environment. These cells were fittingly called place cells. These cells characteristically increase their firing rate when the animal enters a certain location in the environment, i.e. a place cell's respective place field. Outside of a specific place field, place cells hardly signal. But since every place cell has a place field, there is always an active place cell at every location in every environment. In an environment that has been sufficiently explored the array in which different cells fire tends to be stable. The firing pattern does not change in a familiar environment (Hartley, Lever, Burgess, & O'Keefe, 2014). But place cells also exhibit a strikingly different behaviour. They can change their firing pattern completely when they enter an unfamiliar environment. But interestingly, this can also happen when the animal stays in the same environment. The mentioned process is referred to as remapping and can happen, for instance, when visual cues are removed or when a new cue is

introduced in the environment and it might also depend on prior experience in the environment (Bostock, Muller, & Kubie, 1991; Knierim, 2002; Muller & Kubie, 1987).

Another type of spatial cells are head direction cells. These cells were discovered in rats by Ranck (1985) and were later also found to exist in primates (Robertson, Rolls, Georges-François, & Panzeri, 1999). Head direction cells are found both within the hippocampal formation, e.g. in the presubiculum (J. S. Taube, Muller, & Ranck, 1990) and entorhinal cortex (Sargolini et al., 2006) but also in other brain areas like the thalamus (J. Taube, 1992) and striatum (Wiener, 1993). Activity recorded from head direction cells can be compared to the function of an inner compass: each cell shows a maximum in firing when the head of the tested animal is facing in a certain head direction but shows only meagre firing rates when the head is rotated to another direction. Said direction of maximum firing is also commonly referred to as a cell's "*preferred firing direction*" (J. S. Taube et al., 1990). All firing direction are equally represented among head direction cells.

In 2005, the discovery of yet another important set of spatial cells, named grid cells, in the entorhinal cortex (Hafting, Fyhn, Molden, Moser, & Moser, 2005) further refined theories of the cellular basis of spatial cognition. These cells can also be found in different areas within the hippocampal formation (Boccara et al., 2010). Hafting et al. (2005) discovered these cells in rats but they were later shown to also exist in humans (Doeller, Barry & Burgess, 2010; Jacobs et al., 2013). Grid cells differ from place cells and head direction cells as in that every grid cell has many firing fields. These firing fields are spread out in space in a regular pattern of hexagonals. Unlike place cell firing pattern, this grid cell pattern is stable across different environments.

Research has revealed the existence of further specialised cells that exist in the hippocampal formation such as boundary or border cells, that tend to signal when the animal is close to a wall in an environment (Lever, Burton, Jeewajee, O'Keefe, & Burgess, 2009; Solstad, Boccara, Kropff, Moser, & Moser, 2008) or speed cells that can modulate their firing rates according to the velocity with which an animal is moving (Kropff, Carmichael, Moser, & Moser, 2015).

Together, all these spatial cells that are found in the medial temporal lobe are able to determine precisely the current location of a living creature in a given environment and also track a path that has been travelled. This, in turn allows to form a cognitive map of its surroundings. There also exists first evidence that these spatial cells also exist with comparable function in humans (Ekstrom et al., 2003). However, final proof here is still lacking.

A brain region that plays a major role in processing egocentric spatial information has likewise been identified – the dorsal striatum (Brasted, Humby, Dunnett, & Robbins, 1997; De Leonibus, Oliverio, & Mele, 2005). However, the striatum does not only contribute to spatial processing. It is also associated with formation of non-declarative memories (for an overview of the role and characteristics of the hippocampus and the striatum in spatial memory formation properties see Table 1).

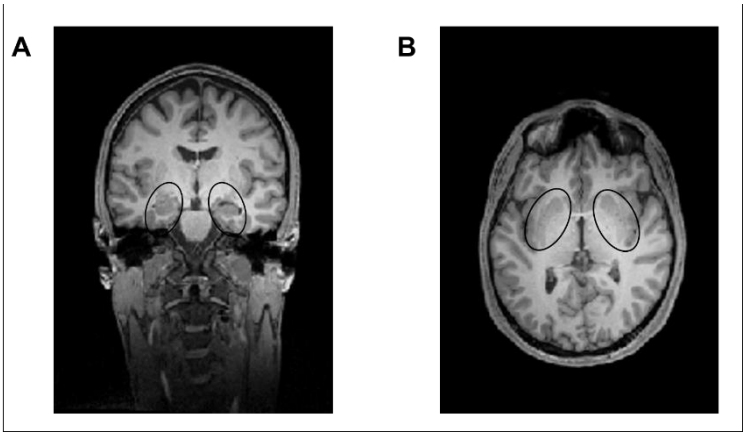

Figure 2: MRI image of the bilateral hippocampi (A) and striata (B).
With kind permission from F. Ott, unpublished data.

Finally, experiments by Doeller and Burgess (2008) have linked the formerly identified brain areas that play a crucial role in spatial navigation to distinct spatial cues. They conducted two experiments set up in a virtual reality. Participants had to learn and relocate object locations within a virtual arena. In an fMRI study they showed that activation in the right posterior hippocampus was seen during learning of object locations in relation to local boundaries while activation in the right dorsal striatum reflected learning of object locations related to a local landmark. The height of activation as seen in fMRI was also directly proportional

to performance. Both activation in the right posterior hippocampus and right dorsal striatum occurred in parallel and independently of the other. Furthermore, in a behavioural experiment, they reported that both systems rely on different learning rules: "*landmark- learning obeys associative reinforcement […] whereas boundary-learning is incidental*" (Doeller & Burgess, 2008, p. 5909).

Table 1: Overview and comparison of Hippocampus and Striatum in research

	Hippocampus		Striatum	
Memory systems	Declarative, especially episodic	*Eichenbaum (2000)* *Poldrack and Packard (2003)* *Tulving and Markowitsch (1998)*	Non-declarative, especially procedural	*Mishkin, Malamut, and Bachevalier (1984)* *Poldrack and Packard (2003)*
Acquisition rate	Fast	*Frank, Stanley, and Brown (2004)* *Wilson and McNaughton (1993)*	Slower	*Barnes, Kubota, Hu, Jin, and Graybiel (2005); (2008)* *Orban et al. (2006)*
Learning in a spatial domain	Place learning	*O'Keefe, Nadel, Keightley, and Kill (1975); Packard and McGaugh (1996)*	Response learning	*Featherstone and McDonald (2004); Packard and McGaugh (1996)*
Spatial frame of reference	Allocentric	*Feigenbaum and Rolls (1991)*	Egocentric	*Brasted et al. (1997); De Leonibus, Oliverio, and Mele (2005);*
Associated spatial representation	Boundaries	*Doeller et al. (2008)*	Landmarks	*Doeller et al. (2008).*
Neural activity	Place cell firing is triggered mainly by local boundaries	*Hartley, Burgess, Lever, Cacucci, and O'Keefe (2000)*	Firing of striatal cells is triggered by egocentric responses	*Berke, Breck, and Eichenbaum (2009)*

1.3. Sleep

Sleep has often been thought to serve as a state for recovery – the body temperature sinks slightly, as do blood pressure, need for oxygen and metabolism rate. In short, ideal premises for recreation and rest. But research has proven that this view falls rather short of the many processes that take place when we are not awake. Many theories have already emerged trying to answer the question as to why we sleep. Is it for regeneration? Is it a way to save energy while the sun is absent? Or are there other processes that can only take place during the off-line state of sleep? To date, some of these questions still lack conclusive answers.

Sleep is not only characterised by a loss of consciousness or the physiological processes mentioned above but also by distinctive changes in EEG pattern (Figure 3). Along with EOG which detects eye movement, and EMG that measures muscle tension, EEG has been used to classify different stages of sleep. Being awake, the EEG shows a β-rhythm, i.e. waves with a low amplitude and high frequency. When a person, has his or her eyes closed and is awake and calm and relaxed, EEG pattern changes to α-waves that have a rate of about 8-12 Hz and a higher amplitude compared to β-waves. Commonly, sleep is divided into REM- and Non-REM-sleep. Non-REM-sleep is subdivided into four stages. The first stage of actual sleep is characterised by θ-waves which have a frequency of about 6 Hz. In sleep stage I, eye movement and muscle tone decrease, a sudden twitching of muscles can occur. After approximately 5 minutes sleep progresses to the next stage, sleep stage II. This stage, that lasts for about 20 minutes is characterised by so-called sleep spindles and K complexes seen in EEG-recordings, which reflect sensory impressions that are still registered but processed subconsciously. Sleep stage III and IV are also referred to as slow-wave sleep because of the emergence of δ-waves - slow waves with a frequency of only 1 to 3 Hz and high amplitudes. After the last and deepest sleep stage, one passes through the preceding sleep stages in reverse order but instead of waking up after this, sleep progresses to REM-sleep or paradoxical sleep. There, the EEG pattern is almost indistinguishable from typical

waking activity and increased heart and breath rate, cerebral blood flow and oxygen consumption as well as rapid eye movements can be seen. Thus, during REM-sleep electrical activity is quite similar to the awake state, as is the activity in the motor cortex. But signalling from this region is blocked by the brain stem so that the body remains – apart from eye muscles and diaphragm – completely paralyzed.

One sleep cycle from sleep stage I / II to REM-sleep takes about 90 minutes. During the course of the night, those sleep cycles are repeated four to six times with a decreasing percentage of stage IV sleep and increasing proportion of REM-sleep. Arousal threshold increases from sleep stage I to sleep stage IV and is also very high during REM-sleep.

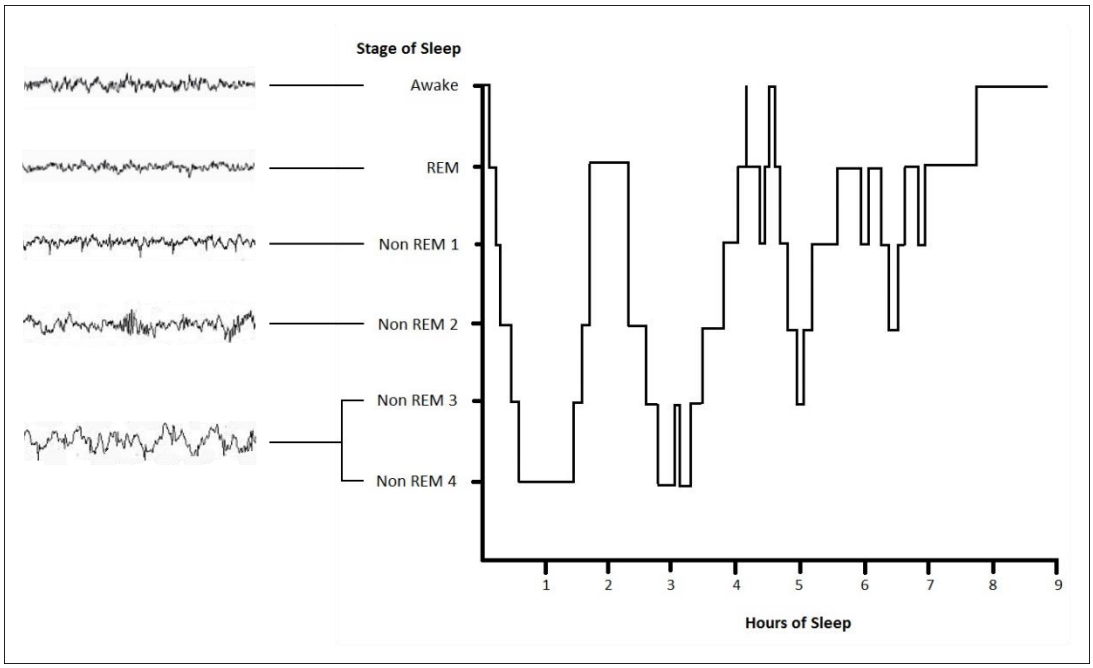

Figure 3: Idealised adult hypnogram with EEG waves corresponding to the different sleep stages. Standard hypnogram of normal sleep by Tash510, Wikimedia Commons

1.3.1. Effects of Sleep Deprivation

In general, an inadequate amount of sleep increases the risk for development of various diseases such as hypertension (Palagini et al., 2013) or coronary heart disease (Chandola, Ferrie, Perski, Akbaraly, & Marmot, 2010), obesity and diabetes (Spiegel, Tasali, Leproult, & Van Cauter, 2009). It furthermore weakens

the immune system (Irwin, 2002) and has a significant influence on mood (Pilcher & Huffcutt, 1996).

Neuroimaging studies using PET or fMRI also revealed a direct impact of sleep deprivation on certain brain areas. For instance, metabolism in thalamus, basal ganglia and frontal lobe visualised via PET decreases after one whole day without sleep. This decrement is furthermore not easily reversible since it can still be detected after a night of recovery sleep (Wu et al., 2006). Also, activation in prefrontal and premotor cortex and parietal lobe is reduced after sleep deprivation (Drummond et al., 1999).

1.4. Memory Formation

A big step for memory research was provided by results from lesion studies in humans, the most famous case being that of Henry Molaison, known as patient H.M. Since childhood he had suffered from severe seizures that got worse during adolescence. As closer examination showed that his seizures began in the temporal lobes of both hemispheres, surgery was performed and both temporal lobes (including the amygdala, a greater part of the hippocampus as well as entorhinal and parahippocampal cortex) were removed. This decreased both amount and severity of his seizures but also led to a profound impairment of memory function for the rest of his life. Patient H.M. could not form new memories (Scoville & Milner, 1957), i.e. he suffered from severe anterograde amnesia. Interestingly, his short-term memory did not seem to have been affected (Wickelgren, 1968), neither was his ability to learn new procedural skills (Corkin, 1968). Memories he had made up to his late teens remained largely intact (Scoville & Milner, 1957) and his IQ showed no deterioration compared to pre-surgery (Corkin, 1984).

From the case of patient H.M. evidence can be drawn that (1) there are different memory types such as STM and LTM and also different subtypes of LTM like hippocampus-dependent and non-hippocampus-dependent, that (2) these different memory types are processed by different brain regions and finally that (3) the medial temporal lobe and namely the hippocampus are crucial for long-

term memory formation. Commonly, LTM is divided into two subsystems: hippocampus-dependent or declarative memory and non-declarative memory that does not depend on the hippocampus (see Figure 4 for a classification of LTM subsystems and corresponding brain regions).

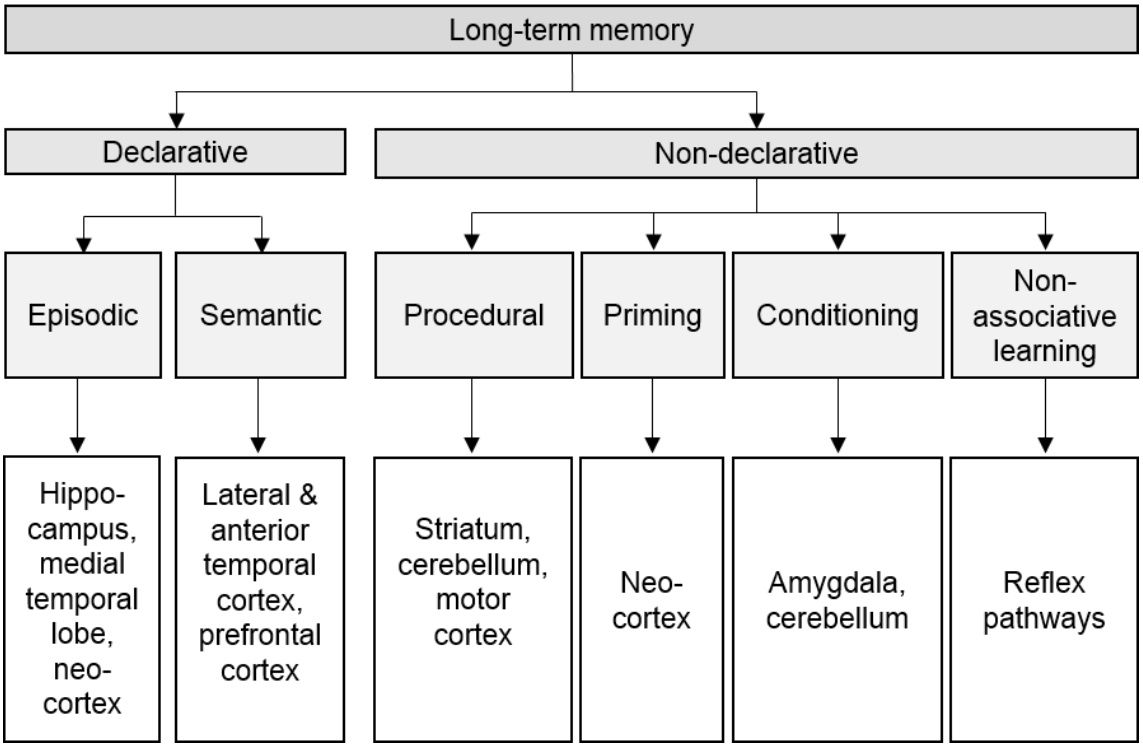

Figure 4: Overview of long-term memory classification and corresponding brain areas
Adated from Bartsch, T. & Butler, C. (2013)

So how do we form new memories? How are memories transferred from short-term storage to LTM? Recent research has tried and in large part succeeded in answering these questions. Formation of new memories proceeds in three steps: encoding, consolidation and retrieval. Sensory input is encoded into short-term memory. But since newly encoded memory traces are quite unstable and in risk of decaying rapidly and thus becoming irretrievably lost, they have to be strengthened. Memory consolidation is a process that converts these new and still unstable memories to stable representations and integrates them into the existing network of long-term memory. More than a hundred years ago, Müller and Pilzecker (1900) proposed that newly acquired memories are stabilised and transferred from short-term memory to long-term memory via consolidation over

time. Consolidation processes can be observed both at a cellular and also at system level.

On a cellular, or rather synaptic level, distinct molecular changes are found both in the structure and also in the physiological function of a neuron. The ability of neurons or whole neural networks to be changed by external influences is called neural plasticity. Already in 1949, Hebb postulated his idea of neural plasticity with the famous phrase "*what fires together, wires together*", meaning that when a synapse is repeatedly activated by another one the connection between the two synapses will gradually become stronger (Hebb, 1949). Fist proof of neural plasticity as proposed by Hebb was found in the hippocampus (Bliss & Lømo, 1973; Schwartzkroin & Wester, 1975). It could be shown that when a presynaptic neuron was repeatedly stimulated with high frequency, the postsynaptic neuron would respond with a significantly increased excitatory postsynaptic potential (EPSP). The induced changes in postsynaptic response pattern proved to be both stable and durable and were thus called long-term potentiation (LTP). Bliss and Gradner-Medwin (1973) later showed that LTP could last for days and even weeks.

Formation of new memories on a system level shall be described here exemplarily with formation of new declarative memories. According to the transformation hypothesis (Wincour et al 2010) fresh memories are initially dependent on the hippocampus and still closely affiliated with the context in which they were formed. As the name suggests, during the process of consolidation, as the memory becomes integrated into the existing network of LTM, it undergoes a transformation to a rather "*schematic version of the original memory which retains some of its essential features […] but few of its contextual detail*" (Wincour et al 2010, p. 2340). In summary, consolidated memories lack in minute detail but conserve the principle features of the original one encoded in the hippocampus.

1.5. The Role of Sleep in Memory Consolidation

While encoding and retrieval processes occur in the awake state, consolidation of memories mainly happens during sleep. Comparing the influence of identically

long intervals of sleeping and waking on memory, a great number of studies proved that both declarative and procedural long-term memory benefit from sleep. Sleep after learning reinforces retention of declarative information (Ellenbogen, Payne, & Stickgold, 2006; Gais & Born, 2004; Plihal & Born, 1997) and also leads to an improvement of performance on procedural tasks (Fischer, Hallschmid, Elsner, & Born, 2002; Plihal & Born, 1997). It does not even need a full night of sleep – beneficial effects of sleep can already be detected after a short nap (Mednick, Nakayama, & Stickgold, 2003). Research in humans has been able to disentangle the complex connection between sleep and memory formation even further by illustrating that different sleep stages have a propitious effect on the consolidation of different types of memory (Walker & Stickgold, 2004). Even though it has to be mentioned that there exists some conflicting evidence to this view (Fogel, Smith, & Cote, 2007; Gais, Plihal, Wagner, & Born, 2000; Rauchs et al., 2004), it is generally assumed that consolidation of hippocampus-dependent, declarative memories profits in particular from SWS (Plihal & Born, 1997; Rasch, Büchel, Gais, & Born, 2007) whereas REM-rich sleep rather promotes consolidation of non-declarative memories (Plihal & Born, 1997, 1999; Wagner, Gais, & Born, 2001). But sleep does not exclusively promote consolidation of declarative memories. Albouy, King, Maquet, and Doyon (2013) reported findings that suggest that procedural memory also benefits from post-learning sleep. In a different study Albouy et al. (2008) could show that activity recorded in the hippocampus during motor sequence learning went hand in hand with a performance enhancement after one night of sleep.

So, what is it that happens during sleep that promotes memory consolidation? Cell recordings from hippocampal neurons tried to shed light upon this question. Wilson and McNaughton (1994) were the first to demonstrate that experiences obtained during waking were re-expressed during non-REM sleep. In 1996 Skaggs and McNaughton reported that whole sets of hippocampal place cells they recorded in rats traversing a path which lead them to food, maintained their overall firing pattern during sleep. Firing during sleep occurred in the same sequence as in the awake state but at a higher frequency. Further studies have

shown that this replay takes place mainly during SWS (Lee & Wilson, 2002) but it is also found during REM-sleep episodes (Louie & Wilson, 2001).
Conversely, it has been shown that hippocampus-dependent memories and performance on spatial navigational tasks are severely impaired after total sleep deprivation in rodents (Campbell, Guinan, & Horowitz, 2002; Guan, Peng, & Fang, 2004; Hagewoud et al., 2010).

In humans, invasive single-cell recordings are not possible, but neuroimaging studies revealed that the hippocampus also shows increased activity after a learning session. A neuroimaging study by Peigneux et al. (2004) found that parts of the hippocampus active during a navigational task show similar activation during slow-wave sleep following the learning phase. Interestingly, they also showed that with increasing hippocampal activation, route retrieval performance also increased. These results support the theory that spatial memories are replayed during sleep in humans and that this leads to an improvement in performance.
To date, the replay of memory traces - as described in the hippocampus - is thought to play a key role in memory formation in both animals and humans by transferring formerly exclusively hippocampal memories to other brain regions, especially to the neocortex (Siapas & Wilson, 1998; Takashima et al., 2006) where they can be stored for days, months, years and even forever. This process is also described by the Active System Consolidation Hypothesis (Diekelmann & Born, 2010). According to this theory, memories are encoded while one is awake both into the hippocampus as well as into the neocortex. During post-learning sleep these fresh memories are reactivated in the hippocampus and redistributed to the neo-cortex. This process of replay and redistribution is orchestrated by the alternation of states of high, global neural activity (up-states) and periods of neuronal silence (down-states) resulting in patterns of slow oscillations as observed at the level of field potentials. Slow oscillations originate from the neocortex during Non-REM-sleep and in turn modulate spindles originating in thalamo-cortical regions. These spindles consecutively trigger hippocampal ripples. Staresina et al. (2015) demonstrated, employing direct EEG-recordings, that these neural firing patterns act in unison and provide a delicate timeframe for

memory transfer from the hippocampus to the neocortex. Interestingly, memory replay is not limited to the hippocampal region alone but can also be seen in other brain areas (for example Ji & Wilson, 2007).

1.6. Spatial Memory and Sleep

Based on the key role sleep plays on memory consolidation in general as well as the effect the hippocampus has on the formation of spatial memories in particular, a number of studies have researched the role of sleep in the formation of spatial memories. The studies discussed here all employed a virtual (Ferrara et al., 2008; Nguyen et al., 2013; Noack et al., 2017; Orban et al., 2006; Peigneux et al., 2004; Rauchs et al., 2008; Wamsley, Tucker, Payne, & Stickgold, 2010) or real-life (Ferrara et al., 2006) environment where subjects had to learn a navigational task. After a retention interval filled with sleep and / or wakefulness, participants were tested again on the learned task. Despite methodological differences, studies by Ferrara et al. (2006); (2008); Nguyen et al. (2013); and Noack et al. (2017) consistently reported an improvement of performance when spatial learning was followed by an interval of sleep. Wamsley et al. (2010) only found a positive effect of sleep concerning navigational performance for participants who already had gained experience with 3D video games. On the other hand, some studies could not detect sleep-related changes in manifest task performance (Orban et al., 2006; Rauchs et al., 2008). However, the latter studies found that sleep after spatial learning does affect fMRI signal. Sleep after learning induces a shift in brain activity detectable by functional neuroimaging techniques that could not be found when wakefulness or sleep deprivation ensued after learning (Orban et al., 2006; Rauchs et al., 2008).

According to a study by Peigneux et al. (2004) areas within the hippocampus active during route learning in a VR environment are reactivated during slow-wave sleep. Furthermore, they found that activity in the hippocampus was proportional to task performance improvement.

1.7. Aim of this Study and Hypothesis

In recent years, a number of studies have researched the effect of sleep on the consolidation of specifically spatial memories. Most of these studies have indeed revealed a beneficial effect of sleep on spatial memory consolidation (for example Ferrara et al., 2008; Nguyen et al., 2013; Noack et al., 2017; Wamsley et al., 2010). However, there are also studies which failed to report a beneficial effect for post-training sleep on task performance (Orban et al., 2006; Rauchs et al., 2008). Interestingly, in the two latter studies sleep after learning did not influence task performance but did affect patterns of brain activation. With regard to experiments by Doeller et al. (2008; 2008) we sought to investigate the effect of sleep on the consolidation of spatial memories with special interest in the different spatial representational systems. We used a virtual reality task adopted from Doeller et al. (2008) that was modified and contained either a single proximal landmark or a circular boundary to address striatum- and hippocampus-dependent spatial representation systems individually. Distal spatial cues were available for orientation. Participants were asked to learn and retrieve object locations in the environment. Retrieval knowledge was tested after an interval filled with sleep or wakefulness. It was hypothesised:

(I) to see sleep-related strengthening of spatial knowledge.

(II) to find a greater benefit from post-learning sleep in the boundary group compared to the landmark group.

2. Methods

2.1. Experiment

2.1.1. Participants

Forty participants volunteered to take part in this study, 19 men and 21 women (mean age 23.8 years ± 2.6 years, range 20-31 years). All participants had normal or corrected to normal vision, did not work night shifts, and had no sleep disturbances or mental diseases. Participants gave written informed consent and were paid for their participation. The study was approved by the local ethic committee (reference number 169/2014BO2).

2.1.2. Design

The present study followed a randomized cross-over design (see Table 2). Participants were randomly assigned to either the boundary or landmark spatial cue group. All participants performed on a sleep and a wake condition, with the order of these conditions being balanced between participants (sleep order: sleepFirst / wakeFirst). Furthermore, two different environment conditions (see Figure 5) were used to minimize carry-over effects from one session to the other. The order of environment conditions was also balanced across conditions.

Table 2: Experimental Design:
Participants were randomly assigned to boundary or landmark cue group. Order of both sleep and environment was counterbalanced across all groups. All experimental subgroups held five participants.

			Session 1			Session 2			
Cue type	Sleep Order	Environment Order	Env. Encoding	Night 1	Env. Retrieval	Env. Encoding	Night 1	Env. Retrieval	No. of Participants
BND	SleepFirst	DesertFirst	Desert	S	Desert	Alpine	W	Alpine	5
	WakeFirst	AlpineFirst	Alpine	W	Alpine	Desert	S	Desert	5
	WakeFirst	DesertFirst	Desert	W	Desert	Alpine	S	Alpine	5
	SleepFirst	AlpineFirst	Alpine	S	Alpine	Desert	W	Desert	5
LM	SleepFirst	DesertFirst	Desert	S	Desert	Alpine	W	Alpine	5
	WakeFirst	AlpineFirst	Alpine	W	Alpine	Desert	S	Desert	5
	WakeFirst	DesertFirst	Desert	W	Desert	Alpine	S	Alpine	5
	SleepFirst	AlpineFirst	Alpine	S	Alpine	Desert	W	Desert	5

2.1.3. Task stimuli

Participants were asked to locate and retrieve objects in a virtual environment that was adapted from Doeller and Burgess (2008). The virtual environment was built using Unreal Engine 2 Runtime Software (Epic Games) and consisted of an even plain surrounded by distant mountains. Importantly, mountains were rendered to infinity such that they provided directional but no distance information. In other words, the mountains did not change size or appearance as the participants navigated through the environment and thus locating objects based on distal cues alone was impossible. Furthermore, we constructed two similar but distinct virtual environments to reduce potential carry-over effects from one session to the other. In addition to a distinct topography, environments differed in their surface characteristics: one had an alpine surface – a grassy plain surrounded by green and snowy mountains – and one had a desert-like appearance on arid ground and brownish mountains (see Figure 5). All subjects were tested in both the alpine and desert virtual environment. For the two experimental groups, a proximal cue was added: either a rocky circular ridge with about 180 virtual meters (vm) in diameter surrounding the area where objects were located, thus serving as boundary, or a traffic cone in the middle of the plain serving as proximal landmark. Neither from the ridge nor the traffic cone the participants could extract any directional information since both were radially symmetric.

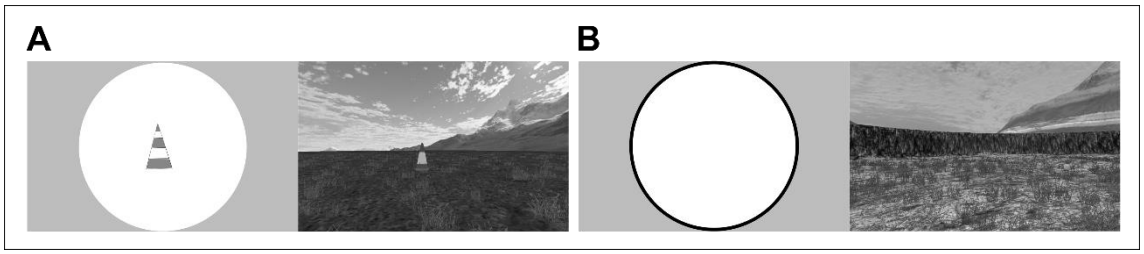

Figure 5: Task stimuli and VR environments
Comparison of both cue types in a schematic view from above: landmark (A left) and boundary (B left) as well as example of the two different environments: alpine (A right) and desert (B right).

2.1.4. General procedure

Participants came to the sleep laboratory at two occasions for an encoding and a retrieval session respectively (see Figure 6). Procedures of the two sessions were similar, except for the sleep/wake condition during the retention interval: participants of the SleepFirst group slept during session one, staying awake during session two and, vice versa, participants of the WakeFirst group stayed awake during session one and slept during session two. There was a break of two weeks between sessions.

Encoding started at 8 p.m. Before the actual experimental task started, participants completed several control tests on short-term memory, vigilance and sleepiness (see Table 3 for details). They then engaged in a training task in a slightly different virtual environment to help them get familiar with task handling. During this familiarisation, a bush and a square boundary as proximal cues were present. After a short break of approximately five minutes participants were informed about whether they would navigate in the arena with the boundary or the traffic cone as proximal landmark and the actual experiment started. As described above, participants were asked to learn the location of six objects while receiving points for their performance. Having completed the experiment, all participants were equipped with Actiwatches to give objective information when they slept and when they were awake. They had to wear the Actiwatches without pause until they returned to the laboratory for the retrieval testing. In the sleep condition, participants went home after the experimental task at about 10 p.m. to follow their regular sleeping schedule. They were instructed not to take any naps during the day and to avoid alcohol and caffeine. In the wake condition, participants had to stay awake during the experimental night. They stayed in the laboratory watching animal documentaries and went for two short walks (20 to 30 minutes) at about 12:00 a.m. and 3:00 a.m.. The experimental wake night ended at 7 a.m. and participants were allowed to go home. The experimenter once more emphasized that participants had to stay awake until 8 p.m. of the same day and to abstain from caffeine and alcohol for the time of the experiment.

The retrieval testing took place precisely 47 hours after encoding. At 7 p.m. participants came to the sleep lab and, after again completing several control tests on reaction time, sleepiness and word fluency, tried to retrieve the object locations they had learned two days previously.

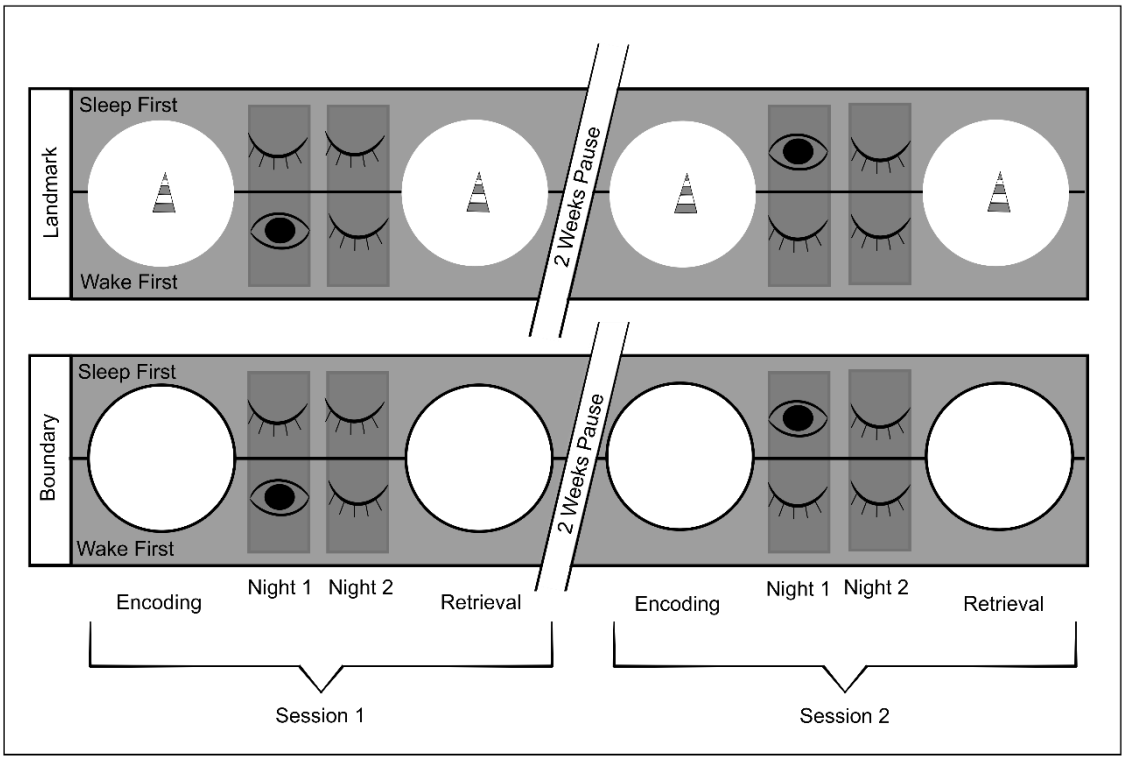

Figure 6: General procedure of the experiment:
Participants came to the sleep laboratory for two sessions. They were randomly assigned to either landmark or boundary group. After encoding, half of every group could go home for two nights of undisturbed sleep whereas the other half had to stay at the laboratory for one night of sleep deprivation followed by a recovery night of undisturbed sleep at home. After that, participants returned to the sleep laboratory for retrieval testing. After a pause of two weeks, the procedure was repeated with interchanged sleep condition – participants who had slept for two nights previously now had one night of sleep deprivation and a subsequent recovery night, formerly sleep deprived subjects could now sleep for two nights. Encoding started at 8:00 p.m. and retrieval started at 7:00 p.m. Picture adapted from: “Sleep support integration of landmark- and boundary-referenced spatial representations”, Noack, Doeller; Born, unpublished data.

2.1.5. Task procedure

Participants had time to get to know the virtual environment before the actual experiment started. During this phase there was no proximal cue present. Participants could navigate in the arena using the left-, right- and up-arrow keys of a standard keypad. When participants felt confident with task handling, the experimental task started. In this task, participants learned the position of six

objects. During encoding, participants were initially familiarized with the six object locations. To this end, participants were placed at a different starting position in the arena and had to navigate to one visible object in each trial. They were asked to pick that object up by moving past it and to memorize the corresponding location as best as possible. Feedback-guided learning (see Figure 7) started after all six object locations had been familiarized. A total of 24 learning trials were presented in four blocks. In every learning trial, one object was presented centrally on a grey background for two seconds. Thereafter, participants started navigation in the arena, taking the corresponding object to the place where they found it during familiarization, and placing it there by pressing the space bar. Having done that, the object appeared at its original location and participants had to pick it up again by walking over it. Time to deposit every object was restricted to 45 seconds. If participants did not respond within that time, the object appeared in its proper location where participants had to pick it up. Participants were explicitly instructed to use these sessions as another chance to improve their learning and to gain better memory of every object's location. Thus, each trial provided a further learning possibility. There were two different sequences of object presentation order, which were counterbalanced between participants. Participants started each trial in a different spot of the arena but always facing the centre.

During retrieval, exactly 47 hours later, long-term consolidation of the object location memory was tested. Retrieval trials were largely similar to encoding trials but lacking the feedback part. That is, an object was presented on a grey screen for two seconds and participants had to navigate to the presumed object's location. In contrast to the encoding trials described above, retrieval trials ended there. Objects were not presented at their original location. Participants performed a total of 18 retrieval trials organized in three blocks and time to complete a trial was limited to 30 seconds.

In order to increase motivation to perform as accurately as possible, participants received points for their performance during all encoding and retrieval trials. Depending on how closely they dropped an object to its original location they could earn zero up to three points. The number of points reached was shown

after each trial. Points were summed up to calculate a monetary bonus (10€ maximum). This was done to foster engagement in the task on the one hand and to increase relevance of the memory traces on the other hand, as relevant memories seem to be particularly susceptible to sleep-related memory consolidation (Stickgold & Walker, 2013; Wilhelm et al., 2011).

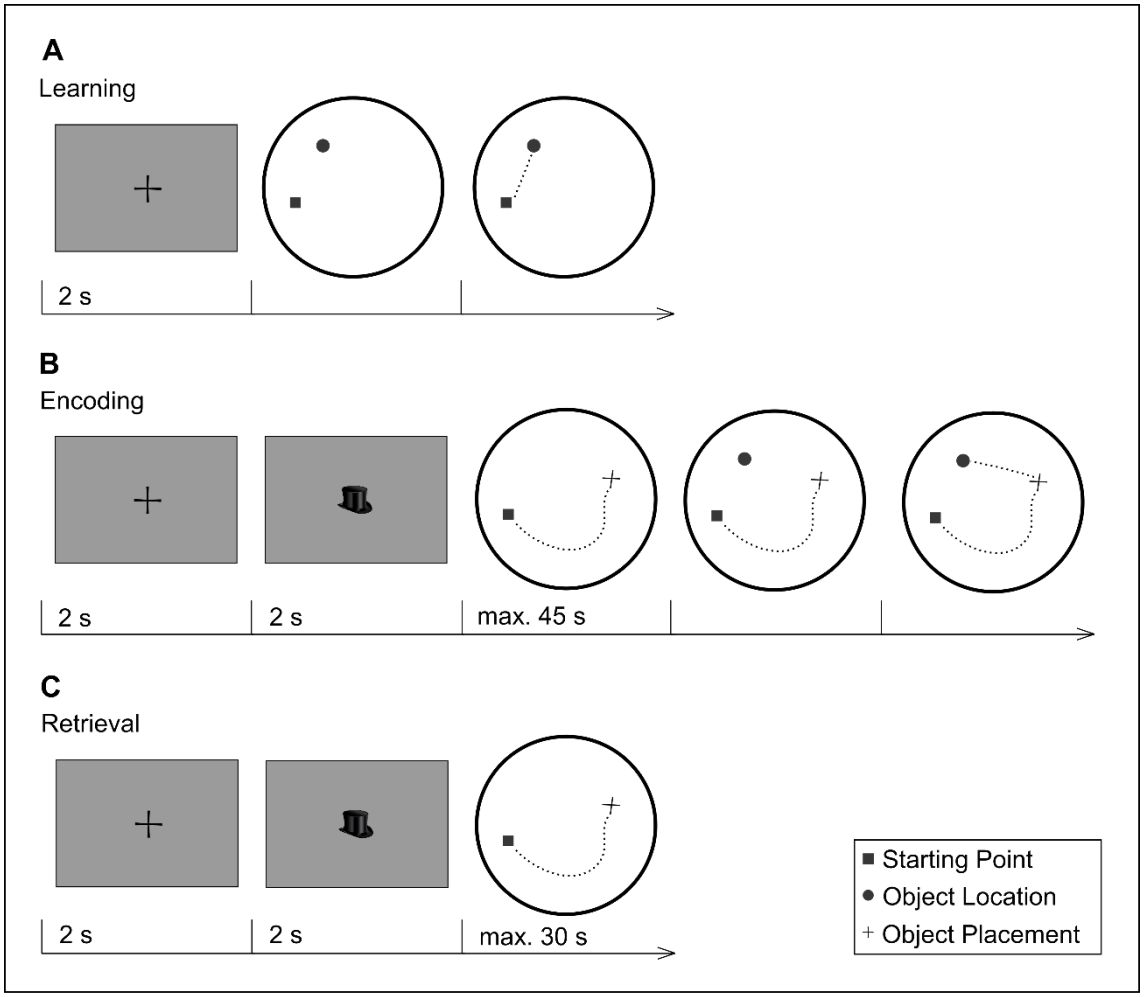

Figure 7: Learning, encoding and retrieval testing overview:
General procedure of learning blocks (A): all six objects were displayed once one after the other to be picked up by the participant. Participants were asked to remember the original object locations as accurately as possible. During encoding blocks (B) an object was displayed for two seconds and participants were asked to return it to its original location. Having done that, the object appeared in its true location to be picked up by the participants. This served as further learning possibility. Furthermore, subjects received points (0 up to 3) for their performance, depending on the distance between retrieved and true location. During retrieval sessions (C) an object was displayed and participants were asked to return it to its original location. Participants received points for their performance. During retrieval the object did not appear in its original location for feedback. Picture adapted from: “Sleep support integration of landmark- and boundary-referenced spatial representations”, Noack, Doeller; Born, unpublished data.

2.2. Control Tests

We assessed a number of covariates in order to control for potential group differences in memory performance (see 2.2.1. Working Memory) and non-specific effects of sleep and wakefulness (see 2.2.3. Stanford Sleepiness Scale). Sleep duration and sleep quality were assessed using a sleep questionnaire and actimeters. All measures and the point in time when they were used are described in Table 3.

Table 3: Collection of control data:
Coming to the sleep laboratory for encoding sessions at session one, participants had to complete Ospan test on working memory. At every session they had to rate their sleepiness using SSS and assess reaction time via PVT. At retrieval testing only, participants had to perform the RWT. After nights when participants were allowed undisturbed sleep, they had to complete SF-A/R in the morning rating their sleep quality, indicating sleep time etc.

Session 1			Session 2		
Encoding	Sleep Nights	Retrieval	Encoding	Sleep Nights	Retrieval
Ospan					
SSS		SSS	SSS		SSS
PVT		PVT	PVT		PVT
		RWT			RWT
	SF-A/R			SF-A/R	

2.2.1. Working Memory

Since it was found that working memory span tasks correlate with the outcome in a variety of cognitive tasks and overall intellectual performance (Conway et al., 2005; Kane et al., 2004; Süß, Oberauer, Wittmann, Wilhelm, & Schulze, 2002), we chose to assess working memory capacity via the operation span (Ospan) task to make sure there would be no major difference between groups. An automated version of the operation span task, as introduced by Unsworth et al. (2005), was used to asses working memory capacity. In this version of the Ospan, participants were asked to remember letters presented to them in their correct order and judge the correctness of solved math operations. First, they had to

complete a practice set consisting of three parts: in part one they were asked to retrieve letters in the same order as presented to them. Then they had to solve math operations and judge whether or not a suggested solution was correct by clicking on a ‘Yes’- or ‘No’-box. Having completed this, subjects practiced both parts together: a math problem was presented and, after having judged the correctness of a given answer, a letter was presented which they had to remember before the next math problem appeared. At the end, they were asked to retrieve the letters in the correct order. Having completed all practice sets, participants had to carry out the actual operation span task which, in fact, was identical to the last practice part, only set sizes varied. Set size ranged from three to seven trials and participants had to complete three sets of every size. Furthermore, participants received feedback on every set completed on how many math errors they had made and how many letters they had remembered in the correct order.

2.2.2. Vigilance

Participants performed on the Psychomotor Vigilance Test (PVT) every time they came to the sleep laboratory before the experiment started. Participants faced a blank black screen. They were instructed to press the space tab immediately when they saw numbers counting up appearing on the screen. In doing so the count stopped and the number at which it stopped was equivalent to participants’ reaction time (in milliseconds). Intervals between each trial varied in length by two to ten seconds. We chose this test because performance in PVT has been shown to be sensitive to sleep deprivation without being prone to learning effects (Dorrian, Rogers, & Dinges, 2005; Lim & Dinges, 2008) in order to determine if sleep deprivation still had an possible effect on participants’ general performance at retrieval testing.

2.2.3. Sleepiness

To quantify subjective sleepiness, participants had to complete Stanford Sleepiness Scale (SSS) (Hoddes, Zarcone, Smythe, Phillips, & Dement, 1973). This scale ranges from 1 – feeling active and vital, alert, wide awake– to 8 – asleep. Participants rated their subjective sleepiness every time they came to the sleep laboratory before the experimental task started.

2.2.4. Sleep Quality Assessment

For every night that participants were allowed to sleep, they were given SF-A/R questionnaires (Schlaffragebogen A; Görtelmeyer, 2011) and instructed to rate their sleep quality and quantity. This questionnaire is used in research as well as diagnosis and therapy of sleep disorders (Habel & Schneider, 2017). The version used in this experiment contained eleven questions about the night, dreams, how participants felt going to bed and waking up the next morning, amongst others. Furthermore, participants had to indicate the time when they fell asleep and woke up. Participants were instructed to complete the sleep questionnaire each morning after they had woken up.

2.2.5. Retrieval Fluency

When participants had to come to the laboratory for retrieval testing, they had to complete the RWT (Regensburger Wortflüssigkeitstest, Aschenbrenner, Tucha, & Lange, 2000). This word fluency test serves as assessment for divergent thinking ability (Aschenbrenner, Tucha, & Lange, 2000). As various studies have shown this kind of divergent, creative thinking is also impaired by sleep loss (Horne, 1988; Wimmer, Hoffmann, Bonato, & Moffitt, 1992). Participants were given a time limit of two minutes to write down as many words as they could, starting either with the letter P or M. Order of the two letters was counterbalances across sessions and participants. Words with the same word stem and proper nouns were excluded. When the time was up, words were counted.

2.2.6. Actiwatch Data

All participants were equipped with Actiwatches when they came to the sleep laboratory for encoding sessions. They were instructed to wear these activity trackers around their wrist at all times during the experimental sessions, except when showering or swimming. They were allowed to take them off after retrieval testing. These trackers recorded subjects' activity thus making it possible to judge whether participants followed the required sleep restrictions (Weiss, Johnson, Berger, & Redline, 2010).

2.3. Statistical Analysis

Statistical analysis was conducted using R 3.2.1 (The R Core Team, 2013) implemented in RStudio for Windows. Landmark and Boundary group were compared via ANOVA (analysis of variance) using the ez 4.40 package (Lawrence, 2016). For the main analysis, a four-factor model was used with spatial cue type (boundary or landmark) and sleep order as between-subjects variables and sleep/wake and encoding/retrieval as within-subjects variables. For analysis of encoding and retrieval performance, 'blocks' was included as within-subjects-variable. There were two dependent variables: navigation accuracy and navigation time. Navigation accuracy represents the distance (in virtual metres) between the position where participants dropped an object and its original position. Navigation time represents the time needed to place an object. Furthermore, standard deviation of mean distance as measure for navigation variability was introduced as dependent variable for analysis of performance over encoding and retrieval blocks. Analysis was done using 12 encoding (block three and four of encoding session) and 18 retrieval trials (all retrieval blocks). Since a study by Wamsley et al. showed a sleep-related benefit for experienced gamers only, we decided to regard initial navigation performance as an additional covariate. Participants were split into high and low performing groups. Therefore, mean distance during encoding of session one for each participant was calculated and the median of all means was set as a cut off value. Participants

with mean distance higher than the overall median were assigned to the low performing group while participants with mean distance lower than overall median were assigned to high performing group.

For analysis of control tests, *t*-tests were used for comparison of group differences concerning performance in the Ospan and RWT and Wilcoxon test was used to assess sleepiness and sleep quality. Performance in the Psychomotor Vigilance Task again was assessed via within-subjects-design using ANOVA and with reaction time as well as number of lapses as dependent variables.

The significance level was set to $\alpha = 0.05$.

3. Results

3.1. Navigation Accuracy

3.1.1. Mean distance

On a general level, we expected a beneficial effect of sleep on spatial memory consolidation. However, contrary to this expectation, we did not observe an effect of overnight sleep or wakefulness, $F(1,38) = 1.22$, $p = 0.28$, $\eta^2 = 0.004$. At the absolute level, however, participants in the landmark group (M = 18.6, SEM 0.68) performed better than participants of the boundary group, mean distance = 32.72, SEM 0.9. $F(1,38) = 7.93$, $p = 0.01$, $\eta^2 = 0.15$.

To see whether other factors of the experimental design influenced the overnight changes in spatial memory performance, sleep order, encoding (blocks 3 and 4 only) and retrieval, gender and order of performance in the alpine or desert environment were included in the analysis. Again, a main effect for cue type was found, $F(1,24) = 11.94$, $p = 0.002$, $\eta^2 = 0.28$, along with a main effect for encoding / retrieval, $F(1,24) = 5.05$, $p = 0.03$, $\eta^2 = 0.01$, and a main effect for gender $F(1,24) = 5.30$, $p = 0.03$, $\eta^2 = 0.15$. Still, we could not report a main effect for sleep $F(1,24) = 1.04$, $p = 0.32$, $\eta^2 < 0.01$.

Besides, there were a number of significant interaction effects: environment order by gender $F(1,24) = 9.61$, $p = 0.005$, $\eta^2 = 0.24$, sleep order by sleep / wake (which corresponds to a main effect of session) $F(1,24) = 7.09$, $p = 0.01$, $\eta^2 = 0.04$, environment order by sleep / wake $F(1,24) = 4.56$, $p = 0.04$, $\eta^2 = 0.02$, sleep order by environment order by sleep wake $F(1,24) = 6.5$, $p = 0.02$, $\eta^2 = 0.03$ (which corresponds to a main effect of session by environment).

3.1.2. Difference of mean distance

To reduce the complexity of analysis, the encoding/retrieval factor was dissolved and instead participants' performance was depicted by difference of mean distance between encoding and retrieval sessions as dependent variable. All four

encoding blocks were included. There were no main effects for cue type $F(1,38) = 0.34$, $p = 0.57$, $\eta^2 = 0.01$ or sleep/wake $F(1,38) = 1.15$, $p = 0.29$, $\eta^2 = 0.01$. What could be found, though, was an interaction effect between cue type and sleep/wake $F(1,38) = 5.08$, $p = 0.03$, $\eta^2 = 0.05$. It can be seen that the performance in the boundary group did not differ greatly between sleep and wake conditions ($mean_{Sleep} = 0.75 \pm 1.88$, $mean_{Wake}$ 2.78 ± 2.19) compared to the landmark group. There, participants displayed a worse overall performance in the wake condition ($mean_{Wake} = -2.43 \pm 2.6$) compared to sleep condition ($mean_{Sleep} = 3.27 \pm 1.25$) (see Table 4).

Table 4: Difference of mean distance between encoding and retrieval.
We found that performance of participants from the landmark group was significantly worse in the wake condition compared to sleep condition. Participants from the boundary group maintained their respective level of performance during sleep and wake condition.

Cue type	Sleep/wake	Difference of mean distance encoding & retrieval	SEM
Boundary	Sleep	0.75	1.88
	Wake	2.78	2.19
Landmark	Sleep	3.27	1.25
	Wake	-2.43	2.60

3.1.3. Encoding Performance over Blocks

Looking at encoding trials we found that participants‘ performance improved significantly from block 1 to block 4 $F(1,38) = 36.65$, $p < 0.001$ $\eta^2 = 0.06$. However, there was again a significant difference concerning cue type groups with participants in the landmark group performing generally at higher accuracy than participants from the boundary group, $F(1,38) = 9.77$, $p = 0.003$, $\eta^2 = .0.15$. Also see Table 5 for details. Performance did not differ significantly between sleep / wake condition $F(1,38) = 0.004$, $p = 0.95$, $\eta^2 < 0.01$ (see Figure 8A).

Table 5: Encoding performance over blocks between boundary (BND) and landmark (LM) group.

		BND		LM	
		pre-sleep	pre-wake	pre-sleep	pre-wake
Block 1	Mean distance (in vm)	38.59	41.56	29.79	25.19
	SD	31.19	34.2	36.19	30.08
	n	114	109	115	114
	SEM	2.92	3.28	3.37	2.82
Block 2	Mean distance (in vm)	35.48	38.65	26.97	18.52
	SD	31.83	29.98	33.24	20.24
	n	116	109	115	114
	SEM	2.96	2.87	3.1	1.9
Block 3	Mean distance (in vm)	32.43	34.8	16.64	20.03
	SD	32.53	32.25	21.53	25.47
	n	115	118	118	115
	SEM	3.03	2.97	1.98	2.38
Block 4	Mean distance (in vm)	27.95	31.8	15.7	15.43
	SD	24.81	34.5	19.72	15.07
	n	118	112	119	117
	SEM	2.28	3.26	1.81	1.39

3.1.4. Retrieval Performance over Blocks

Evaluating retrieval performance (see Figure 8B), we could not find a significant difference in mean distance over retrieval blocks $F(2,68) = 0.13$, $p = 0.88$, $\eta^2 < 0.01$, or between sleep / wake conditions $F(1,34) = 0.02$, $p = 0.90$, $\eta^2 < 0.01$. The performance difference between landmark and boundary groups seen during encoding persisted during retrieval, $F(1,34) = 4.07$, $p = 0.051$, $\eta^2 = 0.07$.

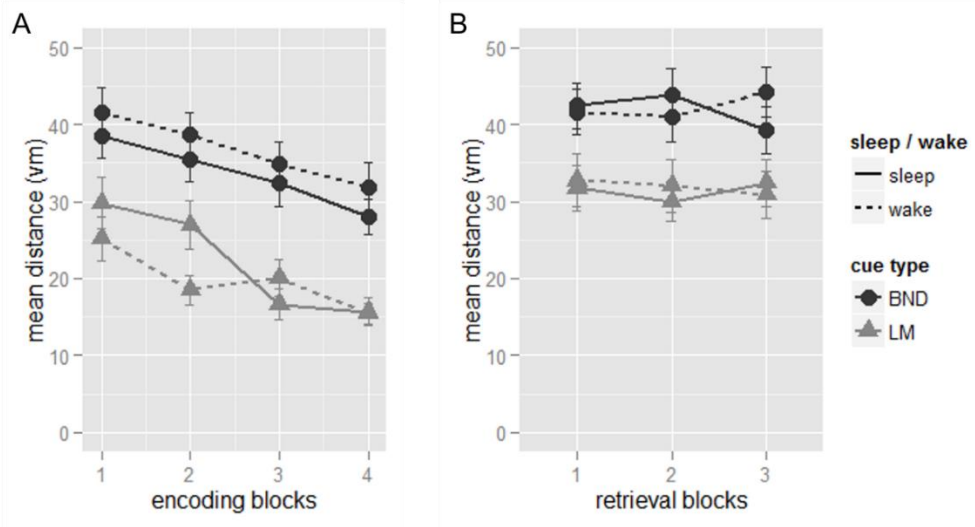

Figure 8: Encoding performance over blocks
A significant difference between landmark (LM) and boundary (BND) groups could be found. When analysing mean distance between original object location and location where participants deposited an object (A) Mean distance continuously decreased over encoding blocks. Strikingly, performance of subjects in the landmark group was much better during both sleep and wake conditions compared to participants' performance in the boundary group. During retrieval blocks (B), performance did not decrease. But again, a manifest difference between cue type groups was seen.

3.1.5. Navigation Variability over Encoding and Retrieval Blocks

As another factor navigation variability, meaning the consistency of finding the same location again, was included in the analysis. We argue that navigation variability reflects the reliability of the spatial representation of an object, where in theory reliability could be independent of absolute displacement if a person would acquire the wrong position and consistently return to it. Looking at individual performance variability using the standard deviation of retrieval distance as dependent variable, a similar outcome was found. During encoding sessions, there were again main effects for blocks $F(1,38) = 20.11$, $p < 0.001$, $\eta^2 = 0.05$ and cue type $F(1,38) = 5.96$, $p = 0.02$, $\eta^2 = 0.08$. Variability of mean distance steadily decreased from block 1 to block 4 and was significantly lower in participants from the landmark group.

Analysis of variability during retrieval sessions showed there was no general effect in variability of either blocks $F(2,68) = 1.73$, $p = 0.18$, $\eta^2 = 0.01$, cue type $F(1,34) = 1.58$, $p = 0.22$, $\eta^2 = 0.01$ or sleep / wake $F(1,34) = 0.02$, $p = 0.89$, $\eta^2 < 0.01$.

3.2. Navigation Time

3.2.1. Mean Navigation Time

Considering that improved spatial memory representations would increase the ease of memory retrieval, we expected to find reduced navigation times after a night of sleep as compared to wakefulness. Yet, there was no general effect of sleep / wake on navigation time, $F < 1$, nor an interaction between sleep/wake and spatial cue, $F(1,38) = 1.63$, $p = 0.21$. Similarly, navigation time was not affected by spatial cue, $F < 1$.

Including sleep order as a control variable for session and encoding / retrieval in the analysis, a significant main effect of encoding / retrieval condition was seen $F(1,36) = 6.32$, $p = 0.02$, $\eta^2 = 0.01$. On average participants' navigation time was

shorter during retrieval trials (mean duration ± SEM: 16.6 ± 0.15) compared to encoding trials (mean duration ± SEM: 17.24 ± 0.19).

3.2.2. Difference of Mean Navigation Time

Using encoding-retrieval difference concerning navigation time, similar results were found. There were no main effects for cue type $F(1,38) = 0.54$, $p = 0.47$, $\eta^2 = 0.01$ or sleep / wake $F(1,38) = 1.84$, $p = 0.18$, $\eta^2 = 0.02$ and, this time, no significant interaction between the two $F(1,38) = 0.18$, $p = 0.68$, $\eta^2 < 0.01$.

3.2.3. Encoding Performance over Blocks

We can see that both groups improved their performance during encoding. There was a decrease in navigation time from block 1 throughout to block 4 (mean ± SEM: block 1: 19.45 ± 0.31, block 2: 18.53 ± 0.28, block 3: 14.48 ± 0.27, block 4: 17.00 ± 0.26) (see Figure 9 A). This difference in performance over blocks was significant $F(1,38) = 32.03$, $p < 0.001$, $\eta^2 = 0.06$.

3.2.4. Retrieval Performance over Blocks

Similarly to encoding, participants significantly decreased their mean navigation time throughout blocks $F(2,68) = 4.1$, $p = 0.02$, $\eta^2 = 0.01$. During retrieval trials there was no significant difference in mean navigation time (see Figure 9 B) between cue types $F(1,34) = 0.02$, $p = 0.89$, $\eta^2 < 0.01$ or between sleep and wake condition $F(1,34) = 0.06$, $p = 0.82$, $\eta^2 < 0.01$.

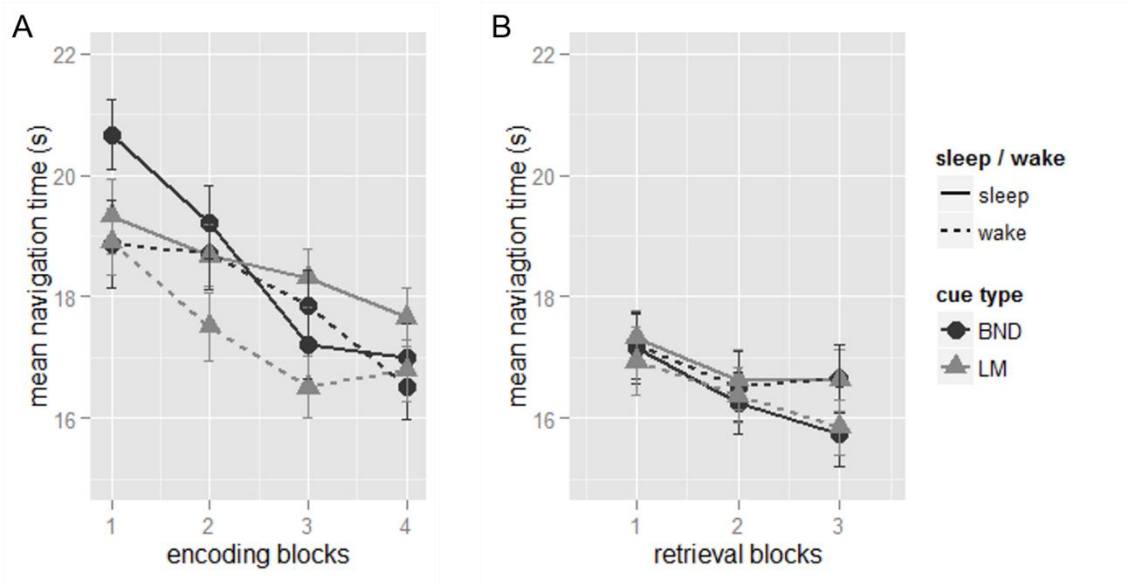

Figure 9: Mean navigation times between cue presentation offset and object placement.
Participants showed a decrease in navigation time over blocks both during encoding (A) and retrieval (B).

3.3. Influence of Design Variables

3.3.1. Session

Looking at performance accuracy, we found that on average participants, regardless of their respective sleep order or sleep/wake condition, improved performance from session one to session two, $mean_{Session1} \pm SEM = 27.77 \pm 0.81$, $mean_{Session2} \pm SEM = 23.88 \pm 0.84$, $F(1,36) = 5.05$, $p = 0.03$, $\eta^2 = 0.02$. However, there was no difference between sessions when looking at mean navigation time $mean_{Session1} \pm SEM = 16.84 \pm 0.17$, $mean_{Session2} \pm SEM = 16.88 \pm 0.16$, $F(1,36) = 0.01$, $p = 0.94$, $\eta^2 < 0.01$ (see also Figure 10).

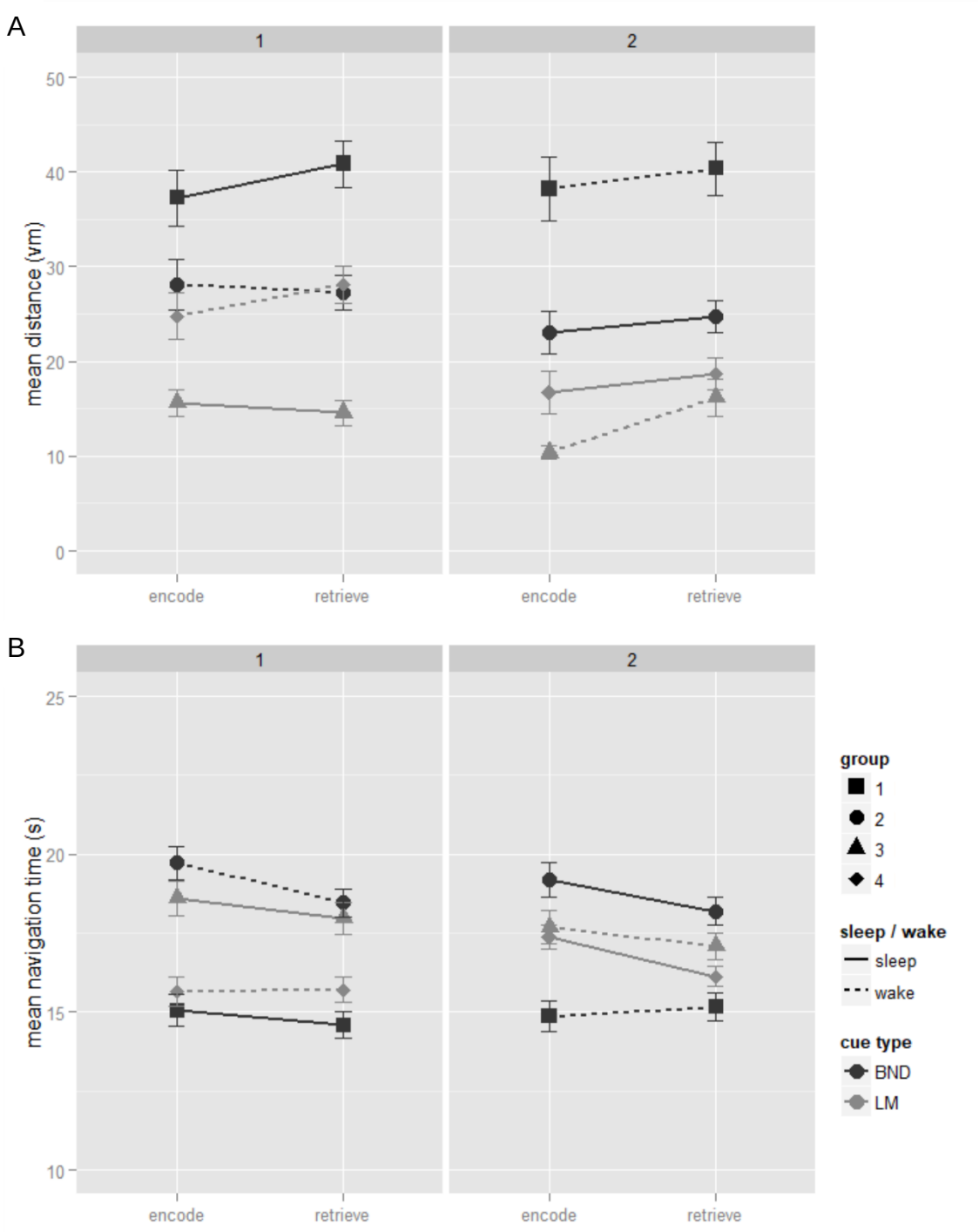

Figure 10: Performance by both cue type groups and sleep / wake condition during session 1 (left) and session 2 (right).
Group one corresponds to participants in the boundary group who slept during session one and were sleep deprived during session two, group two participants that were first sleep deprived and could sleep during session two. Group three includes participants from the landmark group who slept during session one and stayed awake during session two and group four contains participants from the landmark group that were first tested in the wake condition in session one and allowed sleep during session two. (A) depicts performance accuracy by analysing mean distance in virtual metres between original object location and object location where participants deposited an object. (B) depicts participants' mean navigation time in seconds.

3.3.2. Environment

When we looked at the two different environments, participants seemed to find it significantly harder to place objects accurately in the desert environment compared to alpine environment, M_{desert} = 39.93 ± 0.79, M_{alpine} = 25.06 ± 0.67, $F(1,39) = 6.23$, $p = 0.02$, $\eta^2 = 0.02$. The same was true if we looked at navigation time. In the desert environment, participants took significantly longer to locate object locations as compared to the alpine environment M_{desert} = 18.00 ± 0.15, M_{alpine} = 16.93 ± 0.15, $F(1,39) = 7.34$, $p = 0.01$, $\eta^2 = 0.02$.

3.3.3. Gender

Visualizing each participants' performance (Figure 11), six participants with a considerably worse navigation accuracy compared to overall performance could be identified. Since five of them were female and only one male, it was decided to include gender as a factor in the analysis. And indeed, a main effect for gender could be found $F(1,32) = 5.01$, $p = 0.03$, $\eta^2 = 0.11$. On average, women placed objects further away from their original position compared to men (M ± SEM: women 31.86 ± 0.81, men 22.64 ± 0.60). Looking at mean navigation time, however, there was no significant main effect for gender, M ± SEM: women 17.54 ± 0.14, men 17.37 ± 0.15, $F(1,32) = 0.01$, $p = 0.94$, $\eta^2 < 0.01$.

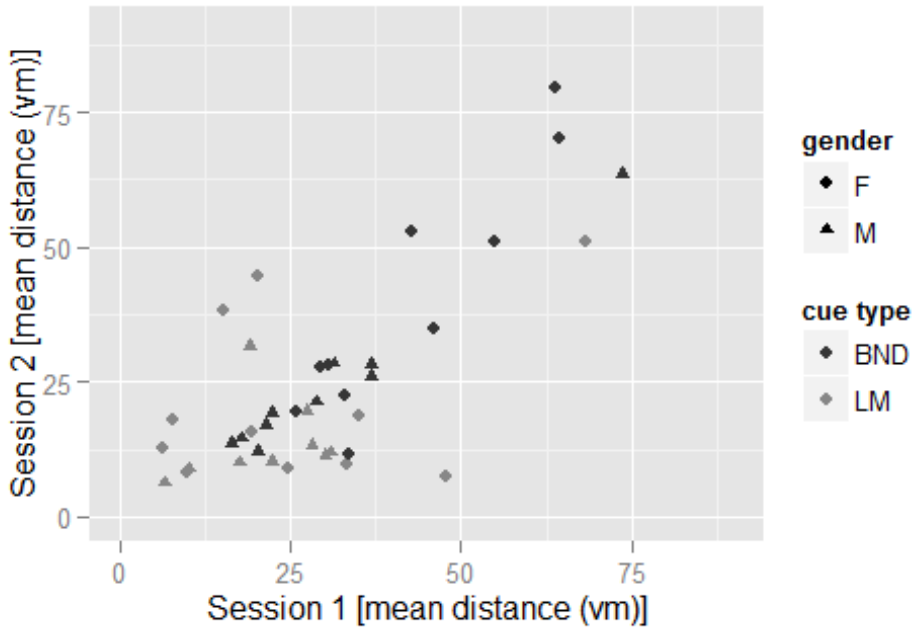

Figure 11: Effect of gender
Participants' performance of boundary (dark grey) and landmark (light grey) groups during session 1 and session 2. Overall, participants maintained their level of performance over sessions. However, there are six outliers, five of them female and all but one from the boundary group.

3.3.4. High and Low Performance Groups

Tucker and Fishbein (2008) showed that the positive effect of sleep on declarative memory task performance depends on the strength of the original task acquisition. Also, Wamsley and colleagues (2011) had found that only experienced video gamers benefitted from sleep in a virtual navigation task. In an attempt to incorporate these previous findings into our analysis, we split our sample into two groups – low and high performers. Median split was performed for both cue type groups separately. As could be expected, there was a significant difference between high and low performance groups $F(1,24) = 20.0$, $p < 0.001$, $\eta^2 = 0.37$. As before, we could also find a main effect for cue type $F(1,24) = 11.23$, $p = 0.003$, $\eta^2 = 0.25$. However, there was no significant effect for sleep / wake condition $F(1,24) = 0.30$, $p = 0.59$, $\eta^2 = 0.002$ and no significant interaction between sleep / wake, cue type and high / low performance $F(1,24) = 0.06$, $p = 0.81$, $\eta^2 < 0.01$.

3.3.5. Navigation Strategy

At the end of the experiment after retrieval testing during session two participants were asked to indicate their strategy used to complete the task. All participants from the landmark group indicated that they had used a landmark-based navigation strategy. No matter what the starting position in the arena was, they consistently returned to the traffic cone first and traced their path to deposit an object from there. Surprisingly, the majority of participants from the boundary group did the same. They chose a specific spot within the arena, mostly directly at the boundary wall, and started every trial by going there first. Only nine out of twenty subjects from the boundary group implied an allocentric navigation strategy. For example, they used compass directions or a clock dial to orient.

3.4. Analysis of Control Tests

3.4.1. Age

Mean age for the group tested with the boundary environment was 24.00 ± 2.85 years and for the group tested in the landmark environment 23.55 ± 2.42 years respectively. Both groups did not show a difference in age distribution with t-test $t = 0.54$, $p = 0.59$, $r = 0.088$ (Table 6).

3.4.2. Ospan

To assess performance in Ospan we looked at number of letters remembered correctly and in the correct order. There was no difference between landmark and boundary group concerning the performance on operation span task, $M_{LM} = 41.05$, $SEM_{LM} = 3.72$, $M_{BND} = 39.10$, $SEM_{BND} = 4.01$, t-test $t = 0.36$, $p = 0.72$, $r = 0.058$ (see Table 6).

Table 6: Age distribution and performance on working memory task (OSPAN)

		Boundary Group	Landmark Group
OSPAN	(mean ± SEM)	39.10 ± 4.01	41.05 ± 3.72
Age	(mean ± SEM)	24.00 ± 2.85 years	23.55 ± 2.42 years

3.4.3. Vigilance

For analysis of variance a model was used with sleep/wake and encoding/retrieval as within-subjects variable. Reaction time was the dependent variable. As anticipated, we could not find a significant interaction between sleep / wake and encoding / retrieval. Whether participants slept for two nights between encoding and retrieval or whether they stayed awake for one night and slept during the other had no significant impact on participants' performance in PVT, $F(1,39) = 0.6$, $p = 0.44$, $\eta^2 < 0.01$ (see Table 7). Also, there were no main effects for either sleep / wake, $F(1,39) = 0.18$, $p = 0.67$, $\eta^2 < 0.01$, or encoding / retrieval, $F(1,39) = 2.89$, $p = 0.1$, $\eta^2 < 0.01$.

Analysis was repeated using number of lapses as dependent variable. As before, there was no main interaction effect between sleep / wake and encoding / retrieval, $F(1,39) = 0.54$, $p = 0.47$, $\eta^2 < 0.01$ as well as main effects for either sleep / wake, $F(1,39) = 0.91$, $p = 0.35$, $\eta^2 < 0.01$, or encoding / retrieval, $F(1,39) = 0.08$, $p = 0.77$, $\eta^2 < 0.01$.

3.4.4. Sleepiness

Since the data collected contained no interval-scaled features, Wilcoxon test was used for analysis. No difference could be found between participants' subjective wakefulness. Comparing encoding blocks we could not find a difference between participants' sleepiness throughout sessions, $\text{Median}_{\text{Session1}} = 3$ $\text{Median}_{\text{Session2}} = 3$, $V = 137.5$, $p = 0.32$. The same was true for retrieval blocks, $\text{Median}_{\text{Session1}} = 3$ $\text{Median}_{\text{Session2}} = 3$, $V = 274.5$, $p = 0.37$. Furthermore, possible differences between sleepiness ratings after sleep deprivation and normal sleep were evaluated. Again, no significant differences could be found, $\text{Median}_{\text{Sleep}} = 3.0$, $\text{Median}_{\text{Wake}} = 3.0$, $V = 284.5$, $p = 0.27$ (Table 7).

3.4.5. Sleep Quality

Analysing SF-A/R, three items were chosen to represent participants' sleep quality – their ratings on how well they had slept, how well rested they felt the day after and how often they had woken up during the night. We examined their answers and compared the results of the second nights of each session, e.g. the recovery night ($Median_{Wake}$) and the second night of undisturbed sleep for every participant ($Median_{Sleep}$). Wilcoxon signed-rank test was used for analysis. Results showed participants slept significantly better during the night after sleep deprivation compared to the night after undisturbed sleep, $Median_{Wake} = 5$, $Median_{Sleep} = 4$, $V = 9.5$, $p < 0.01$. However, analysis of the remaining two items showed no significant difference between the various conditions. Participants felt equally rested after the second night of sleep and after the night of wakefulness, $Median_{Sleep} = 3$, $Median_{Wake} = 4$, $V = 132.5$, $p = 0.26$. Similarly, there was no significant difference concerning how often people woke up during nights, $Median_{Sleep} = 1$, $Median_{Wake} = 0$, $V = 118.0$, $p = 0.35$.

3.4.6. Retrieval Fluency

Dependent variable was number of words in the RWT. Participants generated significantly more words at retrieval in the wake $M_{Wake} = 18.95 \pm 0.81$, as compared to the sleep condition, $M_{Sleep} = 17.55 \pm 0.68$, $t = -2.22$, $p = 0.03$, $r = 0.335$ (see Table 7). To make sure that this finding was not biased by testing order, sleep order was included in the analysis. An ANOVA was performed with sleep order as between-subjects factor and sleep/wake as within-subjects factor. Again, there was a significant main effect of sleep / wake, $F(1,38) = 4.89$, $p = 0.03$, $\eta^2 = 0.02$.

3.4.7. Sleep Duration

To assess and compare sleep duration we focused on sleep durations during recovery nights. There was a reliable sleep / wake condition difference in

participants' sleep duration: Participants slept for 486.175 ± 77.95 minutes (M ± SEM) during sleep nights and 630.75 ± 119.08 minutes (M ± SEM) during recovery nights (Table 7), t = -6.74, p < 0.001. The subjective data as given in SF-A/R corresponded highly to the objective sleep measures taken from the actimeters, r = 0.9988, p = 0.001.

Table 7: Results of SSS, performance in PVT and RWT, Sleep duration throughout experimental conditions
Participants did not indicate a difference during sleep and wake condition using the Stanford Sleepiness Scale (SSS) concerning subjective levels of sleepiness. Likewise, we found no significant difference between sleep and wake condition concerning performance (for both mean reaction time and number of lapses) on the Psychomotor Vigilance Task (PVT). However, results in RWT (Regensburger Wortflüssigkeitstest) were significantly better in the wake condition compared to sleep condition. As expected, sleep duration after a sleep-deprived night was longer compared to undisturbed sleep.

		Sleep	Wake
SSS	(median)	3.0	3.0
PVT	(mean time in s ± SEM)	300.86 ± 3.07	301.85 ± 2.78
	(number of lapses)	0.55 ± 0.1	0.43 ± 0.08
RWT	(mean score ± SEM)	17.55 ± 0.68	18.95 ± 0.81
Sleep Duration	(mean duration in min ± SEM)	486.175 ± 77.95	630.75 ± 119.08

4. Discussion

The aim of the present study was to investigate the influence of sleep on the consolidation of memory representations within two different spatial representation systems: the striatal landmark- and hippocampal boundary-based spatial memory representations system. It was hypothesized to find an overall sleep-related enhancement of spatial knowledge with a particular improvement of performance after sleep within the boundary group. Contrary to our expectations, we can report no such result.

4.1. General Discussion

Patterns of reactivation of spatial activity during sleep have been observed in rodents and humans (Peigneux et al., 2004; Skaggs & McNaughton, 1996; Wilson & McNaughton, 1994). These findings have fuelled the development of theories on the role of sleep in memory consolidation, which suggest that sleep may strengthen and transform memory traces (Diekelmann & Born, 2010; Rasch & Born, 2013). Based on these theories, beneficial effects of sleep on spatial memory must be expected. However, evidence for that prediction is mixed (see e.g. Nguyen et al., 2013; Noack et al., 2017; Orban et al., 2006; Rauchs et al., 2008). The aim of the present study was to investigate the differential effect of sleep on the consolidation of memory representations within two different spatial representation systems: the striatal landmark- and hippocampal boundary-based spatial memory representation system. To this end, we conducted a study using a virtual environment adapted from Doeller et al. (2008) containing either a single proximal landmark or a circular boundary with otherwise identical distal cues for orientation. Participants were randomly assigned to either the boundary or the landmark group, performing on the boundary- or landmark-only environment respectively. They were asked to learn and remember object locations within the environment. After an interval filled with two nights of undisturbed sleep or a night of total sleep deprivation and a consecutive recovery night, memory for previously learned object locations was tested.

4.2. Effect of Sleep and Wakefulness

Contrary to our expectations, we did not observe a beneficial effect of sleep on either boundary- or landmark-based spatial memory. There are a number of studies that reported sleep-related strengthening of navigation performance (see Nguyen et al., 2013; Noack et al., 2017; Peigneux et al., 2004; Wamsley et al., 2010). Other studies by Orban et al. (2006) and Rauchs et al. (2008) also did not detect changes in task performance after sleep. However, they found a sleep-related change in neural activation. In the present study, we did not employ neuroimaging techniques so that we cannot answer the question whether sleep might have had an influence on a neural level.

What should be taken into consideration though, is that in our design we included recovery nights after a night of total sleep deprivation in order to ensure that possible effects of performance are not merely due to tiredness or exhaustion. Interestingly, other studies using a similar experimental design and including recovery nights after sleep deprivation also did not report sleep-related differences in navigation performance (e.g. Ferrara et al., 2008; Orban et al., 2006; Rauchs et al., 2008). Therefore, the direct effects of sleep deprivation on spatial navigation must be taken into account.

Another point is that, after learning in the spatial domain, sleep might exert beneficial effects on memory consolidation even after prolonged wakefulness. However, a large body of evidence contradicts this view (Born, Rasch, & Gais, 2006; Diekelmann & Born, 2010; Rasch & Born, 2013; Stickgold, 2005; Walker, 2008 amongst others). Numerous studies have shown that sleep needs to take place within a few hours after learning (e.g. Gais, Lucas, & Born, 2006; Stickgold, James, & Hobson, 2000). Otherwise, propitious effects on memory consolidation can be lost.

Another possible confounding factor here might be the greatly varying sleep duration during sleep and wake conditions. It has been shown that even short episodes of sleep following learning promote improved memory recall (Lahl, Wispel, Willigens, & Pietrowsky, 2008; Tucker & Fishbein, 2008, 2009; Wamsley et al., 2010). A study by Xu et al. (2011) examining the relation between habitual

sleep duration and memory impairment reported deterioration for both short (i.e. less than seven hours) and long (i.e. more than ten hours) habitual sleep duration. However, there are yet no studies examining the effect of a longer sleep duration of ten hours or more, as was the case in the present study, after just one night of total sleep deprivation on memory. Perhaps future studies should employ a stricter sleep regimen with fixed hours of sleep or wakefulness to ensure comparable sleep lengths throughout the experiment and across all participants. Also, we know from earlier studies that sleep deprivation influences sleep architecture and sleep stages during the following recovery nights (Borbély, Baumann, Brandeis, Strauch, & Lehmann, 1981; Nakazawa, Kotorii, Ohshima, Kotorii, & Hasuzawa, 1978). It has likewise been demonstrated that different sleep stages can benefit the formation of different aspects of memory, respectively (see 1.5 The Role of Sleep on Memory Consolidation). Here, we did not employ polysomnographic measures. Thus, we can only speculate how total sleep deprivation influenced sleep architecture during the recovery night.

To prevent possible sleep effects in this study only to emerge as a result of fatigue ensuing from sleep deprivation, a recovery night was included in the design that allowed participants to follow their normal sleep schedule after a night of wakefulness. And indeed, performance in the Psychomotor Vigilance Test did not show differences in reaction time when sleep and wake condition were compared. The same was true if we only looked at retrieval sessions. However, it was found that on average participants' reaction time significantly increased during retrieval session during session two.

However, a significant difference between sleep and wake condition was revealed when assessing sleep duration. As can be expected, after a night of total sleep deprivation and probably due to exhaustion after prolonged wakefulness, participants slept considerably longer compared to when they were allowed to follow their regular sleep schedule. Differences between sleep and wake condition were also detected when asking for participants' sleep quality using SF-A/R. They indicated that they slept considerably better after sleep deprivation. This might also be a result of exhaustion and fatigue after extended wakefulness. There were no differences concerning the number of time

participants woke up during the night or how rested they felt the next morning. Another unexpected finding was that, assessing divergent thinking ability, participants seemed to have done better after sleep deprivation night and consecutive recovery night than after two nights of normal sleep. Levels of subjective sleepiness did not differ between groups throughout the experiment.
In conclusion, there are mixed results evaluating control tests between sleep and wake conditions. Significant differences were not found concerning alertness (assessed using PVT), SF-A/R rating overall sleep quality or subjective levels of sleepiness. In contrast, average sleep duration and divergent thinking ability varied between sleep and wake condition.

4.3. Effect of Cue Type

As the hippocampus plays a key role in memory processing during sleep (cf. Diekelmann & Born, 2010), we expected to find differential effects of sleep on hippocampal and striatal spatial memory representations respectively. In line with previous findings (Doeller et al., 2008), we reasoned that boundary-based representations, which are dominantly processed by the hippocampus, might profit more from sleep than landmark-based representations, which depend more strongly on striatal representations. However, our data did not support this notion. Despite a strong general difference in navigation performance between the landmark and boundary group there was no interaction with sleep suggesting that the absence of an effect of sleep on spatial memory was not dependent on the specific spatial representation system under study. The basis of the general performance difference between the two spatial cue types remains elusive here. Previous studies using similar tasks and layouts (Doeller et al., 2008) reported similar performance levels for the two cue types, suggesting that the present difference may rather result from chance group performance differences. Evaluating navigation time, however, no significant difference between cue type groups was found.
Interestingly, when analysing performance using the difference of mean distance between encoding and retrieval sessions we found a reliable interaction between

sleep / wake and cue type. It seems that participants from the boundary group did not show a considerable deviation in performance level throughout sleep and wake conditions. However, participants from the landmark group displayed a strong improvement regarding navigation accuracy in the sleep condition. This finding is contrary to our hypothesis.

In addition to mean absolute displacement, we also analysed variability in displacement, i.e. the consistency of finding the same location again. As expected, navigation variability decreased during learning as the single representations were established. Interestingly, we found a reliable difference between cue type groups again: that is, participants from the landmark group returned more consistently to one remembered location than participants from the boundary group.

Participants were explicitly instructed to use encoding blocks as another opportunity to learn. Both navigation accuracy increased and navigation time decreased over encoding blocks, demonstrating that participants improved their knowledge of object locations with every encoding block. In line with this finding, navigation time also significantly decreased during retrieval blocks.

However, learning rates concerning navigation accuracy during encoding blocks again differed significantly between cue type groups. Even though both groups improved consistently from encoding block 1 to encoding block 4, participants from the landmark group generally performed with higher accuracy. Navigation accuracy did not change during retrieval blocks. There, participants did not show improvements regarding performance levels over blocks. A possible explanation for the recurring difference of performance levels between cue type groups might be that distal cues, thought to aid orientation, were in part concealed by the local boundary whereas the view for participants from the landmark group was unobstructed. Orientation within the virtual environment thus might have been harder for participants from the boundary group.

Another possible explanation might be that using a landmark-based strategy for navigation could be more compatible with the 2D-representation that was available in our experiment, as it can be implemented using 2D stimuli only: direction and distance. Distance can be approximated over a certain time at

constant speed. For the precise calibration of place cells, the boundary strategy requires information from boundary cells, which would have to represent the distance to boundaries in different directions. For this purpose, a 3D immersive environment would probably be more important.

Participants also improved navigation accuracy from session one to session two irrespective of sleep and wake condition. The fact that they were already familiar with the task may account for the improvement. Furthermore, during session two they did not have to complete as many control tests as they had to do during the first session of the experiment.

Control tests were included to ensure that experimental groups did not differ in their respective composition and thus ensure comparability. As can be seen, landmark and boundary group were homogenous concerning age and working memory capacity of participants.

4.4. Limitations

4.4.1. Navigation Strategy

Another possible explanation for our results might lie in the different strategies participants used to complete the task. After the last retrieval session participants were asked to describe the navigation strategy they had used to retrieve objects while navigating in the virtual environment. Almost all participants from the landmark group used a landmark-based strategy. Irrespective of their starting position, they almost always went first to the traffic cone, from there determined the direction they had to go in and then deposited the object by judging the distance travelled from the traffic cone.

A notable number of participants from the boundary group implied the same egocentric strategy. They always went to a certain place, mostly a spot directly at the boundary, and started their path to dispose an object from there. Only a minority of participants implied an allocentric strategy. They used compass directions or a clock dial to orient. Thus, validity of our experimental paradigm must be called into doubt here.

It seems likely that the cue type, that means landmark and boundary, implied to address egocentric and allocentric spatial orientation strategies respectively, failed to do so.

Furthermore, participants were not instructed to apply a certain navigation strategy. When asked to describe their strategy, the majority of participants indicated that they used a more landmark-based or egocentric, that is striatum-dependent strategy.

So could it be better to specifically inform participants what navigation strategy to use as it did happen in preceding studies (for example Ferrara et al., 2008)?

What strategy to orient and navigate a person chooses might in large part be their personal disposition (Wolbers & Hegarty, 2010). It seems likely that the virtual reality task, designed to address two different spatial reference frames, in itself is not enough to invoke a certain navigation strategy but that such strategies are innate to a person.

Or perhaps a different task, for example such as proposed by Spriggs, Kirk, and Skelton (2018), might be more apt to address the problem. They introduced a navigation task set in a virtual maze that allows to discern between different navigational strategies. Also, it might be helpful to employ fMRI scans to determine what brain areas or networks are active during the navigational task.

Another idea would be to use VR goggles, and not a 3D video game as the visual stimulus would occupy a larger visual field. In addition, the subjects would have stereo information available and thus a more realistic navigation experience which could improve performance (Tan, Gergle, Scupelli, & Pausch, 2006).

4.4.2. Video Game Experience

A study by Wamsley et al. (2010) reported a performance enhancement when spatial learning was followed by a period of sleep only for participants with experience with 3D video games. In the presents study we did not control for video game experience. Future studies investigating spatial navigation using virtual environments should take this factor into account and assess video game experience. Another idea would be to exclude participants with little experience

with first-person or 3D video games in the first place, as it was done for example in a study by Ferrara et al. (2008).

4.4.3. Environment

To prevent carry-over effects two different virtual environments were designed for testing during two sessions. Analysis revealed a major difference concerning performance between the two environments. Participants seemed to find it much harder to navigate and orient in the desert environment. There, navigation accuracy was considerably lower and it also took participants longer to reach the goal location compared to performance in the alpine environment. So, contrary to our intentions, the two environmental designs used in the current study were not identical with respect to difficulty. However, since the experimental design was carefully counter-balanced and all participants performed both in the alpine and the desert environment, it is rather unlikely that the two different environments with their different levels of difficulty alone can account for the outcome of the present study.

4.4.4. High and Low Performers

Tucker and Fishbein (2008) reported that participants showing only poor performance during a learning task also did not show sleep-related strengthening of performance while participants with an already initially high performance did. Here, we also assigned participants to two groups with high and low performance respectively. We split the set of participants at the median of mean navigation distance. Subjects with mean navigation distance below median were assigned to the group of high performers and subjects with a mean navigation distance above the median were assigned to the group of low performers. But again, and contrarily to our hypothesis, there was no sleep-related strengthening of spatial knowledge, nor could we find a sleep-related benefit for participants in the boundary group. This might have various reasons. One might lie in the means of our statistical analysis. Perhaps participants with low performance were never

able to establish a sufficient object – location representation in the first place, whereas for high performers the representation was already so strong after initial learning that sleep could not exert an additional beneficial effect on performance. Perhaps the representations established during encoding sessions need a certain initial strengths in order to withstand synaptic downscaling (Born & Feld, 2012; Diekelmann & Born, 2010).

4.4.5. Gender

Another finding that was not expected was the striking inconsistency in performance between male and female participants. Commonly and to prevent an influence based on participants' gender a number of studies use only male subjects (for example Doeller & Burgess (2008), Doeller et al. (2008) and Peigneux et al. (2004)). However, preceding studies that also investigated the influence of sleep on spatial memory formation included male and female subjects and did not report stark differences between gender groups (for example Ferrara et al. (2008); Nguyen et al. (2013); Orban et al. (2006) and Rauchs et al. (2008)). The latter two studies included an equal number of male and female participants while the former two included more women than men.

However, navigational performance is well documented to differ greatly between men and women (for example Astur, Ortiz, and Sutherland (1998); Moffat, Hampson, and Hatzipantelis (1998) and Saucier et al. (2002) amongst others). These differences can be seen both in navigational test performance and also in the use of strategies male and female participants employ to solve navigational tasks (Saucier et al., 2002).

Taking these findings into account, it might be expedient to conduct further studies in this field with a balanced number of male and female participants or. for the sake of comparability with other studies, even with male participants only.

4.5. Conclusion

The aim of this study was to investigate the effect of sleep on the consolidation of landmark- and boundary-based spatial memory representations. Numerous preceeding studies described the effects of sleep on spatial memory consolidation (for example Ferrara et al., 2008; Nguyen et al., 2013; Noack et al., 2017; Orban et al., 2006; Peigneux et al., 2004; Rauchs et al., 2008; Wamsley et al., 2010) and consistently reported sleep related benefits on either overall performance or effects on fMRI signal. However, the present study failed to replicate the formerly described beneficial effects of sleep on spatial memory consolidation.

However, by focusing only on behavioural aspects in the present study, it might have been possible that we missed some of the effects and changes sleep might exert over the consolidation of spatial memories as studies by Orban et al. (2006) or Rauchs et al. (2008) have already suggested. They could also not report effects of sleep for behavioural task performance but changes in fMRI response. Perhaps, the present study used too narrow an approach, by focussing only on the behavioural aspects, for too complex a question, trying to assess the diverse interaction of sleep and spatial navigation and differentiate between consolidation of landmark- and boundary-based spatial memory representations.

Traditionally, allocentric and egocentric navigation systems as well as hippocampal and striatal systems are put in contrast with one another. Recent studies show that these systems are more closely connected than previously thought (Goodroe, Starnes, & Brown, 2018). The systems are intertwined and can be dynamically and contextually regulated. The results of the present study might also be an indication that previous theories and their experimental operationalizations are incomplete. Future research in this field needs different experimental designs that enable us to discern between the behavioural differences of naviagtion as well as employing neuroimaging techniques to visualise possible changes in behaviour be reflected on a neural level.

5. Abstract

Studies in both animals and humans have shown that brain activity recorded during route-learning tasks is re-activated during consecutive sleep (Peigneux et al., 2004; Skaggs & McNaughton, 1996; Wilson & McNaughton, 1994). These findings have prompted the development of theories on the role of sleep for memory consolidation. And indeed, there exists a large body of evidence that sleep may both strengthen and transform memory traces (Diekelmann & Born, 2010; Rasch & Born, 2013). Therefore, propitious effects of sleep on the consolidation of spatial memory must be expected. However, evidence for that prediction is mixed (Ferrara et al., 2008; Nguyen et al., 2013; Noack et al., 2017; Orban et al., 2006; Peigneux et al., 2004; Rauchs et al., 2008; Wamsley et al., 2010). The aim of the present study was to investigate the differential effect of sleep on the consolidation of memory representations within two different spatial representation systems: the striatal landmark- and hippocampal boundary-based spatial memory representations system. To this end, we conducted a study using a virtual environment adopted from Doeller et al. (2008) containing either a single proximal landmark or a circular boundary. Distal cues were always available for orientation. Forty participants, both male and female, were randomly assigned to either landmark or boundary group. They were asked to learn and remember object locations within the virtual environment. After an interval of either two nights of normal sleep or one night of total sleep deprivation and a consecutive recovery night, retrieval knowledge was tested. All participants were tested both in the sleep and wake condition. We expected to find a sleep-related strengthening of spatial knowledge with a greater benefit from post-learning sleep within the boundary group in particular. Contrary to our expectations, though, we found no such results. However, our results might be limited because of various factors: we found a strong influence of gender with women's performance significantly worse compared to men's. Furthermore, our cue type, that means landmark and boundary, implied to address egocentric and allocentric spatial orientation strategies respectively, failed to do so. Also, our experimental design, even though carefully counterbalanced across all participants, might have

influenced performance. We used two different virtual realities that differed significantly concerning difficulty. We also did not control for video game experience that has been shown to have an impact on performance in similar studies (Tucker & Fishbein, 2008; Wamsley et al., 2010).

6. Zusammenfassung

Studien sowohl an Tieren als auch am Menschen haben gezeigt, dass Gehirnaktivität, welche während einer Routenlernaufgabe aufgezeichnet werden konnte, in darauffolgenden Schlafepisoden wieder reaktiviert wird (Peigneux et al. 2004; Skaggs und McNaughton 1996; Wilson und McNaughton 1994). Diese Erkenntnisse haben zur Entwicklung von Theorien bezüglich der Rolle des Schlafes für die Gedächtniskonsolidierung im Allgemeinen einen entscheidenden Beitrag geleistet. Tatsächlich gibt es zahlreiche Hinweise darauf, dass Schlaf Gedächtnisspuren sowohl stärken als auch verändern kann (Diekelmann und Born 2010; Rasch und Born 2013). Positive Auswirkungen des Schlafes auf die Konsolidierung des räumlichen Gedächtnisses könen daher erwartet werden. Studien hierzu blieben bisher jedoch ohne eindeutiges Ergebnis (Ferrara et al. 2008; Nguyen et al. 2013; Noack et al. 2017; Orban et al. 2006; Peigneux et al. 2004; Rauchs et al. 2008; Wamsley et al. 2010). Ziel der vorliegenden Studie war es daher die unterschiedliche Wirkung des Schlafs auf die Konsolidierung von Gedächtnisrepräsentationen in zwei verschiedenen räumlichen Repräsentationssystemen zu untersuchen: dem striatalen Orientierungspunkt- und dem hippocampalen, grenzbasierten räumlichen Gedächtnisrepräsentationssystem. Für unsere Studie verwendeten wir eine virtuelle Umgebung von Doeller et al. (2008), welche entweder eine einzelne proximale Landmarke oder eine kreisförmige Begrenzung enthielt. Zur Orientierung standen distale Orientierungspunkte zur Verfügung. 40 Teilnehmer, sowohl Männer als auch Frauen, wurden nach dem Zufallsprinzip entweder der Landmarken- oder der Begrenzungsgruppe zugeordnet. Sie wurden gebeten, Objektpositionen innerhalb der virtuellen Umgebung zu lernen und diese im weiteren Verlauf wieder zu finden. Nach einem Intervall, welches entweder zwei Nächte ungestörten Schlafes oder einer Nacht mit vollständigem Schlafentzug sowie einer anschließenden Erholungsnacht umfasste, wurde das Abrufwissen getestet. Alle Teilnehmer wurden sowohl in der Schlaf- als auch in der Wachbedingung getestet. Wir erwarteten eine schlafabhängige Stärkung des räumlichen Gedächtnisses mit einem größeren Schlafeffekt nach dem Lernen

insbesondere innerhalb der Begrenzungsgruppe. Entgegen unseren Erwartungen können wir jedoch keine derartigen Ergebnisse berichten. Unsere Ergebnisse könnten jedoch aufgrund verschiedener Faktoren in ihrer Aussagekraft limitiert sein: so stellten wir zum Einen einen starken Einfluss des Geschlechts fest. Die Leistung der Frauen war erheblich schlechter als die der Männer. Darüber hinaus hat unsere jeweilige Testbedingung, das heißt Landmarke bzw. Grenze, welche egozentrische und allozentrische räumliche Orientierungsstrategien anzusprechen sollte, dies nicht getan. Auch unser experimentelles Design könnte die Leistung beeinflusst haben. Wir haben zwei verschiedene virtuelle Umwelten verwendet, die sich in Bezug auf den Schwierigkeitsgrad erheblich unterschieden. Zudem wurde die Erfahrung mit Videospielen der Studienteilnehmer hier nicht berücksichtigt, was sich ich in ähnlichen Studien jedoch nachweislich auf die Leistung ausgewirkt hatte (Tucker & Fishbein, 2008; Wamsley et al., 2010).

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Fig.2 (A & B)	Florian Ott Doktorand Fakultät Psychologie Professur für Neuroimaging TU Dresden Chemnitzer Str. 46b 01187 Dresden
Fig. 3	Standard hypnogram of normal sleep, Wikimedia Commons Created by Natasha K. (Tash510) https://upload.wikimedia.org/wikipedia/commons/b/b7/HYPNOGRAM_created_by_Natasha_k.jpg Licensed under Creative Commons Attribution-Share Alike 3.0 Unported license (CC BY-SA 3.0) URL: hhtp://creativecommons.org/licenses/by-sa/3.0/legalcode Picture modiefied (EEG patterns were added)
Fig. 4	Adapted from Bartsch, T. & Butler, C. (2013)
Fig. 5	Own image

Fig. 6	Adapted from: “Sleep support integration of landmark- and boundary-referenced spatial representations”, Noack, Doeller; Born, unpublished data
Fig. 7	Adapted from: “Sleep support integration of landmark- and boundary-referenced spatial representations”, Noack, Doeller; Born, unpublished data
Fig. 8	Own image
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8. Appendix

8.1. Stanford-Sleepiness-Scale

Code:_____

O vor Lernen O vor Abruf

Stanford-Schläfrigkeits-Skala

Probanden-Nr.: Datum: morgens

Im folgenden soll der Grad der Schläfrigkeit (wie wach fühlen Sie sich?) erhoben werden:
Kreuzen Sie bitte das entsprechende Kästchen an.

Schläfrigkeitsgrad	Punktwert
Ich fühle mich aktiv, lebhaft, aufmerksam oder sehr wach	1
Ich kann konzentriert arbeiten, habe aber kein Leistungshoch	2
Ich fühle mich wach, entspannt und aufnahmefähig aber nicht voll konzentriert	3
Ich fühle mich irgendwie träge	4
Ich fühle mich träge, verlangsamt, und könnte mich hinlegen	5
Ich fühle mich schläfrig, benebelt, kämpfe gegen die Müdigkeit und würde mich lieber hinlegen	6
Ich bin kurz vor dem Einschlafen und habe bereits Traumdeutungen	7
Ich schlafe	8

8.2. SF-A/R

Fragebogen zur Schlafqualität

Datum: _____ Ankunft: _____ Uhr

Licht aus: _____ Uhr Eingeschlafen: _____ Uhr

Licht an/Aufgewacht: _____ Uhr

Anleitung:
Die folgenden Fragen beziehen sich darauf, wie Sie in der letzten Nacht geschlafen haben. Kreuzen Sie bitte die Antworten an, die für Sie am ehesten zutreffen. Gehen Sie bei der Beantwortung der Fragen zügig voran und lassen Sie keine Frage aus. Bitte sofort nach dem Aufwachen morgens ausfüllen!

1.) Konnten Sie, nachdem Sie sich schlafen gelegt hatten, gleich einschlafen?

Ja.	
Nein, erst nach 10 min.	
Nein, erst nach 20 min.	
Nein, erst nach 40 min.	
Nein, erst nach 1 Stunde.	
Nein, erst nach mehr als 1 Stunde.	
Ich konnte überhaupt nicht schlafen.	

1.a) Falls Nein, welches waren die Gründe? (Mehrfachnennungen möglich)

Persönliche / berufliche Probleme	
Geräusche im Zimmer oder von draußen	
Beschäftigung mit Tagesereignissen	
Ungewohnte Schlafumgebung	
Sonstige:	

2.) In der Einschlafphase hat man hin und wieder plötzlich deutliche Bildeindrücke. War dies gestern Abend bei Ihnen so?

Nein	Bin nicht sicher	Ja, sehr deutlich

3.) Hatten Sie während der Einschlafphase Muskelzuckungen in den Armen oder Beinen?

Nein	Leicht	Stark

4.) Sind Sie gestern nach dem Einschlafen nachts wieder aufgewacht?

Nein	1x	2x	3x	>3x

4.a) Falls Ja, welches waren die Gründe? (Mehrfachnennungen möglich)

Persönliche / berufliche Probleme	
Geräusche im Zimmer oder von draußen	
Ich musste zur Toilette	
Ich hatte schlecht geträumt	
Sonstige:	

4.b) Falls Ja, wie lange waren Sie ungefähr wach? (Schätzen Sie bitte.)

1. Aufwachen	Dauer (min):	
2. Aufwachen	Dauer (min):	
3. Aufwachen	Dauer (min):	
4. Aufwachen	Dauer (min):	

5.) Können Sie sich erinnern, ob Sie heute Nacht geträumt haben?

Nein, ich kann mich nicht erinnern geträumt zu haben	
Ja, ich habe geträumt, kann mich aber nicht mehr an den Trauminhalt erinnern.	
Ja, ich habe geträumt und kann mich an den Trauminhalt erinnern.	

5a.) Falls ja, welche Gefühle hatten Sie während des Träumens (Mehrfachnennungen möglich)

Angenehm	Neutral	Unangenehm

5b) Falls ja, was war (grob) der Inhalt der Träume

_____

_____

_____

6.) Haben Sie in der letzten Nacht geschwitzt?

Nein	Leicht	Stark

7.) Haben Sie heute Morgen Kopfschmerzen?

Nein	Leicht	Stark

8.) War der gestrige Tag für Sie anstrengend?

Nein	Ein wenig	Sehr

Anleitung:
Auf dieser Seite finden Sie einige Wörter, mit denen Sie beschreiben können, wie Sie sich gestern Abend fühlten, wie Sie heute Nacht geschlafen haben und wie Sie sich heute Morgen fühlen. Kreuzen Sie hinter jedem Wort an, in welchem Ausmaß es für Sie zutrifft. Bitte antworten Sie zügig und lassen Sie keine Zeile aus!

9.) Wie haben Sie letzte Nacht geschlafen?

	Sehr	Ziemlich	Mittel	Wenig	Nicht
a) gleichmäßig					
b) tief					
c) gut					
d) entspannt					
e) ungestört					
f) ruhig					
g) ausgiebig					

10.) Wie fühlten Sie sich gestern vor dem Schlafengehen?

	Sehr	Ziemlich	Mittel	Wenig	Nicht
a) sorglos					
b) erschöpft					
c) schlafbedürftig					
d) überfordert					
e) ausgeglichen					
f) ruhig					
g) müde					
h) entspannt					

11.) Wie fühlen Sie sich heute Morgen?

	Sehr	Ziemlich	Mittel	Wenig	Nicht
a) Ausgeglichen					
b) Dösig					
c) Tatkräftig					
d) munter					
e) frisch					
f) ausgeschlafen					
g) entspannt					

9. Erklärung zum Eigenanteil der Dissertationsschrift

Die Arbeit wurde im Institut für Medizinische Psychologie und Verhaltensneurobiologie der Universität Tübingen unter Betreuung von Prof. Dr. J. Born durchgeführt.
Die Konzeption der Studie erfolgte durch Prof. Dr. J. Born, Direktor des Instituts für Medizinische Psychologie und Verhaltensneurobiologie sowie Dr. rer. nat. Hannes Noack, Postdoktorand.
Die Versuche wurden von mir eigenständig durchgeführt.
Die statistische Auswertung erfolgte nach Anleitung durch Dr. rer. nat. Hannes Noack durch mich.
Ich versichere, das Manuskript selbständig verfasst und keine weiteren als die von mir angegebenen Quellen verwendet zu haben.

Dresden, den 06.11.2020

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