ABSTRACT

Previous studies have demonstrated that a mild increase in skin temperature can induce longer and deeper sleep, particularly during SWS the period of sleep associated with memory consolidation. This study attempted to differentiate the effects of mild skin temperature manipulation on various stages of sleep (SWS and REM) by inducing warm temperature during a single sleep stage and then testing memory consolidation after each condition. Preliminary analysis of individuals who completed at least one condition revealed that memory scores were greatest after the SWS night, as predicted. Compared to control conditions, skin warming during the SWS warming condition showed a slight increase in memory recall in the word-pairing task. Moreover, skin warming during the REM warming condition produced a decline in memory recall compared to both SWS and control conditions. Although, these findings were not corroborated in participants who completed all conditions, the low number of participants may be limiting our ability to detect these effects.

The Effect of Mild Skin Temperature Warming on Stage-Specific Sleep and Memory Consolidation

By Nishath Rahman

A Thesis

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INTRODUCTION

Sleep Defined

Sleep is most commonly defined as a state of rest, opposing the state of wakefulness (Dement, 1999). However, according to William C. Dement, the father of sleep medicine, there are two essential features to sleep. The first is that sleep erects a perceptual wall between the conscious mind and the outside world. The second is that it is immediately reversible. This characteristic defines the difference between sleep and sleep-like states such as comas, hibernation or anesthesia from which a person cannot be immediately awoke (Dement, 1999). The state of sleep is found in all mammals and almost a third of the human lifetime is spent sleeping, but the reason we need sleep is not well understood (Colten, 2006).

Numerous sleep deprivation studies demonstrate the effects lack of sleep has on cognition, learning, attention, stress, memory, health and overall quality of life (Goel, Rao, Durmer, & Dinges, 2009; Alhola & Polo-Kantola, 2007; Ma, Dinges, Basner, & Rao, 2015). The discovery and subsequent research on sleep disorders (e.g sleep apnea, narcolepsy and insomnia) highlight what can go wrong with the body when we cannot sleep properly. Over time, such disorders have long-term consequences on other aspects of health (Dement, 1999). For example while sleep apnea is commonly associated with cardiovascular diseases and diabetes, insomnia has been associated with hypertension, cardiovascular diseases, depression, cognitive and motor impairment as well as many other conditions (Dempsey, Veasey, Morgan, & O'Donnell, 2010; Zhuang et al., 2016). Insufficient sleep over a span of time accumulates into a large sleep debt (Dement, 1999).

Dement acknowledges that people are aware of the dangers of drinking and driving, but not many people are aware that in "nearly every accident linked to alcohol consumption, sleep debt almost certainly plays a major role" (Dement, 1999, p. 68). Given that sleep is tied to so many facets of human health, increased research in this relatively new field is crucial to improving sleep as a preventative regime for other diseases and disorders. Furthermore, research in enhancement of sleep can help improve attention, learning, memory and overall improved quality of life. In order to expand on research in enhancing sleep, understanding the neurophysiology of sleep and its mechanisms at a deeper level is crucial.

Neurophysiology of Sleep

Sleep is also characterized by electrical changes in the brain, which are measured using electroencephalograms (EEGs). Hans Berger, who invented the EEG, found that when two electrodes or more were placed on the head, the voltage between them could be recorded. His experiments showed that in the wake state, the EEG depicted fast but high frequency and small amplitude waves. As a person drifted off into the state of sleep, these waves became slower and less frequent with larger amplitudes.

As a person goes from wake to sleep, heart rate and respiration become slower but more consistent as the muscles relax. Additionally, the temperature of the body also decreases and the cells in the brain that are responsible for the state of wake reduce their firing. The cells that send information from the body's sense organs to the cerebral cortex start to fire in a sequence of rapid bursts subsequently followed by rest periods, thus preventing the flow of sensory information to the brain. This allows the person to ignore any environmental disturbances. This process of rapid bursts of these groups of neurons

is what produces the high amplitude synchronous waves in the EEG, which is a component of sleep known as non-rapid eye movement (NREM) sleep. On the other hand, the rapid-eye movement (REM) component of sleep is a more "active sleep" compared to NREM sleep. It is characterized by bursts of rapid-eye movements and complete loss of muscle tone as the brain works at a faster rate than in periods of wake by increasing the neuronal firings of action potentials in the central nervous system. These 90-min sleep episodes are complemented with ponto-geniculo-occipital (PGO) waves, which in the EEG indicate the intense short-lasting bursts of neural activity that comes from the brain stem and goes to the cortex. While both NREM and REM are two components of sleep, there are several stages within NREM that are differentiated due to their unique characteristics and function within the state of sleep.

Stages of Sleep

In 1953, Nathaniel Kleitman and Eugene Aserinsky discovered the state of REM sleep, a pivotal finding in the field of sleep. Later on in the 1960s, Allan Rechtschaffen and Anthony Kales characterized EEG waves into four stages of sleep. As a result of the two discoveries, sleep can now be seen as two components: NREM and REM. NREM can be further divided into stages 1-4 of sleep.

Stage 1 occurs at the onset of sleep and is the transitional state right between wakefulness and sleep. It is characterized by vertex sharp waves known as alpha rhythm. These vertex sharp waves are characterized by fast, distinct, upward (negative) deflections and are monophasic. Stage 1 is also characterized by slow rolling eye movement, which can be seen in an electrooculogram (EOG), which measures the potential between the cornea and Bruch's membrane at the back of the eye.

Stage 2 is easily distinguishable by two distinct EEG waveforms: the sleep spindle and the K complex. While the sleep spindle essentially looks like a spindle on a spinning machine, the K complex is a sharp negative upward spike that is followed by a slower positive component. Sounds and sensory stimulation can induce a K complex. The name itself comes from the fact that a knock on the door can induce this sharp negative upward spike (Zygierewicz, Malinowska, Suffczynski, Piotrowski, & Durka, 2009). In this stage, the EOG and electromyogram (EMG), which records electrical activity in the skeletal muscles like the chin, are mostly irrelevant and the focus is completely on the EEG. At this stage, sleep is still reversible as the person can be awoken from a loud sound. However, it is a "deeper sleep" than stage one in the sense that if a sound is made in stage 1 that can cause an arousal, then that same sound may only induce a K complex in stage 2 (Dement, 1999).

The last two stages of NREM are stages 3 and 4. Most researchers combine these stages and refer to it as slow-wave sleep (SWS). Both stages are characterized by large delta and theta waves. However, stage 3 is characterized by 20-50 percent of the EEG montage in high amplitude and slow frequency waves, while an EEG montage with more than 50 percent of high voltage, slow frequency waves, characterizes stage 4. Considered our "deepest stage of sleep", SWS is also the stage most associated with memory consolidation, specifically declarative memory consolidation (Marshall & Born, 2007). However, before exploring the function of memory in sleep, it is fundamental to understand what memory is and what its components are.

Types of Memory

Memory can be seen as an adaptive ability, the strength of which determines our success of survival. By forming and retrieving memories, we add to our understanding of the world facilitating our progression in common tasks and experiences. Memory processing happens in three stages: encoding, consolidation and retrieval of the same information. During encoding, the incoming stimuli are taken in as a memory trace, prone to disturbances and decay through forgetfulness. However, during consolidation, the same malleable memory trace is stabilized through a number of short-term memory consolidations and eventually long-term consolidation, solidifying and integrating the traces into a preexisting knowledge base. Retrieval is the process of being able to access and recall that memory.

Memory is composed of two domains or types: short-term and long-term memory. Short-term memory is the process of remembering information immediately after acquiring it. Short-term memory typically holds a small amount of information (7 items or less) in an active state for approximately 10-15 seconds or even up to a minute (Miller, 1956). The transformation of short-term memory to long-term memory is the process of consolidation, which requires rehearsal along with meaningful association (Cowan, 2008). Long-term memory further branches into declarative (explicit) memory and procedural (implicit) memory.

Declarative memory, a component of long-term memory domain, is the memory for facts and events, and it is memory that is consciously stored and retrieved. Declarative memory further branches into episodic and semantic memory. Episodic memory is memory of experiences and events while semantic memory is memory of meanings,

acquired external knowledge of the world, and concepts and meanings that are independent of personal experiences (Cowan, 2008). While declarative memory is "knowing that" of facts and events (e.g., knowing that London is the capital of England), procedural memory is unconscious memory of "knowing how" to do things such as routines or skills (Cohen & Squire, 1980). Rehearsals of routines (e.g., tying ones shoes or riding a bike) are sensorimotor behaviors that are engrained so well that they unconsciously performed due to previous experiences (Matthews, 2015). Both declarative and procedural memories are tied to sleep with certain stages being more associated with procedural memory (e.g., stage 2) and others stages being related to declarative memory (e.g., stage 3 and 4) (Gais & Born, 2004). Regardless, a pivotal relationship between memory consolidation and sleep exists (see review in Rasch, 2013).

Function of Sleep in Memory Consolidation

Memory consolidation refers to the process by which newly learned information (also known as memory traces) is transferred from temporary to permanent storage. In 1900, Müller and Pilzecker proposed the memory consolidation hypothesis. The hypothesis stated that newly acquired memories are initially changeable and prone to disruption before they undergo various biological processes that make the memories more stable (McGaugh, 2000). This hypothesis has become the foundation of memory research. One of the first findings of improved memory consolidation after sleep came from a study done on declarative memory by Jenkins and Dallenbach in 1924 that reported participants forget less nonsense syllables after periods of sleep compared to after periods of wake. Then in 1973, another study found greater retention of associated word pairs when subjects slept during the first half the night compared to being awake

during the day, suggestive of a certain stage of the night being more associated with a declarative memory task. A seminal study done by Guilleminault and Dement (1977) found that as a person got closer to the state of sleep onset, the memory for stimuli presented during wakefulness decreased. The night before the memory task, participants were only given two hours of sleep in order to build sleep pressure. The following day, they were presented with single word stimuli, one minute at a time as they fell asleep. During each sleep onset, participants were either given 30 seconds of sleep or ten minutes of sleep. When they woke up, the participants were given a memory recognition task. The findings of the study showed that when participants slept for no more than 30 seconds, they were able to recall all the words heard before sleep onset. However, if they slept for even ten minutes then participants experienced a deficit for words heard five minutes before sleep onset. The researchers suggested the findings pointed to a "closing gate" or period of information transfer from short-term memory and long-term memory, hence explaining the absence of that information during testing. Therefore, compared to the ten minute sleep condition, the 30 second sleep condition allowed for information to still be present in short term memory for recall.

A neurophysiological model of sleep-memory relationships suggests that sleep facilitates two memory consolidation processes: system consolidation and synaptic consolidation (Born & Wilhelm, 2012). System consolidation is the dialog between the neocortex and hippocampus that enhances newly acquired information over several years. Specifically, system consolidation takes place during SWS rather than REM. System consolidation is an "active" consolidation that suggests that memories are reactivated during sleep for the purpose of selective consolidation. Furthermore, when these

memories shift to long-term memory they undergo qualitative changes before they become permanent (Born and Wilhelm, 2012). Synaptic consolidation is a relatively faster consolidation process that allows for the rewiring and strengthening of the synapses between neurons, solidifying of memory traces, and ultimately producing lasting changes in the efficiency of the previously present synapses (see review in Rasch, 2013). The high frequency EEG and hippocampal theta activity of REM is supportive of the strengthening of synaptic connections compared to the slow EEG frequency present during SWS (see review Giuditta, 1995). It is these synaptic connections that play a role in declarative memory consolidation during SWS.

The Relationship between SWS and Memory Consolidation

Several studies have demonstrated the critical relationship between SWS and memory consolidation (Marshall & Born, 2007; Diekelmann & Born, 2010; Rasch & Born, 2013). These studies date back to 1971, when a differential effect of sleep on memory was found during the first half of the night compared to the second half of the night (Yaroush et al., 1971). In these experiments, participants were put into three different conditions: NREM, REM and wake. Each group got 4 hours of sleep in their respective condition. Participants in the "first half of the night condition" did not sleep before learning while participants in the "second half of the night condition" got four hours of sleep before learning. The participants in the second half of the night were awakened from sleep in order to learn while the participants in the first half were not. Researchers found that memory retention during the first half of the night was greater than either REM or wake conditions. In an assessment of recall for paired-associate lists (declarative memory), the benefit from sleep depended on the sleep phase and the

memory type (Diekelmann & Born, 2010). Recall of paired-associate lists improved more during early sleep, where more SWS is found, relative to late night sleep, where REM is more predominate.

In order to isolate SWS as a factor in improvement of cognitive learning, studies have deprived healthy subjects of SWS (without affecting sleep time or efficiency) and found a lack of improvement in visuo-perceptual and visuo-motor tasks (Bellesi, 2014). Another study enhanced SWS through induction of slow oscillation-like potential fields via transcranial application of oscillating potentials (0.75 Hz) during the stage and found that it boosted the retention of hippocampus-dependent declarative memories in the healthy population (Marshall, Helgadottir, Molle, & Born, 2006). In another study of the role of SWS during a nap, researchers found that taking a 60-minute nap, which comprised of SWS, but not a 10-minute nap without SWS, helped protect memory of a paired association task from subsequent disruption. Together, these studies demonstrate the pivotal relationship that the large EEG delta waves of SWS have in declarative memory consolidation due to the strengthening of the recently formed synaptic connections.

Homeostatic sleep pressure that builds during the day is an indicator of the duration of SWS in a normal night of sleep. However, other factors such as caffeine levels and the environment also play a role in sleep quality during the night. A certain thermal comfort zone for humans is also necessary for proper sleep. Therefore, the way our body regulates internal temperature in relationship with our external environment is a process that is not only necessary to understand but it is also suggestive of novel research that can be done to improve our sleep.

Thermoregulation in Sleep

When considering temperature and the human body, there are two types to consider. The first is core body temperature, which is regulated by the brain and includes the thoracic, abdominal and cranial cavities. The second is the shell temperature, which is composed of the temperature of the distal parts of body such as the hands and feet. The shell area acts as a protection for the core body area. Heat transportation throughout the body is mainly done by blood medium convectively from core to distal areas. The shell area of the blood becomes smaller in a cold environment and larger in a warm environement. When the environment is cold, the shell area of the blood becomes larger while it becomes smaller in a warm environment (Krauchi, 2012). This surface size is regulated by two systems in the sympathetic pathway: the noradrenergic vasoconstrictor system and the active vasodilator system. These systems regulate the constriction or dilation of peripheral blood vessels but mainly of smooth muscles in arterioles, as well as smooth muscles in arteriovenous anastomoses in distal skin regions (Hales, Jessen, Fawcett, & King, 1985). Environmental temperature has a greater affect on the surface temperature, which includes the skin temperature and the tissues and muscles of the subcutaneous layer. Throughout the day, core body temperature and skin temperature show an inverse relationship. Core body temperature stays high during the day and skin temperature stays low. On the other hand, at night the core body temperature experiences a dip and skin temperature rises (McGinty & Szymusiak, 1990). This is due to the body's decreased heat generation and increased heat loss during the night.

During sleep, skin temperature fluctuates between 28-37°C (Koehler, 1996). The fluctuations in skin temperature are regulated by warm-sensitive neurons in the preoptic-

anterior hypothalamus (POAH), the area of the brain adjacent to the superchiasmatic nucleus (SCN) or body's circadian clock. While the pre-optic anterior hypothalamus contains neurons that are sensitive to small changes in the core temperature, it also has neurons that receive input from various spinal and skin thermoreceptors (Boulant, 2000). It integrates the various central and peripheral information it receives to better regulate the body's internal state and external environment. The role of POAH in thermoregulation is supported by evidence that stems from early animal studies testing the thermal stimulation of the area directly. In 1938, Magoun and colleagues elicited panting in anesthetized cats by heating the area of the POAH. Results of the study helped to confirm previous investigations that warmed the carotid blood entering the head in animals and found that it resulted in sweating, peripheral vasodilation and hyperventilation. Another similar study found that when the anterior hypothalamic regions were warmed, shivering was instantaneously suppressed and peripheral vasodilation immediately followed (Hemingway, Rasmussen, Wikoff, & Rasmussen, 1940). However, when the posterior hypothalamus was heated in similar conditions, there was minimal reduction in shivering and no peripheral vasodilation. These studies demonstrate the importance of the preoptic region in thermoregulation and that changes in temperature signals to the hypothalamus regulate and alter physiological and neuronal responses. Armed with the knowledge that a portion of the brain is responsible for regulating specifically skin temperature, it can be practical to suggest that externally changing the skin temperature can have an effect on the warm sensitive neurons in the brain which aid in the thermoregulation of the body.

A previous study found a beneficial effect of external manipulation by demonstrating that a mild skin warming of approximately .4°C from a baseline temperature helps induce deeper and longer full night sleep in adults of all ages (Raymann, Swaab, & Someren, 2008). While there have been few studies on mild skin warming during the full course of a night, there has yet to be an investigation on the effects of mild skin warming on stage-specific sleep. Raymann et al. 2008, found that warming the skin slightly (.4°C) enhanced SWS in young adults. In a similar mild skin temperature manipulation (0.4°C) study of patients with narcolepsy, the location of skin temperature manipulation (e.g., core or distal) had varying effects with SWS and REM (Fronczek, Raymann, Overeem, Romeijn,Van Dijk, Lammers, andVan Someren, 2008). Core body temperature regions suppressed wakefulness and enhanced SWS, while distal skin warming enhanced wakefulness and stage one sleep with SWS and REM stages suffering as a consequence. Therefore, mildly increasing the temperature of the core body regions is suggestive of enhancement of our deepest sleep stage, SWS.

Implications and the Present Study

While SWS is important stage of sleep, demonstrating depth of sleep pressure and being a marker of homeostatic regulation, it also plays a crucial role in declarative memory consolidation. This form of memory consolidation, specifically semantic memory, is pivotal in our daily lives when it comes to learning. Therefore, improving sleep, through specifically increasing SWS suggests a possible mechanism for improving cognition, particularly declarative memory. Raymann and colleagues (2008) showed that a mild increase in temperature could help induce SWS across the age spectrum. Mild skin temperature warming in the core area has been shown to enhance SWS (Fronczek et al.,

2008). Since some stages of sleep (3-4) are more beneficial for learning than others (Wilson, Baran, Pace-Schott, Ivry, & Spencer, 2012), determining whether sleep stages can be independently enhanced with mild skin warming has enormous implications for future research studies on learning and memory. Such research can be momentous for young adolescents, college students and even young professionals. Unlike sleep deprivation, fragmentation or interruption studies that normally occur in the field of sleep research, this study helps boost sleep in order to study the stage-specific effects. By comparing sleep duration during warmed stages with the control night, we aimed to gauge whether warming does indeed affect specific stages more than others.

Since SWS has been associated with memory consolidation (Marshall & Born, 2007; Diekelmann and Born, 2010; Rasch and Born, 2013), our study also tested the effects of memory consolidation as a result of mild skin warming in certain stages of sleep. Previous studies have established a link between mild skin temperature manipulation and SWS (Raymann et al., 2008; Fronczek et al., 2008). Furthermore, the link between SWS and declarative memory consolidation has been found in numerous studies. However, the link between mild skin temperature manipulation, SWS and memory consolidation has yet to be investigated. Based on these previous studies, we hypothesize that mild skin warming during SWS will lengthen time in SWS, and memory consolidation will be greatest following the SWS warming condition. To test this we compared the number of word pairs recalled during a declarative memory task before the night of sleep and after for each condition. We also tested the differences sleep stages durations across the three conditions (e.g SWS, REM and control), with particular focus on SWS. The findings of this study may help the young adult population improve

memory consolidation in both academic and social settings. If significant improvements in SWS (e.g., longer and deeper) are found as a result of mild skin temperature manipulation, this work will provide a tool to enhance memory consolidation in those with poor sleep quality.

METHOD

Participants

Seven healthy men and women, ages 18-30 years, were recruited through flyers in the nearby five college area. A prescreening was done via phone or email, and those who qualified came for the study. Out of 10 recruited participants, three participants dropped out. Participants were excluded if they had a previously diagnosed sleep disorder, a habit of napping, consumed more than 14 cups of coffee or alcohol a week, had prior neurological disorders, or were taking any anti-psychotic or anti-seizure medications/sleep aid medication. Due to the height constraints of the body suit, participants were under 6'2".

Experimental Design

This study was a within-participant experiment design over the course of three nights: SWS, Control and REM nights, which served as the conditions and our independent variables. The dependent variables included the percentage of time spent in each stage along with the change in memory performance from the night before sleep to the morning after sleep.

Materials and Procedure

The study included 4 sessions: one introductory session in which the participant was introduced to the study and the three experimental sessions: REM warming condition, control condition and SWS Condition. The first session was a viewing session in which the participant was able to see the equipment and the apartment in which they were asked to sleep in. The purpose of this session was to ensure that the participant knew exactly what the study entailed. The researchers answered all questions so that the participant was fully educated on the purpose and protocol of the study. The initial visit

also gave participants extra time to think about participating before coming for their first overnight stay. If participants were not comfortable with the protocol, they could opt out of the experiment and were given partial payment for their time. However, they were welcome to reconsider and contact us in the future, in which case the experiment would be restarted from the first session of introducing the experiment. Each participant was given our equipment description sheet (see Figure 1), which outlined where equipment was placed on the body and what type of equipment was used.

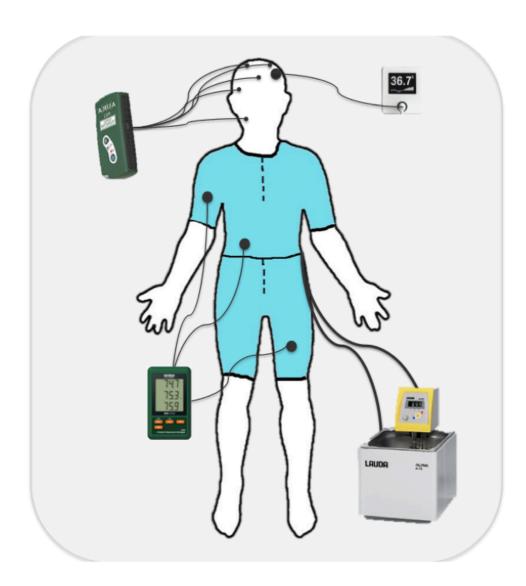


Figure 1. Full Protocol Set Up.

- 1. Three temperature leads (bottom left) measured skin temperature in real-time
- 2. A forehead lead (top right) estimated core temperature via extrapolation
- 3. A water circulating bath (bottom right) heated and maintained water temperature before circulating it through tubes in the suit
- 4. A portable sleep-recording device (top left) monitored sleep stages.

If participants agreed to participate, they were asked to read and sign the informed consent document (see Appendix A). The participants were given several forms to fill out (see Appendix A) including the Epworth Sleepiness Scale (ESS), designed to determine the participant's sleepiness level, or tendency to fall asleep or doze, (during certain everyday activities, such as watching T.V. or having a conversation with someone); the Pittsburgh Sleep Quality Index (PSQI), to measure the sleep quality and sleep disturbances during the participant's past month of sleep; the Morningness-Eveningness Questionnaire (MEQ), designed to determine the participant's preferences to performing tasks and activities during the morning hours or evening hours in order to determine if the person was a 'morning person' or 'night person', and the Stanford Sleepiness Scale (SSS); to determine the participant's sleepiness at the time of the memory tasks. After filling out the consent forms and questionnaires, the participants and the research team discussed and planned three meeting times during which the participant would undergo the experiments.

Word-Pairing Recall Task

Prior to applying the electrodes on the scalp for the EEG, a declarative memory task was done along with a Stanford Sleepiness Scale. In order to measure the formation of new associations in a semantic network, researchers commonly use the unrelated word-pair association task from a word list of single-syllable, high frequency, and concrete nouns (e.g Frame, Shoe). A word-pair task was used to examine declarative memory consolidation (Wilson et al., 2012). The stimuli were 40 semantically-unrelated word pairs consisting of single-syllable nouns. There were four phases in the task included encoding, immediate recall with feedback, immediate recall with no feedback

and delayed recall. Encoding, immediate recall with feedback and immediate recall without feedback were done in that respective order before electrode placement for polysomnography (Figure 2). During encoding, word pairs appeared on a computer monitor for 5s with a 100 ms inter-stimuli interval. Participants viewed the pairs and were recommended to use a mnemonic strategy to help with memory. One specific strategy suggested to participants was to use associations between the word pairs and internal images in their mind. For example if "bush-rope" was presented, participants could imagine holding onto a bush with a rope. Such an instruction was designed to aid in hippocampal-dependent contextual learning, aiding memory recall (Toki et al., 2014). Following this, participants practiced recalling the pairs with feedback. The first word from each pair was presented individually in a random order. The first and last two pairs of the encoded list were removed to eliminate primacy and recency effects, leaving a total of 36 pairs. If the participant's response was incorrect, the correct response was displayed on the computer monitor for 750 ms. If the response was correct, the next stimuli appeared on the screen. Recall practice continued until participants either reached 65% proficiency or the full list of words appeared five times (Mantua, Mahan, Henry, and Spencer, 2015).

After the encoding phase was the immediate recall phase, in which participants were presented with one word from the encoded pairs and were instructed to recall the corresponding word in the pair. In this phase, there was no feedback for incorrect responses. In Session 2, which occurred after a 12-h break (post-night), participants completed the Delayed Recall phase, which was identical to the Immediate Recall Phase.

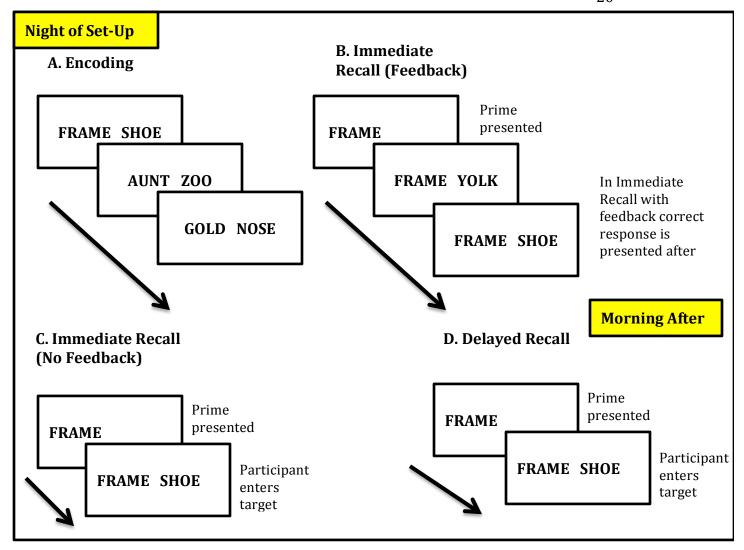


Figure 2. Schematic of the Word Recall Memory Task. At night, the first phase was the encoding (A) of 40 semantically-unrelated word pairs consisting of single-syllable nouns. Following encoding, immediate recall (B) was done with feedback. If the answer was incorrect, the correct answer followed. After achieving either 65% proficiency or the list was repeated 5 times, the immediate recall with feedback ended. The next phase was the immediate recall with no feedback (C) in which a prime was presented and a participant entered the target answer without any indication of whether it was the correct or incorrect answer. The following morning, a delayed recall (D) task, identical to the set up of the immediate recall with no feedback task was done.

Mild Skin Warming

Participants were equipped with the skin-warming suit (a high-density tube suit) during each of the 3 sessions. This spandex-like two-piece suit is equipped with a high volume of thin tubes and has been used in previous studies (Raymann et al., 2008). The tubes on the suit are connected by longer tubes, which connect to a water bath. Water is circulated through the tubes using a water heating/circulating bath (MED-ENG), which has been made especially for research (i.e., suit designed for ease of use with extra zippers for quickly removing the suit in case of bathroom use or discomfort and extra tubes for maximal skin coverage). The brand and model of suit selected for this particular study has been used before to induce mild warming and cooling of skin temperature (Raymann, Swaab, and Someren, 2008).

The water bath is a scientific instrument that can keep water at a constant, steady temperature. The bath circulated water through the tubes so that the warmed water reached the suit and effected skin temperature. Using this bath, subtle temperature manipulation was able to occur at a quick rate (i.e., at the onset of a sleep stage). Importantly, at the end of the stage, water temperature could easily be set back to the baseline skin temperature determined earlier in the night. There was an attached digital thermometer on the water bath that kept a constant reading of the water temperature. Warmed water was the most effective way to induce mild skin warming, as water temperature can be quickly manipulated. If another type of material (a heated blanket, for example) was used, heat would not be able to escape the material immediately, and this lingering heat on the skin would confound results.

Participants were equipped with three temperature-monitoring leads (PT100 thermistors, as used in Raymann et al., 2008 and Fronczek et al., 2008) under the suit so that an objective reading of skin temperature could be obtained throughout the temperature manipulation. These leads were attached to the EXTECH SD200, 3-Channel Temperature Datalogger. One thermometer lead was worn on the thigh, one on the upper arm, and the last on the stomach (Raymann et al., 2008). The wires from these cords were fed out of the suit in a hole designed for this purpose. Temperature leads were taped to the body with medical tape, as done typically in full polysomnographic overnight sleep studies.

Participants were equipped with a core temperature monitor on either side of the forehead, ensuring it would not interfere with the PSG lead that was in the center of the forehead. To do this, researchers asked participants what side they normally sleep on and placed the core temperature monitor on the opposite side in order to reduce discomfort. This monitor (SpotOn Core Temperature Monitoring System), which has been used in previous studies (Iden, Horn, Bein, Bohm, Beese, and Hocker, 2015), offers a reliable measure of core temperature without having to employ the standard method of core temperature measurement (rectal thermometer). The forehead monitor was more comfortable than the standard rectal method of core temperature monitoring and it was easier for the researcher to apply because it did not disturb the sleep of the participant. Previous studies have found that mild skin warming is so subtle that core temperature is not affected (Raymann et al. 2008). Regardless, a core temperature sensor was used to monitor body temperature, to demonstrate no fluctuations in core body temperature when skin temperature warming occurred.

Mild skin temperature manipulation of approximately 1-2°C was done in the REM and SWS warming conditions on the onset of the REM or SWS stage. The temperature was reverted back to baseline after either the period of SWS or REM ended. If baseline temperature was found to be too close to a temperature of 100°F or 37.7°C then temperature was only increased by 1°C in order to prevent awakenings during sleep. In the control condition, participants wore the body suit but the water bath was not turned on and therefore no temperature manipulation occurred. This was done to ensure the control condition that an individual's baseline temperature was not affected by a constant source of warming, which would not occur in a natural setting.

Sessions

Each participant slept in the UMass Cognition and Action lab apartment three times while being observed by a minimum of two researchers. Three sessions were necessary to see whether mild skin warming during these two stages changed the depth and quality of that specific sleep stage (REM and SWS) when compared to the control night. These three sessions (REM, SWS and Control) occurred in a randomized order for each participant. One male and one female researcher were present at all times during the participant's stay in the lab apartment. These two researchers remained awake throughout the night to induce mild skin warming once the proper sleep stage was reached. The researchers, thoroughly trained on sleep-stage identification, had a real-time monitoring system of the sleep recordings and were easily able to see which stage of sleep the participant was in. When it was the appropriate time, mild skin warming not exceeding the threshold of discomfort was induced. The research team checked the temperature monitors to ensure that the target temperature had been reached. The target temperature

was 2°C greater than the average of the three-skin temperature leads at baseline. They then made sure to confirm that the participant had not awakened and did not have any physical or emotional discomfort. Depending on the stage the participant underwent during mild skin warming (REM, SWS) that night, skin warming was induced approximately five times in each stage and in total around ten times each night. Once the participant had left that specific sleep stage, the temperature was returned to baseline. If the participant needed to use the bathroom during the night, the researchers aided in removing the body suit and disabling the polysomonography recording montage of the EEG. The research team reiterated to the participant that he or she could remove the suit/equipment at any point during the experiment and that there would be no negative repercussions for ceasing participation.

Polysomnography

Participants were equipped with the polysomnography (PSG) electrodes in order to record the participant's sleep physiology (sleep stages and other physiological markers) for that night's sleep (see Figure 3-4 below). Polysomnography was recorded with the Aura PSG ambulatory system (Grass Technologies). An electrode montage was applied in the sleep lab approximately 2 hours before their typical bedtime. The montage included 2 EOG leads (right and left ocular canthus), two chin EMG leads, and six cortical EEG leads (F3, F4, C3, C4, O1, O2) with each electrode referenced to CZ and one ground electrode in the center of the forehead. Electrodes (M1 and M2) were also placed on the mastoid bone behind the ear. These electrodes are considered inert references points, which are standard in a PSG protocol. Data analysis was conducted according to the revised AASM manual (Silber et al., 2007). The full protocol set up can

be seen in Figure 3 below. The PSG monitor was used to determine when participants switched from one stage to another (i.e., when to induce or reduce warming).

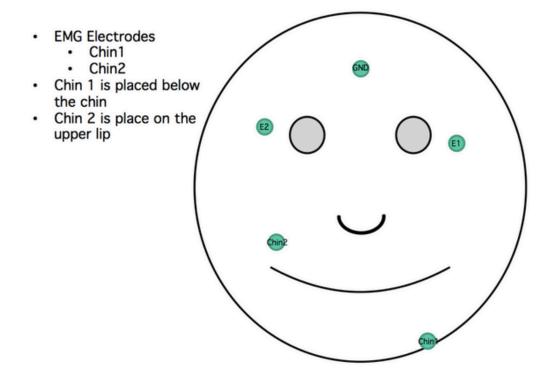


Figure 3. PSG Application Face Placements

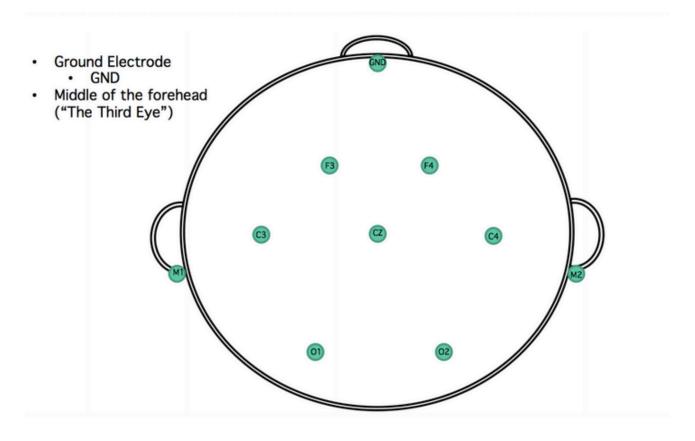


Figure 4. PSG Application Head Placements

Analyses

Polysomnography:

This study was a within-participant design conducted over the course of three nights. The participant's percent of the night in each sleep stage was compared between nights for each condition: REM, SWS, and control night. Polysomnography data were scored using the American Academy of Sleep Medicine (AASM) Manual for the Scoring of Sleep and Associated Events (Silber et al., 2007), identifying periods of wake and sleep stages NREM1, NREM2, SWS, and REM. Total sleep across the night and the percentage in each sleep stage was calculated and compared across all three conditions (control, REM, and SWS). The number of arousals during each stage and each condition was calculated by handscoring each participant's PSG montage. Using SPSS, a 4x3 repeated-measures ANOVA was done to test any differences between the each of the stages (SWS, REM, NREM1 and NREM2) in each of the three conditions: SWS, control and REM with alpha set at .05. No post-hocs were run due to lack of statistical significance in any of the repeated-measures ANOVAs.

Memory Consolidation

In order to see whether there was a difference in memory performance the night before sleep compared to the morning after sleep in each condition, a change in memory performance was calculated using an intersession score formula:

Intercession Score:

$$= \left(\frac{(Accuracy\ of\ Delayed\ Recall) - (Accuracy\ of\ Immediate\ Recall)}{(Accuracy\ of\ Immediate\ Recall)}\right) x\ 100 \tag{1}$$

Word pair data was individually reviewed for total number of correct word pair responses, allowing for misspelling. Recall accuracy was measured as a percentage of the total number of word pairs (of 36 possible) correctly produced. The change in performance between Immediate and Delayed Recall was assessed using an Intersession Change score. Intersession Change in recall was calculated by subtracting the Immediate Recall accuracy from the Delayed Recall accuracy and normalizing to baseline accuracy. This score was our dependent variable and was compared between the pre-night and post-night for all three conditions (REM, SWS, Control).

Results

Skin Temperature:

Skin temperature was increased during both the SWS warming condition and the REM warming condition, generally during the first half of the night and second half respectively. The time it took for the temperature change to hit the target temperature after manipulation was also recorded as the temperature latency. To demonstrate the presence of a temperature warming during the intended stage and time of the night, a representative sample of the average skin temperatures from a participant throughout the night is represented in figures 5-7. Skin temperature fluctuations were more imprecise than planned. Due to the variability in the baseline temperatures of each participant as well as the variability in sleep staging across the night, the average of all seven of the participant's skin temperature leads is not shown. However, through one participant we can see that skin temperature did increase during the second half of the night (figure 5) and during the first half of the night during the SWS condition. In the control condition, the skin temperature did not fluctuate much during the course of the full night of sleep 7-8 hours (Figure 7). This demonstrates that the target temperatures during both REM and SWS warming condition were reached and temperatures during control condition were maintained with little fluctuation as predicted within our hypothesis.

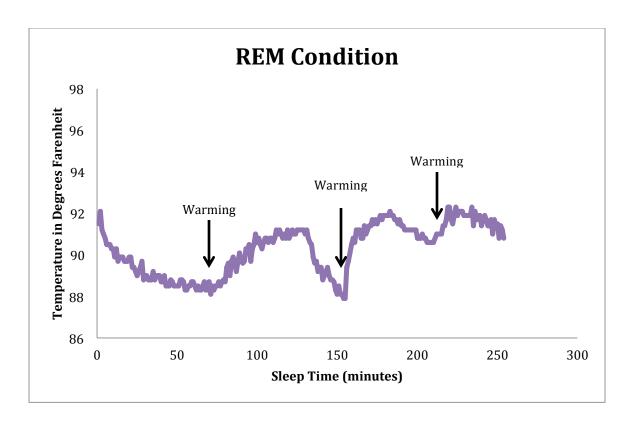


Figure 5. Sample Skin Temperature Manipulation in the REM warming condition for a Participant

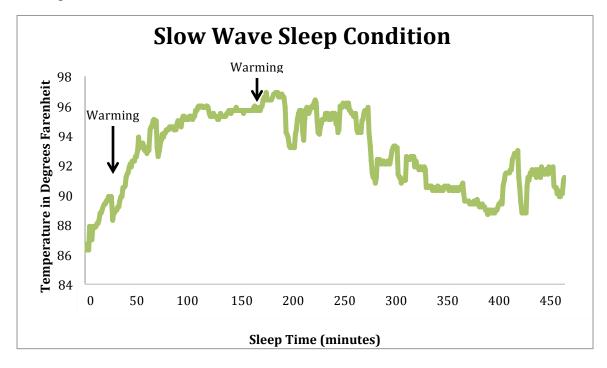


Figure 6. Sample Skin Temperature Manipulation in the SWS Condition for a Participant

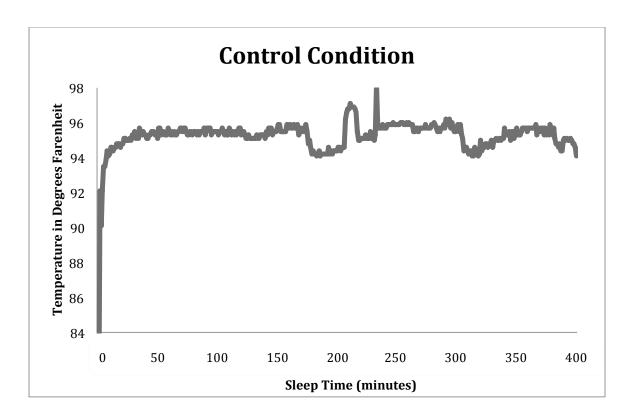


Figure 7. Sample Skin Temperature Manipulation in the Control Condition for a Participant

Sleep Time in Mild Skin Warming

For our analysis, repeated-measures ANOVA tests compared sleep staging among the various conditions and number of arousals between all three conditions. There were no significant differences between conditions (p>.35 in all statistical tests), indicating that all conditions were similar in the distribution of sleep staging throughout the night.

A repeated measures ANOVA was conducted to assess whether there was difference in the total sleep time spent in SWS for the SWS warming condition, control condition or the REM warming condition. There was no statistically significant difference between SWS in any of the conditions: SWS (M=26.67,SD=16.48), control (M=21.35, SD=6.91) or REM (M=27.21, SD=14.68) conditions, $F(_{1.308, 6.540})$ =1.027, MSE=96.31, p=.222. Although there was an expected increase in the duration of time for SWS in the SWS warming condition compared to either the control or REM warming conditions.

In order to test the effects of REM in the SWS, control and REM warming conditions, a repeated measures ANOVA was conducted. The results showed that there was no statistically significant difference between REM in any of the conditions: SWS (M=15.2, SD=8.82), control (M=15.5, SD=5.67) or REM (M=13.3, SD=6.98) conditions. $F(_{1.308, 6.540})=1.027$, MSE=96.31, p=.222. Although there was an expected increase in the duration of time for SWS in the SWS warming condition compared to either the control or REM warming conditions.

For the sake of comparison between sleep stages, a repeated measures ANOVA was conducted to assess the differences in total sleep time of stage 1 (NREM1) in SWS, control and REM warming conditions. The results showed that there was no statistically

significant difference between NREM1 between the following: SWS (M=7.11,SD=14.45), control (M=1.85, SD=1.28) or REM (M=9.58, SD=20.22) conditions, $F(_{1.008, 5.042})=0.843$, MSE=185.68, p=.459. Similarly, a repeated measures ANOVA was conducted to assess the differences in total sleep time of stage 2 in SWS, control and REM warming conditions. The results showed that there was no statistically significant difference between stage 2 and SWS (M=54.65,SD=27.15), control (M=61.23, SD=10.78) or REM (M=52.23, SD=25.25) conditions, $F(_{1.20, 5.99})=.661$, MSE=216.98, p=.537.

In order to examine sleep time of each condition rather than each stage, the total sleep time in each condition was calculated and depicted in figure 8. The total sleep time in SWS was (M=435 minutes, SD=29.31) and in control condition (M=380 minutes, SD=187.11) and finally (M=434, SD=42.49) in the REM warming condition. All nights had sleep within the normal range for young adults (7-9 hours or 420-540 minutes). A repeated measures ANOVA demonstrated no statistically significant difference in the total sleep times among the three conditions, $F(_{1.038, 5.191})$ =.410, MSE=11292.429, p=.675.

The percentage of time spent in different stages was assessed for all three conditions. However, the results did not show any difference between the percentages spent in each of stages across the three conditions. Figure 9 shows the percentage of time spent in different stages (NREM1, NREM2, SWS, and REM) when skin temperature was manipulated in SWS warming condition. Over half of the time (55%) spent in the SWS warming condition was spent in NREM2 (stage 2), followed by SWS with 27%, REM with 15% and 7% spent in REM. Figure 10 shows the percentage of time spent in different stages when a mild skin temperature increase was applied in REM warming

condition. Over half of the night spent (54%) was spent in NREM2 (stage 2), followed by SWS with 26%, REM with 13% and 8% spent in NREM1 (stage 1). Figure 11 shows the percentage of time spent in different stages in the control condition, when no mild skin temperature was applied. Over half of the night spent (61%) was spent in NREM2 (stage 2), followed by SWS with 21%, REM with 16% and 2% spent in NREM1 (stage 1). These percentages reflect a relatively normal percentage of staging for each of the various conditions.

Sleep quality cannot simply be the result of total sleep time in each stage or condition. The number of arousals that disrupted sleep, thus changing the architecture of sleep, may have also had an effect on memory consolidation depending on the stage it is in. Figure 12 depicts the number of NREM (stages 1-4) arousals in each condition when a mild increase in skin temperature was applied in the SWS warming condition. During the control condition there were on average 8.5 arousals, followed by 9.7 arousals in SWS, 12.3 arousals in the REM warming condition. The least number of arousals was found to be in the control condition and the greatest was found to be in the REM warming condition. Figure 13 depicts the number of arousals in each condition when a mild increase in skin temperature was applied in the REM warming condition. The least number of arousals was found in the SWS warming condition with an average 1.3 arousals, followed by REM with 2.6 and finally control with 3.7 arousals during the course of the night.

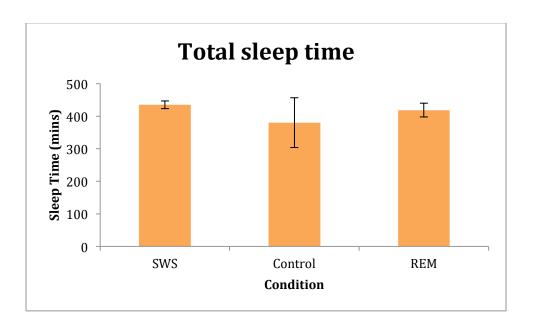


Figure 8: Total sleep time in conditions of SWS, REM and Control Condition.

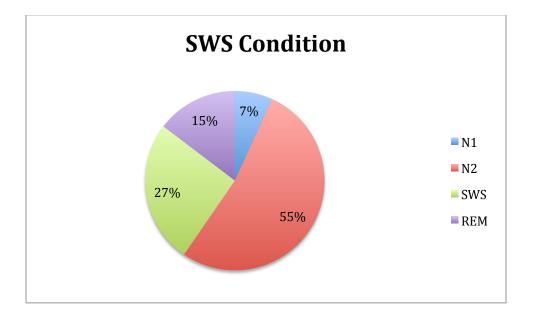


Figure 9: Percentage of time spent in SWS (NREM 3-4) for different stages when skin temperature was manipulated in SWS warming condition.

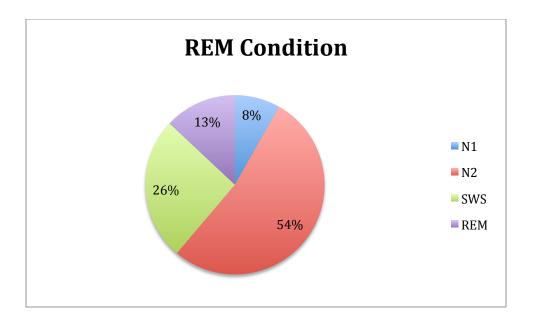


Figure 10: Percentage of time spent in REM for different stages when a mild skin temperature increase was applied in REM warming condition.

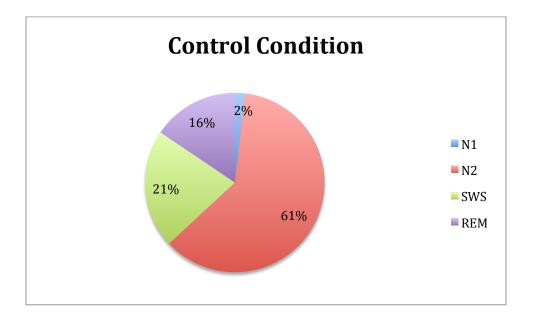


Figure 11: Percentage of time spent in SWS (NREM 3-4) for different stages when skin temperature was manipulated in SWS warming condition.

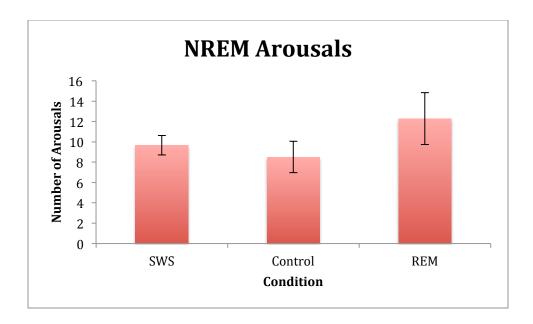


Figure 12: Number of arousals in each condition when a mild increase in skin temperature was applied in the SWS warming condition.

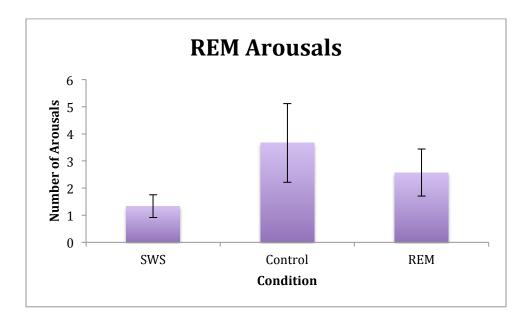


Figure 13: Number of arousals in each condition when a mild increase in skin temperature was applied in the REM warming condition.

Memory Consolidation via Word-Pairing Task

Word pair data was individually reviewed for total number of correct word pair responses, allowing for misspelling. Recall accuracy was measured as a percentage of the total number of word pairs (of 36 possible) correctly produced. The change in performance between Immediate and Delayed Recall was assessed using an Intersession Change score. Intersession Change in recall was calculated by subtracting the Immediate Recall accuracy from the Delayed Recall accuracy and normalizing to baseline accuracy. This score was our dependent variable and was compared between the pre-night and post-night for all three conditions (REM, SWS, Control).

A repeated measures analysis of variance was conducted to assess whether SWS improved memory consolidation compared to control condition and REM warming conditions. The results indicated that there was no statistically significant improvement in memory consolidation during SWS (M=.004, SD=.051) compared to control (M=.148, SD=.431) or REM warming conditions (M=.045, SD=.081), $F(_{1.063, 6.380})$ =1.099, MSE=.133, p=.338.

Results indicated a slight increase of .0054% in memory consolidation post-night in the SWS condition compared to the number of word pairs remembered the night before. During the control condition, there was a decrease of 0.018 % in the control condition. Finally, there was a decrease of 0.056% in word pairs remembered in the post-night condition compared to the night before (see Figure 16). However, a repeated-measures ANOVA showed no significant differences between groups (p=.32), likely because of the small sample size. The results of this behavioral task show a trend towards supporting our hypothesis of an increase in memory performance or greater retention in

the SWS condition. While in the control and REM warming conditions, which served as controls, there was a greater decay of memory recall during the morning after sleep compared to the night before sleep. The results of the two conditions confirmed the hypothesis of no significant improvement being seen in either condition.

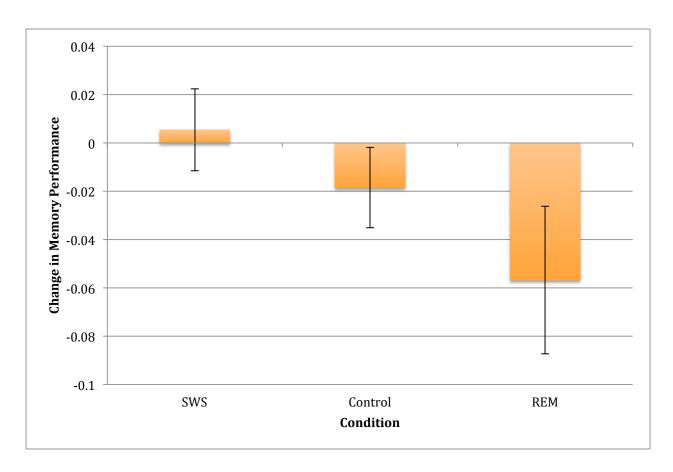


Figure 14. Change in Memory Performance in SWS, Control and REM warming conditions.

DISCUSSION

Sleep Time

In order to see how sleep was affected by mild skin warming, we looked at the total sleep time in each sleep stage for each of the three different conditions (e.g., REM, SWS and control). More specifically, we were interested in the duration of SWS during the SWS warming condition in comparison with SWS sleep time during REM and control conditions when skin temperature was slightly raised. We hypothesized that a mild increase in skin temperature would increase the duration of SWS time during the SWS condition. However, we found no differences for sleep duration in any of our three conditions: SWS, REM or control conditions

Generally, adults spend approximately 50% of their total sleep time in stage 2 sleep, about 20% in REM sleep, and the remaining 30% in NREM1 and SWS (Carskadon and Dement, 2005). Our results showed very slight deviances from the average percentages for each condition for a normal adult (see Figures 9-11). Figure 8 shows the total sleep time in each condition of the experiment including SWS, REM and the control condition. As predicted, the total sleep time was greater in the SWS warming condition compared to control condition and the REM condition by 54 minutes and 16 minutes, respectively. However, these differences were not statistically significance. The actual percentage of time spent in SWS during the SWS warming condition was 27% (Figure 9), which was comparable to the 26% of time spent in SWS during the REM warming condition (Figure 10) and only 6% greater than the 21% of time spent in SWS condition during the control condition (Figure 11). Although no temperature manipulation occurred

during SWS in the REM warming condition, an almost equivalent amount of SWS time was spent in both the REM and the SWS warming conditions (both were greater than the SWS time in control condition as well). Since one brief REM period typically occurs at the beginning of the night (i.e., prior to more SWS later in the night), warming during the first REM period may have affected later SWS even though this was the REM warming condition. This may explain why there were more NREM arousals in the REM warming condition compared to both SWS and control (Figure 12). Although warming occurs during the second half of the night for the REM warming condition, warming during the first REM bout in the first half of the night may have awoken the participants during subsequent SWS and even NREM 2. Alternatively, any warming during the night may have induced SWS, as the suit may have retained heat despite our attempts to allow the skin to cool with time and skin habituates after prolonged exposure to a certain temperature (Castellani & Young, 2016).

A skin warming study gave participants a period of 20 min for cooling (e.g., using an ice pack wrapped in fabric), following a period of warming, and found that their skin temperature did not decrease to baseline (Vuksanovic, Sheppard, and Stefanovska, 2008). During the 30-minute recovery time after the cooling period, it took participants on average an additional eight minutes to reach the baseline temperature. Thus, the physiological response could only be detected well after 20 minutes. Kellogg (2006) suggested that core skin area reaches its highest threshold value when cutaneous vasodilation is fully activated. This is when sweating begins while the body is at rest. It is important to note that this point of sweating is different during exercise or other forms of active movement. In their study, Vukasonovic and colleagues (2008) found skin

temperature thresholds for warming and cooling by studying the correlation between blood flow and skin temperature. Their results suggest that the decrease in blood flow, when temperature fell below 31-32°C, is indicative of a homeostatic response to temperature falling below a lower limit of what is considered the neutral skin temperature zone. Conversely, the upper limit of 36-37°C corresponds to the temperature-related structural changes in hemoglobin that contribute to increased blood flow during the warming periods. During our study, an arbitrary cut-off temperature for skin warming was set at 37.7°C, or 100°F, to ensure no arousals occurred as a result of the warming. However, we may not have warmed the skin enough and if we increased the temperatures beyond 37.7°C, increased vasodilation may have occurred. But this could have also caused more arousals as well.

Arousals

In young adults, arousals are prevalent but not too frequent (Colten, 2006). If they do occur, they normally occur closer to REM onset, thus allowing sleep to remain undisturbed. REM arousals were the most prevalent in the control condition with an average of 3.67 arousals compared to REM warming condition with 2.57 arousals and SWS warming condition with 1.3 arousals. There were no notable differences among the number of arousals in each condition; however, arousals in the control condition may have resulted from unforeseen factors such as being in a new environment, wearing the body suit, or having electrodes placed on the head. Yet these same factors were present in all conditions and may have had the same effects in each condition.

More NREM arousals occurred in the REM warming condition (12.28) than the SWS warming (9.67) and control (8.5) conditions. Previously, it was demonstrated that

fewer arousals occur during a skin warming condition (Raymann et al., 2008). However, this study did not distinguish between NREM and REM arousals. Although we expected more REM arousals to occur, generally skin warming is meant to reduce arousals throughout the night. On the other hand in certain circumstances, imprecise skin warming may have induced unexpected arousals as well. For instance, REM and NREM1 (stage 1) have a similar EEG waveform pattern: a low frequency mixed voltage EEG. Given the real-time skin-warming induction, distinguishing between these two stages may be slightly ambiguous. Incorrect skin warming during NREM1 rather than REM, may have led to more arousals since NREM1 has the lowest arousal threshold (Carskadon & Dement, 2011). However, it could be argued that greater REM arousals should have been expected compared to NREM arousals. This is because greater prevalence in REM arousals compared to NREM arousals may be a protection mechanism to prevent awakenings during NREM in young adults (Djik, 1998).

In animals, the thermoregulatory system is absent during REM, due to the loss of thermo-sensitivity in many of the hypothalamic preoptic neurons (Parmeggiani, 1987). However, in humans this function is not completely lost but rather the thermo-sensitivity is reduced in REM in comparison to NREM and the wake state (Jennings et al. 1993). Sweat rate increases during SWS compared to other sleep stages while in REM there is a delayed onset of sweating, reduced sweat rate, decreased heat dispersal leaving the body and reduced heat tolerance (Sagot, Amoros, Candas, & Libert, 1987). The reduced heat tolerance can be seen as a factor in REM arousals being greater in the REM warming condition compared to REM arousals in the SWS warming condition (Figure 13). Since thermoregulation is absent in REM, it is not surprising that additional heat exposure may

disrupt REM, therefore causing a lower percentage of time spent in REM when mild skin temperature is induced in that stage (Figure 12). In addition to the lower percentage of time spent in REM when temperature is induced in that stage, a greater percentage of time spent in NREM1 can also be an indicator of fragmented sleep. NREM1 has the lowest arousal threshold and a greater percentage of NREM1 is a common sign of disrupted sleep (Carskadon & Dement, 2011). The greatest percentage of NREM1 was found in the REM warming condition (8%) compared to (7%) in SWS and (2%) in the control condition. Therefore, although there was greater SWS in the SWS warming condition (27%) and REM warming condition (26%) compared to control (21%), there was also greater NREM1 compared to control. Therefore, it cannot be conclusively said that the duration of SWS increased as result of mild skin temperature manipulation.

Skin Temperature Manipulation

Mild skin temperature warming of approximately 2°C was induced through a water bath. The temperature was monitored by temperature leads placed on the arm, stomach and calf of the participant's leg within the suit. Temperature was monitored throughout the night by these temperature leads in order to ensure that the induced temperatures actually changed the temperature of the water in the SWS and REM warming condition. The average of the participant's temperature leads was recorded for each condition. During the REM warming condition, increased temperature was prevalent during the second half of the night (Figure 5) for the REM warming condition. This was expected since the REM stage is more prevalent during the second half of the night. In comparison, SWS occurs predominantly during the first half of the night of the night

(Figure 6). The leads also monitored temperature during the control condition. This was done to ensure that the temperature did not fluctuate during the night. According to the average of the skin temperature leads of participants during the control condition, temperature did not fluctuate greatly during the night (Figure 7). Core body temperature was monitored during the night for fluctuation during skin temperature manipulation conditions. No noteworthy core body temperature changes resulted from mild skin temperature manipulation, which has been demonstrated before (Raymann et al., 2008)

Memory Consolidation Behavioral Data

Our hypothesis predicted that a mild increase in skin warming would increase the duration of SWS time during the SWS condition and subsequently increase memory consolidation in that warming condition. Results indicate an increase of .0054% in memory consolidation post-night in the SWS condition compared to the number of word pairs remembered the night before (Figure 14). This result was in line with our hypothesis that mild skin temperature manipulation would induce more SWS, which in turn would improve declarative memory consolidation. However, these results were not significant. During the control condition, there was an unexpected decrease of 0.018 % in the control condition, since no percent change in memory performance was expected for this condition due to absence of skin warming. An old theory suggested that memory decays over time and does so even as a participant is asleep; hence stating that sleep had no effect on memory. It was later found that sleep had a positive effect on memory, thus rejecting the decay theory for the theory of interference (Yaroush et al., 1971). Therefore, a full night's sleep immediate following learning should have either helped retain memory or improve slightly since no deprivation was done. Thus, the decrease in

memory performance was not expected for the control condition or REM in which there was a decrease of 0.056% in word pairs remembered in the REM warming condition (Figure 14). Previous work has attempted to induce odors to reactive neuron firing during REM and SWS and found that there was no effect of odor-induced memory reactivation during REM sleep on declarative memory stability (Cordi, Diekelmann, Born, & Rasch, 2014). Since REM is not associated with declarative memory consolidation, the decrease in memory performance may not be due to decrease in REM time during the REM warming condition (Figure 10). However, disrupted sleep through arousals could have contributed to interference in consolidation during any of the NREM stages, but specifically during SWS. A presence of a REM bout in the first half of the night, may have elicited skin warming that caused arousals during NREM, thus disrupting SWS and any memory consolidation occurring at the time. Ekstrand, Sullivan Parker and West (1971), did not find any differences in memory between REM and stage 4 deprivation for two lists learned through an RI paradigm. However, the possibility exists that this deprivation protocol resulted in many awakenings during the night that may have disrupted the consolidations effects that would be present if the participant had undisturbed sleep (Yaroush et al., 1971). Therefore, arousals may play a greater role in impairing consolidation than expected.

Implications for Study:

SWS is a crucial component of sleep and deprivation of SWS can affect cognitive learning. Raymann et al. (2008) showed that a mild increase in temperature could help induce SWS across the age spectrum. However, since such an effect has only been tested over a full night of sleep, this study tested the effects of mild skin warming in specifically SWS and REM sleep. Since stages of sleep (3-4) are more beneficial for learning than others (Wilson et al., 2012), determining whether sleep stages can be independently enhanced with mild skin warming has enormous implications for future research studies on learning and memory. The findings of this study can help the young adult population improve memory consolidation in both academic and social settings. Greater sample size may be needed in order to reduce error margins and extrapolate findings to a larger population of young adults. Difficulty in differentiating between REM and NREM1 stages may have confounded results by increasing the skin temperature in NREM1 rather than REM. In the future, improved real time EEG analysis of REM staging may aid in properly staging REM sleep, which is commonly confused with NREM1. In improving the ability to distinguish between REM and NREM1, the accuracy of skin warming during the REM stage can improve. A period of cooling may be needed following warming based on research done on skin habituation (Castellani & Young, 2016). This could also compensate for the body suit retaining heat following reduction of temperature to baseline. Future updates in the protocol or another study could potentially use two water baths, one for warming and the other with water of a cooler temperature that is set at baseline skin temperature or lower. However, this would require the use of a new suit design that would be able to include tubes for both water baths, ensuring no cross-circulation.

Based on previous studies, we hypothesized that there will be a greater improvement in memory consolidation as a result of a mild increase in temperature in stage 3 and 4 or SWS. Our results demonstrated a trend depicting mild skin temperature warming in SWS to be better for memory consolidation than control and especially REM, but these results were not significant. Further research is needed to verify whether mild skin warming may help increase duration of SWS and consequently improve memory consolidation. In addition, performing an EEG spectral analysis may also be useful in assessing sleep quality at these specific sleep stages.

APPENDIX A

Stanford Sleepiness Scale (SSS)

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

DATE	TIME	SCALE RATING

Epworth Sleepiness Scale

Name:	Toda	Today's date:		
Your age (Yrs):	Your sex (Male = M, Female = F):		
How likely are you to do tired?	ze off or fall asleep in the following situation	s, in contrast to feeling just		
This refers to your usual	way of life in recent times.			
Even if you haven't done you.	some of these things recently try to work ou	t how they would have affected		
Use the following scale t	o choose the most appropriate number for	each situation:		
It is i	0 = would never doze 1 = slight chance of dozing 2 = moderate chance of do 3 = high chance of dozing important that you answer each question as it	zing		
Situation		Chance of Dozing (0-3)		
Sitting and reading		_ _		
Watching TV		_ _		
Sitting, inactive in a pub	lic place (e.g. a theatre or a meeting)	_ _		
As a passenger in a car f	or an hour without a break	_ _		
Lying down to rest in the	e afternoon when circumstances permit	_ _		
Sitting and talking to sor	neone	_ _		
Sitting quietly after a lun	ich without alcohol	_ _		
	or a few minutes in the traffic			

me				_ Da	ate
	Sleep Quality Assessme	ent (l	PSQI)		
	What is PSQI, and what is it r	neasur	ina?		
erentiates "poo	eep Quality Index (PSQI) is an effective instrument used to mea or" from "good" sleep quality by measuring seven areas (compor sleep efficiency, sleep disturbances, use of sleeping medication	sure the quents): sub	uality and pa jective slee	p quality,	sleep latency,
STRUC	TIONS:				
	stions relate to your usual sleep habits during the past month or the majority of days and nights in the past month. Please answ			ould indica	ite the most
	the past month,				
2. How long (ir	you usually gone to bed? n minutes) has it taken you to fall asleep each night?				
	ave you usually gotten up in the morning? ny hours of actual sleep did you get at night?				
B. How ma	ny hours were you in bed?			_	
5. During the past m	onth, how often have you had trouble sleeping because you	Not during the past month (0)	Less than once a week (1)	Once or twice a week (2)	Three or more times a week (3)
A. Cannot get to s	sleep within 30 minutes				
B. Wake up in the	middle of the night or early morning				
C. Have to get up	to use the bathroom				
D. Cannot breath	e comfortably				
E. Cough or snore	eloudly				
F. Feel too cold					
G. Feel too hot					
H. Have bad drea	ms				
I. Have pain					
J. Other reason (s	s), please describe, including how often you have had trouble sleeping because of this reason (s)	:			
6. During the past m	onth, how often have you taken medicine (prescribed or "over the counter") to help you sleep?				
7. During the past m social activity?	onth, how often have you had trouble staying awake while driving, eating meals, or engaging in				
8. During the past m	onth, how much of a problem has it been for you to keep up enthusiasm to get things done?				
9. During the past m	onth, how would you rate your sleep quality overall?	Very good (0)	Fairly good (1)	Fairly bad (2)	Very bad (3)
	Scoring				
Component 1	#9 Score		С	1	
Component 2	#2 Score (<15min (0), 16-30min (1), 31-60 min (2), >60min (3))				
Component 3	+ #5a Score (if sum is equal 0=0; 1-2=1; 3-4=2; 5-6=3) #4 Score (>7(0), 6-7 (1), 5-6 (2), <5 (3)		C	2 3	<u></u>
Component 4	(total # of hours asleep) / (total # of hours in bed) x 100				
Company F	>85%=0, 75%-84%=!, 65%-74%=2, <65%=3		C	4	
Component 5 Component 6	# sum of scores 5b to 5j (0=0; 1-9=1; 10-18=2; 19-27=3) #6 Score			5 6	

Global PSQI ____ Add the seven component scores together _____

#7 Score + #8 score (0=0; 1-2=1; 3-4=2; 5-6=3)

Component 6

Component 7

REFERENCES

- Ackermann, S., Rasch, B. (2014). Differential effects of non-REM and REM sleep on memory consolidation? *Current Neurology and Neuroscience Reports*, 14(2), 430-013-0430-8. doi:10.1007/s11910-013-0430-8
- Alhola, P., & Polo-Kantola, P. (2007). Sleep deprivation: Impact on cognitive performance. Neuropsychiatric Disease and Treatment, 3(5), 553–567.
- Bellesi, M., Riedner, B. A., Garcia-Molina, G. N., Cirelli, C., Tononi, G. (2014). Enhancement of sleep slow waves: Underlying mechanisms and practical consequences. *Frontiers in Systems Neuroscience*, 8, 208. doi:10.3389/fnsys.2014.00208
- Borbély, A. A. (1982). A two process model of sleep regulation. *Human Neurobiology*, *1*(3), 195-204.
- Born, J., Wilhelm, I. (2012). System consolidation of memory during sleep born, J., wilhelm, I. (2012). system consolidation of memory during sleep. *Psychological Research*, 76(2), 192-203. doi: 10.1007/s00426-011-0335-6
- Boulant, J. A. (2000). Role of the preoptic-anterior hypothalamus in thermoregulation and fever. *Clinical Infectious*, *31 Suppl 5*, S157-61. doi:CID000203 [pii]
- Carskadon, M., Dement, W. C. (2005). Normal human sleep: An overview. M, dement W. normal human sleep: An overview. In M. H. Kryger, T. Roth W. C. Dement (Eds.), *Principles and practice of sleep medicine* (4th ed., pp. 13-23). Philadelphia: Elsevier Saunders.
- Carskadon, M. A., Dement, W. C. (2011). Monitoring and staging human sleep. In M. H. Kryger, T. Roth W. C. Dement (Eds.), *Principles and practice of sleep medicine* (5th ed., pp. 16-26). St Louis: Elsevier Saunders.
- Carskadon, M. A. (1993). *Encyclopedia of sleep and dreaming*. New York: \$bMacmillan Pub. Co.; Toronto; New York: Maxwell Macmillan Canada; Maxwell Macmillan International.
- Castellani, J. W., Young, A. J. (2016). Human physiological responses to cold exposure: Acute responses and acclimatization to prolonged exposure. *Autonomic Neuroscience : Basic Clinical*, doi:S1566-0702(16)30014-5 [pii]

- Clemens, Z., Fabo, D., Halasz, P. (2005). Overnight verbal memory retention correlates with the number of sleep spindles. *Neuroscience*, 132(2), 529-535. doi:S0306-4522(05)00094-1
- Cohen, N. J., & Squire, L. R. (1980). Preserved learning and retention of patternanalyzing skill in amnesia: Dissociation of knowing how and knowing that. Science (New York, N.Y.), 210(4466), 207-210.
- Colten, H. R., Altevogt, B. M., Institute of Medicine. Committee on Sleep Medicine and Research. (2006). *Sleep disorders and sleep deprivation: An unmet public health problem*. Washington, DC: National Academies Press.
- Cordi, M. J., Diekelmann, S., Born, J., Rasch, B. (2014). No effect of odor-induced memory reactivation during REM sleep on declarative memory stability. *Frontiers in Systems Neuroscience*, 8, 157. doi:10.3389/fnsys.2014.00157
- Cowan, N. (2008). What are the differences between long-term, short-term, and working memory? *Progress in Brain Research*, 169, 323-338. doi:10.1016/S0079-6123(07)00020-9
- Delorme, A., Makeig, S. (2004). EEGLAB: An open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of Neuroscience Methods*, 134(1), 1-108.
- Dement, W. C., Vaughan, C. C. (1999). The promise of sleep: A pioneer in sleep medicine explores the vital connection between health, happiness, and a good night sleep. New York: Delacorte Press.
- Dempsey, J. A., Veasey, S. C., Morgan, B. J., & O'Donnell, C. P. (2010). Pathophysiology of Sleep Apnea. Physiological Reviews, 90(1), 47–112. http://doi.org/10.1152/physrev.00043.2008
- Diekelmann, S., Born, J. (2010). The memory function of sleep. *Nature Reviews Neuroscience*, 11(2), 114-126. doi:10.1038/nrn2762
- Dijk, D. (1998). REM sleep as a gate to wakefulness during forced desynchrony in young and older people [Abstract]. *Sleep*, 21(3)
- Ekstrand, B. R., Sullivan, M. J., Parker, D. F., West, J. N. (1971). Spontaneous recovery and sleep. *Journal of Experimental Psychology*, 88(1), 142-144.

- Fischer, S., Drosopoulos, S., Tsen, J., Born, J. (2006). Implicit learning -- explicit knowing: A role for sleep in memory system interaction. *Journal of Cognitive Neuroscience*, 18(3), 311-319.
- Fowler, M. J., Sullivan, M. J., Ekstrand, B. R. (1973). Sleep and memory. *Science*, *179*(4070), 302-304.
- Fronczek, R., Raymann, R. J., Overeem, S., Romeijn, N., van Dijk, J. G., Lammers, G. J., Van Someren, E. J. (2008). Manipulation of skin temperature improves nocturnal sleep in narcolepsy. *Journal of Neurology, Neurosurgery, and Psychiatry*, 79(12), 1354-1357. doi:10.1136/jnnp.2008.143610
- Gais, S., & Born, J. (2004). Declarative memory consolidation: Mechanisms acting during human sleep. Learning & Memory, 11(6), 679–685. http://doi.org/10.1101/lm.80504
- Giuditta, A., Ambrosini, M. V., Montagnese, P., Mandile, P., Cotugno, M., Grassi Zucconi, G., Vescia, S. (1995). The sequential hypothesis of the function of sleep. *Behavioural Brain Research*, 69(1-2), 157-166.
- Goder, R., Scharffetter, F., Aldenhoff, J. B., Fritzer, G. (2007). Visual declarative memory is associated with non-rapid eye movement sleep and sleep cycles in patients with chronic non-restorative sleep. *Sleep Medicine*, 8(5), 503-508. doi:S1389-9457(06)00703-9
- Goel, N., Rao, H., Durmer, J. S., & Dinges, D. F. (2009). Neurocognitive Consequences of Sleep Deprivation. Seminars in Neurology, 29(4), 320–339. http://doi.org/10.1055/s-0029-1237117
- Goodenough, D. R., Sapan, J., Cohen, H., Portnoff, G., Shapiro, A. (1971). Some experiments concerning the effects of sleep on memory. *Psychophysiology*, 8(6), 749-762.
- Guilleminault, C., Dement, W. C. (1977). 235 cases of excessive daytime sleepiness. diagnosis and tentative classification. *Journal of the Neurological Sciences*, 31(1), 13-27.
- Hales, J. R., Jessen, C., Fawcett, A. A., King, R. B. (1985). Skin AVA and capillary dilatation and constriction induced by local skin heating. *European Journal of Physiology*, 404(3), 203-207.

- Hemingway, A., Rasmussen, T., Wikoff, H., Rasmussen, A. T. (1940). Effects of heating hypothalamus of dogs by diathermy. *Journal of Neurophysiology*, *3*(4), 329-338.
- Hoddes, E., Zarcone, V., Smythe, H., Phillips, R., Dement, W. C. (1973). Quantification of sleepiness: A new approach. *Psychophysiology*, *10*(4), 431-436. doi:10.1111/j.1469-8986.1973.tb00801.x
- Holz, J., Piosczyk, H., Feige, B., Spiegelhalder, K., Baglioni, C., Riemann, D., Nissen, C. (2012). EEG sigma and slow-wave activity during NREM sleep correlate with overnight declarative and procedural memory consolidation. *Journal of Sleep Research*, 21(6), 612-619. doi:10.1111/j.1365-2869.2012.01017.
- Iden, T., Horn, E. P., Bein, B., Bohm, R., Beese, J., Hocker, J. (2015). Intraoperative temperature monitoring with zero heat flux technology (3M SpotOn sensor) in comparison with sublingual and nasopharyngeal temperature: An observational study. *European Journal of Anaesthesiology*, 32(6), 387-391. doi:10.1097/EJA.0000000000000232
- Jenkins, J. G., Dallenbach, K. M. (1924). Obliviscence during sleep and waking. *The American Journal of Psychology*, *35*, 605-612. doi:10.2307/1414040
- Jennings, J. R., Reynolds, C. F., 3rd, Bryant, D. S., Berman, S. R., Buysse, D. J., Dahl, R. E., . . . Monk, T. H. (1993). Peripheral thermal responsivity to facial cooling during sleep. *Psychophysiology*, 30(4), 374-382.
- Kellogg, D. L., Jr. (2006). In vivo mechanisms of cutaneous vasodilation and vasoconstriction in humans during thermoregulatory challenges. *Journal of Applied Physiology (Bethesda, Md.: 1985)*, 100(5), 1709-1718. doi:100/5/1709
- Khoury, S., Chouchou, F., Amzica, F., Giguere, J. F., Denis, R., Rouleau, G. A., Lavigne, G. J. (2013). Rapid EEG activity during sleep dominates in mild traumatic brain injury patients with acute pain. *Journal of Neurotrauma*, 30(8), 633-641. doi:10.1089/neu.2012.2519
- Koehler, K. R. (1996).

 Body temperature regulation. University of Cincinnati Raymond Walters College.
- Krauchi, K. (2002). How is the circadian rhythm of core body temperature regulated? Clinical Autonomic Research: Official Journal of the Clinical Autonomic Research Society, 12(3), 147-149.

- Kushida, C. A., Bergmann, B. M., Rechtschaffen, A. (1989). Sleep deprivation in the rat: IV. paradoxical sleep deprivation. *Sleep*, *12*(1), 22-30.
- Ma, N., Dinges, D. F., Basner, M., & Rao, H. (2015). How Acute Total Sleep Loss Affects the Attending Brain: A Meta-Analysis of Neuroimaging Studies. Sleep, 38(2), 233–240. http://doi.org/10.5665/sleep.4404
- Magoun, H. W., Harrison, F., Brobeck, J. R., Ranson, S. W. (1938). Activation of heat loss mechanisms by local heating of the brain. *Journal of Neurophysiology*, 1(2), 101-114.
- Mantua, J., Mahan, K. M., Henry, O. S., Spencer, R. M. (2015). Altered sleep composition after traumatic brain injury does not affect declarative sleep-dependent memory consolidation. *Frontiers in Human Neuroscience*, *9*, 328. doi:10.3389/fnhum.2015.00328
- Marshall, L., Helgadottir, H., Molle, M., Born, J. (2006). Boosting slow oscillations during sleep potentiates memory. *Nature*, 444(7119), 610-613. doi:nature05278
- Marshall, L., & Born, J. (2007). The contribution of sleep to hippocampus-dependent memory consolidation. Trends in Cognitive Sciences, 11(10), 442-450. doi:S1364-6613(07)00212-4 [pii]
- Matthews, B. R. (2015). Memory dysfunction. *Continuum (Minneapolis, Minn.)*, 21(3 Behavioral Neurology and Neuropsychiatry), 613-626. doi:10.1212/01.CON.0000466656.59413.29
- McGaugh, J. L. (2000). Memory--a century of consolidation. *Science* 287(5451), 248-251. doi:8182
- Miller, G. A. (1956). The magical number seven plus or minus two: Some limits on our capacity for processing information. *Psychological Review*, 63(2), 81-97.
- Parmeggiani, P. L. (1987). Interaction between sleep and thermoregulation: An aspect of the control of behavioral states. *Sleep*, *10*(5), 426-435.
- Plihal, W., Born, J. (1997). Effects of early and late nocturnal sleep on declarative and procedural memory. *Journal of Cognitive Neuroscience*, *9*(4), 534-547. doi:10.1162/jocn.1997.9.4.534
- Rasch, B., Born, J. (2013). About sleep's role in memory. *Physiological Reviews*, 93(2), 681-766. doi:10.1152/physrev.00032.2012

- Raymann, R., Swaab, D., Van Someren, E. (2008). Skin deep: Enhanced sleep depth by cutaneous temperature manipulation. *Brain*, *131*(2), 500-513. doi:10.1093/brain/awm315
- Sagot, J. C., Amoros, C., Candas, V., Libert, J. P. (1987). Sweating responses and body temperatures during nocturnal sleep in humans. *The American Journal of Physiology*, 252(3 Pt 2), R462-70.
- Silber, M. H., Ancoli-Israel, S., Bonnet, M. H., Chokroverty, S., Grigg-Damberger, M. M., Hirshkowitz, M., . . . Iber, C. (2007). The visual scoring of sleep in adults. *Journal of Clinical Sleep Medicine*, 3(2), 121-131.
- Smith, C. (2001). Sleep states and memory processes in humans: Procedural versus declarative memory systems. *Sleep Medicine Reviews*, *5*(6), 491-506. doi:S1087-0792(01)90164-9
- Szymusiak, R., Satinoff, E., Schallert, T., Whishaw, I. Q. (1980). Brief skin temperature changes towards thermoneutrality trigger REM sleep in rats. *Physiology Behavior*, 25(2), 305-311.
- Tikuisis, P., Ducharme, M. B. (1996). The effect of postural changes on body temperatures and heat balance. *European Journal of Applied Physiology and Occupational Physiology*, 72(5-6), 451-459.
- Tilley, A. J., Empson, J. A. C. (1978). REM sleep and memory consolidation. *Biological Psychology*, 6(4), 293-300. doi:http://dx.doi.org/10.1016/0301-0511(78)90031-5
- Toki, S., Okamoto, Y., Onoda, K., Matsumoto, T., Yoshimura, S., Kunisato, Y., . . . Yamawaki, S. (2014). Hippocampal activation during associative encoding of word pairs and its relation to symptomatic improvement in depression: A functional and volumetric MRI study. *Journal of Affective Disorders*, 152-154, 462-467. doi:10.1016/j.jad.2013.07.021
- Van Someren, E. J. W. (2004). Sleep propensity is modulated by circadian and behavior-induced changes in cutaneous temperature. *Journal of Thermal Biology*, 29(7–8), 437-444. doi:http://dx.doi.org/10.1016/j.jtherbio.2004.08.003
- Vuksanovic, V., Sheppard, L. W., Stefanovska, A. (2008). Nonlinear relationship between level of blood flow and skin temperature for different dynamics of temperature change. *Biophysical Journal*, *94*(10), L78-80. doi:10.1529/biophysj.107.127860

- Wagner, U., Hallschmid, M., Verleger, R., Born, J. (2003). Signs of REM sleep dependent enhancement of implicit face memory: A repetition priming study. *Biological Psychology*, 62(3), 197-210. doi:S0301051102001254
- Wilson, J. K., Baran, B., Pace-Schott, E. F., Ivry, R. B., Spencer, R. M. (2012). Sleep modulates word-pair learning but not motor sequence learning in healthy older adults. *Neurobiology of Aging*, *33*(5), 991-1000. doi:10.1016/j.neurobiologing.2011.06.029
- Yaroush, R., Sullivan, M. J., Ekstrand, B. R. (1971). Effect of sleep on memory. II. differential effect of the first and second half of the night. *Journal of Experimental Psychology*, 88(3), 361-366.
- Zhuang, J., Zhan, Y., Zhang, F., Tang, Z., Wang, J., Sun, Y., ... Yu, J. (2016). Self-reported insomnia and coronary heart disease in the elderly. Clinical and Experimental Hypertension (New York, N.Y.: 1993), 38(1), 51-55. doi:10.3109/10641963.2015.1060983
- Zygierewicz, J., Malinowska, U., Suffczynski, P., Piotrowski, T., & Durka, P. J. (2009). Event-related desynchronization and synchronization in evoked K-complexes. Acta Neurobiologiae Experimentalis, 69(2), 254-261. doi:6926