The Role of Sleep Spindles and Theta Rhythms in Associative Memory Consolidation of Healthy Young Adults

Thesis by

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Introduction:

Memory consolidation refers to the brain's ability to store experiences and information into long-term memory. As research continues to expand upon this process, we have learned that memory consolidation has been linked intrinsically to sleep quality and quantity[13]. The precise mechanisms behind memory consolidation during sleep are complex and under expanding research. Specific brain patterns called sleep spindles, a unique EEG wave of stage 2 NREM sleep, have sparked interest for their role in learning and memory. Initial research studies have demonstrated sleep spindles during NREM sleep, along with theta rhythm EEG, to have essential roles in memory consolidation[6]. A fascinating area of research in sleep spindles relates to their role in memory consolidation and learning. This study aims to investigate the correlation between sleep spindle quantity in young adults and performance on an associative memory task.

Newer research has identified abnormal sleep spindles in neuropsychiatric disorders such as schizophrenia and autism spectrum disorder[10]. Abnormal sleep spindles have also been linked to neurodegenerative disorders correlated with age such as Alzheimer's disease and Parkinson's disease. However, a lack of abundant research on these brain patterns exists in the healthy young adult[12]. Examining sleep spindles and theta activity and linking their density to performance on a memory paradigm will provide insight into memory consolidation during sleep of young adults.

To understand the role of NREM sleep spindles, REM theta rhythms, and their role in memory for healthy young adults, this experiment performed in the Wheeler Lab will use a portable sleep EEG device to measure brain waves of college students and young adults ages 18-25 years old. Data analysis will be performed to examine whether links between sleep spindle density, REM sleep theta activity, and accuracy and reaction time on the memory task exist.

Understanding markers of memory consolidation during sleep in a healthy population will provide a basis to compare abnormal sleep spindles and theta activity to in medical studies. With this information, treatments can be targeted when abnormal brain pattern activity during sleep is identified in younger adults, and the progression of cognitive deficits and disease can be prevented.

Literature Review:

During sleep, the presence of certain brain waves varies depending on the sleep stage. Amongst these different oscillations, sleep spindles are characterized in the 11-16 Hertz frequency range and are markers of NREM 2 sleep[16]. Spindle generation lies in the thalamocortical network and occurs due to reverberating excitatory and inhibitory activity in the thalamocortical loop compromised of the thalamus, thalamic reticular nuclei, and neocortex[16].

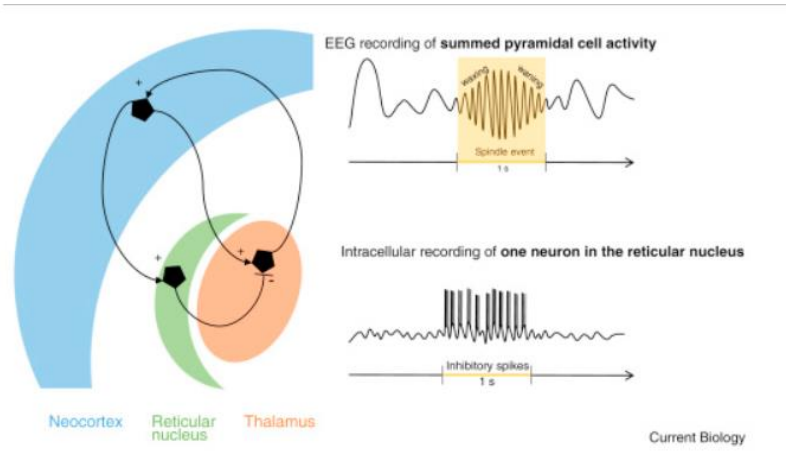


Figure 1 Spindle generation in the thalamocortical network.

Image Citation : Figure 1 (Schönauer, M., & Pöhlchen, D).

There is a consensus amongst researchers that sleep spindles play a crucial role in memory consolidation, although the exact mechanisms behind their contribution to memory are a relatively novel area. One type of memory is associative memory, which refers to the ability to

form relationships between unrelated items and can be episodic in nature. In these episodic memories, the hippocampus aids in constructing associations while it receives inputs from medial temporal areas repetitively[11]. There is evidence to suggest that during sleep, not only does memory consolidation occur but also the formation of associative schemata, particularly by the integration of new memories into neocortical networks through synchronized activity of slow wave sleep and sleep spindles[4].

This slow wave sleep during NREM sleep, along with REM sleep, play different roles in memory consolidation. Thalamocortical spindles are associated with long-term storage of memory representations as both human and rat studies display an increase in spindle density during NREM sleep after learning declarative tasks. Following NREM sleep, theta rhythms during REM sleep have extensively shown memory-consolidation effects[13].These theta rhythms propagate from the nuclei of the thalamus, particularly the anterior thalamic nuclei, and are linked to episodic memory formation[6]. As the thalamus also plays an essential role in the thalamocortical loop during sleep spindle generation, decades of research display the pivotal role of the thalamus in sleep spindles during NREM sleep and in theta oscillations during REM sleep, all contributing to memory consolidation.

Furthermore, another factor to consider regarding sleep spindles are how they change with aging. Sleep spindle density has been shown to decline with age, likely due to the known reduction in thalamocortical connectivity[14]. A study done on adults aged 50-91 years old demonstrated higher spindle density predicted better performance on declarative verbal memory, working memory, and verbal fluency [8]. Research subjects under forty have been shown to have an increase in fast spindle density during the night[14]. A matter of interest is that sleep spindle density is shown to peak around age twenty. However, there is a lack of sufficient research on

the density and architecture of sleep spindles in young adults. This research study aims to provide more insight into sleep spindle characteristics in healthy young adults.

Deficits in sleep spindles have been associated with psychiatric disorders and neurodegenerative disorders such as Alzheimer's and Parkinson's diseases. For example, impairments in sleep dependent memory consolidation related to spindle density have been linked to the cognitive deficits seen in schizophrenia [10]. Neurophysiological models of schizophrenia show abnormalities in thalamic reticular nuclei, the same ones needed for sleep spindle formation. This suggests thalamocortical hyperconnectivity from reduced inhibition of thalamocortical neurons. For neurodegenerative disorders such as Alzheimer's disease, the characteristic tau tangles have been linked to reduced spindle density during N2 sleep and may possibly explain why tau worsens memory consolidation [7]. As Alzheimer's disease is highly age-dependent, understanding the mechanism in which sleep spindles change as humans age and the identification of sleep spindle deficits in an aging population can serve as a marker for identifying the early stages of cognitive memory decline. In Parkinson's disease, reduced sleep spindle density and amplitude was found in those patients in the early stages of the disease who went on develop to dementia versus those who did not in a longitudinal study and suggest spindle density reduction as a dementia marker [9].

Recognizing the vital role of sleep spindles in both the healthy brain and disorder-affected brain, future research lies in therapeutic interventions for restoring and stimulating sleep spindles and slow wave sleep. These interventions can lie in pharmacological treatments or the use of neurotechnology. For example, pharmacological treatments such as eszopiclone have been shown to increase spindle density, but with no positive effect on memory. This is likely due to the decrease in hippocampal ripple power[10]. Neurotechnology such as wearable EEG has been

able to induce slow wave sleep oscillations using auditory stimulation, however these stimulations are a novel area and have potential for future studies[3]. Therefore, evaluating different sleep medications and neurotechnology can provide a greater understanding of their effects on sleep spindles and memory.

The existing literature points to various future areas of research regarding sleep spindles, and it also reveals a need for more information on sleep spindles in young adults. This proposed study aims to provide insight into understanding sleep spindles in healthy young adults ages 18-25 years old and their role in memory consolidation. With this information, future studies can further evaluate sleep spindles as a marker for cognitive decline and neurodegeneration in the aging brain. Having a greater understanding of what occurs in healthy young adults will set a basis for detection of abnormal sleep spindle activity in young adults showing symptoms of psychiatric and neurologic disorders.

Methodology

Participants

The study will recruit healthy adults aged 18-25 years old. Participants will be recruited from the Georgia Tech SONA participant database after obtaining Institutional Review Board approval. All participants will undergo a phone pre-screening to determine eligibility based off their age and any potential neurological, psychiatric, sleep disorders, or medical exclusions that would prevent them for participating in the study. Upon arrival, participants will be informed of any benefits and risks of the study and be asked to sign an informed consent document provided to them. Compensation for the study will include one SONA credit per hour. All participants and

research personnel will follow COVID-19 laboratory research guidelines mandated such as wearing masks and pre- and post-experiment lab sanitation.

Task& Procedure

To collect sleep and EEG data, the wearable EEG Dreem 2 headband will be used. The device is equipped with EEG sensors, a pulse sensor, and an accelerometer. The benefit of using a wearable EEG device in comparison to traditional EEG methods is that it allows the researcher to examine habitual sleep over an extended period rather than a single night in a sleep lab.

On the initial visit to the lab, the participant will complete the memory task which presents images and words on a computer screen. Participants will be given practice utilizing a memory encoding strategy and will be asked to utilize this strategy to remember as many of the word-picture pairs as possible. After the memory encoding session is complete, participants will be instructed on how to wear the EEG device properly. Cognitive tests will be administered to assess normal cognitive abilities, while sleep-related questionnaire will measure perceptions of their sleep quality. The full cognitive battery includes the Digit Span test, Mini Mental Status Examination, Weschler Adult Intelligence Scale Visual Puzzles, Weschler Adult Intelligence Scale Visual Similarities and Puzzles, Pittsburgh Sleep Quality Index, Big Five Personality Index, Insomnia Severity Index, and the Morningness Questionnaire. Participants will then complete an immediate memory recall test, and upon completion, will be given a sleep log to record sleep and wake times for a period of three days. The initial session will take approximately ninety minutes.

The participant will return to the lab after a period of week and will complete the same delayed memory recall task presented the week before. The headband will be retrieved along with the sleep log.

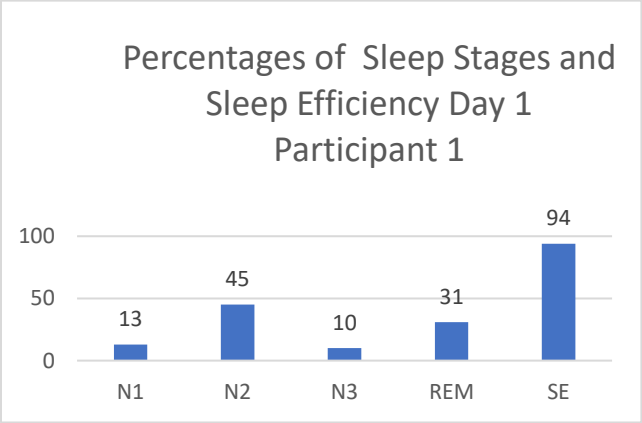
Data Analysis

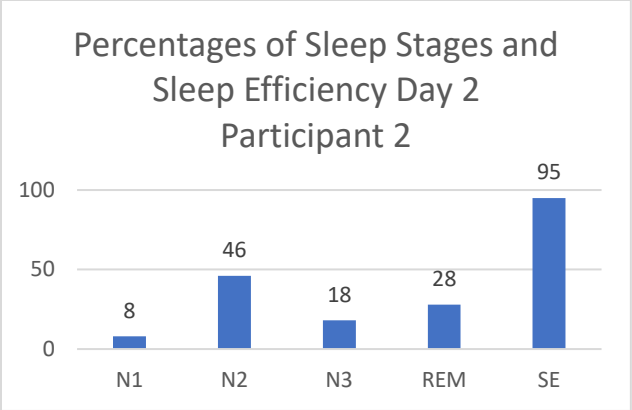
The EEG data will be assessed using the software present in the Dreem 2 EEG device and the *LunaR* signal processing computer program and system for researchers. The memory paradigm uses *PsychoPy* experiment design software. Accuracy and reaction time on the memory task will be analyzed using ANOVA statistical tests.

Results

The study is currently collecting data from participants. However, preliminary data from the first participant can be seen below.

Data obtained from the Dreem2device revealed that on Day 1 of the study is shown in the figures below.





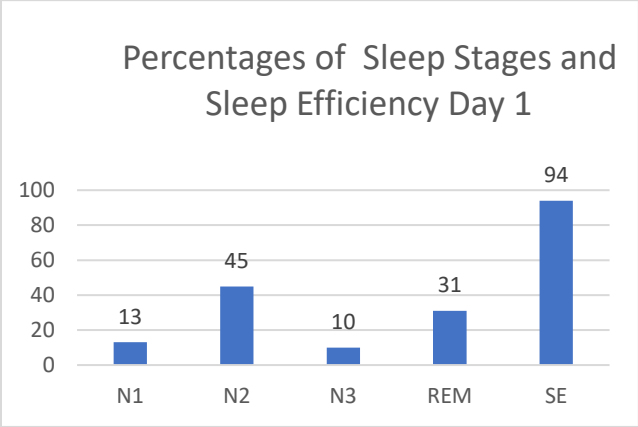


Figure 2: Data from Participant 1 Days 1-3 using Dreem2 overnight.

Discussion

The discussion will be completed after more results have been obtained and analyzed.

Future Directions

Future directions will include studies expanding the range of ages examined to an older group (65-80 years old) due to sleep spindle architecture and density changing as one ages. Understanding sleep spindles in a young adult population as this study intends to help scientists have a marker for identifying abnormal sleep architecture in aging populations that can be a sign of developing neurological disease.

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