

Enhancing memory consolidation with targeted reactivation during sleep

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Introduction

Our short-term newly acquired memories get stabilized into long-term ones through the process of memory consolidation. As our memories are not static, constant memory storage update is needed. This depends on the spontaneous and random memory reactivation of previously learned content during wakefulness and sleep. However, sleep-dependent preferential consolidation is crucial for systems and procedural memory stabilization specifically during Slow Wave Sleep or stage N3 of NREM sleep. It has been recently shown that such consolidation can be artificially enhanced using the method of TMR: Targeted Memory Reactivation. This technique can affect the selectivity of memory storage using auditory cues associated with learning. It reactivates relevant neural representations utilized in learning, that are reflected by certain hippocampal firing patterns. This project aims to further explore and create a DIY replica of the research conducted by James W. Antony, Ken Norman, and Ken Paller from Princeton and Northwestern Universities on this matter. Is it that we remember better or forget less?

Result: SWS can be detected in real time EEG due to the presence of Delta waves and sleep spindles

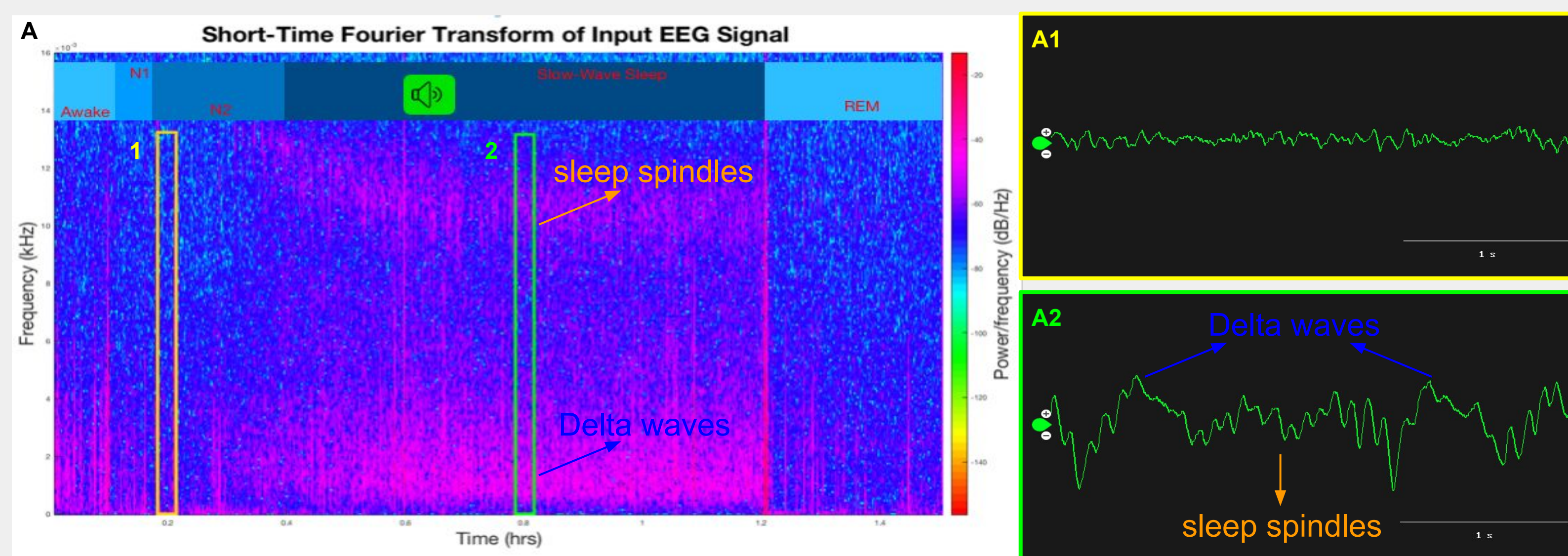


Figure 4: Spectrogram of EEG recording taken from one subject

Result: Cued sounds during SWS showed better recall after sleep than uncued sounds

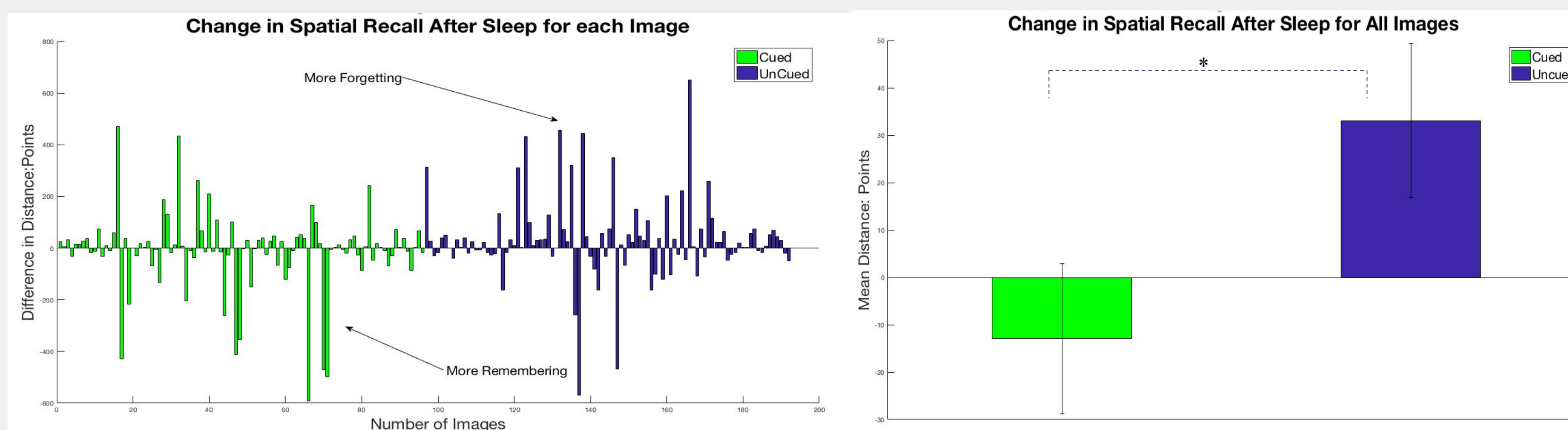


Figure 5: Better recall for cued images (-12.95 points +/- 15.80 SE) compared to uncued images (33.09 points +/- 16.26 SE), using two-sample independent t-test (p = 0.04)

Discussion

The DIY version of Targeted Memory Reactivation (TMR) technique could potentially enhance memory consolidation during SWS and have suitable applications in learning and teaching in the future. It can be seen that TMR can effectively bias spatial associative memory consolidation, by altering the level of forgetness, more than providing pure gain of remembering cued images better. Our project would still need to be tested on more subjects for accurate significance conclusions. Control experiments involving cueing with no sleep were conducted on two subjects. Instead of a 90 minute nap, subjects performed a continuous reaction game. Results show the same trend of the experiment. However, forgetness levels were slightly higher (p<0.05). Since it was conducted on only 2 subjects, this could still indicate the importance of SWS in the consolidation process. Sleep does provide a finite time window for memory processing and storage.

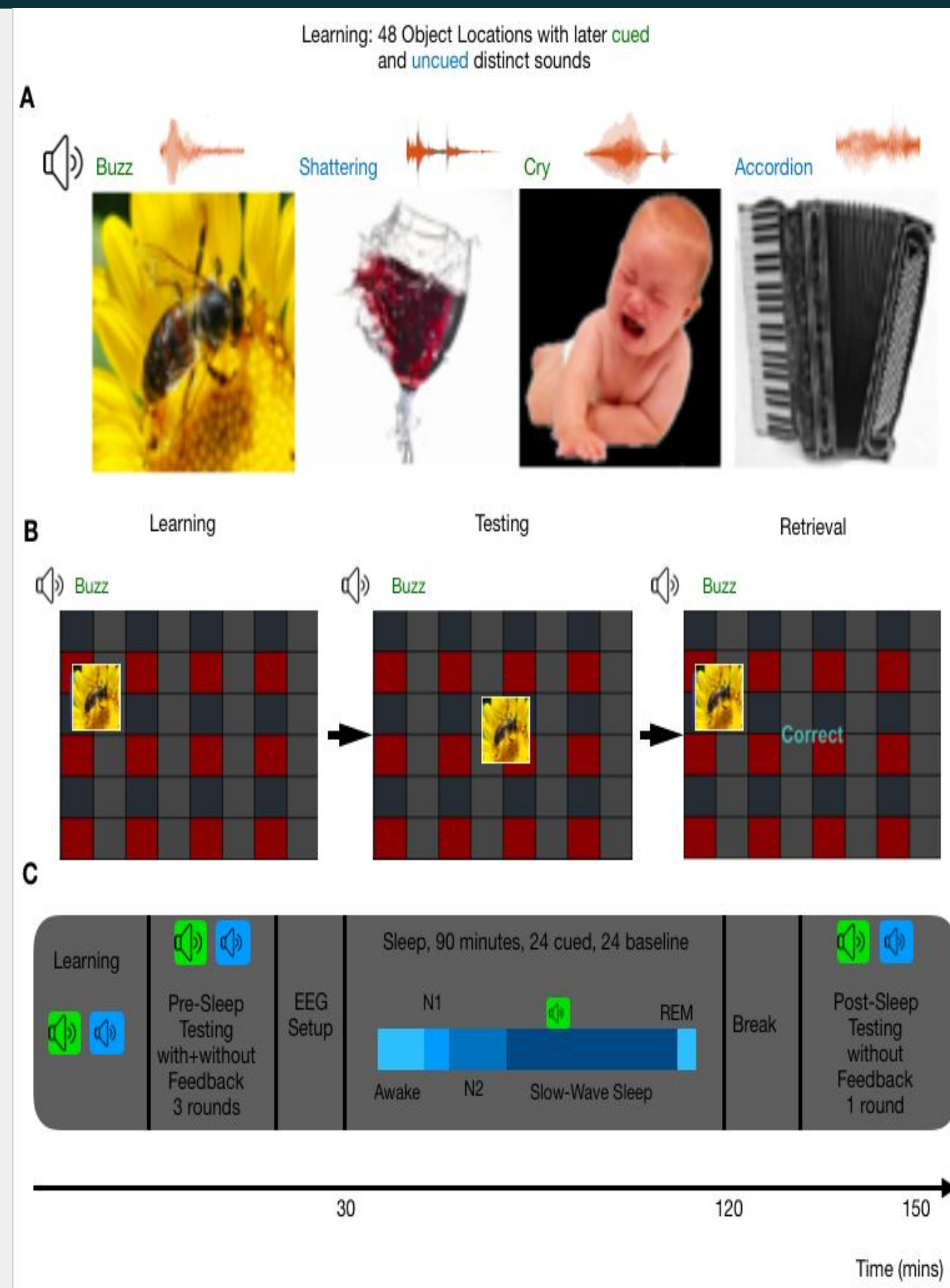
Future work would be focusing on detecting SWS and cueing sounds automatically during sleep using machine learning. This would allow this DIY project to be fully functional, where people can have their own "mini sleep lab", and be able to experiment with different parameters of TMR. Will cueing sounds at different sleep stages still have an effect? Would repetition or multiple cueing provide better enhancement? TMR could be used to help PTSD patients overcome traumatic memories, or provide more insight into Alzheimer's research!

Methods

Figure 1: (A) TMR iOS application. Images with their distinct sounds in learning phase appear in random locations on the screen for 3000ms, 1000ms blank interval inbetween. Subjects memorize positions.

(B) Subjects perform 2 rounds of testing phase before sleep with feedback (correct vs. incorrect). Correct/Incorrect determined by comparing the distance in points (between where the user clicks and original location of the image using distance formula) to a 15% of screen width set threshold. Round 3 of testing phase is with no feedback. Pre-sleep test results are taken from it.

(C) Subjects sleep for around 90 minutes. 48 sounds play during SWS, 24 are cued or targeted, in which the subject heard during performing the memory task. The other 24 are uncued or baseline sounds, in which the subject never listened to before. Each sound is 200-500ms in duration. White noise played during sleep. Simulation once, 1 sound every 5 seconds. Subjects perform post-sleep task after waking up.



Subject	Treatment	Age	Sleep Duration (hrs)	SWS Duration (mins)	SWS Observation
3	Sleep + Cueing	30	1:41:42	36 - 48	Continuous Delta waves and sleep spindles
4	Sleep + Cueing	28	1:20:07	36-72	Continuous Delta waves and sleep spindles
8	Sleep + Cueing	20	1:42:15	18-66	Continuous Delta waves and sleep spindles
14	Sleep + Cueing	19	1:47:20	60-102	Continuous Delta waves and sleep spindles 2 rounds of cueing tried. No significance difference
6	Sleep+HeardCues	55	1:31:49	36-72	36-42: Delta waves present but no sleep spindles after cueing ended 45-60: Sleep spindles present but no Delta waves 62-72: Both Delta waves and sleep spindles present but not strong
11	Sleep+Disqualified	35	1:34:37	60-84	Unclear Delta waves and sleep spindles Segmented Cues played at very early SWS start Subject does not remember hearing cues
12	Sleep+Disqualified	22	1:30:22	30-72	Radio Shack speaker used to deliver cues picked up radio station signal Continuous sounds played during SWS, interfering with TMR cueing Session was conducted at a different location, with more surrounding noise
13	Sleep+Disqualified	31	1:33:02	24-66	42-48: Delta waves present but no sleep spindles during cueing Then continuous Delta waves and sleep spindles Subject does not remember hearing cues
5	Could not sleep	28	36:50:00	NA	NA
7	Could not sleep	19	19:10	NA	NA
9	Could not sleep	22	1:23:15	NA	NA
10	Could not sleep	16	1:08:29	NA	NA

Figure 6: Full database of all subject participants in this research

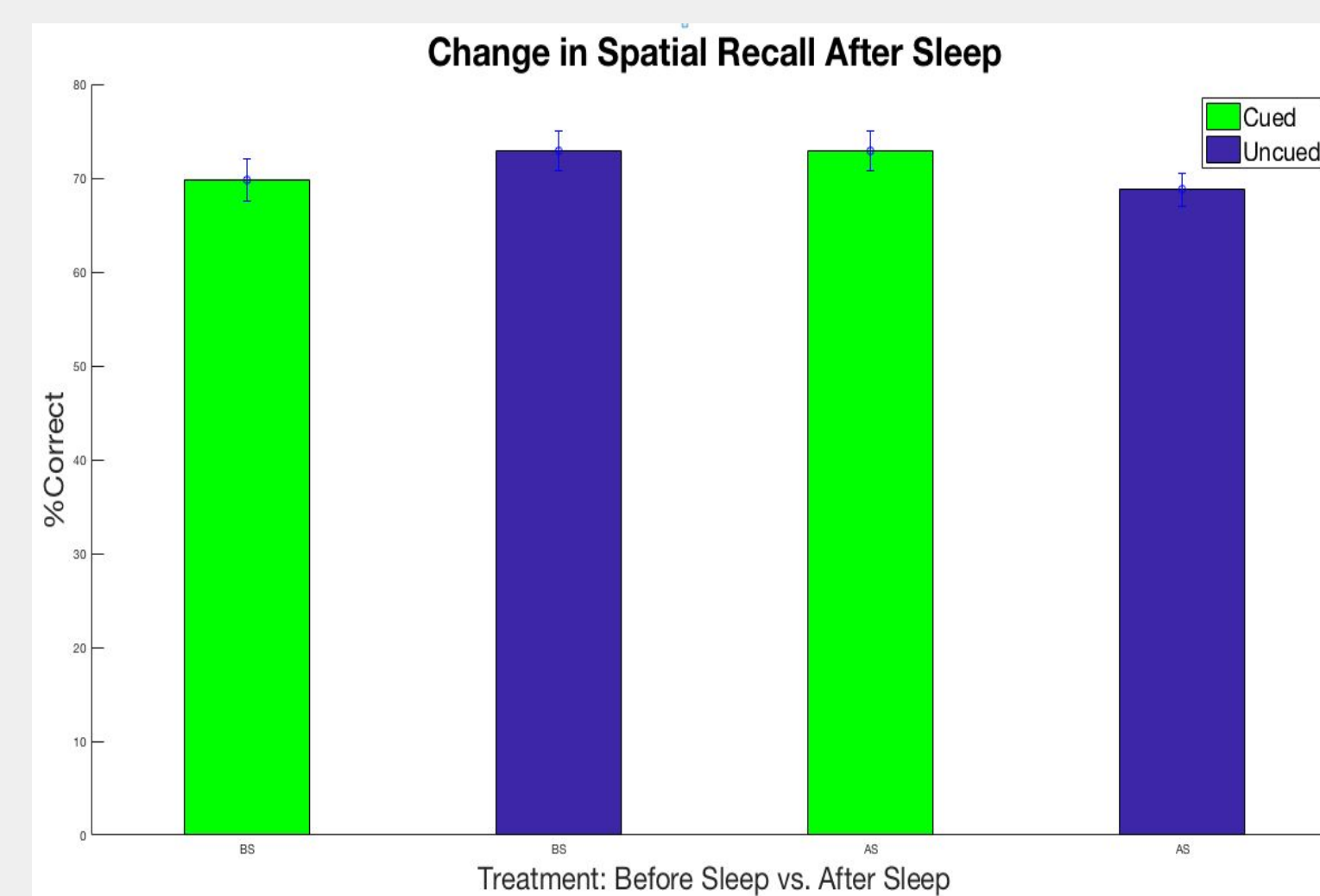


Figure 7: Improvement in performance on the memory test for cued images. Decline in performance for uncued images

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References

Antony, J. W., E. W. Gobel, JK O'Hare, P. J. Reber, and K. A. Paller. 2012. *Cued memory reactivation during sleep influences skill learning*. Vol. 15. Oudiette, D., J. W. Antony, J. D. Greery, and K. A. Paller. 2013. *The role of memory reactivation during wakefulness and sleep in determining which memories endure*. Vol. 33. Oudiette, Delphine, James W. Antony, and Ken A. Paller. 2014. *Spotlight: Fear not: Manipulating sleep might help you forget*. *Trends in Cognitive Sciences* 18 : 3-4. Rudoy, John D., Joel L. Voss, Carmen E. Westerberg, and Ken A. Paller. 2009. *Strengthening individual memories by reactivating them during sleep*. *Science*(5956): 1079.

Setup

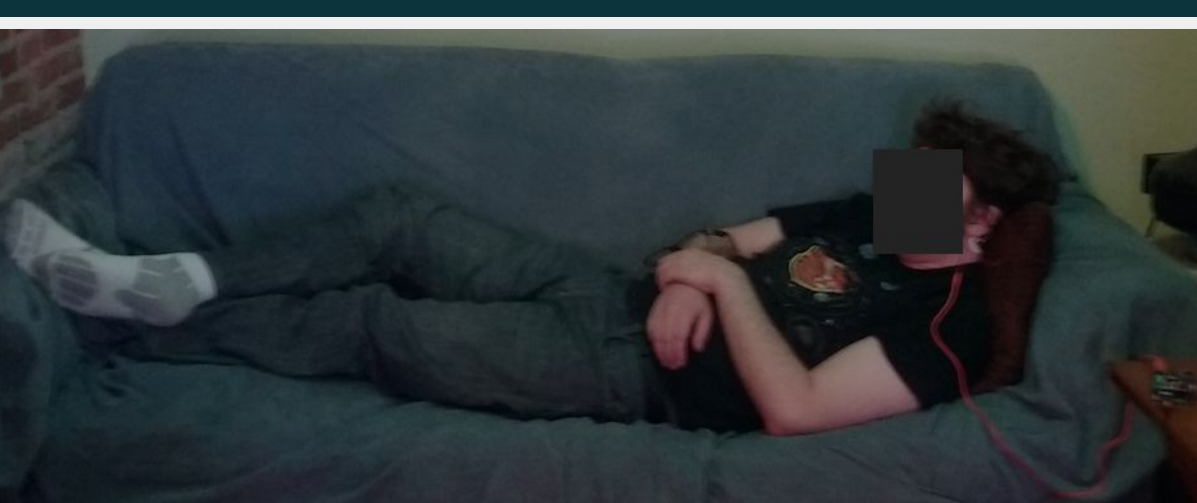


Figure 2: Heart and Brain SpikerShield connected to a computer for EEG real time detection using SpikeRecorder software.

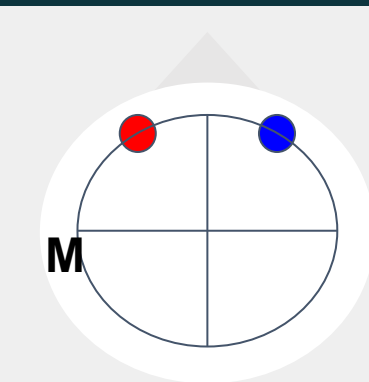


Figure 3: Blue: Active Electrode, Red: Ground, M: Reference Electrode