Can We Manipulate Sleep Spindles? *

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Faulty memory consolidation during sleep might be a contributing factor to age-related memory decline. The timing between two electrical brain activities, slow oscillations (SO), and sleep spindles is thought to be important in this process. Studies have shown that precisely timed sound stimulation presented during SO up-states can enhance SO amplitude, which improves participants' memory consolidation. However, it is not known if sound can influence the amplitude of sleep spindles synchronized to SO and if the effect differs when the sound is presented at different spindle phases. In this within-subjects design, 4 young adults received sound stimulation during sleep timed to hit peaks of SO. A trend emerged from the preliminary results of a possible influence of sound on sleep spindles' amplitude, with an effect that differed by the sleep spindles' phase divisions. If sleep spindles can be manipulated and possibly enhanced, like SO, their timing can possibly be influenced, providing a new method to improve deteriorating memory processes.

Memory deteriorates with normal and pathological aging, which is evident in those with mild cognitive impairment and Alzheimer's Disease [1,2]. Stimulation techniques might be used to influence memory processes that are decaying during normal aging such as encoding, consolidation, and retrieval [3]. During the encoding of a memory, neurons of brain areas that are relevant for a task are active. Pavlides and Winson have found a similar re-activation of brain areas during sleep to the ones involved in the encoding of the memory [4]. The process of re-activation is thought to be critical in consolidating newly encoded experiences from short- term to long-term storage [5]. Particularly, sleep is important in the consolidation of memories and patterns of neuronal activation are thought to contribute to age-related memory decline [1]. Thus, stimulation of these neuronal activities might be part of the solution to lessen the effects of memory deterioration.

Sleep is divided into two categories: non-rapid eye movement sleep (NREM) and rapid eye-movement sleep (REM). The NREM sleep is predominant in the beginning of the night and can be further subdivided into three stages, while REM represents a single stage, predominate in the latter half of the night [3]. In sleep research an electroencephalogram (EEG) measures electrical brain activity in frequencies, an electromyogram (EMG) measures muscular activity, and an electrooculogram (EOG) measures eye movement throughout the night [6]. Each sleep stage is defined by the outputs of these three devices and is characterized by different electrical rhythms, representing communications between populations of neurons. The first stage of NREM sleep can be described as light sleep. The second and third stages of the NREM sleep are of particular interest to the memory consolidation process [7]. During these stages, electrical activity sleep bursts of 11-16Hz, named sleep spindles, occur. Additionally, slower waves with a frequency of 0.5-1.5 Hz, named slow oscillations (SO) are also present [3]. NREM 2 is characterized by a higher proportion of sleep spindles, whereas during NREM 3 there is a higher SO occurrence [3, 5]. SO and sleep spindles have separate, but related roles in the sleep-dependent memory consolidation. SO originate in the neocortex through the hyperpolarization and depolarization of populations of neurons and they

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are thought to synchronize neuronal activity such as sleep spindles [8]. The process of sleep spindle generation in the reticular nucleus of the thalamus seems to be driven by depolarized neurons being close to their firing threshold and the synchronicity of their firing. Researchers propose that once generated, spindles re-instate newly formed memories, by the modulation of neocortical activity through cortico-thalamic loops [9, 10]. Specifically, these oscillations would modulate the re-activation of neurons initially active during the encoding of the memory. In addition to the individual roles of SO and sleep spindles in memory consolidation, it appears that their interaction is essential as well [11].

Sleep spindles and SO interact by being precisely timed, meaning that they can work in synchrony and the timing between them influences sleep dependent memory consolidation [1, 11, 12]. Mikutta and colleagues found that participants with a higher number of sleep spindles coupled to the SO up-states during sleep (i.e., rising phase of the wave) performed better on the morning recall of a learning task completed the night prior, compared to participants with fewer sleep spindles coupled to the up-states of SO [11]. Therefore, the optimal timing between the two waves for memory consolidation seems to be the coupling of a sleep spindle to the up-state of a SO [10, 13-15]. The optimal coupling phase is also apparent from studies with older participants who displayed a delayed coupling related to decreased retention scores [1]. A possible solution to improve memory consolidation processes in older adults is to influence sleep spindles and SO, and to repair the delayed coupling between them.

An intervention that influences SO and possibly sleep spindles is sound stimulation [13]. Sound stimulation is a common technique used in sleep research as it is a non-invasive tool and auditory information continues to be processed through cortical pathways during sleep [16-18]. Different techniques such as open-loop (OLAS) and closed-loop auditory stimulation (CLAS) can be used to send an auditory stimulus during the occurrence of specific brain waves. The former delivers a sound at a time that is pre-programmed and independent of brain activity whereas the latter sends the sound when a specific brain activity is detected. CLAS targeting SO independent from spindles has been successfully done. Ngo and colleagues [13] found that CLAS sent during the up-state of SO enhanced the SO rhythm, the coupling proportion between spindles and SO, and memory recall, in comparison to a random stimulation condition. Therefore, it appears the up-state phase of SO is a successful target for sound stimulation of memory consolidation. In contrast, sending sounds during sleep spindles occurring in the up-states of SO, using a mix of CLAS and OLAS was unsuccessful in improving memory recall [18]. One explanation is that the sound stimulus was not timed to the endogenous activity of the spindle. The phase of spindles might be of importance to potentially influence their amplitude, such that during SO up-states the neuronal membranes are more depolarized and have a higher probability of firing. A similar property of sleep spindles' neuronal membranes may be expected, as well as a different effect of sound stimulation at various sleep spindle phases.

The aim of this study was to further the understanding of how spindles may be manipulated. Thus, auditory stimulation was presented during sleep spindles, through a mix of OLAS and CLAS. First, the general change in amplitude following spindle stimulation was investigated. A novel investigation in the field was pursued through our second goal, which was to determine whether the effect of sound differed based on the phase of the spindle to which the auditory stimulus was presented. It was hypothesized that the sound stimulus presented to a spindle in a SO up-state would influence the sleep spindles' amplitude. Additionally, if an effect of sound on sleep spindles was present it would differ based on the phase of the spindles during which the

sound was presented.

Method

Participants

Participants were recruited through word-of-mouth. The participants were not eligible if they had: cognitive and hearing impairments; sleep disorders; were pregnant or breastfeeding; had a history of cardiac, neurological, and psychiatric conditions in the past 12 months; or were using any sleep or wakefulness altering drugs, which affect spindle density [19]. Participants received a monetary compensation for their participation of $150. The research study received approval from Concordia's Ethical Research Board and all participants provided informed consent to take part in the experiment.

Measures

The participants were asked to fill in a sleep diary (adapted from Himmer and colleagues [20]), which measured total time in bed and roughly total time asleep (e.g., When did you go to bed?). Before the experiment, participants were asked to complete the Munich Chrono Type Questionnaire (MCTQ) which confirmed the participants' normal sleep patterns (a full night of sleep with no awakenings) and thus eligibility to the study [21]. An example of a question from the MCTQ is "On workdays I have to get up at [blank] o'clock", the participants were then asked to fill in the blank using short answers. The MCTQ's reliability cannot be determined as it is a scale, however, Di Milia and colleagues [22] have characterized the MCTQ's level of agreement with the Morningness-Eveningness Questionnaire (a questionnaire that assesses chronotype with a high level of reliability of 0.80) as satisfactory.

Apparatus

The Endpoint Connected Hilbert Transformation (ECHT) Box, which takes EEG measurements and outputs sounds, was used [23]. The EEG data was gathered using one recording electrode (forehead placement) and a reference electrode (mastoid bone placement). The sound stimulus (40ms pink noise) was presented binaurally at 55dB SPL through Etymotic ER-3C earphones with insert foam tips [24]. The sound level was decided based on previous similar literature [13,25]. The ECHT box was set to employ a CLAS of SO. The system was programmed to output two types of auditory stimulation: sound for 5 minutes and sham the next 5 minutes. The sound stimulation consisted of detection of sleep spindles and sound output. The sham condition comprised only the detection of sleep spindles for further analysis with no output of sound. The sleep spindles that received sound were compared to those that received sham, with a further analysis of the sleep spindles' phases to which the two conditions were presented.

Procedure

Following recruitment, the participants were briefed about the study. The equipment was later delivered to the participants' home address. Participants gave their written consent and were asked to fill out the sleep diary two days prior to the first experimental night and throughout the nights slept with the equipment. Furthermore, instructions and support for the setup of the apparatus and data collection were provided.

Participants were asked to use the equipment during a total of 5 nights. The duration of the

experiment was determined based on previous research [26]. During one night of sleep, an approximate 20% of sleep spindles were found to be coupled to the SO up-states [26]. Thus, in this study, to maximize the amount of sleep spindles that were stimulated, a 5 nights design was used. In total, 10 days were allocated for the completion of the experiment.

Before going to sleep the participants started a program on the laptop, which was set to present the sound stimulus 30 minutes after start, to allow the participants to fall asleep and enter the NREM 2 [23]. The recording was stopped by the participant in the morning after waking up and the sleep diary was then completed.

Data Collection

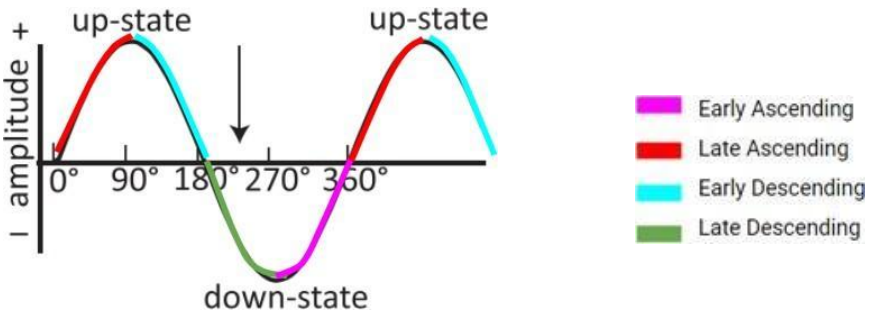
To target sleep spindles nesting in the SO up-states, a mix of OLAS and CLAS was run using a sound (55dB) and a sham (0dB) stimulus. The data acquisition was performed using a sampling rate of 500Hz. An intervention using both OLAS and CLAS was necessary to detect shorter durations than SO (i.e., sleep spindles) as CLAS does not operate fast enough to detect a spindle and send a sound stimulation during it (typically 0.5-3 seconds). The current study design consisted of first targeting the SO-upstates using CLAS by outputting an auditory stimulus fast enough to fall on the up-state of SO. Secondly, based on previous research it was expected that SO would coincide with sleep spindles [26,27]. As a result, only spindles indirectly targeted through stimulation of SO were considered in this study using OLAS.

Data Processing

Once the EEG data was collected, it was analyzed with Python Version 3.8.10 [28] using a custom script that outputted: the time points of auditory and sham stimulation, and raw EEG data. The data were then analyzed using a custom MATLAB script [29]. A filter of 0.1-40Hz was applied to the raw EEG data to filter out low and high frequencies and a customized algorithm of sleep spindle detection was applied [30]. Once the sleep spindles were detected, the oscillations forming the sleep spindle were considered as separate waves and subdivided into four different phase groups based on their electrical activity (named bins): early ascending (bin 1), late ascending (bin 2), early descending (bin 3), and late descending (bin 4). This division of sleep spindles by phases was based on a similar investigation done with SO by Batterink and colleagues [31]. The division of SO is shown in Figure 1 and similar phase categories of sleep spindles are shown in Figure 2 [31]. The EEG data were then fragmented into time windows, (i.e., epochs of 1000ms before the presentation of the sound stimulus and 1000ms after). As a result, each participant had epochs containing sleep spindles that have received sound or sham. A distinction between spindles' phases that have received sound and those that have received sham were made. Spindle amplitude post stimulation was used as a quantifying measure of the effect of sound on sleep spindles.

Figure 1

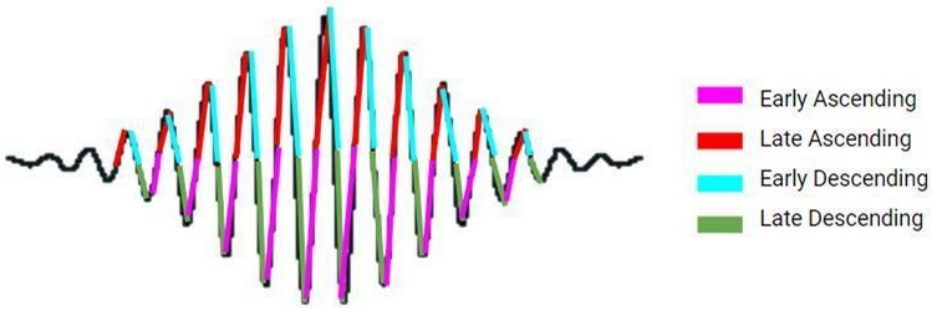
Division of a slow wave by its phases



Note. The figure depicts a SO separated in four parts based on its phases, shown in colour. The legend is provided for comparison with this project's division of sleep spindles. The arrow depicts the optimal phase to which the sound should be presented to participants. Y-axis: Amplitude of the wave; X-axis: Phase of the wave. Figure adapted from Batterink and colleagues (2016; see reference for any other information).

Figure 2

Division of a sleep spindle by its phases



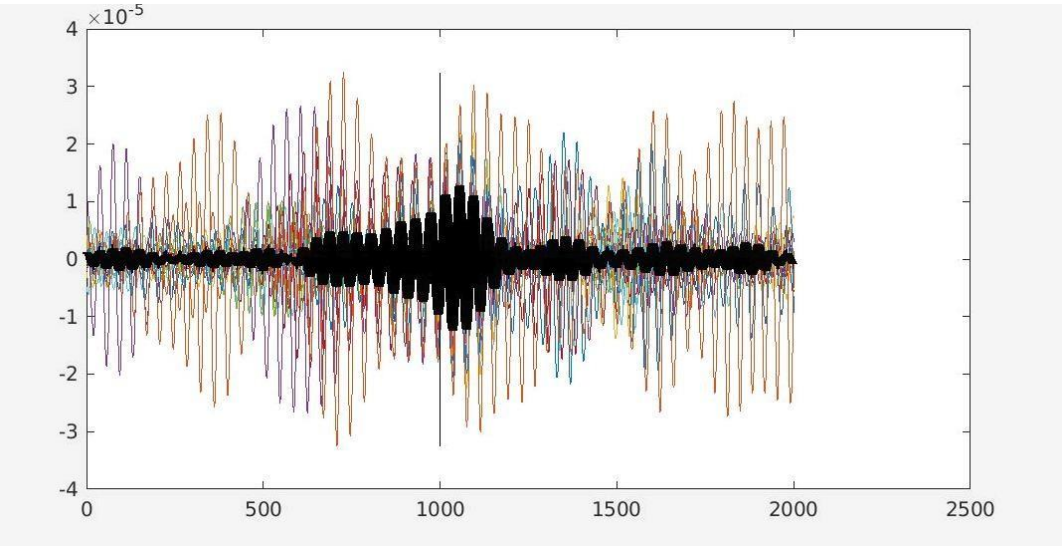
Note. The figure shows the proposed division of a sleep spindle into four phase parts, i.e. bins, which was done during the analysis. The time series for the research and control group, i.e. the phases of the sleep spindles when stimulation occurred and did not occur, will be averaged over time. Each bin is color-coded and assigned a descriptive name.

Data Analysis

The sleep spindles were visualized to determine the appropriate time windows for amplitude comparisons using R2018a MATLAB version [29]. As shown in Figure 3, the average activity of sleep spindles decreases within 1 sec after the presentation of the auditory stimulus. This time interval is adequate as sleep spindles are on average 1000-2000ms and there is approximately a maximum of half of the spindle left following stimulation [32]. The epochs considered in the analysis contain sleep spindles following the time of sound entry.

Figure 3

Average Sleep Spindle Signal in Bin 1 for 1 Night



Note. Visualization of sleep spindles pre and post stimulation from a sample participant and spindle bin. In color: sleep spindles in bin 1 during 1 night of participant 3. In black: average signal of the sleep spindles. X axis: datapoints; Y axis: Voltage (microVolts). Line at 1000 datapoints represents the sound stimulation. For reference 500 datapoints is 1 sec, thus it can be seen that the sleep spindle power decreases around 1 sec after sound stimulation.

Root Mean Square (RMS) values were used to quantify the sleep spindles' amplitude. The power of sleep spindles was considered through RMS values from the moment that the auditory stimulation was presented up to 1 second afterward. RMS values were compared between sound and sham conditions within this time interval. Global RMS averages (of all spindles) were computed in the two conditions to explore a possible effect of sound stimulation on sleep spindles. RMS averages for the four bins, in the sound and sham conditions, were used to look at how the effect might differ based on the phase of the sleep spindle to which the auditory stimulus was presented.

In the present study median values of the sleep spindles in both stimulation conditions were compared within each individual participant. The Mann-Whitney U test was employed and bootstrapped 95% Monte Carlo confidence intervals (CI) based on 10,000 samples were computed. The alpha level was specified at 0.05 and the hypotheses tested in both research questions were two-tailed. The effect size reported was Pearson's r and it was calculated by hand [33]. The effect sizes were interpreted as small at .1, medium at .3, and large at .5 and they were indicative of the proportion of variability between the two conditions accounted for by the sound stimulus [33, 34]. The negative values of the effect size are explained by the sound condition being subtracted from the sham condition in the statistics. Thus, a negative value indicates a higher median in the sound condition. It is important to note that statistical significance and effect sizes must be interpreted with caution considering the small sample size of the study.

Results

Demographics

The original sample of the current study was comprised of 5 individuals, however, following one drop out due to the participant's reported low quality of sleep, the final sample consisted of 4 individuals. The majority of the sample were males (75%) with an average age of 25 (*SD* = 1.70, range = 23-26 years).

Through communications during the experiment and the sleep diary, participants have reported having similar sleep quality and duration during the experiment compared to their usual sleep, with no awakenings caused by the sound stimulation. All the participants reported a normal sleep pattern throughout the experiment and no equipment malfunctions. In this study, participants slept an average of 6.75 hours and displayed a mean of 359.80 sleep spindles coupled to the SO upstates (*SD* = 167.80) for the total duration of the experiment were detected for each participant, which is consistent with a healthy sleep architecture observed in previous studies [26,27]. The results for each participant are presented separately, for both research questions.

Participant 1

The Effect of Sound on Sleep Spindles' Amplitude

A statistically significant difference was found between the sleep spindle amplitude (*Mdn* = 4.32e-6) in the sound stimulation condition and that of the sham stimulation condition (*Mdn*= 3.46e-6; *U* = 31029.00, $p < .001$, r = - 0.15, 95% CI [0.00; 4.77e-4]). This implies a higher median of sleep spindle amplitude in the sound condition than in the sham one (see Table 1). The negative small effect size is indicative of a small proportion of variability between the two conditions accounted for by the stimuli introduced in the sound condition.

Table 1

Results of Mann Whitney U Test for Stimulation Condition on Sleep Spindle Amplitude

RMS Global	*U*	*p*	Pearson's *r*	95% CI	
				Lower	Upper
Participant 1	31029.00	<.001**	*-0.15*	0	4.77e-4
Participant 2	15610.00	.27	*-0.06*	.26	.28
Participant 3	17043.00	.43	*-0.04*	.42	.44
Participant 4	2364.00	.55	*-0.05*	.54	.56

Note. RMS Global = all of the RMS values in both stimulation conditions (sound and sham); CI = confidence interval.
**p<.05, **p<.001.*

The Effect of Sound on Sleep Spindles' Amplitude Based on Phase Divisions

To further explore if the phase of the sleep spindles which the sound was presented exhibited

a different effect on the sleep spindles' amplitude, the phase categories "bins" were compared in the sound and sham condition (see Table 2). The comparison between sound (*Mdn* = 4.37e-6) and sham (*Mdn* = 3.14e-6) stimulations presented to bin 3 resulted in a statistically significant difference between the medians of the 2 groups (*U* = 3662.50, *p* < .001, *r* = -0.25, 95% CI [1.82e-4; 0.001]). It can be concluded that the sleep spindle amplitude in the sound condition was higher than that of the sham condition. The effect size indicates a medium proportion of this difference to be explained by the introduced sound. No significant effects were found of sound on the RMS values of sleep spindles in the other bins. However, small effect sizes were apparent.

Table 2

Mann Whitney U Test for Stimulation Condition on Sleep Spindle Amplitude by Phase Divisions

RMS Divided	Bins	*U*	*p*	Pearson's *r*	95% CI	
					Lower	Upper
Participant 1	Bin 1	646.00	.42	*-0.09*	.41	.43
	Bin 2	4458.00	.28	*-0.08*	.27	.29
	Bin 3	3662.50	<.001**	*-0.26*	1.82e-4	.001
	Bin 4	543.50	.54	*-0.07*	.544	.564
Participant 2	Bin 1	172.00	.03*	*-0.32*	.025	.032
	Bin 2	1556.00	.27	*-0.10*	.26	.27
	Bin 3	2849.00	.10	*-0.13*	.09	.11
	Bin 4	96.00	.16	*-0.24*	.15	.17
Participant 3	Bin 1	498.50	.14	*-0.18*	.135	.149
	Bin 2	2024.00	.53	*-0.06*	.515	.534
	Bin 3	2121.50	.38	*-0.08*	.37	.39
	Bin 4	114.00	.04*	*-0.33*	.038	.046
Participant 4	Bin 1	34.00	.72	*-0.10*	.71	.73
	Bin 2	231.00	.36	*-0.14*	.35	0.37
	Bin 3	236.50	.09	*-0.23*	.088	.099
	Bin 4	68.50	.73	*-0.07*	.72	.74

Note. RMS Divided= all of the RMS values in both stimulation conditions (sound and sham) divided by bins; CI= confidence interval.
**p<.05, **p<.001*.

Participant 2

The Effect of Sound on Sleep Spindles' Amplitude

Overall, no statistically significant difference was found when comparing the amplitude of sleep spindles in the sound condition to the sham one (U = 15610.00, p < .27, r = -0.06, 95% CI [0.26; 0.28]. However, a small effect size was present.

The Effect of Sound on Sleep Spindles' Amplitude Based on Phase Divisions

A significant difference and a medium effect size were found in the first bin's sleep spindle amplitude in the sound condition (*Mdn* = 1.82e-6) compared to the sham one (*Mdn* = 1.43e-6; U = 172.00, p = .03, r = -0.32, 95% CI [0.025; 0.032]). No statistically significant difference of medians was found in bin 2, bin 3 or bin 4 (see Table 2). However, small effect sizes were observed.

Participant 3

The Effect of Sound on Sleep Spindles' Amplitude

The difference in the amplitude of sleep spindles between the sound and sham condition was not statistically significant (U = 17043.00, p < .43, r = -0.04, 95% CI [0.42; 0.44]). A small effect size was present, suggesting that there is virtually no variability between conditions in this analysis accounted by the stimuli introduced in the sound condition.

The Effect of Sound on Sleep Spindles' Amplitude Based on Phase Divisions

In contrast, the sound stimulation condition (*Mdn* = 1.46e-6) exhibited a statistically significant effect in bin 4 (U = 114.00, p = .04, r = -0.33, 95% CI [0.038; 0.046]) compared to the sham condition (*Mdn* = 1.16e-6). As well, a medium effect size is suggestive of a medium proportion of the variance between the sleep spindles amplitude in conditions being accounted for by the introduced stimuli. No statistically significant difference was found between the two conditions for bin 1, bin 2, and bin 3 (see Table 2). This was further supported by small effect sizes.

Participant 4

The Effect of Sound on Sleep Spindles' Amplitude

No statistically significant difference and a small effect size were found between the sleep spindle amplitude in the sound and sham conditions (U = 2364.00, p < .55, r = -0.05, 95% CI [0.54; 0.56]).

The Effect of Sound on Sleep Spindles' Amplitude Based on Phase Divisions

A similar pattern of results emerged in the investigation of differences for the bin divisions. None of the bins had a statistically significant difference between the stimulation conditions (see Table 2). Bin 1 (r = -0.10), bin 2 (r = -0.14), bin 3 (r = -0.23) and bin 4 (r = -0.07) have exhibited small effect sizes. Mixed results can be concluded from the data of participant 4.

Discussion

The goal of this study was to investigate the possibility of stimulating sleep spindles' amplitude with sound, specifically, if spindles differ in their sensitivity to sound by phase. The preliminary results suggest a trend of sound increasing sleep spindles' amplitude following stimulation, however this was not consistent across participants. Mixed results were found regarding specific

phases being more sensitive to sound stimulation than others with bin 1, bin 3 and bin 4 of interest. These findings agree with previous research, which has shown an influence of sound on sleep spindles [16-18]. The hypothesis that sound will affect the amplitude of sleep spindles coupled to the SO up-states was supported only by data collected from participant 1. That is, the sound stimuli increased sleep spindles' amplitude immediately after stimulation. A successful stimulation of sleep spindles may render influencing the timing between SO and spindles possible. If the timing between the two waves can be influenced, the memory processes that are related to the coupling might be affected as well, which is of relevance in older adults. However, a similar study to the present one did not find an effect on sleep spindles via sound [18]. One limitation that is shared by Ngo and colleagues' and the current study was considering the whole spindles and not taking the sleep spindles' phases into account (relating to the endogenous activity of the waves). Thus, it is possible that the effect of sound on individual bins could not be resolved when the data was considered as a whole, because the RMS values might have averaged out in the analysis. This limitation is addressed in the second analysis of this study by tackling the effect of sound on sleep spindles by phase divisions, which is a novel investigation in the field.

The increase of spindle amplitude following stimulation was found to be dependent upon the phase of the spindle to which sound was presented to. The female participant (i.e., participant #2) showed a significant stimulation of the ascending phase (bin 1) of the sleep spindle sensitive to sound, compared to the male counterparts that showed sensitivity in the descending phases of the spindles (bin 3 and bin 4). Overall, hormonal differences between sexes affect sleep, such as total amount of sleep, specific stage duration, and oscillatory activity in frequency bands, more specifically females have shown higher spindle density, duration and amplitude compared to males [35-37]. Thus, sex differences might affect the activity or properties of sleep spindles, which in turn could explain a different phase sensitivity to sound. Nevertheless, more studies on the phase-dependent intrinsic properties of sleep spindles need to be conducted to tie the above results to the differences in sleep spindle activity between sexes. Overall, spindles seem to be influenced by sound stimuli.

Furthermore, during sleep, spindles are thought to protect the individual from stimuli, including sounds that may disrupt their sleep [38]. This property might explain the increase of amplitude of the sleep spindles following presentation of the sound stimulus. Thus, the results of this study are mostly consistent with previous work that has found an increase in the number of spindles during sleep and spindle density, defined as number of spindles per minute, following sound stimulation [16,17]. Particularly, the sensitivity of the spindle bins to sound found in this study followed the SO stimulation literature. The up-states of SO are an effective target for sound stimulation; thus, the same train of thought might be assumed for sleep spindles, due to the close interaction between the two waves [13-15].

This study was affected by limitations stemming from the spindle detection algorithm, sample size and tools used. First, faulty detections of sleep spindles could have been included by the automatic sleep spindle detection algorithm used, however, this limitation can only be addressed by improving the algorithms currently available to researchers [30]. Second, the small sample size of the study calls for caution in the interpretation of the findings. This study provides preliminary results as methodological refinement, not generalizability, was the primary goal of this study.

It is important to note that this data set was collected from a young adult sample, thus no generalization claims toward older individuals can be made. As well, measures of memory con-

solidation were not used. That is, the goal accomplished by this experiment was to determine if an effect on sleep spindles using sound stimulation is possible. Future studies can use these findings as basis to investigate the potential influences of sound on memory consolidation achieved through stimulation of sleep spindles and SO in younger and older samples. More specifically, future studies could focus on other variables of sleep spindles that might be affected by sound rather than amplitude, such as spindle density (defined as the number of spindles per minute). Further, for the purposes of this project the EEG signal used was only filtered to the spindle frequency from the signal collected. An effect of sound might not be limited to solely the spindle activity band post stimulation, but other bands as well. Similarly, when sound stimulation was presented during SO, the effects of the stimulation manifested not only in the SO activity band, but the faster spindle band as well [13-15]. Lastly, it's important to note that this study only used one frontally-placed electrode to determine SO and sleep spindles. EEG signals may appear differently based on electrode placements and should be considered when comparing results.

In summary, the results suggest a potential influence of sound stimulation on sleep spindles. This effect seems to be directional toward an increase of sleep spindles' amplitude following sound stimulation. Additionally, targeting specific phases of sleep spindles seems to be of importance, because some participants showed phase-dependent specificity to sound. If spindles are indeed sensitive to sound stimulation by phase, this information can be used to successfully target their oscillations and possibly affect memory consolidation processes. This study supplements the current understanding of how sleep spindles might be manipulated using sound stimulation and brings a novel interest of investigation by phase of spindles [16-18]. Subsequent research should investigate whether presenting sounds can stimulate sleep spindles separately from SO. These findings would suggest that these electrical signals could be rhythmically influenced and potentially be used as a treatment intervention for cognitive impairments in older adults [1, 12]. Once more information on the manipulation of sleep spindles is available, this may lead to the opportunity to explore the re-alignment of SO and sleep spindles that is lost with age and is crucial to the memory consolidation process.

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