Acoustic stimulation during deep sleep using a mobile EEG system at home

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Introduction

Sleep has a crucial impact on health and memory consolidation (Rasch and Born 2013). Memory consolidation mainly takes place during the slow oscillations (SO) typical of the N3 deep sleep stage. SO are characterised by frequencies around 0.8 Hz and high amplitudes. The underlying neuronal activity appears to synchronise in an up-and down-phase, reflecting membrane depolarisation and hyperpolarisation, respectively (Massimini et al. 2004). Brief acoustic stimulations during the up-phase of SO showed increased SO amplitudes and improved memory consolidation (Ngo et al. 2013; Ong et al. 2016). Ngo and colleagues (2013) demonstrated that if the stimulus is set out of phase, the SO activity is disrupted, and memory consolidation is not improved. Sleep EEG data are typically derived in a laborious process at a sleep laboratory. High-quality sleep EEG data can be recorded in a home environment using unobtrusive, easy-to-apply EEG electrode grids worn around the ear (Da Silva Souto et al. 2021). Moreover, a recent development relevant for sleep EEG is the trEEGrid sensor, which consists of nine single-use self-adhesive gel electrodes placed around the ear, one eye, the forehead, and the chin. Linear combinations of trEEGrid channels can be used to approximate the EEG that would be recorded at PSG-relevant scalp positions (Da Silva Souto et al. 2022). Here we developed a real-time acoustic SO approach to be used in a home setting with the trEEGrid layout.

Method

A closed-loop method detects the up-phase of SO, representing a phase-dependent acoustic stimulation. The control circuit is based on three processes: detecting the SO during sleep in real-time in the EEG, triggering and setting an acoustic pulse during the up-phase to amplify the SO amplitude. The acoustic stimuli are pink noise bursts of 50 ms and a level of 55 dB SPL. This algorithm identifies a local minimum in the EEG and presents an acoustic stimulus afterwards. Since the amplitudes in N3 sleep are higher than in the other sleep stages, this should also ensure a N3 classification. This approach is based on a paper by Ngo et al. (2013). The channel combination Fpz-M1 identifies the stimulation points. An initial threshold was determined from an already collected sleep dataset from 12 participants (Da Silva Souto et al. 2022) and set at -45 microvolts. The incoming EEG signal is buffered for five seconds and then bandpass-filtered between 0.25 Hz and 4 Hz (phase true Butterworth filter of 4th order). An acoustic stimulus is presented if a sample of the last

half period duration exceeds the negative threshold and represents a local minimum. The delay between negative peak and acoustic stimulation is adaptive to ensure synchronous stimulation with the SO up-phase. Every time the minimum is found, the following maximum is sought. The time interval between minimum and maximum is stored. The time delay from minimum to stimulation is adapted to one-half of the median of the last ten min-max distances. Every two seconds, the threshold under which the minimum must lie is adjusted to the root mean square of the last five seconds, provided it is below the initial threshold.

In an offline evaluation, the signal was divided into sections around the stimuli to evaluate the accuracy of the desired phase matches. The negative peak before and the positive peak after the stimulus was found. The time between these peaks is the rising slope of the SO. The rising slope was divided into four section equal in length, and it was determined in which section the stimuli have been set; sections two to four were considered most ideal in terms of stimulus presentation to ensure that stimulation is not too early (i.e., close to the minimum) and therefore compromising SO activity. To evaluate the developed algorithm a pilot experiment was conducted. One participant slept two nights with the at-home system (this data is further referred to as pilot measurement). The algorithm operated online and detected the appropriate time points to trigger an acoustic stimulus as described above. To investigate the effect of acoustic stimulation on SO amplitude in only half of the instances an acoustic stimulus was actually presented. In the other half, only a marker was sent by the system, but no acoustic stimulus was played.

Results

Previously collected data from 12 participants were used to test the algorithm (Da Silva Souto et al. 2022). Of the 12 data sets, the median of setting the stimulus trigger in the targeted phase (i.e., sections 2-4) was 83 % (SD = 4.8 %). The pilot measurements suggest that the algorithm also works in an online setting. The stimulation was restricted to the first 4 hours of the night when N3 sleep tends to be more prominent compared to the second half of the night. The acoustic stimulus was presented in the targeted phase in 76.6 % (SD = 6.9 %) of the detected SO. Two measurements (i.e. two nights) with the same participant were divided into intervals with and without stimulation. In the interval without stimulation the time point for stimulation is marked but no actual stimulus is presented. Figure 1 represents the mean (±SEM) of all SO time-locked to the detected negative peak.

The positive peak amplitudes following the stimulation markers were significantly larger for the intervals with acoustic stimulation (red) against those without stimulation (blue).

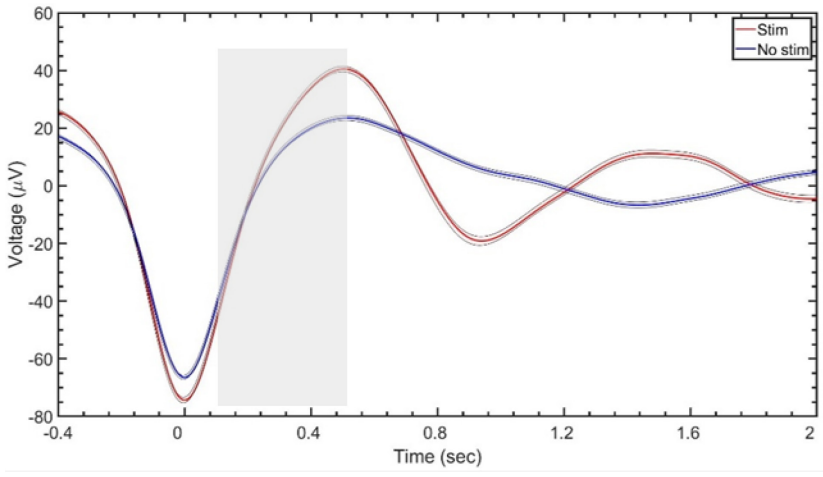

Figure 2: SO, time locked to negative peaks (0 ms); mean (±SEM) of the interval of two measurements (i.e. two nights) with intervals of acoustic stimulation (red) and intervals without acoustic stimulation (blue). Gray box indicates the time interval of acoustic stimulation

Outlook

So far, the focus was placed on developing and fine-tuning the algorithm. Up until now only limited pilot measurements were conducted. Even though the results are promising it is too early to draw definitive conclusions, particularly on the functional level with respect to cognitive effects. The setup will continue to be evaluated in healthy participants to determine whether the described approach modulates the amplitude of SO and contributes to improving memory consolidation. Each participant will be measured for two nights, one with a stim- and one with a sham condition. The stim condition places the stimuli during the rising slope of the up-phase, while the sham condition places the stimuli in a random phase of the EEG signal. A memory task will be performed in the evening and then tested the morning after.

The here-described approach for an acoustic closed-loop system provides promising results as a basis for an easy-to-use at-home system to modulate SO during sleep. This could be of particular interest in the context of neurodegenerative diseases. Papalambros and colleagues (2017) suggested that an SO enhancement associated with overnight memory improvement in people with amnestic mild cognitive impairment (aMCI) by acoustic stimulation offers a potential intervention approach.

References

Da Silva Souto, Carlos F.; Pätzold, Wiebke; Paul, Marina; Debener, Stefan; Wolf, Karen Insa (2022): Pre-gelled Electrode Grid for Self-Applied EEG Sleep Monitoring at Home. In: *Frontiers in neuroscience* 16, S. 883966. DOI: 10.3389/fnins.2022.883966.

Da Silva Souto, Carlos F.; Pätzold, Wiebke; Wolf, Karen Insa; Paul, Marina; Matthiesen, Ida; Bleichner, Martin G.; Debener, Stefan (2021): Flex-Printed Ear-EEG Sensors for Adequate Sleep Staging at Home. In: *Front. Digit. Health* 3, S. 688122. DOI: 10.3389/fdgth.2021.688122.

Massimini, Marcello; Huber, Reto; Ferrarelli, Fabio; Hill, Sean; Tononi, Giulio (2004): The sleep slow oscillation as a traveling wave. In: *J. Neurosci.* 24 (31), S. 6862–6870. DOI: 10.1523/JNEUROSCI.1318-04.2004.

Ngo, Hong-Viet V.; Martinetz, Thomas; Born, Jan; Mölle, Matthias (2013): Auditory closed-loop stimulation of the sleep slow oscillation enhances memory. In: *Neuron* 78 (3), S. 545–553. DOI: 10.1016/j.neuron.2013.03.006.

Ong, Ju Lynn; Lo, June C.; Chee, Nicholas I. Y. N.; Santostasi, Giovanni; Paller, Ken A.; Zee, Phyllis C.; Chee, Michael W. L. (2016): Effects of phase-locked acoustic stimulation during a nap on EEG spectra and declarative memory consolidation. In: *Sleep Medicine* 20, S. 88–97. DOI: 10.1016/j.sleep.2015.10.016.

Papalambros, Nelly A.; Santostasi, Giovanni; Malkani, Roneil G.; Braun, Rosemary; Weintraub, Sandra; Paller, Ken A.; Zee, Phyllis C. (2017): Acoustic Enhancement of Sleep Slow Oscillations and Concomitant Memory Improvement in Older Adults. In: *Front. Hum. Neurosci.* 11, S. 109. DOI: 10.3389/fnhum.2017.00109.

Rasch, Björn; Born, Jan (2013): About sleep's role in memory. In: *Physiological reviews* 93 (2), S. 681–766. DOI: 10.1152/physrev.00032.2012.