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MANIPULATING MEMORY DURING SLEEP

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Introduction: Targeted Memory Reactivation (TMR) is the deliberate reactivation of a memory trace by presenting learning-related cues during sleep. TMR is thought to selectively enhance memory consolidation during Slow-Wave Sleep (SWS). The hallmark of SWS is the slow-wave, characterized in the electro-encephalogram (EEG) as a wave with amplitude >75

μV and frequency around 1 Hz. The slow-wave reflects global synchronous neuronal depolarisation and increased excitability in the so-called up-state, followed by a widespread neuronal hyperpolarisation in the down-state. In this study, our aim was to present learned stimuli during either a slow-wave up- or down-state. Our expectations were that stimuli cued during the up-state would enhance vocabulary memory the most, since the up-state is associated with neuronal depolarisation and increased excitability.

Materials and methods: 65 Native Dutch speakers participated in the study. They learned 120 Danish nouns before sleep. We developed a closed-loop method that allows targeting stimuli to any oscillatory phase by modelling and predicting the oscillatory brain activity. We used this method to predict either up- or down-states in slow-waves. In the "Up" group (N=23), half of the learned words were aurally cued again during predicted slow-wave up-states. In the "Down" group (N=19), half of the learned words were cued during predicted slow-wave down-states. The "Sham" group (N=23) did not receive any cues during the night. Auditory TMR started at the beginning of SWS and continued for 3 hours. The following morning, participants had to retrieve all 120 words in a cued recall test.

Results: Our results show that memory for words cued in the up-state of a slow-wave was improved, i.e. on average participants knew more of the cued words after sleep (107%±12%) compared to the uncued words (99%±10%, p=.03). Moreover, we are the first to show that memory traces seem to deteriorate when cued in a slow-wave down-state (95%±11%) compared to uncued words (102%±10%, p=.04). The sham group knew on average the same amount of words after sleep compared to the learned amount before sleep (100%±8%). Event-Related Potentials (ERPs) show an induced slow-wave-like pattern after cueing at the beginning of a slow-wave up-state, which is not present in an ongoing "sham" slow-wave. Presenting a cue at the beginning of a down-state seems to disrupt this pattern, resulting in a phase shift of the induced slow-wave-like pattern. Time-frequency analysis reveals an early enhancement in the fast spindle/beta power range (14-21 Hz) for the up-state cued words compared to the down-state cued words. Interestingly, both TMR cued groups show more SWS (17%±6%) compared to the sham group (11%±7%, p=.01).

Conclusions: Applying TMR in an ongoing slow-wave up-state enhances post-sleep memory, whereas reactivation in the slow-wave down-state depresses memory. Thus, by taking into account the oscillation phase of the slow-wave, it is possible to manipulate the fate of a memory trace during sleep. These results open perspective for exciting future research, such as strengthening deliberate memory traces with a device wearable at home when learning, or even deteriorating memory traces in PTSD patients.