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## Memory

### ENHANCING OR DEPRESSING MEMORIES, WHILE DEEPENING SLEEP, BY EEG-GUIDED NEUROSTIMULATION

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**Introduction:** Over recent years we have developed a pioneering technique that allows us to interact with the sleeping brain in real-time. An automated loop, involving real-time modeling and prediction of electrophysiological brain signals, targets stimuli to specific patterns in ongoing brain activity. This sophisticated form of manipulation, termed closed-loop neurostimulation (CLNS), enables innovative experimentation and exciting applications.

**Materials and methods:** We used CLNS to test the hypothesis that sleep-related memory reactivation and consolidation are specifically linked to the depolarized phase of slow oscillations (SO's). Participants were exposed to a foreign vocabulary-learning task in the evening and tested for vocabulary acquisition the next morning. During sleep, memory reactivation was induced through subtle, auditory presentation of foreign words, locked to a specific phase of the slow oscillation.

**Results:** Using this approach, we showed that the alignment of memory cues to the SO depolarising slope enhances memory for cued vocabulary items. Conversely, cues targeted to the down-going slope promote forgetting. Moreover, subtle auditory stimuli locked to SO zero-crossings can boost the slow oscillation dynamic, inducing long SO trains that effectively increase the duration and percentage of deep sleep across the night.

**Conclusions:** These results provide strong evidence for the notion that sleep-related memory consolidation occurs during the depolarised phase of slow oscillations. Moreover, they show that declarative memory traces can be either enhanced or suppressed during sleep, depending on the precise alignment of reactivating cues to specific neural activity patterns. Finally, we show for the first time that sleep, as whole, can be deepened using intermittent, SO phase-locked sound stimulation during NREM sleep.

These findings provide important insights into sleep-related memory reprocessing and point the way to possible applications of CLSN in the treatment of sleep problems and disorders involving maladaptive memories, such as PTSD, phobia and addiction.