Supporting Information

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SI Methods

Memory Tasks in Exp. 1. Four memory tasks were used, and for all tasks, parallel versions (A, B) were used in the subject's two experimental sessions. To assess declarative memory, a word paired-associate learning task was used (1, 2). Forty-six semantically related pairs of German nouns (e.g., bird-claw) were sequentially presented on a monitor with a rate of 1/5 s and an interstimulus interval of 100 ms. Also, four dummy pairs of words at the beginning and end of each list served to buffer primacy and recency effects, respectively. At learning, before the retention period, presentation of the list was immediately followed by a cued recall, i.e., the subject was to respond by naming the second word on presentation of the first (cue) word of each pair, whereby the 46 stimulus words of the word list appeared on the screen in a different order than during the foregoing presentation. The subject had unlimited time to recall the appropriate response word. If a minimum of 60% correct responses was not obtained on a run, word-pairs were presented again in a newly randomized order (to prevent serial learning) and cued recall was repeated. At retrieval testing (17:00 h) in the afternoon cue words were again displayed in a newly randomized order, and the subject was required to recall the appropriate response words. Retention was measured by the difference in the number of words recalled at retrieval minus the number of words reproduced correctly at the last run of the learning period.

On a second declarative nonverbal paired-associate task, subjects were shown on the monitor a list of 16 evenly balanced pairs of either geometric or nongeometric line-drawings, adapted from ref. 3. During learning, presentation of the list was followed by a cued recognition task, in which subjects had unlimited time to recall the appropriate response drawing from a group of seven simultaneously presented other drawings. Learning ended when a minimum of 10 correct responses (60%) was reached on a run. At retrieval testing the cued recognition task was repeated using a newly randomized order of presentations. Retention was measured by the difference in the number of correctly retrieved drawings at retrieval testing minus the number of drawings correctly recognized at the last run of the learning period.

To test procedural memory, a finger sequence tapping task was used, adapted from ref. 4. Subjects were required to repeatedly finger-tap with the nondominant left hand a five-element sequence presented on a computer monitor as fast and accurately as possible on a key board. The two sequences used were "4-2-3-1-4" and "4-1-3-2-4." The training period before sleep consisted of 12 30-s intervals with 30-s breaks between trials. Retrieval testing consisted of a practice run followed by three 30-s test intervals. A working memory component of the task was excluded by continuous presentation of the sequence on the screen. No feedback was given on pressing keys. Each 30-s interval was scored for the number of correctly completed sequences and the number of errors made. Performance at learning and retrieval testing was defined by averaged scores from the final three intervals during the learning period, and from three intervals of the retrieval period, respectively. Retention performance was defined by the difference between performance at retrieval testing minus performance during the learning period.

Also, procedural memory was evaluated by the mirror tracing task, adapted from refs. 2 and 5. In this task, subjects had to trace as fast and as accurately as possible line-drawn meaningless figures while these figures (with 26 to 27 angles and curved corners) and their hand movements were visible only through a mirror. Subjects traced each figure with an electronic stylus starting and ending at the same point. Drawing speed and error rate were registered. An error consisted of moving the stylus off the line of the figure. At learning, subjects first performed practice runs with a star-like figure until draw time was <1 min and <12 errors were made (the learning criteria), and then continued with 4 runs with the test figure. At retrieval testing, after one practice run, performance on 4 runs on the test figure was examined. On each occasion, the total time to trace a figure, and the number of errors were measured and averaged across the 4 runs. Retention was defined by the difference in performance on the test figure at retrieval testing and during the learning period.

The word fluency task conducted at retrieval testing to assess the general capability to retrieve information from long-term memory (6) requires the subject to write down within 2-min periods, respectively, as many kinds of either jobs or hobbies, and words starting with either the letter "M" or "P." For the digit span test of the Wechsler Adult Intelligence Scale (7) subjects were to repeat accurately lists of orally presented digits forward and backward.

Transcranial Slow Oscillation Stimulation (tSOS). tSOS was applied for five 5-min epochs separated by 1-min stimulation free intervals. Stimulation parameters were the same as in a previous study of our lab (1, 8) and as follows. Size of stimulation electrodes, 0.502 cm^2; current strength, 260 μV; current density, 0.517 $\mathrm{mA/cm}^2$. The overall duration of 25-min of stimulation had been selected in our previous study as this duration is approximately equivalent to the length of the first slow wave sleep (SWS) epoch during nocturnal sleep. Stimulation was interrupted by 1-min stimulation-free intervals to enable the assessment of immediate effects of stimulation, because an uncontaminated EEG cannot be recorded during ongoing stimulation. Although EEG activity during these intervals cannot a priori be taken to reflect ongoing EEG activity during the 5-min stimulation epoch, there is strong evidence that activity immediately after stimulation with weak electric fields indeed reflects neuronal activity that has become entrained to the stimulation (9–12).

Results

Transcranial SOS During Quiet Wake Does Not Consolidate Memories. Changes in Performance Across the 7-h Retention Interval. Mean (±SEM) performance at learning and retention performance on the four different memory tasks in the stimulation and sham condition are summarized in Table 1 of the main text. Independent of the tSOS condition, performance on the declarative word paired-associate task remained unchanged (time: $F_{1,15} = 0.42$, $P > 0.5$) and decreased on the nonverbal paired-associate task (time: $F_{1,15} = 6.43$, $P < 0.03$) across the retention interval. Performance speed on both procedural finger sequence tapping (time: $F_{1,15} = 23.46$, $P < 0.001$) and the mirror tracing (time: $F_{1,15} = 60.28$, $P < 0.001$) increased across the wake retention period. Error rate on the finger sequence tapping task did not change across time ($F_{1,15} = 1.61$, $P > 0.2$), but decreased in the mirror tracing task ($F_{1,15} = 8.97$, $P < 0.05$), altogether indicating that improvements on these procedural tasks was not merely due to speed-accuracy trade-offs.

Improved Retention of Verbal Memory by tSOS Applied During Learning (Exp. 2). We additionally examined whether the effect of tSOS applied during encoding would manifest itself also at a delayed recall test 30 min later. Number of words recalled at this delay after testing on word list R6 was indeed increased after tSOS as compared with sham stimulation (sham: 13.08 ± 0.43, tSOS: 13.92 ± 0.42, $P < 0.05$). There was no significant difference in the number of errors (sham: 0.75 ± 0.28, tSOS: 0.33 ± 0.14, $P > 0.1$).

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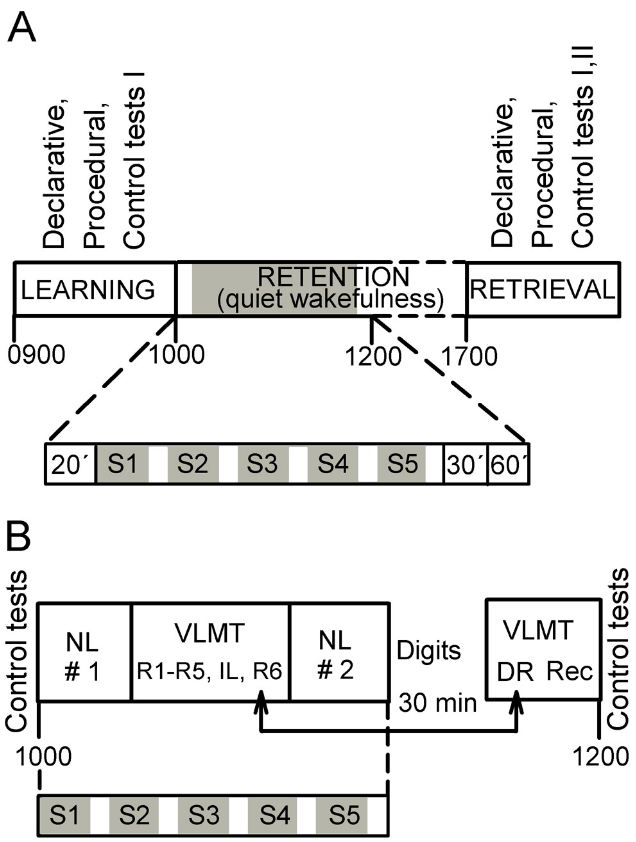

Fig. S1. Experimental procedures of Exp. 1 and 2. (*A*) In Exp. 1, subjects ($n = 16$) participated in two sessions (tSOS and sham condition), with each consisting of a learning period, a 7-hour retention interval and subsequent retrieval testing. In the learning period, subjects acquired declarative (word paired-associates, nonverbal paired-associates) and procedural memories (finger tapping, mirror tracing). ''Control tests 1'' to assess mood, motivation and activation level [Positive and Negative Affect Schedule (PANAS), adjective check list] were conducted before learning and retrieval testing. Subjects spent the first 2 h of the retention interval in the laboratory sitting quietly and listening to relaxing music while the EEG was recorded continuously. Stimulation or sham stimulation was applied 20 min after the learning period. Stimulation consisted of five 5-min intervals of transcranial slowly oscillating electrical stimulation (S1-S5) each followed by a 1-min stimulation-free interval (white areas) used for EEG analyses. A 1-min interval immediately preceding S1 served as baseline. EEG analyses were also performed for 1-min intervals after stimulation by 30 and 60 min. At ≈12:00 h, subjects were released from the laboratory and engaged in standardized activities of low cognitive and physical demand. During the retrieval period, performance on the declarative and procedural tasks was retested. Subsequent ''Control tests 2'' assessed working memory and retrieval function per se (digit span, word fluency). (*B*) In Exp. 2, subjects ($n = 12$) participated in two sessions (tSOS and sham condition). After assessment of self-reported tiredness, mood and motivation in Control tests (Standford Sleepiness Scale, PANAS, adjective check list) subjects performed on two learning tasks, the number list learning task (NL), and the adapted Verbal Learning and Memory Test (VLMT) while either tSOS or sham stimulation was applied. As in Exp. 1, stimulation consisted of five 5-min intervals (S1-S5) each followed by 1-min stimulation-free intervals (white area). The period of stimulation and the learning tasks began simultaneously after a 2-min period of quiet wakefulness. Learning of the tasks took place essentially only during acute tSOS intervals. The number list learning task was conducted twice (no. 1, no. 2) with two different lists. The VLMT consisted of 5 presentations of the standard word list each immediately followed by a free recall (R1-R5), then an interference list (IL) of words was presented, which was to be immediately recalled before free recall of the standard word list was tested again (R6). Working memory performance on the digit span test (Digits) was tested immediately after the 5th interval of stimulation.

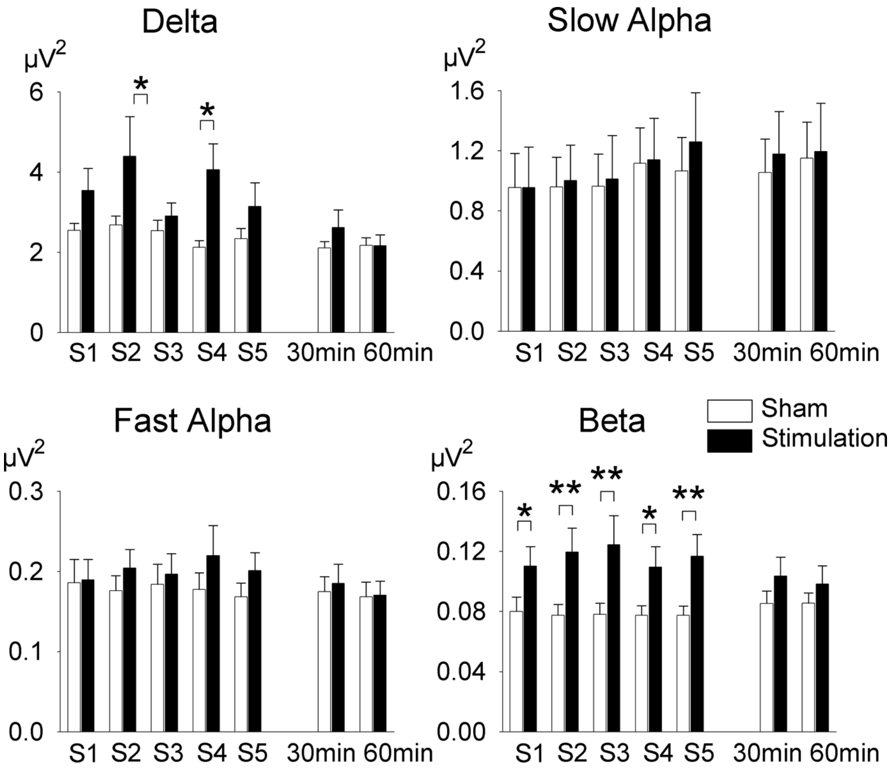

Fig. S2. Changes over time in EEG spectral power in delta, alpha, and beta bands of Exp. 1. EEG spectral power across the five 1-min intervals immediately succeeding the stimulation intervals and 30 and 60 min after termination of stimulation in the delta (1–4 Hz), slow alpha (8–12 Hz), fast alpha (12–15 Hz), and beta bands (15–25 Hz) averaged across all locations. **, $P < 0.01$; *, $P < 0.05$ (*t* test) for comparisons between the stimulation and sham condition ($n = 16$). Note, during some intervals, strong modifications in the theta frequency band affected adjacent activity in the delta band, resulting in increased activity as compared with sham stimulation for the 2nd and 4th stimulation-free intervals (stimulation × time: $F_{7,105} = 3.85$, $P < 0.05$).

Table S1. Performance on the psychometric control tests in experiment 1 (n = 16; mean ± SEM)

Test	Sham	Stimulation
Before learning		
PANAS, positive score	5.11 ± 0.52	5.23 ± 0.59
PANAS, negative score	3.70 ± 0.41	3.74 ± 0.37
After retrieval		
Digit span forward (digits)	8.18 ± 0.21	8.38 ± 0.22
Digit span backward (digits)	6.62 ± 0.32	6.94 ± 0.30
Word fluency (words)	22.50 ± 1.30	25.25 ± 1.41
Stanford Sleepiness Scale	2.37 ± 0.36	2.50 ± 0.35
PANAS, positive score	4.88 ± 0.47	5.14 ± 0.51
PANAS, negative score	3.48 ± 0.36	3.73 ± 0.38

For all measures, sham vs. stimulation comparisons were nonsignificant.

Table S2. Error subtypes on the VLMT in Exp. 2 (n = 12; mean ± SEM)

Type of error	Sham	Stimulation	*P*
False memories (word not in the standard list)	0.17 ± 0.09	0.21 ± 0.13	0.81
Perseverations (repetitions)	0.46 ± 0.19	0.16 ± 0.10	0.16
Accuracy (ratio of total correct words by total cited words)	0.96 ± 0.01	0.97 ± 0.01	0.35

For all measures, sham vs. stimulation comparisons were nonsignificant.