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Word encoding during sleep is suggested by correlations between word-evoked up-states and post-sleep semantic priming

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Abstract

To test whether humans can encode words during sleep we played everyday words to men while they were napping and assessed priming from sleep-played words following waking. Words were presented during non-rapid eye movement (NREM) sleep. Priming was assessed using a semantic and a perceptual priming test. These tests measured differences in the processing of words that had been or had not been played during sleep. Synonyms to sleep-played words were the targets in the semantic priming test that tapped the meaning of sleep-played words. All men responded to sleep-played words by producing up-states in their electroencephalogram. Up-states are NREM sleep-specific phases of briefly increased neuronal excitability. The word-evoked up-states might have promoted word processing during sleep. Yet, the mean performance in the priming tests administered following sleep was at chance level, which suggests that participants as a group failed to show priming following sleep. However, performance in the two priming tests was positively correlated to each other and to the magnitude of the word-evoked up-states. Hence, the larger a participant's word-evoked up-states, the larger his perceptual and semantic priming. Those participants who scored high on all variables must have encoded words during sleep. We conclude that some humans are able to encode words during sleep, but more research is needed to pin down the factors that modulate this ability.

40 **1 Introduction**

41 Although sleep is a state of reduced consciousness, we still process sensory information while
42 asleep. The sleeping brain responds differently to semantically congruent versus incongruent sentences
43 (Daltrozzo et al., 2012), to semantically related versus unrelated words (Brualla et al., 1998), and to
44 one's own name vs. names of others (Perrin et al., 1999) reflecting word understanding. If words are
45 understood during sleep (Brualla et al., 1998; Daltrozzo et al., 2012; Perrin et al., 1999), we speculate
46 that they might be stored as well which might alter subsequent processing of these words due to
47 priming. But sound evidence for this claim is missing (see Aarons, 1976; Eich, 1990; Hoskovec, 1966;
48 Simon and Emmons, 1955 for reviews on sleep-learning studies). So far, there are only reports of non-
49 verbal learning during sleep (Arzi et al., 2012; Ikeda and Morotomi, 1996; Hauner et al., 2013). For
50 example, Arzi et al. (2012) showed that humans take deeper breaths if they hear a tone that was
51 repeatedly associated with a pleasant odor during sleep. Hauner et al. (2013) further demonstrated
52 extinction learning during sleep if slumbering participants are re-exposed to an odor that was used as
53 context odor during a contextual fear conditioning task. Tone-odor conditioning and extinction learning
54 do not involve processing of conceptual information and might mainly rely on subcortical and
55 hippocampal networks. Evidence of verbal learning during sleep would demonstrate that the sleeping
56 brain is also able to acquire abstract conceptual knowledge whose processing depends on the neocortex.

57 The success of word encoding during sleep might depend on the sleep stage, during which words
58 are presented. Although rapid eye-movement (REM) sleep is characterized by dreaming (Siclari et al.,
59 2013) and wake-like cerebral activity, non-rapid eye-movement (NREM) sleep might actually provide
60 better conditions for word encoding due to its role in memory consolidation (Diekelmann and Born,
61 2010; Rasch and Born, 2013). NREM sleep consists of stage 1 sleep (S1) that builds the transition
62 between wakefulness and sleep, stage 2 (S2) or light sleep, and deep sleep stages 3 and 4 (S3/S4) which
63 are often referred to as slow-wave sleep (SWS). S2 sleep is characterized by the presence of spindles
64 and k-complexes in the electroencephalogram (EEG). Sleep spindles are brief oscillatory events at
65 frequencies between 9-16 Hz. They are most frequent during S2 but are also present in SWS. K-
66 complexes are sharp negative signal deflections followed by a slower positive component. They bear
67 much similarity with the high-amplitude, slow-frequency (< 4 Hz) activity that characterizes the deep
68 NREM sleep SWS. In SWS, EEG activity is dominated by slow-oscillations with peak frequencies at
69 about 0.8 Hz (Mölle et al., 2002). These oscillations are generated in neocortical neurons which slowly
70 and synchronously alternate between phases of membrane depolarization accompanied by increased
71 firing (up-states), and phases of membrane hyperpolarization with reduced firing (down-states) (Mölle
72 et al., 2002; Steriade et al., 1993). Slow-oscillations and especially up-states are thought to play a vital
73 role in memory consolidation. Much evidence suggests that memories formed during the day are
74 reactivated and thereby strengthened during NREM sleep (Diekelmann and Born, 2010; Rasch and
75 Born, 2013). Reactivation benefits from the increased neuronal activity and excitability that is provided
76 by up-states. Up-states are thought to boost neuronal plasticity, which helps to strengthen reactivated
77 memories. We hypothesize that the activity and plasticity provided by neocortical up-states might also
78 assist word encoding.

79 We played single words in a rhythmic manner while participants were in deep NREM sleep during
80 an afternoon nap. Several studies suggested that the rhythmic presentation of sounds during NREM
81 sleep entrains slow-oscillations such that up-states start to occur regularly upon sound presentation
82 (Ngo et al., 2013a, 2013b). These investigators observed up to two entrained slow-oscillations within
83 3 seconds upon sound presentation. To investigate whether slow-oscillations are similarly entrained by

84 rhythmically played words, we analyzed event-related EEG activity within the 3 s following word
85 onset. We correlated the size of the word-evoked up-states with performance in the two priming tests
86 that were administered following the nap to find out whether entrained up-states contribute to word
87 priming. Because up-states provide windows of increased neocortical plasticity, we hypothesized that
88 large word-evoked up-states would benefit word encoding. Following the nap, we administered two
89 behavioral tests that assessed priming from sleep-played words. We hypothesized that successful
90 encoding of words during sleep would improve the subsequent processing of these and semantically
91 related words due to priming. Priming is thought to be a by-product of the modification of existing
92 knowledge (Bowers, 2003; Marsolek, 2003) and thus reflects a simple form of learning. Because
93 priming effects are long-lived (Tulving et al., 1982; Woltz and Shute, 1995) and even observed in
94 amnesic patients with impaired explicit memory (Carlesimo, 1994), tests of priming are suitable to
95 look for an imprint that sleep-played words leave on memory.

96 **2 Materials and methods**

97 **2.1 Participants**

98 We tested 26 healthy men who reported normal sleep routines. Participation was compensated with 90
99 Swiss Francs (~90\$). Ten men were excluded after data collection because of poor polysomnography
100 ($n = 2$) or because less than 2/3 of the planned stimuli could be presented during NREM sleep due to
101 insufficient sleeping time ($n=8$). We report the data of the remaining 16 participants (age: mean \pm SD
102 = 23.75 ± 2.44 years). The study was introduced as an investigation of the effect of noise on sleep
103 quality to keep participants naïve to word presentations during sleep. This was necessary to promote
104 unconsciousness of word presentation. Written semi-informed consent was obtained from all
105 participants before experimentation. The fact that words were played during sleep was revealed
106 following sleep. The study was approved by the local ethics committee “Kantonale Ethikkommission
107 Bern (KEK)”, in Bern, Switzerland and was conducted in accordance with the guidelines of the
108 Declaration of Helsinki.

109 **2.2 Procedure**

110 Participants were instructed to sleep from 2 to 7 a.m. and to abstain from caffeine on the day of
111 testing to promote sleep during the afternoon nap. Actigraphy and semi-structured interviews indicated
112 good compliance with these instructions. Upon arrival at the sleep laboratory, participants were
113 prepared for polysomnography. Next, we assessed whether the minimal volume defined for stimulation
114 during sleep was within participants’ hearing range. Based on a pilot study, we used a preset volume
115 of 53.2 dB(A) for presenting words during sleep. If this preset volume disturbed an individual’s sleep,
116 we reduced the volume to levels above the lower bound of 47.2 db(A). To confirm that this lower
117 bound was within hearing range, we measured the minimal volume at which each participant could
118 detect pseudowords embedded in background noise (noise that was later played during sleep). This
119 assessment was introduced as a hearing test. The minimal volume was the point where the presence of
120 noise-embedded pseudowords could just be detected in 98% of presentations. This volume ranged
121 between 36.2 and 42.6 dB(A) and was below the lower bound of 47.2 db(A).

122 At 1.30 p.m., participants took their nap. They were not informed of sleep-played words.
123 Throughout the entire nap a pleasant mixture of brown and pink noise was playing at an unobtrusive
124 volume of 56.6 dB(A). This background noise should reduce the salience of words and should thereby
125 promote unconsciousness of word encoding. When participants entered stable NREM sleep, as

126 indicated by visible slow-wave (1-4 Hz) activity at frontal electrodes during at least 30 s, word
127 presentation was initiated. We started by presenting pseudowords at a very low volume level to
128 habituate participants to noise-embedded words. Then, the presentation volume was increased to 53.2
129 dB(A) and the words were presented. Word presentation was stopped if an arousal (evoked by various
130 reasons) appeared in the sleep-EEG. The average number of stops per participant was 4.75 ± 5.79 (SD).
131 In case of repeated arousals upon word presentation, we lowered the volume from 53.2 dB(A) but kept
132 it above the lower bound of 47.2 dB(A). Consequently, volumes varied both within participants (range:
133 47.2 dB(A) - 53.2 dB(A)) and between participants (range of average volume: 50.2 dB(A) - 53.2
134 dB(A)).

135 A total of 56 nouns were presented during NREM sleep. Half were played once and half six times
136 to boost sleep-learning through repetition. Yet, some participants' sleep was too short to present the
137 complete set of words. In several of these participants the number of available trials was too low to
138 reliably assess differences between once and repeatedly played words. Therefore, we pooled data over
139 conditions (see Statistical Analyses). We presented words intermixed between conditions avoiding the
140 immediate repetition of a word. Participants were awakened, when either all words were presented or
141 when they failed to fall back into stable NREM sleep after an arousal. The 16 analyzed participants
142 spent on average 14.87 minutes in slow-wave sleep (SWS) and 23.31 minutes in sleep stage 2 (S2).
143 We aimed at word learning mainly during SWS: Of 178.63 presentations during NREM sleep (SD =
144 23.27, range: 124 – 196) as much as 154.44 (SD = 41.88) presentations were conducted during SWS
145 and only 24.19 (SD = 34.4) during S2.

146 2.2.1 *Semantic priming test*

147 Following waking, participants were given a break of 15 minutes to recover from sleep inertia. Then,
148 we administered a semantic priming test to find out whether participants would show priming of the
149 meaning of sleep-played words (Figure 1). This test recorded the minimal volume at which participants
150 identified synonyms to sleep-played words versus new words (control condition). If the sleeping brain
151 had encoded and stored the meaning of a word like 'soldier', it should be prepared to identify a
152 semantically related word like 'warrior' more easily – i.e., at lower volumes – than a new word. This
153 test was introduced as a hearing test. The background noise that played during sleep kept playing at
154 56.6 dB(A) during this test. On each trial, a word was repeatedly presented with increasing volume
155 until the participant could identify it. Identification was signaled by button press and the pronunciation
156 of the heard word. Only correctly identified words went into analysis. Each word was initially
157 presented with a volume of 38.7 dB(A). This volume was increased with each word repetition by 2.5
158 dB(A). The average identification volume was 53.7 dB(A). Of the 56 words played for identification,
159 14 were synonyms to one-fold and 14 to six-fold sleep-played words. Another 28 words were new and
160 belonged to the control condition. Words were presented intermixed between conditions. The
161 difference between the mean identification volume for new words (higher) and synonyms (lower due
162 to priming) was the score of semantic priming. We chose this priming test because Stuart and Jones
163 (1995, 1996) had found that this test is sensitive to perceptual priming. Before the main experiment,
164 we had carried out a pilot study to make sure that the task is also susceptible to semantic priming. In
165 the encoding part of this pilot study, 19 participants performed an auditory attention task during which
166 prime words were played in the background for incidental encoding. Incidental encoding was used to
167 mimic word-encoding during sleep. The attention task required participants to indicate on which ear a
168 repeatedly playing beep tone was presented. This task ensured that participants focused on the auditory
169 modality. Each prime word was played ten times in sequence during a 6 s encoding episode. Following

170 each encoding episode, either a synonym of the prime word or a semantically unrelated new word was
171 presented as target in the word identification task. Participants identified synonyms to played prime
172 words at lower volumes than unrelated words (mean and SEM of volume difference: 0.87 ± 0.31 dB(A),
173 $t(18) = 2.77$, $p = .01$, $r = .55$). Hence, this test was considered adequate for our sleep study.

174 2.2.2 Perceptual priming test

175 Next, we administered a test of perceptual priming to find out whether participants remembered
176 sleep-played words explicitly (consciously) or implicitly (unconsciously). Before we applied this test,
177 we informed participants that words were embedded in the noise that played during sleep. All
178 participants were surprised to hear this and assured that they were not aware of any words. The
179 perceptual retrieval test should provide a more objective measure of word awareness during sleep,
180 namely forced-choice accuracy. On each of 28 trials, participants were played with normal volume
181 either a one-fold or a six-fold sleep-played word plus a new word to decide which word had been
182 presented during sleep (answer by button press). The order of the two words in a pair was randomized.
183 Participants were forced to guess because they were not aware of sleep-played words. The percentage
184 of correct choices served as an objective measure of word awareness during the nap. The reaction times
185 for correct and false responses served as an implicit measure that reflects perceptual word priming.
186 Perceptual priming was hypothesized to reflect in the difference between the mean reaction latency for
187 incorrect minus correct choices. Previous studies had suggested that participants respond faster when
188 correctly retrieving unconsciously learned information (e.g. Henke et al., 2003; Duss et al., 2011). A
189 positive difference score between incorrect minus correct responses was thus assumed to reflect
190 perceptual priming of sleep-played words. The percept may be the sound or rhythm of the spoken word.

191 2.3 Hardware and software

192 We used the software Presentation® (14.5, Neurobehavioral Systems, <http://www.neurobs.com>) for
193 stimulus delivery. Sounds were produced using the audio interface Audio 2 DJ by Native Instruments
194 (<http://www.native-instruments.com>) and in-ear headphones CX300II by Sennheiser. The EEG was
195 recorded with the amplifier N7000™ and the software Somnologica Studio Version 5.1.1 by Embla
196 (<http://www.embla.com/>).

197 2.4 Stimuli

198 We presented two-syllabic German nouns during sleep. Playing only two-syllabic words was
199 assumed to help create a rhythmic auditory stimulation pattern that entrains slow-oscillations. The
200 retention of half of sleep-played nouns was assessed in the semantic priming test and the retention of
201 the other half in the perceptual priming test. In the semantic priming test, targets were synonyms to
202 sleep-played nouns and distracters were semantically unrelated nouns. In the perceptual priming test,
203 targets were the sleep-played nouns and distracters were also semantically unrelated nouns. The
204 procedure for creating the stimuli for the two priming tests was the following: we formed word triplets
205 that consisted of a two-syllabic sleep-played prime word, a synonym of varying word length and
206 syllable count for the semantic test, and a semantically unrelated, frequency-matched two-syllabic
207 distracter noun for the perceptual test. These word triplets were assigned to six lists (A-F) of 14 triplets
208 each (all words and data on word-frequency, duration of spoken words, syllable counts of synonyms,
209 and word concreteness are presented in the Supplementary Table 1). Four lists (e.g. A-D) were used to
210 play prime words during sleep. The primes and distracter nouns of two of these lists (e.g. A, B) were
211 later used for the perceptual priming test. The synonyms of the other two lists (e.g. C, D) were used

212 for the semantic priming test. Because synonyms varied regarding word length across word triplets,
213 whereas the primes and distracters were always two-syllabic, we used the synonyms of prime words
214 from the two remaining lists (e.g. E, F) that were not presented during sleep as new words (distracters)
215 in the control condition of the semantic priming test. This guaranteed that word length was similarly
216 distributed in targets (synonyms two sleep-played nouns) and distracters. Lists were counterbalanced
217 over tasks between participants, such that each list was equally often used for the perceptual and the
218 semantic test. Furthermore, primes and distracters were interchanged in half of the instances where a
219 specific word list was used for the perceptual priming task. For the semantic priming task, primes and
220 synonyms were never interchanged because synonyms varied regarding syllable count, whereas primes
221 were always two-syllabic.

222 The six stimulus lists were matched for word-frequency, duration of spoken words, syllable count,
223 and concreteness. Supplementary Tables 2 to 5 provide descriptive statistics for these variables per
224 word list and word type (prime, synonym, distracter). We used logarithmized frequency data provided
225 by the Leipzig Wortschatz Lexicon (<http://corpora.informatik.uni-leipzig.de/>) to match lists regarding
226 word frequency. Syllable counts were also drawn from the Leipzig Wortschatz Lexicon. Two raters
227 classified concreteness of words on a binary scale (100% rater agreement). The time from word onset
228 to offset in the recorded sound files was the duration of spoken words.

229 Word lists differed neither regarding word frequency nor word duration nor syllable count nor
230 concreteness (all $F(5,78) < 1.12$, all $p > .36$, all $\eta_p^2 < .07$). This was suggested by separate ANOVAs
231 run for each matching criterion (frequency, duration, concreteness) and each word type (primes,
232 synonyms, distracters) where word list was entered as sole factor. Furthermore, prime and distracter
233 words were statistically equal regarding word frequency, word duration, and concreteness. This was
234 tested with separate repeated-measures ANOVAs for each matching criterion where word-type (prime
235 vs. distracter) was entered as within- and word-list as between-subjects factor. Measures of frequency,
236 duration, and concreteness were equal between word-lists (all $F(5,78) < 0.15$, $p > .98$, $\eta_p^2 > .01$), word-
237 types (all $F(1,78) < 1.92$, $p > .17$, $\eta_p^2 < .02$), and combinations of word-lists and word-types (all $F(5,78)$
238 < 0.88 , $p > .50$, $\eta_p^2 < .05$ for the word-list X word-type interaction).

239 The semantic relatedness between primes and their synonyms was assessed in two pilot studies
240 using priming tests that differed from the test used in the main experiment. In both studies, 19
241 participants listened to prime words while performing an auditory attention task. Each prime word was
242 played ten times in sequence during a 6 s encoding episode. Each encoding episode was followed by a
243 word identification task (see semantic priming test) in pilot study 1, and an auditory lexical decision
244 task in pilot study 2. The critical variable in the word identification task was the stimulus volume at
245 which participants could identify synonyms to prime words versus distracters. Primed synonyms were
246 identified at lower volumes than unrelated words (mean and SEM of volume difference: 0.87 ± 0.31
247 dB(A), $t(18) = 2.77$, $p = .01$, $r = .55$) reflecting semantic priming. In the lexical decision task, encoding
248 of a prime word was followed by the presentation of either a synonym to the prime word or a distracter.
249 Correct classification was faster for synonyms versus distracters (mean and SEM of difference in
250 response latencies: 34.70 ± 11.22 ms, $t(18) = 3.09$, $p < .01$, $r = .59$). Both pilot studies confirm that the
251 semantic relatedness between primes and their synonyms is behaviorally relevant.

252 All words were spoken by a female voice and were recorded using professional audio equipment.
253 Sounds were edited and volume-level normalized using the software Audacity®

254 (<http://audacity.sourceforge.net/>). The duration of sleep-played words ranged between 0.45 and 0.95 s
255 (mean = 0.65 s, SD = 0.1 s).

256 2.5 Polysomnography and sleep scoring

257 Sleep was monitored by standard polysomnography (Iber et al., 2007) which included
258 electroencephalography (EEG), electrooculography, electromyography, and electrocardiography. The
259 EEG was recorded at 500 Hz and was obtained from F3, Fz, F4, C3, Cz, C4, P3, Pz, P4, O1, Oz, O2,
260 with Fpz as ground and contralateral mastoids as reference electrodes. Sleep scorings were carried out
261 according to Rechtschaffen and Kales (1968) by three scorers, who were blinded to periods where
262 words were presented.

263 2.6 EEG analysis

264 Only EEG data that were scored as NREM sleep were analyzed. Data segments that contained
265 arousal, which consists of an abrupt shift to high frequency activity (Iber et al., 2007), or motor and
266 other artefacts were visually identified and excluded from data analysis. If a word was played in the
267 3s-period before a rejected EEG segment, it did not enter EEG and behavioral data analysis. If a word
268 belonging to the “word repetition” condition was excluded, we also excluded the EEG response to this
269 word’s repetition at other time points during sleep. The selected unfiltered EEG data were re-referenced
270 to pooled mastoids and were segmented into epochs ranging from 1 s before to 3 s following word
271 onset.

272 To analyze event-related potentials (ERPs), each epoch was baseline-corrected by subtracting the
273 mean voltage of the 1 s pre-stimulus time period. We used 1 s pre-stimulus period - rather than a shorter
274 period - for baseline correction in order to obtain signals that are unaffected by the current phase of the
275 large-amplitude 1 Hz frequency, which dominates deep NREM sleep. The baseline-corrected epochs
276 were averaged per participant.

277 To analyze event-related changes in spectral power (ERSPs), the data of each epoch were
278 decomposed into the time-frequency domain using the function *newtimef()* by EEGLAB. We used
279 sinusoidal wavelet transforms with 3 cycles in length at the lowest frequency of 4 Hz, increasing
280 linearly with frequency to 20.0625 cycles at the highest frequency of 53.5 Hz. The time window was
281 834 ms. The decomposition produced a linear frequency space with 100 frequencies ranging from 4 to
282 53.5 Hz, and a time space with 200 time points ranging from -582 ms to 2582 ms. The raw power
283 values at each time-frequency point for each epoch were divided by the mean raw power of the same
284 frequency averaged across the entire epoch. The resulting relative power values were baseline corrected
285 by subtracting the mean relative power of the prestimulus time window (-582 ms to 0 ms) of the
286 corresponding frequency. These baseline-corrected epochs were then averaged per participant.
287 Preprocessing was performed with the Matlab® toolbox EEGLAB (<http://sccn.ucsd.edu/eeglab/>) by
288 Delorme and Makeig (2004).

289 We used a cluster-based nonparametric approach as proposed by Maris and Oostenveld (2007) to
290 find peaks where the event-related signal (ERP) and spectral power (ERSP) deviated significantly from
291 the pre-stimulus baseline. In brief, we (1) computed t-tests against the baseline (i.e., zero) for each time
292 point or time-frequency point and each electrode. Next, we (2) identified coherent points in time-
293 electrode space or time-frequency-electrode space, where all t-values were significant at the 5% level.
294 For each cluster of connected points, the cluster mass (3) was then computed as the sum of the t-values

295 of all included points. To test whether a specific cluster reflected a significant deviation from baseline,
296 we compared its cluster mass with the permutation distribution, i.e., the distribution of the mass of
297 clusters obtained from randomly permuted data sets. We obtained the permutation distribution by
298 repeatedly permuting the data. To this aim, we randomly interchanged the evoked signal and the
299 baseline in arbitrarily selected participants. We finally extracted the cluster mass of the largest cluster
300 by performing steps (1) through (3) with each permuted data set. The 5000-fold repetition of this
301 procedure yielded a valid estimation of the permutation distribution of the maximal mass of clusters in
302 random data sets. The p-value of a specific cluster in the original data set was computed as the
303 percentage of clusters in the permutation distribution that had the same or a larger mass. A cluster was
304 accepted as a significant peak, if less than 5% of the clusters in the permutation distribution exhibited
305 an equal or larger mass. The resulting peaks reflect deviations in the EEG that must have been evoked
306 by played words.

307 We validated the results of this analysis for the ERP data by running a topographic consistency test
308 (Koenig and Melie-García, 2010; Koenig et al., 2011). This test produced qualitatively similar results.

309 To assess whether word evoked brain responses during sleep predicted subsequent word priming,
310 we correlated the magnitude of evoked ERPs with participants' performance scores attained in each
311 priming test. ERP magnitude was computed separately for each participant and each cluster by
312 averaging the amplitude (μV) across all points in time-electrode space for the respective significant
313 cluster.

314 The next aim was to determine whether the occurrence of slow-oscillations was influenced by word
315 presentation. We identified discrete slow-oscillations in the frontal electrode Fz using an algorithm of
316 Mölle et al. (2009). Slow-oscillations detected with this algorithm had been found to be relevant to
317 memory consolidation (Ruch et al., 2012). We applied a low-pass filter at 30 Hz, down-sampled the
318 data to 250 Hz, and then applied a band-pass filter of 0.15 to 2 Hz. All epochs of the residual data that
319 contained two consecutive positive-to-negative zero-crossings were selected as potential slow-
320 oscillations. We computed the local minimum (negative peak) and maximum (positive peak) per epoch.
321 An epoch was accepted as a discrete slow-oscillation, if (1) it had a duration between 0.9 and 2 s, (2)
322 the amplitude of the negative peak was more negative than $2/3$ of the average amplitude of all negative
323 peaks, and (3) the difference between the amplitudes of the positive and negative peak was larger than
324 $2/3$ of all amplitude differences. To analyze the temporal association between word presentation and
325 slow-oscillations, we counted the number of up-states (positive peaks) of discrete slow-oscillations
326 occurring within the 0.2 s time bins from 1 s before to 3 s after stimulus onset. These counts were first
327 z-transformed per participant and then averaged over participants (Figure 2 c). We further averaged
328 the z-transformed peak amplitudes of these up-states per time-bin to analyze the modulation of up-state
329 amplitudes by word presentation (Figure 2 d).

330 Assuming that word-evoked brain responses reflect entrained slow-oscillations, we compared the
331 topographies of evoked responses with the topographies of spontaneously occurring slow-oscillations.
332 For the evoked brain responses, individual amplitudes at the peak time of the averaged ERPs (see Table
333 1) were normalized by the subject's mean and standard deviation. For spontaneous slow-oscillations,
334 we averaged the EEG data of all discrete slow-oscillations centered around the transition from down-
335 to up-states for each participant. Amplitudes at the down-state peak (196 ms before the transition to
336 the up-state) and up-state peak (176 ms after the transition to the up-state) were normalized by the
337 subject's mean and standard deviation of the respective topography. The resulting normalized

338 topographies were contrasted using repeated-measures ANOVAs with the two within-subject factors
339 Topography (reflecting the 12 electrodes) and Event (evoked ERPs vs. spontaneous up-state or down-
340 states).

341 2.7 Statistical analysis

342 Data of the two conditions (one-fold versus six-fold word presentation) were pooled for all statistical
343 analyses to gain more statistical power. Data pooling was necessary because some participants slept
344 too short to present them with the complete set of words (i.e., loss of trials). Data pooling was
345 acceptable because word repetitions did not seem to modulate the word-evoked EEG responses nor
346 priming performance. Due to the small sample size, nonparametric Spearman correlation coefficients
347 r_s are reported. Note that Pearson coefficients and the corresponding significance levels were very
348 similar and are therefore not reported. We computed two-tailed p-values for all reported correlations
349 and t-tests. For t-tests, r is reported as measure of effect size.

350 3 Results

351 3.1 Word processing during sleep

352 Event-related potentials (ERPs) to word presentation during NREM sleep indicated that participants
353 noted words while asleep (Figure 2 a). Words elicited a negative ERP around 500 ms and two positive
354 ERPs at 1000 ms and 2400 ms following word-onset (all $p < .05$; see Table 1 for descriptive statistics
355 and Figure 3 for plots of the ERPs at all recorded electrodes). We interpret these EEG responses as
356 down-states (at 500 ms) and up-states (up-state 1 and 2 at 1000 and 2400 ms) of entrained slow-
357 oscillations. Although slow-oscillations occur spontaneously during NREM sleep, they can be
358 entrained by rhythmic presentations of sounds (Ngo et al., 2013a) such that they start to consistently
359 appear following sounds. We suggest that the rhythmic presentation of words entrained a sequence of
360 two slow-oscillations with down-states at 500 ms and up-states at 1000 and 2400 ms following word
361 onset. Up-states were of special interest to us because they provide brief windows of increased
362 neocortical excitability (Bergmann et al., 2012; Schabus et al., 2012) that promote neocortical
363 processing such as the consolidation of previously formed memories (Ngo et al., 2013b). The word-
364 entrained up-states in our study reflect sleep-specific brain states that might assist the initial word
365 processing or the ensuing consolidation of the sound and meaning of the encoded words.

366 The analysis of automatically identified discrete slow-oscillations (Möller et al., 2009) confirmed
367 that the ERPs at 1000 and 2400 ms reflect entrained up-states. Discrete up-states occurred more
368 frequently and with higher peak-amplitudes at around 1000 ms and 2400 ms following word-onset
369 (Figure 2 c and d). The number of up-states occurring per second was significantly elevated during the
370 time windows of the ERPs at 1000 ms (mean \pm SEM: 0.450 ± 0.011 up-states/s; $t(15) = 4.34$, $p < .001$,
371 $r = .75$) and 2400 ms (0.464 ± 0.019 up-states/s; $t(15) = 4.17$, $p < .001$, $r = .73$) when contrasted with
372 the ERP at 500 ms (0.343 ± 0.020 up-states/s).

373 Event-related changes in spectral power (ERSP) suggested that the ERP at 500 ms was accompanied
374 by slow sleep spindles, while the ERP at 1000 ms was accompanied by fast spindles. Sleep spindles
375 are NREM-sleep specific oscillatory events at frequencies between 9-16 Hz and with durations of 0.5
376 to 3 s (De Gennaro and Ferrara, 2003; Lüthi, 2013). They are separated into slow spindles (<12 Hz)
377 that occur preferably during down-states and fast spindles (>12 Hz) that occur more frequently during
378 up-states of both naturally occurring (Möller et al., 2011, 2002) and entrained slow-oscillations (Ngo et

379 al., 2013b, 2013a). We found a significant word-induced power increase in the slow-spindle frequency
380 band (see SS+ in Figure 2 b) that co-occurred with the negative response at 500 ms, followed by a
381 power increase (FS+) in fast spindle frequencies within the time window of the ERP at 1000 ms
382 response. The FS+ was followed by a decrease (FS-) in fast spindle activity. These power changes in
383 the spindle frequency range were significant at $p < .01$ (see Table 2 for descriptive statistics and Figure
384 4 for ERSP plots of all recorded electrodes). Because slow-oscillations are known to drive fast spindles
385 to up-states and slow spindles to down-states (Möller et al., 2011, 2002), the co-occurrence of the ERP
386 at 500 ms with slow- and the ERP at 1000 ms with fast-spindle activity further indicates that the
387 reported ERPs reflect slow-oscillations.

388 Although spontaneously occurring up-states showed the typical fronto-central maximum at
389 electrode Fz, entrained up-states peaked at centro-parietal sites (see Figure 5). This was suggested by
390 the analyses of normalized topographies of the peaks of all averaged spontaneous up-states and the
391 peaks of entrained up-states 1 and 2. Repeated measures ANOVAs with the within-subject factors
392 Topography (the 12 electrodes) and Event (spontaneous versus entrained) revealed that the topographic
393 differences were significant. This was suggested by the significant Topography X Event interactions
394 if up-state 1 ($F(11,165) = 24.20, p < .01, \eta_p^2 = .62$) and up-state 2 ($F(11,165) = 12.27, p < .01, \eta_p^2 =$
395 $.45$) were contrasted with spontaneously occurring up-states. Spontaneous and entrained down-states
396 showed visually similar topographies with maximal negativity over fronto-central sites. However, the
397 significant interaction term in the ANOVA still indicated that the topographies differed between
398 spontaneous and entrained down-states ($F(11,165) = 5.00, p < .01, \eta_p^2 = .25$) because the difference
399 between frontal and posterior negativity was less pronounced in the entrained compared to spontaneous
400 down-states.

401 The analysis of ERSPs did not reveal a general increase in high-frequency activity that would be
402 observed if sleep-played words had reduced sleep depth. Thus, word presentation did not awake our
403 participants. To underscore this conclusion, we contrasted the mean spectral power following word-
404 onset with the mean power of the pre-stimulus time window for the theta (4-8 Hz), alpha (4-12 Hz),
405 sigma (11-16 Hz), beta (12-24 Hz), and gamma (> 24 – 50 Hz) frequency band. Mean spectral activity
406 was not significantly altered by word presentation in any of these bands (all $t(15) < 1.8$, all uncorrected
407 $p > .09$, all $r < .42$).

408 In sum, we have reasons to believe that word presentations during sleep did not wake our
409 participants but entrained their slow oscillations and modulated their sleep spindle activity.

410 3.2 Implicit retrieval of sleep-played words following waking

411 The performance on both priming tests was at chance level for participants as a group (Figure 6 a).
412 Performance in the semantic priming test was expressed as the difference in identification volumes for
413 new words (mean \pm SEM = 54.07 ± 0.58 dB(A)) minus synonyms to sleep-played words (53.89 ± 0.57
414 dB(A)). This difference score did not significantly diverge from zero ($t(15) = 0.58, p = .57, r = .15$).
415 The perceptual priming scores contained the difference in response latencies between incorrect word
416 choices (2720 ± 232 ms) minus correct word choices (2750 ± 229 ms). Again, these scores did not
417 significantly diverge from zero ($t(15) = -0.33, p = .75, r = -.09$). Hence, participants showed no implicit
418 memory for sleep-played words, when tested at the group-level.

419 However, performance on the two priming tests was linearly correlated between participants ($r_s =$
420 $.53$, $p = .04$, Figure 6 a), which hints at perceptual and semantic priming effects in some but not all
421 participants. Because different subsets of sleep-played words were used in the two tests, the significant
422 correlation is not a product of carry-over effects from the first to the second priming test. This
423 significant correlation suggests that the priming scores reflect true interindividual cognitive differences
424 rather than mere noise. These cognitive differences must mirror different degrees of word priming
425 because success on both tests cannot be mediated by any other psychological or stimulus-inherent
426 factor. Hence, those participants who yielded high priming scores on both tests must have been able to
427 encode the percept and the meaning of sleep-played words. Moreover, the magnitude of word-entrained
428 up-states predicted the amount of priming on both tests. Participants with larger mean amplitudes in
429 up-state 1 and 2 performed better on both priming tests. The amplitude of up-state 2 correlated
430 positively with perceptual priming (Figure 6 d; $r_s = .62$, $p = .01$) and with semantic priming (Figure 6
431 b; $r_s = .57$, $p = .02$). The amplitude of up-state 1 correlated positively with perceptual priming (Figure
432 6 c; $r_s = .55$, $p = .03$), but not semantic priming ($r_s = .03$, $p = .83$). These findings suggest that up-states
433 contributed to word encoding. It appears that those participants who consistently increased their
434 neocortical excitability to a large extent in response to words were capable of forming enduring neural
435 representations of words that facilitated priming following sleep. Note that the magnitude of the
436 entrained down-state was not related to performance in either test (all $|r_s| < .36$, all $p > .17$).

437 Which factors account for successful word encoding during sleep? We looked at various variables
438 underlying sleep quality but none was predictive of the amount of priming in either test (all $|r_s| < .39$,
439 all $p > .13$). These variables were time spent in NREM sleep, number of words presented during sleep,
440 average sleep depth during word presentation, the number of stops during word presentation due to
441 arousals, mean amplitude of all detected up-states, and the average volume at which participants
442 identified words in the semantic test. However, we found that the mean individual volume at which
443 words were played during sleep was correlated with the amplitude of the entrained down-state ($r_s = -$
444 $.53$, $p = .04$) and by trend with the amplitude of the first ($r_s = .46$, $p = .07$) but not the second ($r_s = .23$,
445 $p = .38$) entrained up-state. This suggests that the entrainment of slow-oscillations was influenced by
446 stimulus volume. However, the mean presentation volume was not correlated with semantic or
447 perceptual priming (all $|r_s| < .22$, all $p > .40$). Thus, presentation volume did not directly contribute to
448 word encoding and to subsequent priming.

449 Words were not processed consciously during sleep. Participants asserted that they had not heard
450 any words while asleep. Furthermore, choice accuracy reflecting conscious recognition in the
451 perceptual forced-choice test was at the guessing level of 50% (mean \pm SEM = $49.03 \pm 2.21\%$, $t(15) =$
452 -0.44 , $p = .68$, $r = .11$). Furthermore, choice accuracy was uncorrelated with up-state amplitude (all $|r_s|$
453 $< .30$, all $p > .26$), semantic priming ($r_s = -.45$, $p = .08$), and perceptual priming ($r_s = -.06$, $p = .82$). This
454 is evidence that sleep-played words left no consciously accessible memory traces following waking.

455 4 Discussion

456 To investigate whether humans can encode familiar everyday words during sleep, we played single
457 words while participants were in NREM sleep during an afternoon nap. Words were presented
458 rhythmically every 4 s which entrained sleep-specific slow-oscillations with up-states at around 1000
459 and 2400 ms following word onset. Following the nap, we administered a perceptual and a semantic
460 priming test to tap participants' implicit memory for sleep-played words. Participants as a group
461 performed at chance level in both priming tests. Nevertheless, some participants in the group must have

462 encoded words during sleep as suggested by correlation analyses. Priming scores of both tests were
463 positively correlated and were predicted by the magnitude of word-entrained up-states. Hence,
464 participants with stronger entrainment of up-states – as reflected in larger word-related up-state
465 amplitudes – showed stronger priming on both tests. These correlations indicate that some participants
466 have encoded sleep-played words in a way that allowed them to reactivate the words' percepts and
467 meanings following waking. The findings further suggest that up-states might have contributed to
468 sleep-encoding. We conclude that the encoding of everyday words is feasible during sleep for some
469 but not all individuals and benefits from up-states of slow-oscillations.

470 Sleep-played words were processed unconsciously and did not induce wakefulness as indicated by
471 polysomnographic data recorded during sleep. Moreover, participants were unable to recognize sleep-
472 played words following waking, which suggests that their sleep was not interrupted. EEG data of the
473 polysomnogram suggested that word presentation entrained specific features of NREM sleep, namely
474 slow-oscillations and spindles. The presence of slow-oscillations indicates that participants remained
475 asleep and thus unconscious while words were being played for encoding. Unconsciousness of
476 encoding was fostered by the low volume level used for word presentation. In addition, sleep-played
477 words were partially masked by the constantly playing background noise. Following the nap, none of
478 the participants reported having noticed words during sleep. Furthermore, conscious recognition of
479 sleep-played words was at chance level and was neither correlated with the performance on the implicit
480 memory measures nor with the size of the entrained up-states. Our behavioral data thus confirm the
481 polysomnographic data suggesting complete unconsciousness of word encoding.

482 Polysomnographic data suggest that rhythmic presentation of words during sleep entrained a
483 sequence of two slow-oscillations with up-states occurring at around 1000 and 2400 ms following word
484 onset. The time delay of about 1.4 s between up-states indicates that entrained slow-oscillations
485 appeared at a rate of 0.7 Hz. This rate reflects the characteristic frequency (0.7 – 0.8 Hz) of spontaneous
486 slow-oscillations in humans (Achermann and Borbély, 1997). Previous studies reported entrainment
487 of slow-oscillations at very similar rates (Ngo et al., 2013a, 2013b). In these studies, noise sounds of
488 50 ms duration were played at rates of 0.8 or 0.93 Hz (one sound every 1.25 or 1.075 s), which entrained
489 slow-oscillations at just these frequencies. Although we used two-syllabic nouns of varying duration
490 and played them at a rate of 0.25 Hz (1 word every 4 seconds), entrained slow-oscillations still appeared
491 at their characteristic rate of 0.7 Hz. This suggests that entrainment of slow-oscillations is possible
492 using meaningful sounds and does not depend on the exact duration of sounds or on a presentation rate
493 that lies within the slow-oscillations frequency range. We assume that entrainment is successful as long
494 as sounds are presented at regular intervals that leave sufficient time for one or several full slow-
495 oscillations to unfold between two consecutive stimuli. Random intervals (Ngo et al., 2013a) and
496 intervals shorter than one slow-oscillation cycle (Ngo et al., 2013b) were indeed shown to interfere
497 with slow-oscillation activity.

498 Auditory stimuli frequently evoke K-complexes in the EEG of NREM sleep but we think that word-
499 evoked brain responses were not affected by these electroencephalographic events. K-complexes are
500 marked by a strong hyperpolarization followed by a depolarization and are very similar to slow-
501 oscillations regarding morphology and generating mechanism (Amzica and Steriade, 2002; Cash et al.,
502 2009; Colrain, 2005). However, K-complexes are singular events that rarely occur in groups. Because
503 slow-oscillations occur in groups of 2 to 3 cycles (Möller et al., 2011), the long-lasting oscillatory
504 activity (up-state 2) observed here is more likely to reflect slow-oscillations than K-complexes.
505 Furthermore, evoked K-complexes are rare if stimuli are presented at high rates (once every 5 seconds),

506 especially during deep NREM sleep (Bastien and Campbell, 1994). Slow-oscillations on the other hand
507 are specific to deep sleep and are entrained by rhythmic and frequent stimuli (Ngo et al., 2013a, 2013b).
508 Because we presented words at high rates and targeted presentation to deep NREM sleep, we are
509 confident that the reported brain responses were mainly driven by slow-oscillation activity. However,
510 even if K-complexes contributed to evoked responses, the similarity between K-complexes and slow-
511 oscillations suggests that the hyperpolarized phase of K-complexes could foster plastic synaptic
512 changes in similar ways as up-states of slow-oscillations.

513 Word-entrained up-states seemed to have different neural generators than spontaneously occurring
514 up-states. This was suggested by the finding that entrained up-states reached maximum around centro-
515 parietal sites, whereas spontaneous up-states showed the typical topography with a maximum over
516 fronto-central sites. Previous studies reported that sound-entrained and spontaneous up-states produce
517 very similar topographies and might thus be generated by similar neuronal mechanisms (Ngo et al.,
518 2013b). However, these studies used non-verbal sounds to entrain slow-oscillations. It is possible that
519 the altered neural generators of word-entrained up-states reflect word-specific processing. But this
520 interpretation remains speculative because our design entailed no control condition such as the play of
521 nonsense words. Hence, a comparison between meaningful words and nonsense words cannot be
522 computed to demonstrate a topographical difference due to semantic word processing.

523 Mean performance was at chance level in the two priming tests that probed implicit memory for
524 sleep-played words. This makes believe that participants did not encode sleep-played words and
525 showed no priming effects following sleep. However, performance on both priming tests was positively
526 correlated with participants exhibiting higher semantic priming scores also exhibiting higher perceptual
527 priming scores. Moreover, performance on both priming tests was correlated with word-evoked up-
528 state amplitudes. The significant correlations between these three variables cannot be products of noise
529 or chance. The relation between these three variables must have a biological origin. We assume that
530 participants had encoded the sleep-played words to varying degrees with some participants showing
531 positive priming and others negative priming. It should be noted that some participants displayed
532 negative priming scores on both tests. Negative priming scores reflect impaired processing of the
533 percepts and meanings of sleep-played words following waking. It is thus possible that successful
534 encoding of words during sleep induced consistent positive priming in some and negative priming in
535 other participants leading to zero net priming at the group level. This phenomenon is known from
536 experiments on subliminal priming. Snodgrass and Shevrin (2006) found that a main effect of priming
537 was absent because some participants showed positive priming, while others displayed negative
538 priming due to differences in stimulus preferences and processing strategies. We assume that positive
539 and negative priming are two natural consequences of encoding during sleep. According to Newman
540 and Norman (2010), the direction of priming depends on the strength of activation of prime
541 representations. The authors argued that strong activation of stimulus representations improves these
542 representations and leads to positive priming, whereas weak activation impairs representations and
543 yields negative priming. Their assumption is supported by the finding that stimuli which are masked
544 or ignored and are thus only weakly activated induce negative priming (Newman and Norman, 2010;
545 Ortells and Tudela, 1996; Noguera et al., 2007; Bermeitinger et al., 2012). Negative priming in our
546 study was most pronounced in participants with minimal entrainment of up-states. We speculate that
547 NREM sleep and especially down-states (Schabus et al., 2012) prevented strong activation of words'
548 representations. Thus, the state of sleep might actually have impaired or weakened neuronal
549 representations of percepts and concepts that were triggered by words – unless words were followed
550 by up-states. We assume that the neuronal excitability and plasticity provided by up-states allowed a

551 stronger activation of words during sleep, leading to a strengthening of words' representations. Because
552 most participants displayed entrainment to some degree, the excitability provided by entrained up-
553 states counteracted the weakening of word representations. In participants who consistently produced
554 precisely timed large amplitude up-states upon word-onset, word activation was sufficient to even
555 induce a strengthening of representations, leading to positive priming.

556 Performance on the priming tests administered after sleep was predicted by the magnitude of word-
557 entrained up-states. Hence, up-states of slow-oscillations might have contributed to word encoding and
558 to the strengthening of words' representations during sleep. Entrained up-states are not a specific
559 indicator of word processing. In fact, up-states appear naturally, in the absence of any external triggers,
560 and can be entrained by various non-verbal stimuli, such as pure tones (Ngo et al., 2013a, 2013b),
561 transcranial direct current stimulation (Marshall et al., 2006), and transcranial magnetic stimulation
562 (Massimini et al., 2007). However, up-states reflect a brain-state that could serve as a window of
563 opportunity for unconscious encoding. So far, slow-oscillations and up-states have only been
564 associated with the consolidation of memories that were encoded before and not during sleep (Ngo et
565 al., 2013b; Marshall et al., 2006, 2004). The sleeping brain repeatedly reactivates and replays the
566 neuronal activity that represents memories learned before going to sleep (Skaggs and McNaughton,
567 1996; Ji and Wilson, 2007). This replay is thought to strengthen memory traces (Rudoy et al., 2009;
568 van Dongen et al., 2012) by inducing synaptic changes within the networks that represent the memory
569 traces. Importantly, memory replay occurs predominantly during up-states of slow-oscillations (Ji and
570 Wilson, 2007) because synaptic plasticity is increased during up-states. The plasticity provided by up-
571 states should also contribute to the acquisition of new information during sleep. The coupling of words
572 with up-states in the EEG suggests that the neuronal networks supporting word encoding were in a
573 state of plasticity that allowed for long-term synaptic modifications. These synaptic changes may
574 outlast the state of sleep to facilitate the perceptual and semantic processing of the same words or
575 semantically related words following sleep. Evidence for this is provided by the finding of a larger
576 entrainment of up-states in those participants, who yielded strong positive priming. It appears that
577 participants who consistently produced large-amplitude up-states at 1000 and 2400 ms after word onset
578 exhibited a facilitated perceptual and semantic processing of sleep-played words or their synonyms
579 following sleep.

580 The excitability and plasticity provided by up-states could in principle assist both, the initial
581 processing and the ensuing consolidation of sleep-played words. Our study design did not allow
582 capturing the early ERPs that represent the initial sensory and semantic analysis of sleep-played words.
583 The sensory component was obscured by different word lengths. The semantic component could not
584 be isolated because the appropriate control condition (e.g., presentation of nonsense words) was
585 lacking. But drawing from previous studies of sleep-played words, we assume that the initial perceptual
586 analysis occurred around 100 ms following word onset (Perrin et al., 1999, 2002) and the semantic
587 analysis around 400 to 700 ms following word onset (Brualla et al., 1998; Daltrozzo et al., 2012; Perrin
588 et al., 1999). Thus, encoding was terminated before the onset of the first entrained up-state at about
589 800 ms. This indicates that up-states contributed rather to the consolidation than the initial encoding of
590 the words' sounds and meanings. Interestingly, entrained up-states that followed early after word
591 presentation (up-state 1) were predictive of perceptual priming, whereas later up-states (up-state 2)
592 predicted both perceptual and semantic priming. This indicates that early up-states assisted the
593 consolidation of appearance characteristics of words such as the rhythm or sound of words, while later
594 up-states assisted the strengthening of word meaning.

595 We are not the first to postulate that humans might encode words during sleep (e.g. Bierman and
596 Winter, 1989; Elliott, 1968; Fox and Robbin, 1952; Levy et al., 1972). However, previous reports of
597 sleep-encoding lack convincing proof that participants were sleeping continuously during verbal
598 stimulation (for reviews see Aarons, 1976; Eich, 1990; Hoskovec, 1966; Simon and Emmons, 1955).
599 It is possible that encoding was mediated by brief phases of wakefulness in these studies. Studies that
600 properly monitored the absence of wakefulness did not find evidence of sleep-encoding. It is likely that
601 evidence of encoding was absent in these studies because stimuli were presented during REM instead
602 of NREM sleep (Wood et al., 1992; Tani and Yoshii, 1970) or because explicit instead of implicit
603 retrieval tests were used to assess memory for sleep-played contents (Emmons and Simon, 1956; Simon
604 and Emmons, 1956; Koukkou and Lehmann, 1968; Lehmann and Koukkou, 1974). The sleep stage,
605 during which information is presented, might determine the success of sleep-encoding. Because only
606 NREM but not REM sleep is thought to actively contribute to memory consolidation (Diekelmann and
607 Born, 2010; Deliens et al., 2013), only NREM sleep might provide the necessary conditions for the
608 long-term storage of new information. Indeed, Arzi et al. (2012) found that sleep-learned tone-odor
609 associations are retained into wakefulness if they were acquired during NREM rather than REM sleep.
610 Yet, not only the sleep stage of encoding but also the type of retrieval test decides about the success of
611 sleep-encoding. Sleep-formed memories are acquired in a state of unconsciousness and might therefore
612 not be remembered consciously in explicit tests after waking up (Wood et al., 1992; Arzi et al., 2012).
613 Therefore, implicit tests need to be applied as they are tailored to tap unconscious expressions of
614 memories.

615 Although the correlations between word-entrained up-states and perceptual and semantic priming
616 suggest that up-states contributed to the encoding of sleep-played words and their meanings, we
617 recognize that our findings are not necessarily specific to verbal information. Up-states are sleep-
618 specific brain states of increased neuronal activity that might benefit various cognitive processes and
619 that can be entrained by various non-verbal stimuli (Ngo et al., 2013a, 2013b; Marshall et al., 2006;
620 Massimini et al., 2007). Thus, entrained up-states might also contribute to the encoding of nonverbal
621 stimuli such as environmental sounds or simple melodies and might facilitate subsequent processing
622 of these stimuli due to priming.

623 Encoding during sleep is not a pervasive phenomenon as suggested by the fact that only part of our
624 participants displayed positive perceptual and semantic word priming. Because sleep quality and other
625 external factors did not correlate with the size of priming, we speculate that perceptual or psychological
626 factors might explain the difference between individuals regarding sleep-encoding. We found that the
627 volume of sleep-played words tended to correlate with the magnitude of the first entrained up-state. If
628 entrained up-states reflect stimulus intensity, they might also mirror participants' auditory sensitivity
629 during sleep. Participants who are more sensitive to auditory stimuli during sleep might have responded
630 with stronger entrainment of up-states upon word presentation which improved their ability to encode
631 and consolidate the sleep-played words. Whether psychological factors such as motivation to learn
632 during sleep or openness to experience affected entrainment of up-states and word-encoding remains
633 elusive as we did not measure any psychological characteristics. Many more studies are necessary to
634 pin down the factors that modulate encoding during sleep.

635 **5 Conflict of interest statement**

636 The authors declare that the research was conducted in the absence of any commercial or financial
637 relationships that could be construed as a potential conflict of interest.

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646 **7 References**

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813 9280.1992.tb00035.x.

815

816 **8 Figure legends**

817 **Figure 1. Design.** Word presentation during sleep was followed by two priming tests. In the
818 semantic test, identification volumes for synonyms to sleep-played words and new words were
819 contrasted. In the perceptual test, response latencies for correct and incorrect responses in a two-
820 alternative forced-choice recognition test for sleep-played words were compared.

821 **Figure 2. Electric brain responses at electrode Fz to word presentation during sleep.** Event-
822 related potentials (A) and event-related spectral power changes (B) to word-presentation during sleep.
823 Temporal overlaps of the down-state with the increase in slow-spindle power (SS+) and of the up-state
824 1 with the increase in fast-spindle power (FS+) are highlighted. Normalized count (C) and peak-
825 amplitudes (D) of discrete slow-oscillation up-states identified before and after word presentation. Both
826 the number and the amplitudes of up-states are increased during the time windows of the ERPs
827 identified as up-states 1 and 2, which indicates that these ERPs reflect up-states. * $p < .05$, # $p < .10$
828 (uncorrected p-values for two-tailed t-tests).

829

830 **Figure 3. Event-related brain potentials (ERPs) to word presentation during sleep.**

831

832 **Figure 4. Event-related changes in spectral power (ERSPs) to word presentation during sleep.**

833

834 **Figure 5. Topographic plots for naturally occurring and entrained down- and up-states.**
835 Topographies were normalized within each participant and were then averaged across participants.
836 Plots display the topography at the peak of the ERP for all discretely identified down- and up-states
837 (top line, left and right), and of the ERPs reflecting the entrained down-state and entrained up-states 1
838 and 2 (bottom line, left and right plots).

839

840 **Figure 6. Correlations between word-related brain responses and the amount of priming.** (A)
841 Although the amount of priming was at chance level in both tests (triangles with lines reflect mean and
842 standard deviation), perceptual and semantic priming were correlated. (B) The mean amplitude of the
843 word-evoked up-state 1 predicted the amount of semantic priming. The mean amplitude of the word-
844 evoked up-state 1 (C) and 2 (D) predicted the amount of perceptual priming. r_s : Spearman correlations;
845 * $p < .05$.

846

847 **9 Tables**848 **Table 1: Descriptive statistics for the event-related potentials that were evoked by words**
849 **presented during sleep.**

| Response | Duration (ms) | | *p-value | Locus of maximal deviation from baseline | | |
|-----------------|----------------------|------------|-----------------|---|---------------------|------------------|
| | Start | End | | electrode | peak t-value | peak time |
| down-state | 452 | - 806 | 0.032 | C4 | -9.974 | 670 |
| up-state 1 | 868 | - 1668 | < .001 | P4 | 6.858 | 1168 |
| up-state 2 | 2078 | - 2672 | < .001 | P4 | 6.958 | 2400 |

*Note: p-values are based on non-parametric statistics as suggested by Maris, E., and Oostenveld, R. (2007). Nonparametric statistical testing of EEG- and MEG-data. *J. Neurosci. Methods* 164, 177–190. doi:10.1016/j.jneumeth.2007.03.024.

850

851 **Table 2: Descriptive statistics for the event-related changes in spectral power that were evoked**
852 **by words presented during sleep.**

| #Response | Duration (ms) | | Frequency (Hz) | | *p-value | Locus of maximal deviation from baseline | | | |
|------------------|----------------------|------------|-----------------------|-------------|-----------------|---|-------------|------------------|----------------|
| | Start | End | min. | max. | | electrode | time | frequency | t-value |
| SS+ | 340 | 928 | 4 | 11 | 0.001 | Fz | 562 | 5.5 | 10.5187 |
| FS+ | 832 | 1722 | 8.5 | 21.5 | 0.002 | F3 | 1294 | 15.5 | 7.1544 |
| FS- | 1706 | 2470 | 12 | 21.5 | 0.005 | P4 | 1930 | 17.5 | -5.5267 |

*Note: p-values are based on non-parametric statistics as suggested by Maris, E., and Oostenveld, R. (2007). Nonparametric statistical testing of EEG- and MEG-data. *J. Neurosci. Methods* 164, 177–190. doi:10.1016/j.jneumeth.2007.03.024.

*Responses: increases (+) and decreases (-) in slow- and fast-spindle (SS and FS respectively) frequencies.

853

Figure 1.TIF

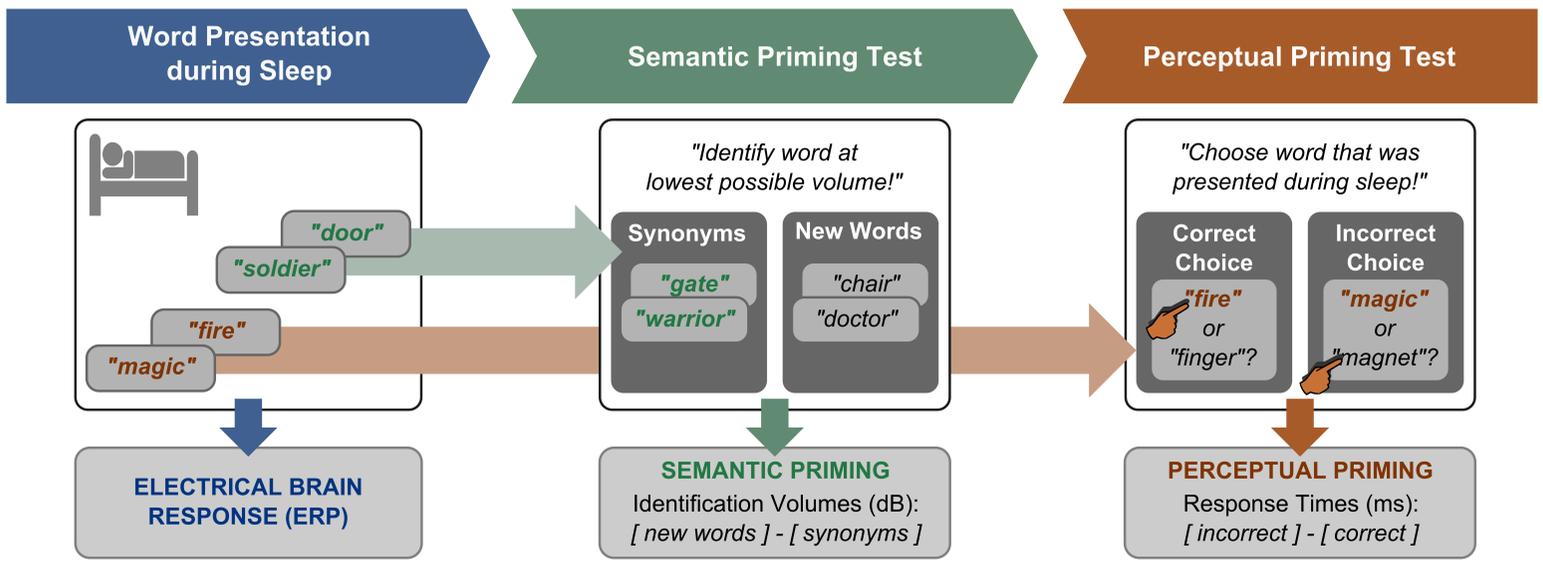


Figure 2.TIF

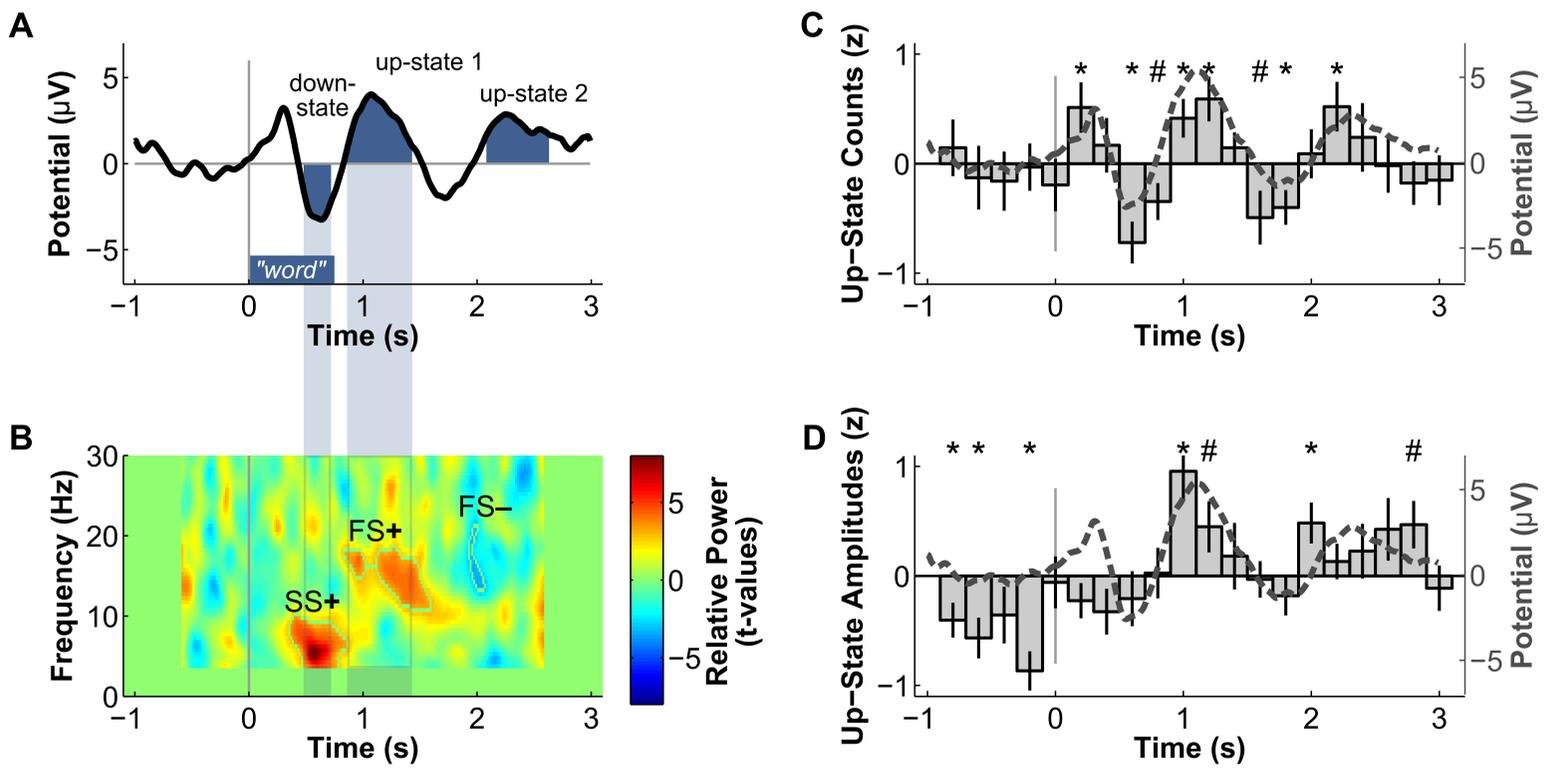


Figure 3.TIF

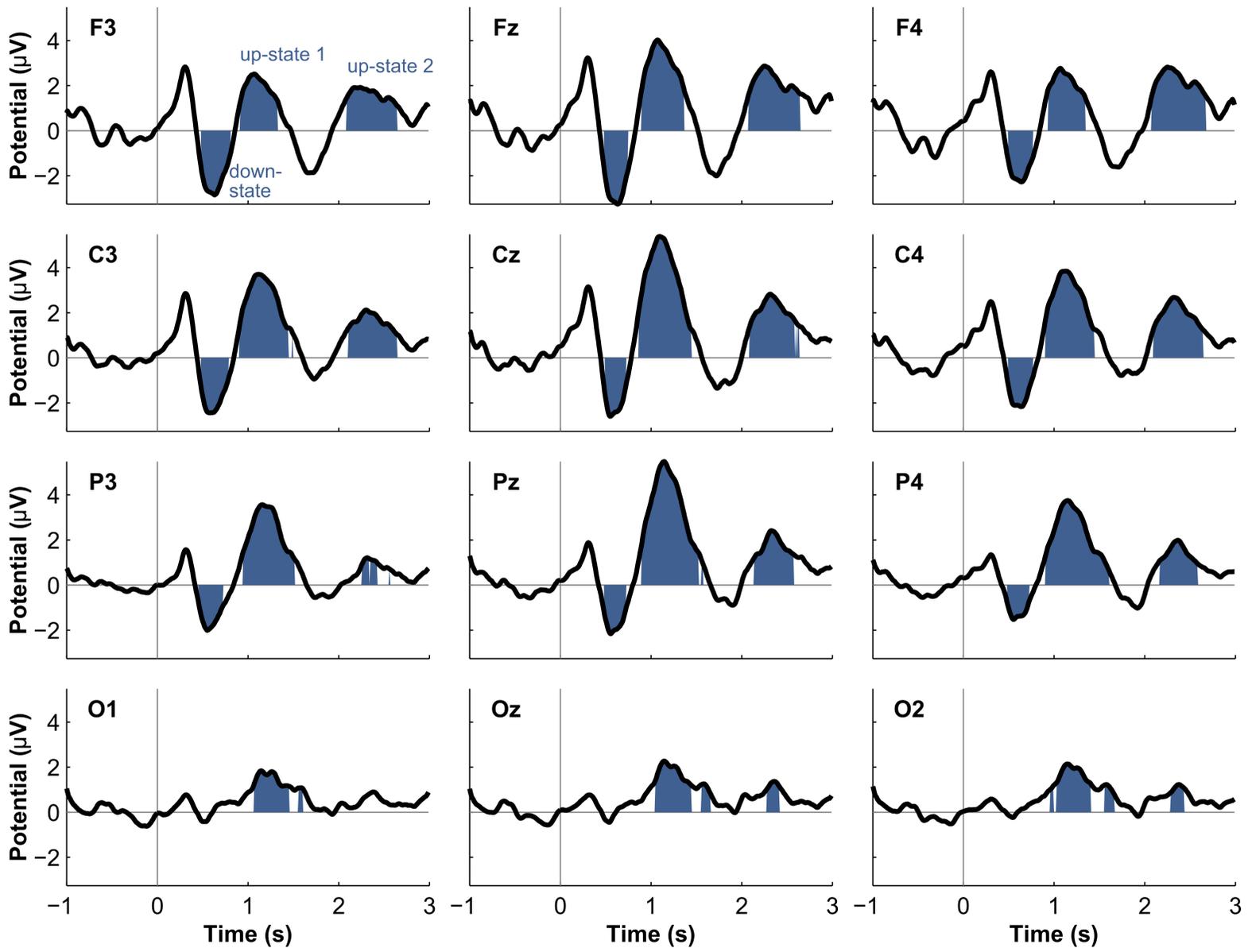


Figure 4.TIF

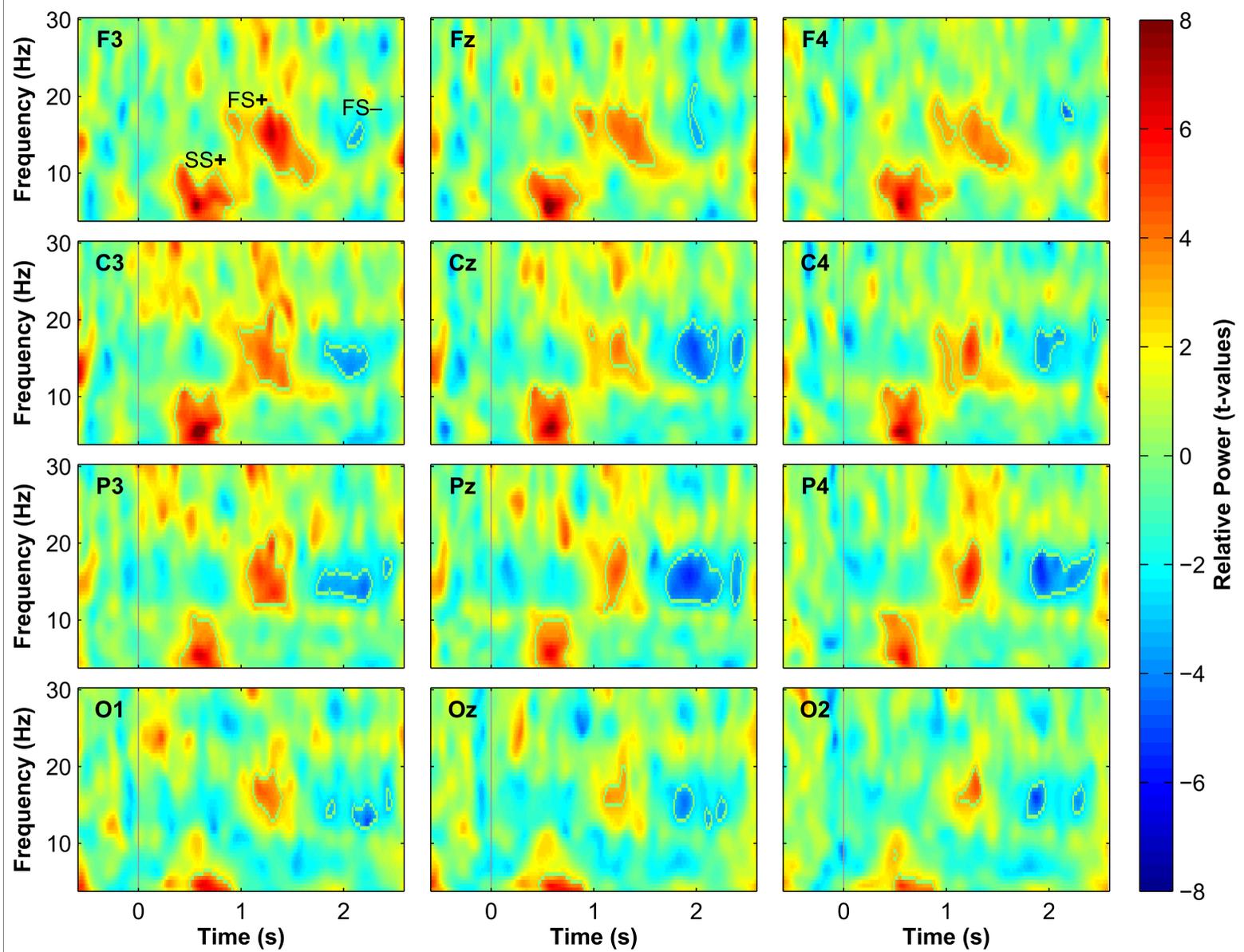


Figure 5.TIF

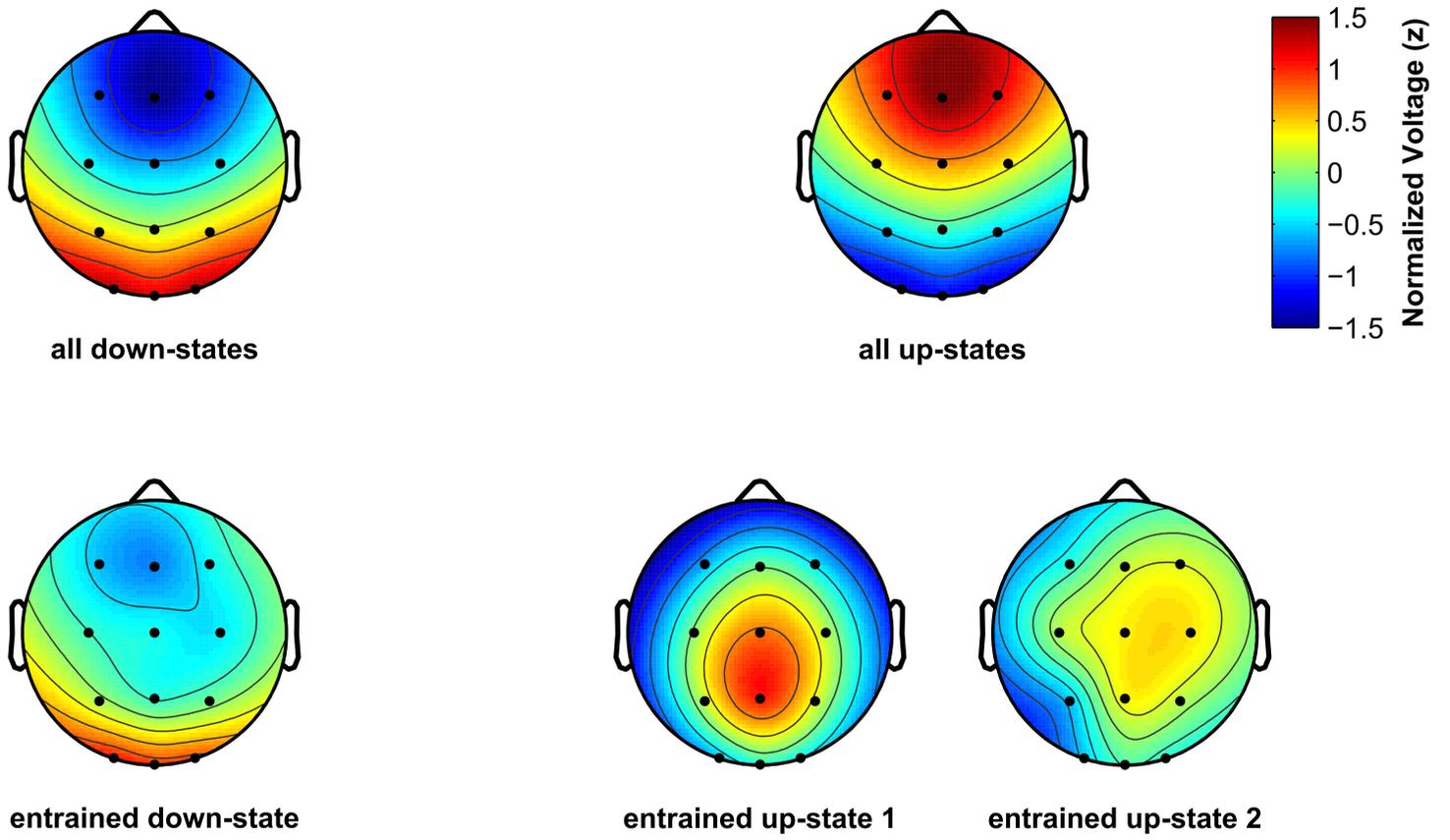


Figure 6.TIF

