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The brain selectively tunes to unfamiliar voices during sleep.

[Abbreviated title: Sleeping brain and unfamiliar voices]

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35 **Abstract**

36 The brain continues to respond selectively to environmental stimuli during sleep. However,
37 the functional role of such responses, and whether they reflect information processing or
38 rather sensory inhibition is not fully understood.

39 Here, we present 17 human sleepers (14 females) with their own name and two unfamiliar
40 first names, spoken by either a familiar voice (FV) or an unfamiliar voice (UFV), while
41 recording polysomnography during a full night's sleep. We detect K-complexes, sleep
42 spindles, and micro-arousals, and assess event-related, and frequency responses as well as
43 inter-trial phase synchronization to the different stimuli presented during non-rapid eye
44 movement (NREM) sleep.

45 We show that UFVs evoke more K-complexes and micro-arousals than FVs. When both
46 stimuli evoke a K-complex, we observe larger evoked potentials, more precise time-locking
47 of brain responses in the delta band (1-4 Hz), and stronger activity in the high frequency
48 (>16Hz) range, in response to UFVs relative to FVs. Crucially, these differences in brain
49 responses disappear completely when no K-complexes are evoked by the auditory stimuli.

50 Our findings highlight discrepancies in brain responses to auditory stimuli based on their
51 relevance to the sleeper and propose a key role for K-complexes in the modulation of
52 sensory processing during sleep. We argue that such content-specific, dynamic reactivity to
53 external sensory information enables the brain to enter a 'sentinel processing mode' in which
54 it engages in the important internal processes that are ongoing during sleep while still
55 maintaining the ability to process vital external sensory information.

56 **Keywords: Auditory stimulation, Sleep, K-complexes, Micro-arousals, EEG,**
57 **Information processing**

58 **Significance statement**

59 Previous research has shown that sensory processing continues during sleep. Here, we
60 studied the capacity of the sleeping brain to extract and process relevant sensory
61 information. We presented sleepers with their own names and unfamiliar names spoken by
62 either a familiar (FV) or an unfamiliar voice (UFV). During non-rapid eye movement (NREM)
63 sleep, UFVs elicited more K-complexes and micro-arousals than FVs. By contrasting stimuli
64 that evoked K-complexes, we demonstrate that UFVs evoked larger, more synchronized
65 brain responses as well as stronger power at high frequencies (>16Hz) relative to FVs.
66 These differences in brain responses disappeared when no K-complexes were evoked. Our
67 results suggest a pivotal role for K-complexes in the selective processing of relevant
68 information during NREM sleep.

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1. Introduction

During sleep, the brain continues to respond to auditory stimuli in a selective fashion (Portas et al., 2000; Andrillon et al., 2016; Blume et al., 2017; 2018). Previous studies have demonstrated that, for instance, the subject's own name (SON) evokes stronger brain responses than other names during sleep (Oswald et al., 1960; Perrin et al., 1999; Pratt et al., 1999). Recently, Blume et al. (2018) showed that during all stages of sleep, brain responses to SON and other unfamiliar names (UNs) did not differ; however, names uttered by an unfamiliar voice (UFV) evoked stronger brain responses as compared to a familiar voice (FV).

The discrepancy in brain responses to different stimuli implies the presence of an initial, presumably low-level, sensory processing during sleep that enables the brain to differentiate between sensory signals (Blume et al., 2018). However, knowledge about the functions of such responses is still lacking. That is, the selective brain responses to specific sounds during sleep might reflect inhibitory processes that protect sleep from disruptions. Conversely, they might indicate further, higher level, processing that ensures the connectedness of the sleeping brain to the surrounding.

In this study, we investigated the purpose of such selective brain responses to sounds presented during non-rapid eye movement (NREM) sleep. We focused on sleep-specific events that have been previously linked to information processing, sensory inhibition, or both. That is, we focused on three cardinal sleep-specific electroencephalography (EEG) events, namely, the K-complex (KC), sleep spindles, and micro-arousals.

KCs are ~1Hz oscillations and a hallmark of N2 sleep (Loomis et al., 1938, Colrain, 2005; Halász, 2005). KCs occur either spontaneously or in response to sensory stimuli.

Spontaneous KCs appear in the EEG signal as well-defined sharp negative wave followed by a positive component with a total duration of at least 0.5s (Rechtschaffen and Kales, 1968; Hori et al., 2001). Following sensory perturbation, KCs appear to have two main components; a sharp negative deflection at ~550ms (N550) followed by a longer-lasting

positive wave at ~900ms (P900) (Bastien & Campbell, 1992; Cote et al., 1999; Colrain, 2005; Halász, 2005). Some studies have considered an early positive peak that appears around 200ms (P200, Laurino et al., 2014; 2019) and another negative peak around 350ms (N350, Bastien & Campbell, 1992; Cote et al., 1999) to be parts of the KC, albeit these components can occur without a KC being elicited. Relevant stimuli have higher propensity to trigger KCs (Halász, 2005). Recent theories suggest that KCs can serve both sleep-protecting as well as arousal-inducing processes (Halász, 2005; Jahnke et al., 2012; Forget et al., 2014; Laurino et al., 2014; Blume et al., 2017; 2018; Legendre et al., 2019; Latreille et al., 2020).

Sleep spindles are also characteristic of N2 sleep. Spindles are thalamocortical oscillations of 11-15 Hz that last around 0.5 to 2s (De Gennaro and Ferrara, 2003; Fernandez and Lüthi, 2020) that can be triggered by sensory stimuli (Antony and Paller, 2017). They have been repeatedly shown to inhibit sensory processing during sleep (McCormick & Bal, 1994, Schabus et al., 2012; Blume et al., 2018; Fernandez and Lüthi, 2020). However, recent work challenges this notion (Sela et al., 2016) and even associates spindles with the processing of memory-related sounds presented during NREM sleep (Cairney et al., 2018).

Finally, micro-arousals are abrupt shifts in the EEG signal towards theta, alpha and/or high beta (>16 Hz) frequencies (Halász et al., 1979; American Sleep Disorders Association, 1992; Halász et al., 2004) that appear in all sleep stages and are considered windows of information processing during sleep (dos Santos Lima et al., 2019; Halász et al., 2004; Halász, 2005). Micro-arousals are usually preceded by KCs (Colrain 2005; Halász, 2005), yet they have been shown to be correlated with a lower incidence of sleep spindles in the preceding 10s of EEG signal (Ehrhart et al., 1981).

Here, we re-analysed the dataset used in Blume et al. (2018) who recorded polysomnography while presenting SONs and two UNs spoken by either a FV or an UFV during a whole night of sleep. We detected KCs, spindles, and micro-arousals in response

135 to these sounds during NREM sleep and hypothesized that the selective auditory-evoked
 136 responses support the extraction and processing of relevant sensory information.

137 **2. Materials and methods**

138 **2.1. Participants:** We recruited 20 healthy participants with no reported history of
 139 neurological or psychological problems as well as no reported sleep disorders. However, one
 140 participant dropped out after the adaptation night and we had to exclude two participants due
 141 to technical problems during EEG acquisition. Therefore, we performed the analyses we
 142 report here on 17 participants (14 females) with a median age of 22.6 ± 2.3 years. Before
 143 beginning the experiment, all participants signed written informed consents. The experiment
 144 was approved by the ethics committee of the University of Salzburg.

145 **2.2. Experimental design:** Before the start of the experiment, participants were
 146 advised to maintain a regular sleep/wake cycle (~8h of sleep) for at least four days which we
 147 monitored via actigraphy (Fig. 1A). Subsequently, participants spent two nights in the sleep
 148 laboratory of the University of Salzburg. The first night was an adaptation night, during which
 149 we recorded polysomnography (PSG) data with no auditory stimulation. The second night
 150 was an experimental night, during which we recorded PSG data while presenting sounds via
 151 loudspeakers throughout the night. In both nights, participants were tested during
 152 wakefulness before and after sleep. Briefly, the wakefulness testing consisted of two
 153 sessions, a passive-listening session and an active-listening session. Passive listening
 154 entails that the participants had to listen to the repeatedly presented auditory stimuli; while
 155 active listening means that, they had to count the number of presentations of one specific
 156 stimulus chosen by the experimenters. Before the wakefulness testing, participants were
 157 stimulated with either a bright (blue-enriched) light or an inactive (sham) light for one hour.
 158 The order of the light-stimulation conditions was counterbalanced between the adaptation
 159 and the experimental nights across participants. However, the light condition is irrelevant to
 160 this study, as we grouped our data over both light conditions. For the purpose of this paper,
 161 we will focus primarily on the sleep part of the experimental night. For more details on the

162 wakefulness part of the experiment, please refer to Blume et al. (2018). During the
 163 experimental night, participants went to bed around their habitual bedtime (8:30pm –
 164 11:30pm). Time in bed (TiB) was approximately 8 hours. After 8 hours TiB, we waited for
 165 light NREM or REM sleep before waking up the participants (median sleep duration = $480 \pm$
 166 2.5 minutes). The auditory stimulation started directly after participants went to bed and
 167 continued throughout the whole night. We presented auditory stimuli continuously for 90
 168 minutes (*Stimulation periods*) then paused the presentation for 30 minutes (*No-stimulation*
 169 *periods*) to allow for periods of undisturbed sleep. This resulted in a 120-minute cycle that we
 170 repeated four times throughout the night (Fig. 1B).

171 **2.3. Stimuli:** We presented six different auditory stimuli (Fig. 1C) that we
 172 personalized for each participant. The stimuli were the subject's own name (SON) and two
 173 unfamiliar names (thereafter referred to as UNs) spoken by either a familiar voice (FV) or an
 174 unfamiliar voice (UFV). A FV was the voice of someone close to the participant, for example
 175 one of the parents. An UFV was the voice of someone unknown to the participant. We did
 176 not control for the sex of the voices, but they were matched, that is, the familiar and
 177 unfamiliar voices were always both either male or female. We chose UNs that matched the
 178 SON in the number of syllables and the frequency of occurrence in the population. The
 179 volume for stimulus presentation was adjusted individually for each participant so that the
 180 participant could clearly hear the stimulus and still be able to fall asleep. Each stimulus was
 181 presented 690 times and the mean duration was $808\text{ms} \pm 110\text{ms}$. Stimuli were presented in
 182 a pseudo-random order and no stimulus was presented twice in a row. The inter-stimulus
 183 intervals during sleep were jittered between 2800ms to 7800ms in 500ms steps. Stimulus
 184 pre-processing, i.e. denoising and normalization, was done using Audacity© software
 185 (<http://audacityteam.org/>). Stimulus delivery was controlled by Matlab® (Mathworks, Natick,
 186 USA).

187 **[Please inset Figure 1 about here]**

188 **2.4. Brain Data Acquisition:** We recorded ongoing brain activity using a high-density
 189 EEG 256-channel GSN HydroCel Geodesic Sensor Net (Electrical 478 Geodesics Inc.,
 190 Eugene, Oregon, USA) and a Net Amps 400 amplifier. The PSG recordings included two
 191 electrooculography (EOG) and two chin electromyography (EMG) channels. Data were
 192 acquired at a sampling rate of 250 Hz and Cz served as the online reference.

193 **2.5 Sleep staging:** Sleep staging was performed on 30s epochs using the computer-
 194 assisted sleep classification system developed by the SIESTA group (Somnolyzer 24x7; The
 195 SIESTA Group Schlafanalyse GmbH, Vienna, Austria; [Anderer et al., 2005](#); [Anderer et al.,](#)
 196 [2010](#)) following the standard criteria recommended by the American Association for Sleep
 197 Medicine (AASM, [American Academy of Sleep Medicine & Iber, 2007](#)). We have previously
 198 shown that level of agreement between this algorithm and expert human scorers is similar to
 199 the level of agreement between human experts ([Ameen et al., 2019](#)).

200 **2.6. The detection of sleep microstructures:**

201 **2.6.1. KC detection:** We detected KCs automatically with a wavelet-detection
 202 algorithm that was developed by the SIESTA group (The SIESTA Group Schlafanalyse
 203 GmbH., Vienna, Austria). The development and validation procedures have been described
 204 in detail in Parapatics et al. ([2015](#)) and Schwarz et al. ([2017](#)), respectively. Briefly, 12
 205 experienced human scorers visually scored KCs in 873 10-minute-epochs of PSG recordings
 206 from 189 control subjects and 90 patients. The features of the visually scored KCs were used
 207 to set the criteria for detection as well as to create a template KC that worked as a gold
 208 standard for the automatic detection. The detection itself is a two-step process; first, the
 209 algorithm detects possible KCs via an approach that combines a matched-filtering detection
 210 method and a slow-wave detection method ([Woertz et al., 2004](#)). Accordingly, the detection
 211 criteria for possible KCs were: 1) a minimum negative-to-positive peak-to-peak amplitude of
 212 50 μ v, and 2) a duration between 480ms and 1500ms. Second, all possible KCs are matched
 213 to the prototypical KC template via wavelet analysis and the results are submitted to a linear
 214 discriminant analysis (LDA) to select only “real” KCs. For our analysis, we considered real

KCs to be events that have an LDA score (how likely a specific EEG segment is a KC) of 0.8 or higher. This LDA score corresponds to $61.87\% \pm 9.14$ of all detected KCs and a mean correlation to the template of 0.87 ± 0.007 over all subjects and is a compromise between reliable detections and a sufficient number of detected events for our analyses. Note that an LDA score of 1.7 reflects 98% detection specificity. Before running the detection algorithm, raw data were down-sampled to 128Hz and re-referenced to the contralateral mastoid. We detected KCs at C3 and C4. We only report results from C3 as the detections were similar between C3 and C4. We only considered events that occurred during N2 and N3 sleep and fulfilled the standard criteria for KC detection (Rechtschaffen and Kales, 1968; Hori et al., 2001). For N3 detections, however, we applied a more strict amplitude criterion as we only selected events with a peak-to-peak amplitude of $75\mu\text{V}$ or higher (Cote et al., 1999; Nir et al., 2011). We marked the start of KC events as the point of the negative-going zero-crossing of the signal prior to the negative peak. We defined evoked KCs as those events which occurred (started) in the 2000ms post-stimulus-onset window. Fig. 2 demonstrates the LDA distribution of the detected KCs as well as some examples of the detected events.

[Please insert Figure 2 about here]

2.6.2. Spindle detection: Sleep spindles were detected using an algorithm developed by the SIESTA group (ASK analyser, The Siesta Group Schlafanalyse GmbH., Vienna, Austria, Gruber et al., 2015). First, we filtered the raw data between 11 and 16 Hz and then detected spindle events at frontal (F3, F4, Fz) and central leads (C3, C4 & Cz) channels re-referenced to the average of mastoids. We used the criteria described in Schimicek et al. (1994). Only events with an amplitude $>12\mu\text{V}$ and duration between 500ms and 2000ms were considered. Further validation of the detected spindles was done using LDA in which the detected spindles were compared to a template that is generated based on the visual scoring of sleep spindles in 8730 minutes of PSG data from 189 healthy participants and 90 participants with sleep disorders. For our analyses, we only considered events that occurred during N2 and N3 sleep with an LDA score of 1.7 or higher (for more details see: Anderer et

242 [al., 2005](#)). In order to identify the frequency of each spindle event, the algorithm preforms
 243 period-amplitude analysis of the band-pass filtered signal in the time domain. We subdivided
 244 spindles into slow (11-13 Hz) and fast (13-15Hz) spindles based on the dichotomy in their
 245 topography and functions ([Schabus et al., 2007](#)). We report results from fast spindles
 246 detected at C3 and slow spindles detected at F3.

247 **2.6.3. Micro-arousal detection:** We detected micro-arousals semi-automatically using
 248 an algorithm developed by the SIESTA group (The Siesta Group Schlafanalyse GmbH,
 249 Vienna, Austria), and has been described in details in ([Anderer et al., 2010](#)). Briefly, the
 250 algorithm was developed using the scoring of 12 PSG recordings by six independent experts.
 251 It incorporates information from central and occipital channels. First, the algorithm compares
 252 the absolute and relative power of nine frequency bands including theta, alpha and high beta
 253 (> 16 Hz) frequencies between a 3-second test window and a moving ten-second baseline
 254 via a series of LDA separately for each channel. Second, the start and end of each event are
 255 determined by combining the posterior probabilities of all channels so that the number of
 256 micro-arousals per total sleep time is the same for both automatic and visual detections.
 257 Although, EMG increases are not necessary for the identification of micro-arousals that occur
 258 during NREM sleep, some of the detected micro-arousals showed a concurrent increase in
 259 the amplitude of the EMG signal; however, this increase in EMG activity was not time-locked
 260 to the high-frequency shifts of the EEG signal. The algorithm detects micro-arousals in all
 261 sleep stages, however, for the purpose of this study; we selected micro-arousals that
 262 occurred during N2 and N3 only (for examples of the detected micro-arousals see: [Fig. 3](#)).

263 **[Please insert Figure 3 about here]**

264 **2.6.4. The detection of transient microstates (micro-measures of alertness):** The
 265 detection of sleep microstates provides a more fine-grained scoring that detects transient
 266 changes in sleep architecture in 4s epochs rather than 30s, using an algorithm described in
 267 Jagannathan et al. ([2018](#)). The algorithm uses the Hori scale ([Tanaka et al., 1996](#)) to classify
 268 the epochs into either awake, drowsy (N1), or asleep (N2) based on the signal from a subset

269 of 14 electrodes distributed over frontal, central, parietal, occipital and temporal regions. We
 270 extracted stimuli from N2 sleep only and removed stimuli with inter-stimulus intervals of less
 271 than 4000ms. Then, we filtered the data between 0.1 and 30Hz before running the algorithm
 272 on an equal number of epochs in all conditions.

273 **2.7. EEG pre-processing and analyses:**

274 **2.7.1. Pre-processing:** We performed all the pre-processing steps in EEGLAB
 275 v14.1.1b (Delorme & Makeig, 2004). First, we excluded face and neck channels and down-
 276 sampled the raw data from 183 EEG channels to 128 Hz. Then, we filtered the data between
 277 0.1 and 40 Hz using a Butterworth bandpass filter. We performed bad channels rejection and
 278 interpolation as well as re-referencing to an average reference using the PREP pipeline
 279 described in Bigdely-Shamlo et al. (2015). Finally, we performed independent component
 280 analysis using the Adaptive Mixture Independent Component analysis (AMICA) toolbox and
 281 visually detected and discarded eye and muscle artefacts. **2.7.2. Event-related analysis:** We
 282 epoched the pre-processed data into 3000ms trials (-1000ms to 2000ms relative to stimulus-
 283 onset). For each participant, we converted ERPs into percent power change relative to the
 284 500ms pre-stimulus-onset window using the formula: $(\text{Data} - \text{mean baseline values}) / \text{mean}$
 285 baseline values . **2.7.3. Time-frequency analysis:** Time-frequency representations (TFRs)
 286 were computed over 8000ms epochs, (-4000ms to 4000ms relative to stimulus onset). We
 287 choose relatively long epochs to avoid edge artefacts due to the transformation. We
 288 calculated TFRs by applying a 500ms hanning window as taper on frequencies from 0.5 to
 289 30 Hz in 0.5Hz frequency steps and 5ms temporal steps. Similar to ERPs, we converted
 290 participant-specific TFRs into percent power change relative to the 500ms pre-stimulus-onset
 291 window. **2.7.4. Inter-trial phase coherence estimate (ITPC):** Following time-frequency
 292 transformation, we extracted the complex Fourier coefficient for each channel, frequency,
 293 and time point in every single trial. Then we computed the phase angles in each trial before
 294 finally, averaging the single-trial ITPC values over all trials per subject. We performed all
 295 analyses in Fieldtrip (Oostenveld et al., 2011; <http://fieldtriptoolbox.org>).

2.8. Statistical Analyses:

For all of our analyses, we randomly selected an equal number of events/epochs per condition from N2 and N3. Evoked events were defined as events that are detected by our algorithms in the 2000ms post-stimulus-onset window. Due to violations to the assumptions of parametric testing, we applied rank-based non-parametric tests using the *nparLD* function implemented in the *nparLD* package available in R (Ngouchi et al., 2012). We report ANOVA-type statistics (ATS), p-values (alpha = 0.05, two-sided), as well as effect sizes using relative treatment effects (RTE). Generally, RTEs represent the probability of the values from the whole dataset being smaller than a randomly chosen observation from the respective group. Therefore, RTE values range between zero and one. An RTE value of 0.5 means no effect. The higher the RTE value of one condition the higher the probability that a randomly chosen value from that condition is larger than that randomly drawn from the whole dataset, and vice versa. When applicable, we performed post-hoc tests via the '*NparLD*' function with Bonferroni's correction for multiple comparisons. For repeated measures at different time points, we performed non-linear mixed regression via generalized linear mixed models (GLMMs) implemented in the '*glmer*' function of the '*lme4*' package in R (Bates et al., 2015). Both KC and micro-arousals were non-normally distributed. For K-complexes, we used a GLMM with a Poisson distribution. For micro-arousals, due to the presence of a notable amount of zero counts, we used the zero-inflated Poisson distribution implemented in the '*pscl*' package (Zeileis et al., 2008). We added our subjects as effect with random intercepts and slopes. We report the estimates of the fixed effects ($\hat{\beta}$) and their standard errors, z-values, and p-values. We performed post-hoc interaction tests using marginal means estimates as implemented in the '*emmeans*' package in R with Tukey's correction for multiple comparisons and we report Cohen's d effect sizes.

For the more temporally resolved analysis to compare between the latencies of the detected events, we binned the 2000ms post-stimulus intervals into bins of 100ms, then we calculated the mean of the number of events in each bin for each subject and condition, before finally

323 submitting these results to the permutation analysis in Fieldtrip. The choice of the bin-size is
 324 a compromise between a meaningful temporal resolution and a sufficient statistical power.

325 For ERP, TFR, and ITPC analyses, we selected equal numbers of epochs per condition
 326 (66.47 ± 56.25) for each subject. For this analysis, we averaged the signal from six frontal
 327 channels (F3, F4, F7, F8, Fcz and Fz), using a time window from -500ms to 2000ms relative
 328 to stimulus onset. We calculated the grand average over all subjects in each condition before
 329 submitting the results to the non-parametric cluster-based permutation analysis in fieldtrip
 330 (Maris and Oostenveld, 2007). We performed two-sided paired-sample t-tests followed by
 331 Monte Carlo's approximation with 5000 permutations (cluster-alpha = 0.05 and critical alpha
 332 = 0.025). We report the sum of the t-values ($\sum t$), as well as Cohen's d effect sizes calculated
 333 over all possible permutations, channels, time points, and frequencies in the cluster.

334 **3. Results**

335 **3.1. Auditory stimulation influenced sleep microstructure but not macrostructure.**

336 First, we assessed the effects of auditory stimulation on sleep macrostructure. We found that
 337 auditory stimulation during sleep does not influence sleep macrostructure. That is, we found
 338 no change in sleep macrostructure from the adaptation to the experimental night (Fig. 4A).
 339 Specifically, we found an effect of *Stage* ($ATS(2.61) = 62.75$, $p < 0.001$, $RTE_{wake} = 0.24$,
 340 $RTE_{N1} = 0.26$, $RTE_{N2} = 0.79$, $RTE_{N3} = 0.70$, $RTE_{REM} = 0.51$), no effect of the night ($ATS(1) =$
 341 0.04 , $p = 0.84$, $RTE_{Nostim} = 0.48$, $RTE_{stim} = 0.52$) and no interaction *Night X Stage* ($ATS(2.56)$
 342 $= 0.75$, $p = 0.51$). Similarly, during the experimental night, we found no difference in sleep
 343 macrostructure between periods of stimulation and periods of no-stimulation (Fig. 4B). We
 344 found a main effects for stage ($ATS(2.51) = 53.30$, $p < 0.001$, $RTE_{wake} = 0.28$, $RTE_{N1} = 0.18$,
 345 $RTE_{N2} = 0.82$, $RTE_{N3} = 0.74$, $RTE_{REM} = 0.47$). There was no effect of the stimulation ($ATS(1)$
 346 $= 3.36$, $p = 0.07$, $RTE_{ADAPT} = 0.5$, $RTE_{EXP} = 0.5$), and no interaction *Stimulation X Stage*
 347 ($ATS(2.08) = 0.68$, $p = 0.52$). Even when we opted for a more time-resolved analysis of sleep
 348 stages based on the Hori scoring system (Jagannathan et al., 2018; Tanaka et al., 1996) that
 349 uses 4s epochs instead of the classical 30s staging. Again, we found a main effect for stage

350 ($ATS(1.64) = 146.26$, $p < 0.001$, $RTE_{wake} = 0.28$, $RTE_{N1} = 0.18$, $RTE_{N2} = 0.82$, $RTE_{N3} = 0.74$,
 351 $RTE_{REM} = 0.47$). However, there was no effect of the stimulation ($ATS(1.69) = 3.36$, $p = 0.19$,
 352 $RTE_{ADAPT} = 0.5$, $RTE_{EXP} = 0.5$), but a significant interaction *Stimulation X Stage* ($ATS(1.47) =$
 353 8.17 , $p = 0.02$). Post-hoc pairwise test with Bonferroni's correction for multiple comparisons
 354 revealed that auditory stimulation resulted in higher number of sleep epochs ($ATS(1) =$
 355 12.84 , $p < 0.001$, $RTE_{stim} = 0.62$, $RTE_{nostim} = 0.38$) and lower number of drowsy epochs
 356 ($ATS(1) = 10.88$, $p < 0.001$, $RTE_{stim} = 0.4$, $RTE_{nostim} = 0.6$), suggesting even deeper sleep
 357 during stimulation periods.

358 On the level of sleep microstructure, we compared the densities, i.e. the numbers of events
 359 per minute of N2 and N3, of KCs, slow and fast spindles, as well as micro-arousals between
 360 stimulation and no-stimulation periods. We show that auditory stimulation significantly
 361 increased the densities of KCs (Fig. 4D; $ATS(1) = 19.68$, $p < 0.001$, $RTE_{stim} = 0.59$, $RTE_{nostim} =$
 362 0.41) and spindles (Fig. 4E; slow: $ATS(1) = 19.68$, $p < 0.001$, $RTE_{stim} = 0.58$, $RTE_{nostim} =$
 363 0.42 – fast: $ATS(1) = 8$, $p = 0.005$, $RTE_{stim} = 0.58$, $RTE_{nostim} = 0.42$). However, the increase
 364 in the density of micro-arousals did not reach statistical significance (Fig. 4F; $ATS(1) = 1.01$,
 365 $p = 0.31$, $RTE_{stim} = 0.53$, $RTE_{nostim} = 0.47$).

366 **[Please insert Figure 4 about here]**

367 Next, we performed a more temporally resolved analysis of the auditory-induced changes in
 368 sleep microstructure. Specifically, we compared the numbers of KCs, spindles, and micro-
 369 arousals between Stimulus-ON and Stimulus-OFF periods during the experimental night.
 370 Stimulus-ON periods are 2000ms post-stimulus intervals (0 to 2000ms relative to stimulus-
 371 onset), while stimulus-OFF periods are 2000ms intervals that start at least 2000ms after the
 372 onset of the previous stimulus and during which no sounds are presented (Fig. 5A). We
 373 found significantly higher numbers of KCs ($ATS(1) = 54.77$, $p < 0.001$, $RTE_{ON} = 0.68$, $RTE_{OFF} =$
 374 0.32), slow spindles ($ATS(1) = 9.13$, $p = 0.002$, $RTE_{ON} = 0.57$, $RTE_{OFF} = 0.43$), fast spindles
 375 ($ATS(1) = 20.16$, $p < 0.001$, $RTE_{ON} = 0.55$, $RTE_{OFF} = 0.45$), and micro-arousals ($ATS(1) =$

376 8.45, $p = 0.003$, $RTE_{ON} = 0.58$, $RTE_{OFF} = 0.42$), in the stimulus-ON than in the stimulus-OFF
 377 periods (Fig. 5B-E).

378 [Please insert Figure 5 about here]

379 3.2. The brain responds selectively to unfamiliar voices during NREM sleep.

380 We subsequently sought to investigate whether brain responses to auditory stimuli differ
 381 depending on their content, i.e. the names and/or voices used in the stimulus. We employed
 382 a non-parametric test from the *npard* package with two within factors, i.e. *Name* (SON and
 383 UNs) and *Voice* (FV and UFV). KC responses to auditory stimuli showed a significant effect
 384 of *Voice*, as UFVs triggered more KCs than FVs (Fig. 6A, $ATS(1) = 16.10$, $p > 0.001$, RTE_{UFV}
 385 $= 0.76$, $RTE_{FV} = 0.24$), no effect of *Name* ($ATS(1) = 0.09$, $p = 0.76$, $RTE_{SON} = 0.48$, $RTE_{UNs} =$
 386 0.52), and a significant interaction *Name* $\times$ *Voice* ($ATS(1) = 11.86$, $p = 0.001$). Post-hoc tests
 387 revealed that the amount of KCs triggered by the combination FV-SON was marginally
 388 higher than that triggered by the combination FV-UNs ($ATS(1) = 4.17$, $p_{bonf} = 0.08$, RTE_{FVSON}
 389 $= 0.56$, $RTE_{FVUNs} = 0.44$), while there was no difference between UFV-SON and UFV-UNs
 390 ($ATS(1) = 4.17$, $p_{bonf} = 0.19$, $RTE_{UFVSON} = 0.53$, $RTE_{UFVUNs} = 0.47$).

391 For fast and slow spindles, however, there was no effect of *Voice* (Fig. 6B-C; slow:
 392 $ATS(1,16) < 0.001$, $p = 0.99$, $RTE_{UFV} = 0.5$, $RTE_{FV} = 0.5$ - fast: $ATS(1,16) = 2.71$, $p = 0.10$,
 393 $RTE_{UFV} = 0.53$, $RTE_{FV} = 0.47$), no effect of *Name* (slow: $ATS(1,16) = 0.46$, $p = 0.5$, $RTE_{SON} =$
 394 0.51 , $RTE_{UNs} = 0.49$ - fast: $ATS(1,16) = 0.62$, $p = 0.43$, $RTE_{SON} = 0.49$, $RTE_{UNs} = 0.51$), and
 395 no interaction *Name* $\times$ *Voice* (slow: $ATS(1,16) = 0.11$, $p = 0.74$, $RTE_{UFVSON} = 0.51$, RTE_{UFVUNs}
 396 $= 0.49$, $RTE_{FVSON} = 0.52$, $RTE_{FVUNs} = 0.48$ - fast: $ATS(1,16) = 2.63$, $p = 0.10$, $RTE_{UFVSON} =$
 397 0.50 , $RTE_{UFVUNs} = 0.55$, $RTE_{FVSON} = 0.47$, $RTE_{FVUNs} = 0.47$). Micro-arousals showed a main
 398 effect of *Voice* (Fig. 6D, $ATS(1) = 9.14$, $p = 0.002$, $RTE_{UFV} = 0.59$, $RTE_{FV} = 0.41$), no effect of
 399 *Name* ($ATS(1) = 1.16$, $p = 0.29$, $RTE_{SON} = 0.53$, $RTE_{UNs} = 0.47$) and no interaction *Name* $\times$
 400 *Voice* ($ATS(1) = 0.19$, $p = 0.66$, $RTE_{UFVSON} = 0.61$, $RTE_{UFVUNs} = 0.58$, $RTE_{FVSON} = 0.44$,
 401 $RTE_{FVUNs} = 0.37$).

Fig. 6E depicts the number of KCs and micro-arousals evoked by different stimulus types as compared to a 2000ms no-stimulation period. Further, a temporally-resolved analysis (see section 2.8) showed that the difference in the evoked KCs between FVs and UFVs occurred in the 100ms – 800ms post-stimulus window (Fig. 6F, $\sum t(16) = 25.35$, $p = 0.002$, $d = 1.02$). For micro-arousals (Fig. 6G), the difference appeared 200ms post-stimulus-onset, i.e. 100ms later than that of KCs, and was significant between 200ms and 700ms post-stimulus (200-400ms: $t(16) = 5.92$, $p = 0.01$, $d = 0.84$; 500-700ms: $t(16) = 5.19$, $p = 0.02$, $d = 0.76$). It is worth mentioning that we observed a transient increase in the number of micro-arousals around 200ms before the onset of UFV stimuli, however, this increase did not yield a significant statistical difference.

[Please insert Figure 6 about here]

To illustrate whether the unfamiliarity of the voice is candidly the main cause of the difference in KC and micro-arousal responses, we divided the night into halves and hypothesized that brain responses to UFVs, but not to FVs, will decrease from the first to the second half, as the UFVs become more familiar with time. We modelled the change in the number of KCs from the first to the second half of the night using a GLMM with Poisson distribution fit by maximum likelihood (Fig. 7A). We found a main effect of *Voice* ($\hat{B} = 1.17 \pm 0.16$, $z = 7.51$, $p < 0.001$), no effect of *Time* ($\hat{B} = -0.08 \pm 0.11$, $z = -0.77$, $p = 0.44$), and a significant interaction *Time X Voice* ($z = -2.28$, $p = 0.02$). Post-hoc tests revealed a significant decrease of the UFV-triggered KCs from the first to the second half of the night ($\hat{B} = -0.31 \pm 0.08$, $z = 3.54$, $p = 0.002$, $d = 0.31$), while FV-evoked KCs did not change ($\hat{B} = -0.08 \pm 0.11$, $z = 0.77$, $p = 0.87$, $d = 0.08$). Conversely, for micro-arousals, a GLMM with zero-inflated Poisson distribution (Fig. 7B) demonstrated a marginally significant effect of *Voice* ($\hat{B} = 0.89 \pm 0.51$, $z = 1.75$, $p = 0.08$), no effect of *Time* ($\hat{B} = -0.19 \pm 0.27$, $z = 0.73$, $p = 0.98$), and no interaction *Time X Voice* ($\hat{B} = -0.09 \pm 0.33$, $z = -0.27$, $p = 0.55$). We provide a more detailed description of the GLMMs results in Fig. 7C-D.

[Please insert Figure 7 about here]

3.3. UFVs evoke stronger K-complex mediated brain responses during NREM sleep.

Next, we aimed to examine the neural dynamics underlying the aforementioned differences in sleep microstructure. Therefore, we compared the ERPs between FVs and UFVs in two conditions: 1) when the stimuli triggered KCs, 2) when no KCs were triggered. We found that when KCs were triggered, UFVs evoked a larger, more pronounced negative peak (Fig. 8A, $\sum t(16) = -436.35$, $p > 0.001$, $d = 0.96$) that resembles the KC's N550 in its temporal and morphological characteristics. Importantly, however, we observed that the peak of the N550 potential occurred later (~750-800ms) than the usual time window (500-550ms) and had a much smaller amplitude (20 - 50 μ v) than that (~100 μ v) previously reported in the literature (Colrain, 2005; Halász, 2005; Laurino et al., 2014). We illustrate that these discrepancies with previous literature are due to the relatively large temporal window we defined for the detection of evoked KCs (2000ms) as well as our decision to use an average reference as compared to the mastoid reference used in earlier studies (Bastien and Campbell, 1992; 1994; Colrain, 2005; Halász, 2005; Laurino, 2014). Fig. 8-1 and Fig. 8-2 in the extended data show the difference in the amplitude of the N550 according to the different referencing procedures as well as the latency jitter of the N550 peak on the single-trial level. Further, to confirm that the difference in the ERPs does not reflect a difference in the amplitude of the evoked KCs, we compared the peak-to-peak amplitudes of the evoked KCs, as measured by the detection algorithm, between FVs and UFVs (Fig. 8B). Peak-to-peak amplitudes showed no significant effect of *Voice* ($ATS(1) = 1.47$, $p = 0.23$, $RTE_{UFV} = 0.48$, $RTE_{FV} = 0.52$), *Name* ($ATS(1) = 0.71$, $p = 0.39$, $RTE_{SON} = 0.52$, $RTE_{UNs} = 0.48$), and no interaction *Voice X Name* ($ATS(1) = 1.47$, $p = 0.23$, $RTE_{UFVSON} = 0.49$, $RTE_{UFVUNs} = 0.47$, $RTE_{FVSON} = 0.54$, $RTE_{FVUNs} = 0.50$). Intriguingly, when no KCs are evoked, we found no difference in the amplitude of the ERPs between UFVs and FVs (Fig. 8C, 0.3 - 0.37s: $\sum t(16) = 27.31$, $p = 0.13$).

[Please insert Figure 8 about here]

3.4. K-complex mediated brain responses to UFVs reflect sensory processing

455 We then speculated that the difference in the amplitude of the ERPs, if not due to a
 456 difference in the amplitude of the evoked KCs, might reflect more synchronized evoked
 457 responses to UFVs as compared to FVs. Therefore, we compared the phase consistency of
 458 brain responses between FVs and UFVs via the inter-trial phase coherence metric (ITPC,
 459 Tallon-Baudry et al. 1996). We observed stronger ITPC following UFVs as compared to FVs
 460 in the delta band (1-4Hz; Fig 9A, $\sum t(16) = 2413.98$, $p = 0.003$, $d = 1.06$) indicating more
 461 synchronized brain responses to UFVs. Fig. 9B shows the ITPC contrast between FVs and
 462 UFVs indicating that difference in the IPTC is a product of stronger time-locked responses to
 463 UFVs. Similar to our ERP analysis, in the absence of the evoked KCs, IPTC values did not
 464 differ between FVs and UFVs (Fig. 9C, $\sum t(16) = 2521.7$, $p = 0.001$).
 465 Finally, we performed spectral analysis of brain responses to UFVs and FVs in the presence
 466 and absence of evoked KCs. We observed stronger low frequency response (delta band; 1-
 467 4Hz) to UFVs as compared to FVs (Fig. 9D-E) that started around 250ms post stimulus
 468 onset. This delta responses appeared independent of the presence (Fig. 9D, $\sum t(16) =$
 469 9395.64 , $p < 0.001$, $d = 1.25$), or absence (Fig. 9E, $\sum t(16) = 4097.56$, $p = 0.013$, $d = 0.86$) of
 470 the evoked KC.
 471 Crucially, only in the presence of KCs, UFVs additionally elicited a significant increase in the
 472 power of higher frequencies (>16Hz) as compared to FVs (Fig. 9D, $\sum t(16) = 5020.62$, $p =$
 473 0.006 , $d = 1.04$) starting around 500ms post-stimulus.

474 **[Please insert Figure 9 about here]**

475 **4. Discussion**

476 In this study, we presented sleepers with their own first names (SON) and two unfamiliar
 477 names (UNs) spoken by either a familiar voice (FV) or an unfamiliar voice (UFV) during a full
 478 night of sleep with polysomnography. We show that although auditory stimulation did change
 479 sleep architecture (Fig. 4A-C); they induced prominent, stimulus-specific changes in sleep
 480 microstructure. Generally, presenting auditory stimuli during NREM sleep increased the
 481 number of KCs, spindles, and micro-arousals (Fig. 5). UFVs triggered more KCs (Fig. 6A)

482 and micro-arousals (Fig. 6D) than FVs. However, we found no difference in the amount of
 483 triggered KCs, spindles, or micro-arousals between SONs and UNs. The difference in the
 484 numbers of evoked KCs and micro-arousals between FVs and UFVs appeared around
 485 100ms post-stimulus (200ms for micro-arousals) and extended over the whole duration of the
 486 stimuli ~800ms (Fig. 6F-G). While the number of the UFV-triggered KCs decreased in the
 487 second half of the night, the numbers of evoked micro-arousals remained relatively stable
 488 throughout the night (Fig. 7). Moreover, in the presence of the auditory-evoked KC, UFVs
 489 triggered larger evoked responses (Fig. 8A) that did not reflect a difference in the amplitudes
 490 of the evoked KCs (Fig. 8B-C) but rather more-synchronized brain responses to UFVs
 491 relative to FVs (Fig. 9A-B). Similarly, brain responses to UFVs demonstrated an increase in
 492 the power of high frequencies (>16 Hz), suggesting a stronger arousal reaction to UFVs (Fig.
 493 9D). Crucially, we were not able to detect such differential brain responses between FVs and
 494 UFVs in the absence of the evoked KC.

495 It has previously been suggested that the more relevant the stimulus, the higher its tendency
 496 to trigger KCs (Halász, 2005). In this regard, our results pose UFVs as more relevant - or in
 497 evolutionary terms potentially more threatening (Blume et al., 2018) – and consequently
 498 more arousing to the sleeper than FVs. Indeed, the increase in micro-arousals following
 499 UFVs suggests a transient shift towards external processing of “vital” environmental stimuli.
 500 In the same vein, the decrease in the number of UFV-evoked KCs in the second half as
 501 compared to the first half of the night (Fig. 7A) supports the notion that the sleeping brain
 502 continues to learn new information during sleep (Züst et al., 2019). That is, homeostatic
 503 regulatory processes alone cannot explain this observation, since the number of FV-evoked
 504 KCs did not change, indicating a stimulus-specific attenuation of brain responses. It might be
 505 that the sleeping brain learns, through repeated processing, that an initially unfamiliar
 506 stimulus poses no immediate threat to the sleeper and consequently decreases its response
 507 to it. Conversely, in a safe sleep environment, the brain might be “expecting” to hear FVs and
 508 consistently inhibits any response to such stimuli to preserve sleep (see Fig. 6E). Although
 509 this assumption remains speculative, it entails a thorough investigation of the brain’s ability to

510 generate top-down predictions of the external sensory world during sleep. Nevertheless, our
 511 results suggest that the unfamiliarity of voice is a strong promoter of brain responses during
 512 NREM sleep.

513 What is the role of the auditory-evoked brain responses during NREM sleep? Central to such
 514 responses is the KC, i.e. the most prominent sleep-specific response to sensory stimulation.
 515 To answer this question, we contrasted trials during which FVs and UFVs triggered KCs. In
 516 such trials, UFVs evoked a larger negative potential that resembles the N550 component of
 517 the KC (Fig. 7A). The N550 has been associated with large-scale neuronal silencing that
 518 protects sleep (Cash et al., 2009; Laurino et al., 2014), and conversely, an arousal reaction
 519 that facilitates stimulus processing (Atienza et al., 2001). In our study, the amplitudes of the
 520 evoked KCs did not differ between FVs and UFVs corroborating previous literature
 521 presenting the evoked KC as an all-or-non phenomenon (Bastein and Campbell, 1992).
 522 Rather, the difference in the N550-amplitude between FVs and UFVs was due to more
 523 synchronized brain responses to UFVs as indicated by the ITPC values (Fig. 9A). Stimulus-
 524 induced phase modulations have been suggested to promote information processing and
 525 transmission in the cortex (Canavier, 2015; Lakatos et al., 2013; Voloh and Womelsdorf,
 526 2016), and increased ITPC values have been associated with better cognitive performance
 527 (Hanslmayr et al., 2005; Eidelman-Rothman et al., 2019) and enhanced attention (Joon Kim
 528 et al., 2007) during wakefulness. Together, our results suggest that the preferential brain
 529 responses to UFVs during NREM sleep reflect sensory processing. Importantly, the shorter
 530 post-stimulus time window during which UFVs elicited KCs as compared to FVs, as indicated
 531 by the narrower peak in Fig. 6F, implies better temporal alignment of KCs following UFVs
 532 and emphasizes the contribution of the evoked KCs to the observed phase modulations.
 533 Finally, the stronger high frequency responses (>16Hz, Fig. 9) to UFVs that appeared only in
 534 the presence of KCs corroborate the role of the auditory-evoked KCs in promoting sensory
 535 processing of relevant information. Together, our findings suggest a central role for KCs in
 536 the extraction and processing of relevant external sensory information during NREM sleep.

537 We did not find any differences in brain responses between SON and UNs in contrast
 538 to previous literature (Oswald et al., 1960; Perrin et al., 1999). One explanation might be that
 539 while sleep preserves low-level auditory processing, it attenuates higher-order linguistic
 540 tracking (Makov et al., 2017). We speculate that this is due to the disruption of the activity of
 541 the large-scale networks necessary for higher-order name processing (Démonet et al., 1992;
 542 Luke et al., 2002), due to the loss of long-range cortical connectivity during sleep (Massimini
 543 et al., 2005). Further research should elucidate the mechanisms of language tracking during
 544 sleep.

545 We show that the auditory-evoked spindles are not influenced by specific
 546 characteristics of the auditory stimuli (i.e., name or voice). However, the role of spindles in
 547 response to sensory stimuli during sleep is far from clear. Previous research has shown
 548 spindles attenuate or even inhibit the processing of auditory information (De Gennaro and
 549 Ferrera, 2003; Schabus et al., 2012; Blume et al., 2018). Other work suggests that brain
 550 responses are preserved during spindles (Sela et al., 2016) and even argues for a role for
 551 spindles in the processing of memory-related sensory information (Antony et al. 2018;
 552 Cairney et al. 2018; Jegou et al. 2019). More research should investigate the role of spindles
 553 in response to sensory information irrelevant to ongoing memory processes.

554 Finally, we found no relevant changes in sleep macrostructure and architecture due to
 555 auditory stimulation (Fig. 4). In fact, micro-arousals represent an integral part of healthy sleep
 556 as they ensure its reversibility (Halász et al., 2004). Hence, their slight increase should not
 557 be viewed as a disruption to normal sleep. Further, the analysis of microstates even indicates
 558 a shift towards deeper sleep in response to UVF stimuli (Fig. 4C), which is most likely a by-
 559 product of more auditory-evoked KCs that influenced the staging. However, the classical 30s
 560 sleep staging might not be sensitive enough to capture subtle changes in sleep
 561 microstructure. Hence, the development and refinement of new fine-grained methods, such
 562 as the Hori-based microstate classification (Jagannathan et al., 2018) promises better
 563 monitoring of transient sleep fluctuations, especially in the presence of sensory perturbation.

564 In summary, sleep appears to be far from a homogenous state of unconsciousness.
 565 There are temporal windows in sleep during which the brain filters, extracts, and processes
 566 relevant external information. We speculate that such content-specific, dynamic reactivity to
 567 sensory signals enables the brain to enter a “sentinel processing mode” (Blume et al., 2018)
 568 during which it preserves the ability to efficiently engage in the important internal processes
 569 that are ongoing during sleep while remaining connected to the surrounding environment.

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6. Figure legends:

Figure 1. Experimental design. A) Protocol: participants were invited for an initial screening interview during which they were given the wrist-worn actigraphy and advised to keep a regular sleep-wake cycle. Participants slept in the sleep laboratory during two nights: an adaptation night during which PSG was recorded but no stimuli were presented, and an experimental night during which we recorded PSG and presented auditory stimuli throughout the night. B) Procedure of the experimental night: participants slept for approximately eight hours with PSG and auditory stimulation. All participants went through a stimulation session in the evening before sleep; however, this session is irrelevant to the current manuscript. The auditory stimuli started directly after going to bed and continued for 90 minutes, then paused for ~30 minutes to allow for a period of undisturbed sleep. This cycle was repeated four times accounting for the whole duration of the night. C) (Top) Stimuli: We presented the subject's own name (SON) and two unfamiliar names (UN1 & UN2) spoken by either a familiar voice (FV) or an unfamiliar voice (UFV). (Bottom): an exemplary sequence of stimulus presentation. Stimuli were presented in a pseudo-random order; each stimulus was presented 690 times and the inter-stimulus intervals ranged between 2800ms to 7800ms.

761 **Figure 2. K-complex detection and examples.** A) Linear discriminant analysis (LDA)
 762 scores for the all detected K-complexes for all subjects. The dashed line represents our
 763 minimum cut-off at an LDA value of 0.8, which is the threshold used for the selection of
 764 reliable K-complex events. The percentage of the events used in our analyses from all the
 765 detected events for each subject are indicated in red at the bottom. B) Examples of the
 766 detected K-complexes at channel C3 referenced to the contralateral mastoid. We show the
 767 standard EEG montage that we used for sleep staging as well as event detections.
 768 Specifically, we used channels (from top to bottom): F3, F4, C3, C4, O1, and O2 referenced
 769 to the contralateral mastoid. Moreover, we show one EMG and two EOG channels as well as
 770 the average of both mastoids. Examples one and two show K-complexes detected in N2
 771 sleep from one subject, while examples three and four are K-complexes detected during N3
 772 in a different subject.

773 **Figure 3. Examples of the detected micro-arousals.** We show the standard EEG montage
 774 that is used for sleep staging as well as event detections. Specifically, we used channels
 775 (from top to bottom): F3, F4, C3, C4, O1, and O2 referenced to the contralateral mastoid.
 776 Moreover, we show one EMG and two EOG channels as well as the average of both
 777 mastoids. Examples 1 and 2 are events detected in N2 sleep from one subject. Example 2
 778 shows a micro-arousal that is preceded by a K-complex. Example 3 is from an N3 epoch
 779 from a different subject.

780 **Figure 4. Auditory stimulation influenced sleep microstructure but not macrostructure.**
 781 In each participant, we selected equal numbers of epochs for all conditions. A) Difference in
 782 sleep architecture, i.e. the distribution of sleep stages, between the adaptation and the
 783 experimental night. To account for the effect of sleep-onset latency, we discarded all epochs
 784 that preceded the first N1 epoch. We found no difference between the architectures of both
 785 nights. B) Difference in sleep architecture between stimulation and no-stimulation periods
 786 during the experimental night. The experimental night consisted of periods of continuous
 787 auditory stimulation and period of no stimulation. We found no difference in the sleep

788 architecture between those periods. C) Microstate differences between the stimulation and
 789 the no stimulation periods. To circumvent the poor temporal resolution of classical sleep
 790 staging in 30sec epochs, we opted for a more time-resolved analysis of sleep stages based
 791 on the Hori scoring system. We found a higher number of sleep epochs and lower number of
 792 drowsy epochs during the stimulation periods suggesting deeper sleep during auditory
 793 stimulation. D-F) A comparison of the densities of sleep microstructure between stimulation
 794 and no-stimulation periods. D) K-complex density during the stimulation periods is higher
 795 than that in the no-stimulation periods. E) Slow and Fast spindles densities are higher during
 796 the stimulation periods. F) Micro-arousal density, however, did not differ between stimulation
 797 and no-stimulation periods. Boxplots show the median and the whiskers depict the 25% and
 798 the 75% quartiles. Each dot/triangle represents one participant in one condition. * $p<0.05$,
 799 ** $p<0.001$.

800 **Figure 5. Auditory stimulation increased the occurrence sleep microstructures.** A) A
 801 graphical illustration of the stimulus-ON and stimulus-OFF windows used for the analysis.
 802 We detected events in the 2000ms post-stimulus window (Stimulus-ON; green), as well as
 803 during 2000ms pre-stimulus windows that are at least 2000ms after the last stimulus
 804 (Stimulus-OFF, orange). The numbers of (B) K-complexes, (C) slow spindles, (D) fast
 805 spindles, as well as (E) micro-arousals were significantly higher during the stimulus-ON than
 806 the stimulus-OFF periods. Y-axis depicts the percentage of epochs in which events were
 807 detected. Boxplots show the median and the whiskers depict the 25% and the 75% quartiles.
 808 Each dot/triangle represents one participant in one condition. * $p<0.05$, ** $p<0.001$.

809 **Figure 6. Selective sleep-specific responses to unfamiliar voices during NREM sleep.**
 810 A) Differences in the triggered K-complexes between familiar voices (FV) and unfamiliar
 811 voices (UFV) in the 2000ms post-stimulus-onset window. UFVs triggered more K-complexes
 812 than FVs. However, the numbers of (B) slow and (C) fast spindles did not differ between FV
 813 and UFVs. D) Differences in triggered micro-arousals between FVs and UFVs demonstrating
 814 the higher number of micro-arousals triggered by UFVs. E) The amount of triggered K-

815 complexes and micro-arousals by all of our stimulus categories and compared to the same
 816 number of 2000ms no-stimulation epochs. F-G) Temporal aspects of the difference in the
 817 triggered K-complexes and micro-arousals. F) The difference between UFV and FV in the
 818 number of triggered K-complexes was significant from 100ms to 800ms (indicated by bar and
 819 asterisks). G) The difference in the number of micro-arousals between FVs and UFVs was
 820 significant in the periods from 200 to 400ms, and from 500 to 700ms. Boxplots show the
 821 median and the whiskers depict the 25% and the 75% quartiles. Each dot/triangle represents
 822 one participant in one condition. In panels F and G The dashed horizontal line on top of the
 823 plots represent the mean duration of our stimuli (808ms), the lines depicts the means of the
 824 bins, and the shadings show the standard error of the mean. * $p < 0.05$, ** $p < 0.001$, SONs:
 825 Subject's own name, UNs: Unfamiliar names. FVSON: familiar voice speaking the subject's
 826 own name. UFVSON: unfamiliar voice speaking the subject's own name, FVUNs: familiar
 827 voice speaking two unfamiliar names, and UFVUNs: unfamiliar voice speaking two unfamiliar
 828 names.

829 **Figure 7. The effect of time on sleep-specific responses to unfamiliar voices during**
 830 **NREM sleep.** A) The difference in the numbers of triggered K-complexes to familiar voices
 831 (FV) and unfamiliar voices (UFV) from the first to the second half of the night. A GLMM using
 832 Poisson distribution revealed a significant interaction *Time x Voice*, as only the amount of
 833 UFV-triggered K-complexes decreased in the second half. B) The number of triggered micro-
 834 arousals did not change from the first and the second half of the night. C) A statistical report
 835 of the GLM model of K-complexes. We added Time (first half & second half), and Voices
 836 (familiar and unfamiliar voices) as fixed effects. Moreover, we assigned random intercepts
 837 and slopes for each subject. We found a significant main effect of voice, no effect of time,
 838 and a significant interaction *Time X Voice*. D) Statistical report of the zero-inflated Poisson
 839 GLM of micro-arousals. Similar to K-complexes, we added Time (first half & second half),
 840 and Voices (familiar and unfamiliar voices) as fixed effects and random intercepts and slopes
 841 for each subject. No main effect of time and no interaction *Time x Voice*, indicating that the
 842 amount of triggered micro-arousals did not change from the first to the second half of the

843 night. * $p < 0.05$, SONs: Subject's own name, UNs: Unfamiliar names. Boxplots show the
 844 median and the whiskers depict the 25% and the 75% quartiles. Each dot/triangle represents
 845 one participant in one condition

846 **Figure 8. Unfamiliar voices elicited stronger brain responses in the presence of the**
 847 **evoked K-complex.** A) ERP contrast between familiar voice (FV) and unfamiliar voices
 848 (UFV) stimuli in the presence of the auditory-evoked K-complexes. UFVs triggered a larger
 849 amplitude of the evoked response between 510ms to 1400ms as shown by the grey
 850 shadings. Figures 8-1 and 8-2 illustrate the methodological underpinnings of the
 851 discrepancies between the amplitude and latency of the negative component in panel A as
 852 compared to the conventional amplitude and latency of the N550 in the literature. B)
 853 Comparison of the peak-to-peak amplitude (P2P; N550 to P900) of the evoked K-complexes
 854 showing no difference in the amplitudes of the evoked K-complexes between FVs and UFVs.
 855 C) ERP responses to FVs and UFVs in the absence of evoked K-complexes. There was no
 856 difference in the ERP amplitudes between FVs and UFVs when no K-complexes were
 857 evoked. The solid blue and red lines and the shadings represent the mean and the standard
 858 error of the mean respectively. The dashed horizontal line on top of the plots represent the
 859 mean duration of our stimuli (808ms). Vertical dashed lines (at $x = 0$) represent stimulus
 860 onset. The red dots on the topographical plots at the bottom-left side of the plots indicate the
 861 locations of the channels used for the analysis. Boxplots show the median and the whiskers
 862 depict the 25% and the 75% quartiles. Each dot/triangle represents one participant in one
 863 condition.

864 **Figure 8-1. K-complex trials referenced to contralateral mastoids.** In the upper row, we
 865 show the comparison between the evoked K-complexes to FVs and UFVs centered on the
 866 start of the K-complex, i.e. negative-going zero-crossing of the K-complex. In more details,
 867 we extracted the K-complexes that were detected by our algorithm in the 2000ms post-
 868 stimulus window and created epochs from -0.5s to 2s around the start of the K-complex
 869 events (negative going zero-crossing). The bottom row depicts the trials where a K-complex

870 was evoked, centered on the start of the stimulus (zero = stimulus onset). We show the
 871 grand average ERP over all subjects (left panel). Note that the amplitude of the negative
 872 wave exceeds 100uv and that there is no difference in the amplitude of the ERPs between
 873 FVs and UFVs. We also show the single subject data of the K-complex averaged over trials
 874 for each subject (middle panel). Finally, we show single trials ($n = 20$ trials per condition)
 875 from one subject (right panel). Together, this figure corroborates our claim that the difference
 876 in the ERPs between FVs and UFVs shown in Fig. 8A of the manuscript is due to difference
 877 in time-locking rather than the amplitude of the evoked K-complexes. K-complexes were
 878 detected at C3. We show data from one electrode F3, referenced to the contralateral mastoid
 879 (A2). Shadings reflect the standard error of the mean. Vertical dashed lines (at $x=0$)
 880 represent the start of the evoked K-complex detected by our algorithm (top) or stimulus onset
 881 (bottom). Shadings represent the standard error of the mean.

882 **Figure 8-2. K-complex trials referenced to an average reference.** Similar to Fig. 8-1, in
 883 the upper row we show the evoked K-complexes to FV and UFV centered on start of the K-
 884 complexes (the zero-crossing of the signal from positive to negative), while the bottom row
 885 depicts the trials when a K-complex was evoked centered around the start of the stimuli. The
 886 difference between Fig. 8-1 and Fig 8-2 is the choice of the reference. Note the decrease in
 887 the amplitude of the ERPs from Fig 8-1 to Fig 8-2 due to changing the reference (from a
 888 mastoid reference in Fig. 8-1 to an average reference in Fig. 8-2). Left panel: Grand average
 889 ERPs over all subjects for both conditions FVs and UFVs. Middle panel: single subject data
 890 for the K-complex trials averaged over all trials. Right panel: Single trial data ($n=20$ per
 891 condition) from one subject. K-complexes were detected at C3. We show ERPs from one
 892 electrode (F3) referenced to an average reference. Vertical dashed lines (at $x=0$) represent
 893 the start of the K-complex event (top) or stimulus onset (bottom). Shadings represent the
 894 standard error of the mean.

895 **Figure 9. Brain responses to unfamiliar voices in the presence of the evoked K-**
 896 **complex reflect further processing.** A) The difference in ITPC values between familiar

897 voice (FV) and unfamiliar voice (UFV) stimuli in the presence of the evoked K-complex.
898 UFVs evoked significantly higher ITPC than FV in the delta (1-4Hz) frequency band. Note
899 that the largest difference in phase locking overlaps with the difference between the ERPs in
900 Fig. 8A. B) Separate ITPC plots for Familiar voices (top) and unfamiliar voices (bottom)
901 showing stronger ITPC values following UFVs and indicating that the difference in ITPC
902 values is due to an increase in ITPC following UFVs. C) ITPC difference between UFVs and
903 FVs in the absence of the evoked K-complexes. There is no difference in ITPC between FVs
904 and UFVs in the absence of evoked K-complexes. D-E) Spectral power maps of the power
905 differences between FVs and UFVs. We demonstrate stronger responses to UFV in a broad
906 frequency range (~1-10Hz) regardless of the presence (D) or the absence (E) of K-
907 complexes. However, stronger high frequency (>16Hz) responses to UFVs appeared only in
908 the presence of K-complexes. The dashed horizontal line on top of the plots represent the
909 mean duration of our stimuli (808ms). Vertical dashed lines (at $x=0$) represent stimulus
910 onset. The red dots on the topographical plots at the bottom-left side of the plots indicate the
911 locations of the channels used for the analysis.

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