

Research report

## Local functional state differences between rat cortical columns

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### Abstract

Surface evoked potentials (SEPs) during auditory clicks and whisker twitches are usually larger during quiet sleep (QS) over waking and REM sleep. However, SEP amplitudes from single trials fluctuate periodically between high and low values regardless of sleep–wake cycle. To test the hypothesis that state-independent fluctuations represent local functional sleep-like states of individual cortical columns, we examined single trial SEP amplitudes from multiple cortical locations across sleep–wake cycles. Bilateral stimuli produced SEP amplitude fluctuations in each hemisphere that usually covaried ( $r = 0.4$ ), but with frequent hemispheric differences. Two neighboring whiskers, twitched simultaneously on the same side, produced highly correlated SEPs in neighboring cortical columns ( $r = 0.9$ ) with frequent divergences. We found 50% more disparity during QS over waking, indicating that the differences did not result from recording noise or stimulus inconsistency. Local SEP fluctuations also followed local differences in the delta wave signal during QS ( $r = 0.4$ ), suggesting that similar mechanisms may modulate the SEP. The duration of the localized sleep-like (high SEP amplitude) state was dependent on the duration of prior wake-like (low SEP amplitude) state ( $r = 0.5$ ), suggesting a use dependence of prior functional state period. Since SEP indicators fluctuated independently from whole animal sleep state, and were frequently different between hemispheres and nearby cortical columns, these data support the theory that sleep-like functional states may be localized to brain regions at least as small as cortical columns.

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### 1. Introduction

In order to understand sleep regulation, a number of recent studies have characterized localized EEG patterns and asymmetries across different brain regions during sleep/wake states [14,21,30,60,62,65,81,85]. Regional differences in the depth of slow-wave sleep can also be use-dependent [20,31,34,79]. A clearer understanding of these regional differences may help us explain how sleep is generated and provide insights into sleep function.

Several investigators [8,9,35,39,41,70] consider sleep a distributed process. Built primarily from a biochemical point of view, distributed theories of sleep regulation make few predictions concerning the electrophysiological behavior of individual or small groups of cells. These theories posit that as synapses and circuits are used, induction and release of sleep regulatory substances (SRSs) are responsible for synaptic sculpturing (the neurotrophin hypothesis) [40,63,67]. In an autocrine fashion, these activity-dependent substances alter synaptic efficacy via nuclear transcription events and translation mechanisms targeted to the specific synapses that were activated. Sleep regulatory substances can also act in a paracrine fashion, affecting the electrical properties of nearby neurons such that a given input results in a different output. Within a

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group of cells, SRS-induced alterations in input–output relationships can be considered a state shift. We consider such groups of cells to be equivalent to cortical columns representing groups of tightly interconnected and functionally related cells.

Typical EEG and sleep studies consider only that the whole animal is asleep or awake. If sleep begins at the neuronal level, a variety of output features will be modulated by the particular state of the cortical column, independently of whole animal state. Since animals and humans experience a loss of reportable conscious stimuli perception during sleep, a misconception has developed that thalamic transmission of sensory inputs is blocked during sleep. Indeed, the processing of sensory information is present during sleep even though profound modifications occur [10,19,25,38,53,64,76–78]. These findings led us to hypothesize that local sleep-like functional states could be measured using local surface field potentials from individual cortical columns. This study aims to assess different temporal patterns of local surface evoked field potentials (SEPs) across sleep states and to develop characteristic indicators for physiological state of local regions.

We measured the physiological or functional state of local brain regions by assessing the electrical output they produce when probed with an input stimulus. The output is made up of several parameters including unit firing

patterns [74], several classes of population evoked post-synaptic potentials [6,86], and high-frequency oscillatory activity generated by the neuronal group in response to stimulation [13,27,32,33]. Other potential indicators of local neuronal group functional state include recruitment of metabolic factors such as blood oxygenation and volume [18] and molecular markers. This report is focused on long-term recording of individual SEPs in response to probing sensory stimuli.

## 2. Materials and methods

The state dependence of SEPs was investigated by chronically instrumenting five Sprague–Dawley rats with two pairs of cortical screw electrodes over the sensory cortex; one pair on each hemisphere (Fig. 1). In another four animals, a  $5 \times 5$  electrode array was placed over the whisker barrel cortex of one hemisphere (Fig. 1E). Whisker barrels on the same hemisphere were identified by plotting 3D surface maps of the SEPs after twitching the two whiskers independently. The surface plots in the right panel of Fig. 1 illustrate how we identified the appropriate electrode within the electrode array which corresponded to the whisker barrel being activated. All animals were instrumented for standard sleep state recording using an EEG stainless steel screw implanted

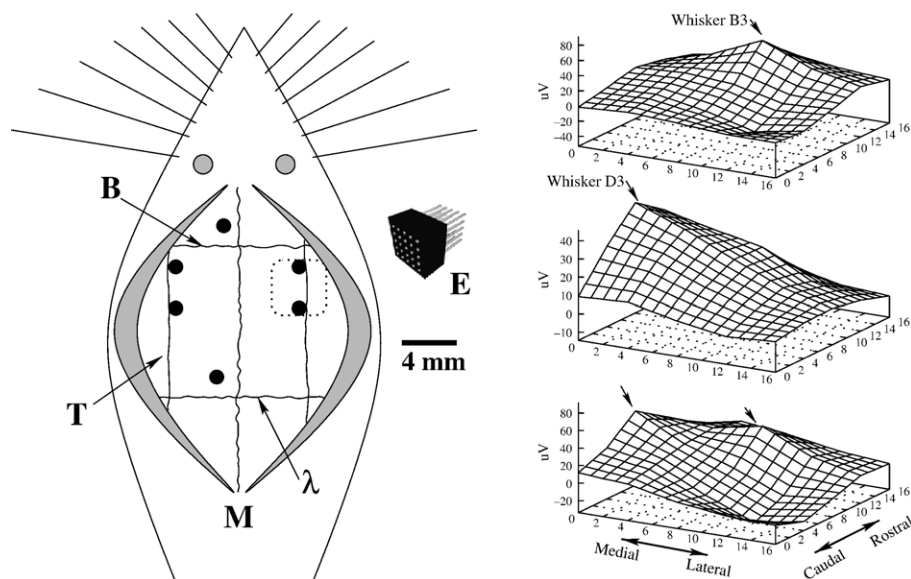


Fig. 1. Schematic diagram of electrode placement. Circles indicate placement of EEG screw electrodes and 25-electrode array (E). For some rats, two pairs of stainless steel screw electrodes were placed 4 mm apart over the somatosensory cortex on the temporal ridge (T), 1 mm caudal to bregma (B). Some rats received a 25-electrode array constructed from black Delrin and 0.2 mm stainless steel wires spaced 0.4 mm apart. A squared opening in the skull over the somatosensory cortex, outlined by the dotted line, allowed placement of the array on the cortical surface. One screw electrode was placed rostral to bregma near the midline (M) for frontal lobe EEG and one placed near lambda ( $\lambda$ ) for ground reference. For animals that were implanted with a 25-electrode surface array, the location of each whisker barrel was mapped by twitching whiskers in sequence while generating 3D surface maps of electrical potentials. For example, twitching whisker B3 and D3 each produced unique maps (upper right panels) with the peak amplitude corresponding to the location of the whisker barrel associated with that whisker. When the two whiskers are twitched simultaneously, the lower right panel shows that the two peaks appear at the same time. The 3D surface maps were used to identify the corresponding electrodes to use for the comparisons in Fig. 8.

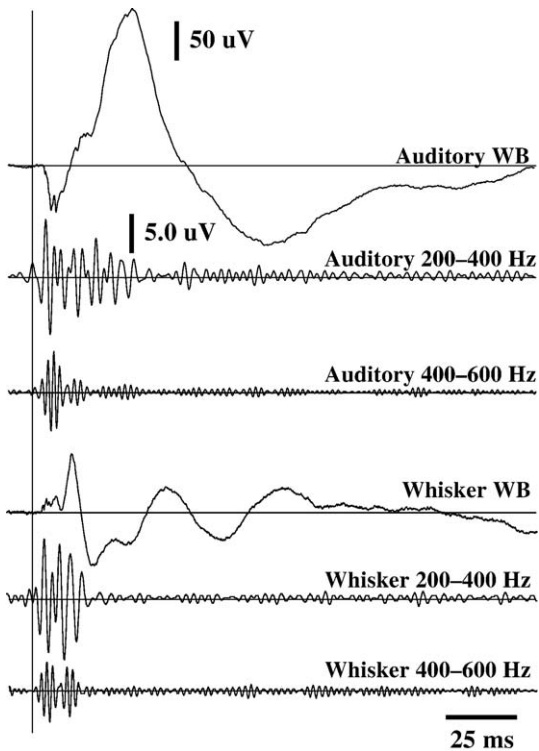


Fig. 2. Typical evoked responses and high-frequency oscillations after auditory clicks or whisker twitches. Each trace represents the time-triggered average of 20 to 40 stimuli that begin at the time indicated by the vertical line. In each example, the data are digitized at 20 kHz and displayed without filtering in the wideband trace (WB). Since all signals were referenced to an occipital skull screw, more localized signals were derived by subtracting signals from adjacent electrodes. Each wideband trace is then subjected to an FFT filtering algorithm between 200 and 400 Hz or between 400 and 600 Hz which shows a high-frequency burst of waves that precede the first major peak of the evoked response. The high-frequency burst is typically much smaller in amplitude than the evoked response; thus, the vertical scale bar for the top trace applies to the two evoked responses, and the second vertical scale bar is associated with the filter traces. Positive differential potential between adjacent electrodes is displayed in the upward direction.

over the frontal cortex. A pair of multi-stranded stainless steel wires inserted into the neck muscles served as EMG electrodes. Another pair of multi-stranded stainless steel wires was inserted subcutaneously on either side of the lower rib cage to record respiration and cardiac activity. A ground reference screw was placed 1 mm rostral and 1 mm lateral to the lambda–midline intersection. Food and water were continuously available under a 12–12-h light (60 lx)–dark cycle and ambient temperature was regulated at 25 °C. Animals were recorded at the same time of the light cycle to control for possible circadian effects. All procedures were reviewed and approved by the Washington State University Animal Care and Use Committee.

Long-term whisker stimulation in behaving rats is difficult, and has been accomplished only by a few investigators (e.g., 19,43,47)]. Unfortunately, studies that

require sleep usually employ measures such as sleep deprivation to achieve sleep in the restrained condition. Additionally, rats in a natural sleep position will tuck one side of their whiskers under their forelimb, making it difficult to stimulate whiskers. We thus developed training procedures to accommodate rats to restrained conditions so that they would sleep without sleep deprivation during their normal sleeping period. The training procedures were important for these studies to control for potential sleep deprivation effects on state-dependent changes in the evoked responses and local sleep parameters. Additionally, we used both auditory and whisker stimulation to test if state-dependent responses could be independent of sensory modality. Since the auditory stimulation paradigm did not require handling or restraint, it also provided an

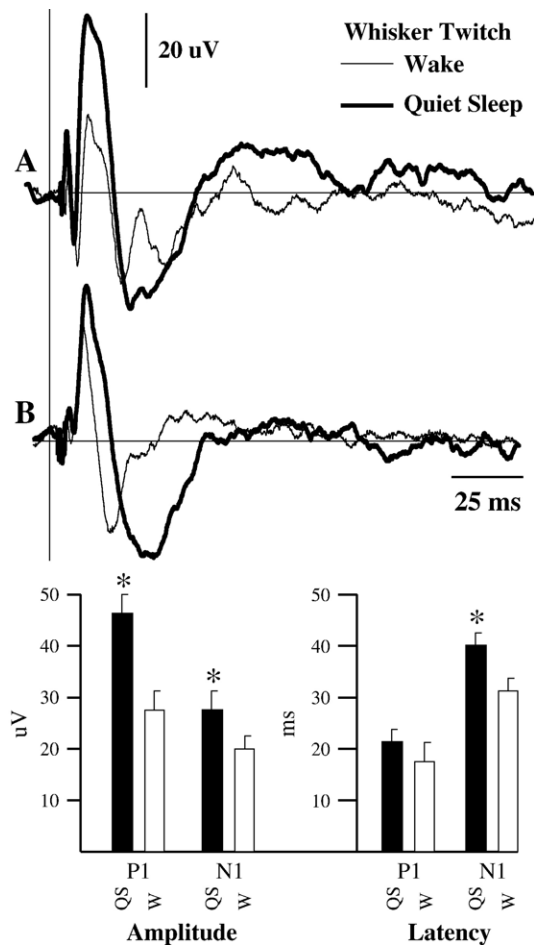


Fig. 3. State-dependent whisker SEPs. Examples of time-triggered average traces after whisker twitches during wake (W) and quiet sleep (QS) from two animals (A and B) show a significantly bigger evoked response, and longer latency to the time of the trough. Standard error for all recordings from all 5 animals is displayed with the vertical bars on top of each bar in the summary bar graph. Asterisks indicate comparisons that were significantly different ( $P < 0.01$ ). Positive differential potential between adjacent electrodes is displayed in the upward direction.

appropriate control for potential influences of the restraint procedures. Rats were trained to sleep under restrained conditions by daily gentle handling and restraining for increasing time periods. Initially, rats were restrained for 5 min, working up to 2 or more hours. Training typically required 3 to 6 weeks. A rat was considered a good candidate for surgery and electrode placement when it showed signs of sleeping and was quiet in the restraint for more than 2 h. To assess training progress, we implemented an ethogram protocol to evaluate the animal's behavior during training.

Seven days post-surgical recovery, rats were connected to the digitizing hardware for continuous streaming of electrophysiology to a 200-GB hard drive. Our software also provided online strip chart display, FFT analysis, state display, and time-triggered averages of evoked responses. All channels were digitized at 20 kHz and stored on a computer [61]. For sleep scoring, the frontal lobe EEG was digitally filtered in 0.5-Hz bins between 0.5 Hz and 40 Hz by means of fast fourier transformation for consecutive epochs and averaged every 2 or 10 s. The

high sampling rate was necessary to adequately resolve the high-frequency oscillation (200–600 Hz) component of the evoked response.

During a typical 2- to 3-h recording, we continuously presented animals (1 to 2 s randomized intervals) with either 0.2-ms (5 dB) auditory clicks, or 0.2-ms (75  $\mu$ m) whisker twitches. Whiskers were twitched with a solenoid coupled to a piece of hypodermic tubing into which the whisker was inserted. To compare cortical column state across different whiskers, two whiskers were stimulated at the same time, either on opposite hemispheres for probing interhemispheric differences, or on the same side for probing ipsilateral differences. Auditory clicks were provided by a 2-in., 8- $\Omega$  speaker placed 20 cm above the animal's head and driven by a 0.2-ms, 5-V square wave. Animals were under constant surveillance to assess movement and position.

We identified vigilance states using frontal EEG and EMG records reconstituted on the computer screen together with the EEG spectra. Sleep state was determined in 2-s epochs as quiet sleep (QS), REM sleep, and

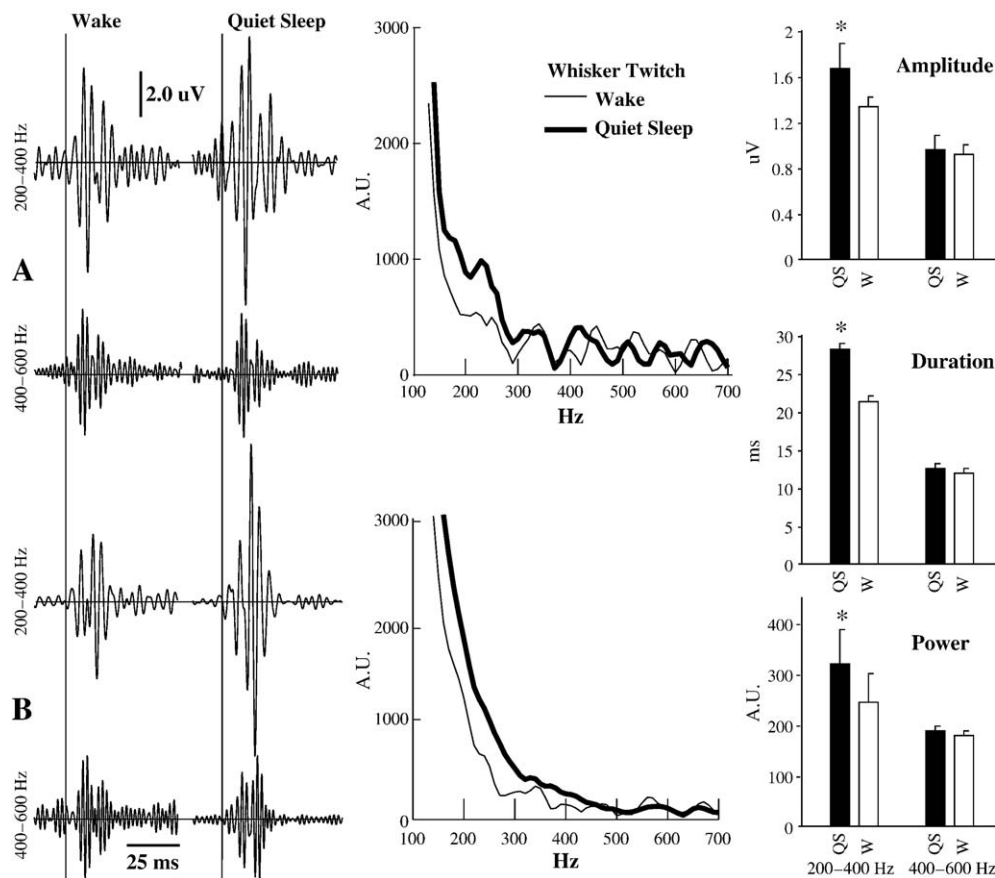


Fig. 4. State-dependent whisker high-frequency oscillations. The same two example evoked responses (A and B) as illustrated in Fig. 3 were filtered using FFT procedures between 200 and 400 Hz and 400 and 600 Hz for wake (W) and quiet sleep (QS) states. The middle two panels show the frequency power spectrum from 100 to 700 Hz. All measures of the high-frequency burst (RMS amplitude, duration, and power) were significantly larger for the 200–400 Hz range during quiet sleep, but not for the 400–600 Hz range ( $P < 0.01$ ).

wakefulness using both visual parsing of the record, and scattergram plots of EMG power vs. frontal lobe EEG delta power (0.5 to 4.0 Hz). Local surface evoked field potentials (SEPs) were derived by subtracting signals from neighboring electrodes. The trace was then filtered between 1 and 3 Hz to assess delta wave signal amplitude, 10–200 Hz to measure the amplitude of the evoked response, 200–400 Hz and 400–600 Hz to assess the high-frequency response. Each evoked response was grouped into sleep state categories as determined by whole animal sleep, scored from the frontal lobe electrode. Triggered averages of the SEPs binned for each state provided a quantitative measure of the temporal pattern for each state. Individual time-triggered responses were also plotted continuously for the whole record to assess the progression of the SEP changes across state. The defining components of the evoked potentials in rat have been reviewed in a parametric study by Knight et al. [38], comparing the various waveforms to human generated auditory potentials. For each SEP, the P1/N1 amplitude difference was measured, registered in time with the scoring bins, and plotted across time smoothed with a 5-point moving box car algorithm.

For each SEP P1/N1 amplitude plot, the mean value was calculated, and we normalized the traces by subtracting the mean from all moment-to-moment values, then divided each value by the mean. This procedure allowed us to compare between recording channels. The Pearson's correlation between regions across all values in the recording provided an index of similarity between locations. To identify time periods when the SEP amplitude was different between channels, we calculated the moment-to-moment studentized (or *z*-score) values (each value minus the mean and divided by the standard deviation), subtracted the studentized values between channels, then squared the result. This created a plot that illustrated when the two channels differed significantly above the 90% significance level. To measure the duration that the SEP remained in a particular functional state, a line drawn through each P1/N1 amplitude record at the mean value provided a reference for high and low shifts in amplitude. When the P1/N1 amplitude rose 10% above the mean line, the subsequent period was considered in the high-amplitude, sleep-like state. When the P1/N1 amplitude dropped below 10% of the mean value, this marked the beginning of the low-amplitude, wake-like state. In this way, the fraction of time spent in the high-amplitude and subsequent low-amplitude states was plotted and correlated for each 5-min interval of all records.

### 3. Results

Auditory and whisker stimuli across all behavioral states produced SEPs with 200–400 and 400–600 Hz

high-frequency oscillations (Fig. 2). Under head and body restraint used during whisker twitching, we have not been able to record deep levels of QS and REM sleep in rats. When average SEPs to whisker twitches were separated into whole animal waking and QS, we found an average 60% increase in SEP amplitude (Fig. 3). There was also a significant increase in the 200- to 400-Hz oscillation amplitude, power, and duration, but no significant difference in the 400- to 600-Hz oscillation during QS when compared to waking (Fig. 4).

Both deep QS and REM sleep were present when animals were unrestrained, freely moving in their home cage, connected through a tether, and subjected to auditory clicks. A similar relationship in the SEPs (Fig. 5) and high-frequency oscillations (Fig. 6) was found as that during whisker twitches during QS and waking. However, responses during REM sleep were

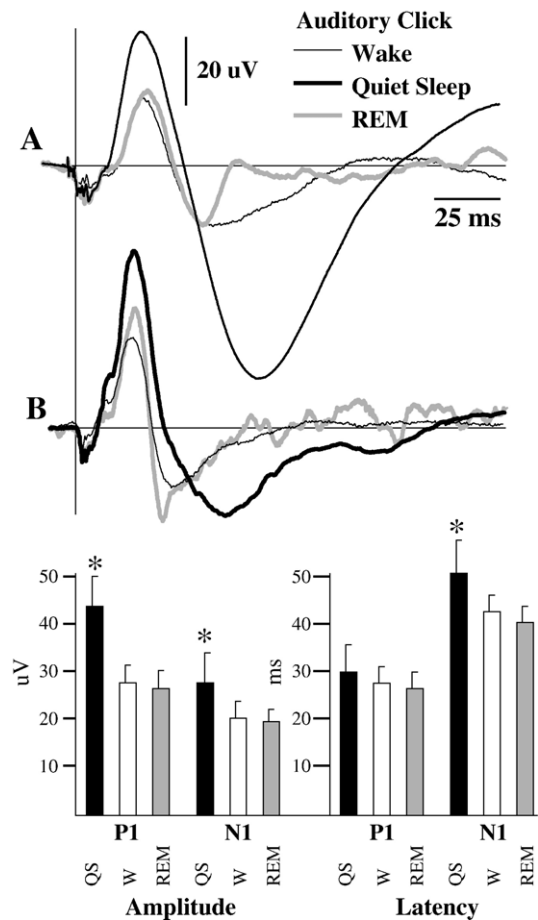


Fig. 5. State-dependent auditory SEPs. Two examples of evoked responses after auditory clicks show bigger amplitudes and longer trough latencies during quiet sleep (QS) over both waking (W) and rapid eye movement (REM) sleep. Standard error for all recordings from all 5 animals is displayed with the vertical bars on top of each bar in the summary bar graph. Asterisks indicate comparisons that were significantly different ( $P < 0.01$ ). Positive differential potential between adjacent electrodes is displayed in the upward direction.

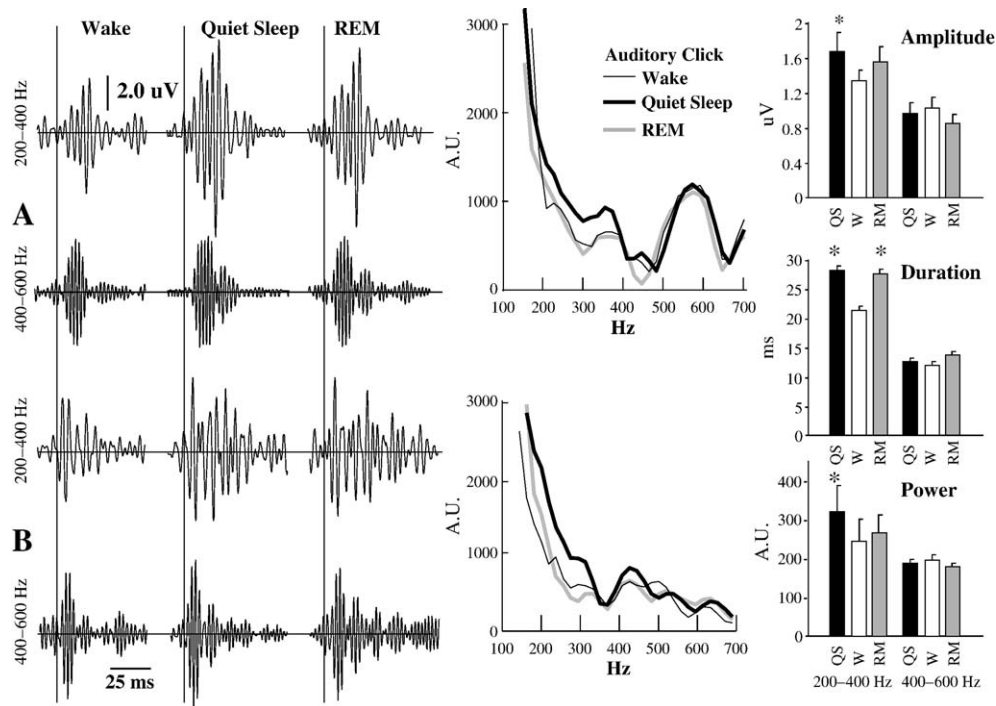


Fig. 6. State-dependent auditory high-frequency oscillations. The same two example evoked responses (A and B) as illustrated in Fig. 5 were filtered using FFT procedures between 200 and 400 Hz and 400 and 600 Hz for wake (W), quiet sleep (QS), and rapid eye movement (REM) sleep states. The middle two panels show the frequency power spectrum from 100 to 700 Hz. All measures of the high-frequency burst (RMS amplitude, duration, and power) were significantly larger for the 200–400 Hz range during quiet sleep, but not for the 400–600 Hz range ( $P < 0.01$ ). Evoked responses during REM was not significantly different from waking for any comparison, except 200–400 Hz burst duration.

not different from waking. Late temporal responses were always enhanced in waking and REM sleep compared to QS.

Changes in the SEPs across state were easily recognized by following the P1/N1 amplitude difference of individual SEPs across time. We observed significant fluctuations between high- and low-amplitude SEPs in individual brain regions during sleep states, even though the trend followed the sleep state of the whole animal (Fig. 7). These fluctuations were different across corresponding contralateral regions during both auditory clicks and whisker stimulation and were different between different whisker barrels of the same hemisphere, suggesting an independent and localized origin (Fig. 8). The SEP differences between recording sites was significantly higher during QS compared to waking and REM (Fig. 9). Local differences in SEP amplitude also followed local differences in the delta wave signal ( $r = -0.4$ ) such that when the local delta wave was at a high level, the SEP P1/N1 amplitude was low, and when the delta wave was low, the SEP amplitude was high. The fraction of time that each cortical column spent in the low-amplitude, wake-like state plotted against the fraction of subsequent time in the high-amplitude, sleep-like state showed a mean positive correlation of  $0.54 \pm 0.21$  ( $P < 0.01$ , Fig. 10).

#### 4. Discussion

Our results show that several aspects of the SEP are state dependent. The size and shape of the post-synaptic potentials were significantly larger and less complex during QS, and the 200- to 400-Hz high-frequency component burst was bigger and longer lasting. We found a high correlation in the SEP amplitude across channels; however, significant deviations in amplitude across brain regions, especially during QS, illustrates that the signals can be unique to a particular brain area and not a product of a brain wide phenomenon. Since the SEP response during QS is less spatially coherent than wake, this measure differs from the EEG, which exhibits higher coherence. Higher disparity in the SEP amplitude during QS supports the hypothesis that these differences are related to local functional states, and not noise in the recording or stimulus inconsistencies because we would expect both of these artifacts to produce higher disparity during waking.

The SEP fluctuations could represent the state changes of individual neural groups or cortical columns that are independent from the organism as a whole. Since our observations were similar between whisker and auditory stimulation, the effects may be independent of sensory modality and not significantly altered by the restraint

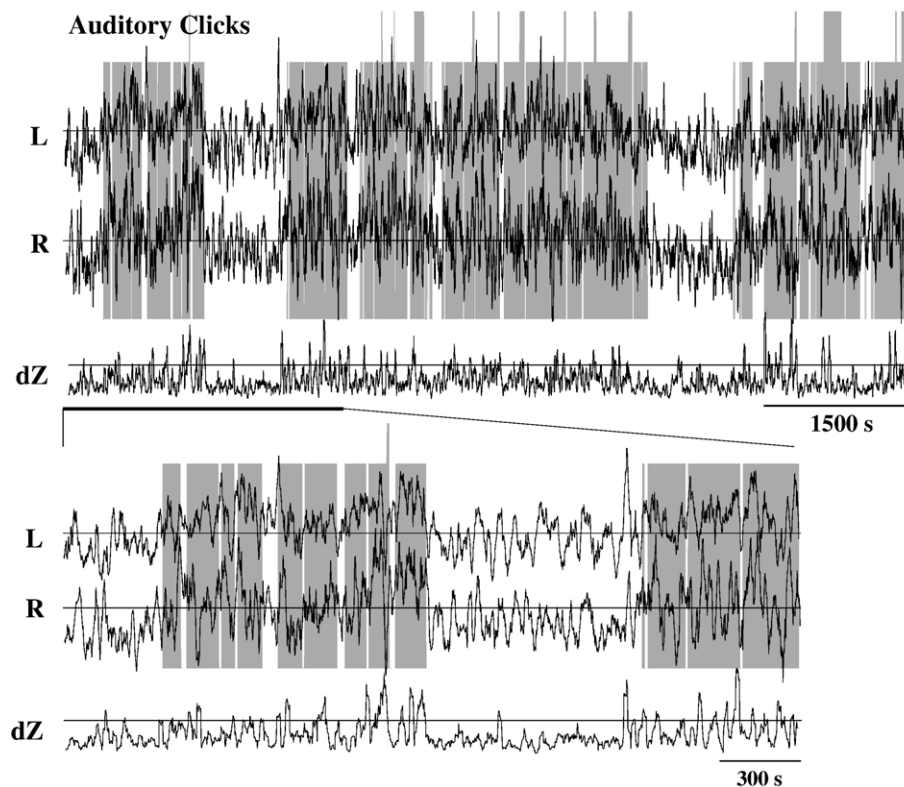


Fig. 7. Hemispheric differences in SEP amplitude. Continuous P1/N1 amplitude plots during auditory clicks across a typical recording shows large inter-trial SEP variability. Each point in the plot is the normalized peak-to-peak amplitude of each evoked response throughout the recording. The horizontal line through each trace represents the mean amplitude for the entire trace (Left: 57  $\mu$ V, Right: 63  $\mu$ V). Absolute SEP amplitudes varied between 0 and 100  $\mu$ V. A hypnogram for the record is plotted behind the traces such that quiet sleep (QS) periods are colored gray, with higher extending gray blocks representing REM epochs. Two pairs of electrodes on both hemispheres allow us to plot left side (L) responses separately from the right side responses (R). The traces show surprisingly similar patterns (Pearson's correlation,  $r = 0.45$ ) with low and high amplitudes that generally correspond to the wake and QS states, respectively. REM sleep periods show a lower amplitude as seen in the average response curves. Moment-to-moment fluctuations could correspond to localized states (e.g., wake-like state during whole animal sleep and vice versa). Below the left and right channel plots, we show the square of the moment-to-moment studentized difference values (dZ) between hemispheres. The horizontal line drawn on each dZ trace shows when the hemispheric differences rise above the 90% significance level, and illustrates significant deviations in evoked response amplitude between the different hemispheres. Such deviations suggest hemispheric differences in the modulation of the evoked response. Since the differences were greater during QS, we can reject the possibility that local differences are caused by recording noise, or stimulus inconsistencies.

required for whisker stimulation. A key concept of a distributed theory of sleep brain organization is that individual cortical columns transition through states of wakefulness and sleep as a function of prior neuronal activity. Since the duration of the localized sleep-like (high SEP amplitude) state was dependent on the duration of the prior wake-like (low SEP amplitude), individual cortical column sleep transitions are also use-dependent.

Weitzman and Kremen [83] first described an increase in the SEP as the waking state gave way to drowsiness. Systematic analysis of individual evoked responses were not possible until modern computer techniques allowed continuous long-term EEG recordings where stimuli could be controlled and individual evoked responses could be identified, classified, and averaged across sleep state. Since then, changes in evoked cortical potentials that accompany the behavioral changes of sleep have been

described in many animals including rats [25,42,45, 46,74,77], guinea pigs [58], cats, monkeys [11,50], and humans [7,12,15–17,23,26,48,49,52,54,55,57,66,73, 80,82–84,87]. Of significant importance to the primary sensory cortex, several investigators have identified differential processing of more complex sensory paradigms across sleep states [53,59,76], which is altered by several types of pathological conditions [15], and can also be correlated to local brain regions used during learning tasks [31]. However, only a few of these studies characterized individual SEP events, and none of them attempted to explain the large variability in SEP amplitude between individual trials. The results of the present study provide a foundation to further explore local SEP trial-to-trial variability, and provides a definition of functional states for cortical columns.

During the early portion of the SEP, brief low-amplitude, high-frequency (200–600 Hz) spike-like wave-

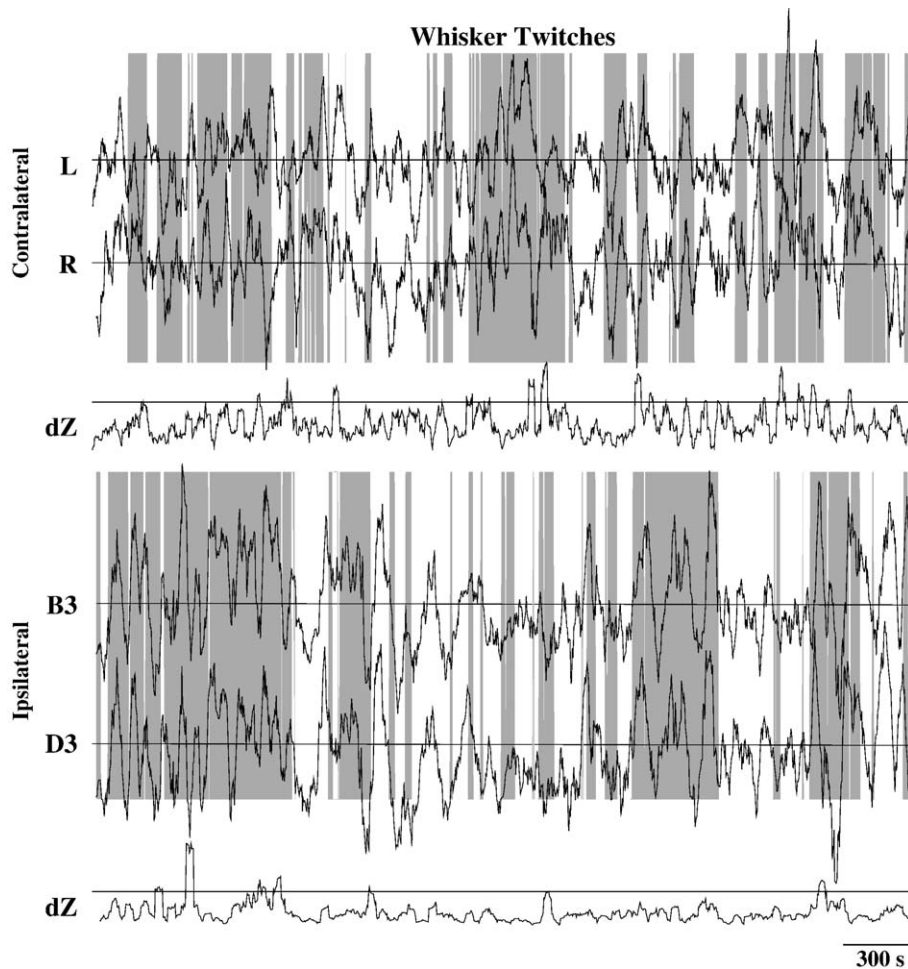


Fig. 8. SEP differences between neighboring cortical columns. An expanded time view of normalized evoked response P1/N1 amplitude across the recording during whisker twitches shows surprisingly similar temporal patterns with occasional and significant periods of discrepancy as seen during auditory clicks in Fig. 7. The horizontal lines through the traces represent the mean peak-to-peak amplitude across the record (Upper Panel Left: 55  $\mu$ V, Right: 42  $\mu$ V, Lower Panel B3: 314  $\mu$ V, D3: 308  $\mu$ V). The gray blocks in the background mark quiet sleep (QS) periods. During restraint with whisker twitching, only waking (W) and QS were attained. Data from the upper panel was collected from two pairs of screw electrodes over the somatosensory cortex of the left (L) and right (R) hemispheres while the B1 whisker on each side of the face was twitched at the same time. Data in the lower panel was collected from two electrodes of the 25-electrode array placed on the right hemisphere while whiskers B3 and D3 were twitched at the same time. The electrodes were selected based on 3D surface maps of the evoked responses from each whisker twitched separately (Fig. 1). Temporal patterns of the evoked response amplitudes followed similar generalized high and low trends as would be expected by sleep state, again with similar fluctuations between hemispheres (Pearson's correlation,  $r = 0.37$ ). The highest moment-to-moment correlation was achieved between electrodes on the same hemisphere (Pearson's correlation,  $r = 0.91$ ); however, in both the upper and lower panels, there were short periods of discrepancy as highlighted by the studentized difference traces below each panel (dZ). Horizontal lines on the difference traces show the 90% significance level for differences between channels. These discrepancies are indications that there are both hemispheric and columnar differences in the modulation of evoked response amplitudes.

let bursts were superimposed on the SEP. With sufficient filter bandwidth and amplification, high-frequency bursts can be recorded from scalp EEG electrodes in humans and with screw electrodes or surface electrodes in animals. This activity burst most likely arises from thalamo-cortical circuits within the cortical layers or local cortical circuits alone which oscillate at these high frequencies [13,22,24,27–29,32,33,36,37] and may play a critical role in information processing. Since the high-frequency bursts represent an oscillatory behavior that is generated by a combination of thalamic input and local

circuitry within the sensory cortex, when a particular brain region is defined as in the sleep state, we would expect changes in the burst pattern and SEP as reported here.

The state-related differences in the SEP amplitude could be a result of several mechanisms related to fluctuations of sleep regulatory substances in the brain (e.g., NO). State-related fluctuations in cortical excitability under the influence of subcortical structures could involve general modulatory systems. For example, phasic changes in brain stem activity could affect cortical

excitability through ascending connections [44,69], though local effects may not be explained by this mechanism. Several investigators also report state-related fluctuations in the excitability of intracortical neuronal networks with state-related and spontaneous changes in their synaptic and metabolic activity [68,70]. These investigators separated the fluctuations into “up” (excitable) and “down” (inhibited) states which could be related to larger and smaller evoked responses, respectively. This hypothesis is supported by the moderate correlation of the SEP amplitude with delta wave activity. If local delta waves indeed follow the local up and down states of the cortical column, then we would expect local differences in the SEP amplitude to follow the delta wave signal.

Modulation of spindle activity by 0.1 to 0.5 Hz slow oscillations can also contribute to periodic changes of SEP amplitude [1,2]. During the active “up” period of the slow oscillations, cortical neurons receive a balanced, strong barrage of inhibitory and excitatory synaptic potentials from the thalamus, resulting in depolarization interleaved with periods of relative quiescent “down” states [3,4,68,71,72,75]. Local cortical–thalamic pathways could result in local changes in cortical excitability which can be restricted to individual columns or larger brain regions as is seen in marine mammals [5,51,56].

Localized appearance of sleep-like states may underlie anomalous sleep/wake phenomenon such as sleep inertia, sleep paralysis, sleep walking, cataplexy, and REM sleep behavior disorder. Such behavior can be explained by parts of the brain being functionally wake,

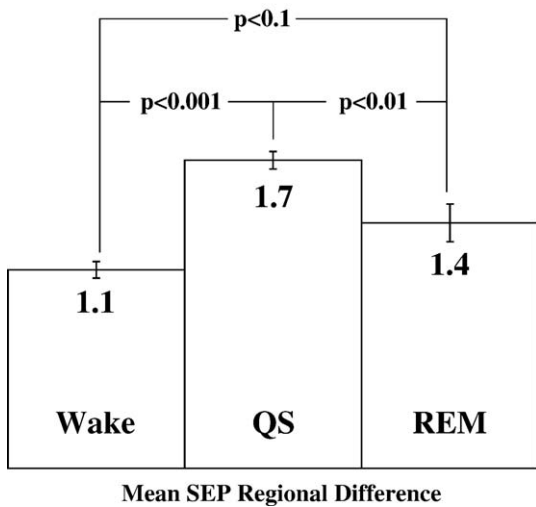


Fig. 9. State-dependent regional SEP disparity. When averaged across state, the mean regional differences in studentized SEP amplitude show a significantly greater amount of local disparity during QS when compared to waking and REM. Numerical values represent the mean of the moment-to-moment SEP studentized difference between regions, and the error bars represent the standard error of the mean.

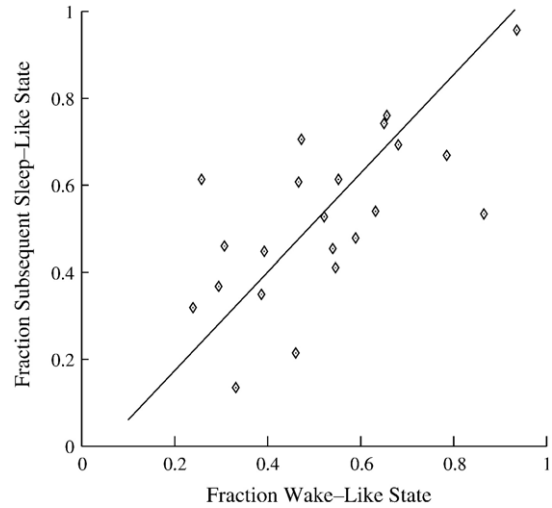


Fig. 10. Functional state dependence on prior state. All records were divided into 5-min epochs and the fraction of time spent in the wake-like state (low amplitude) was plotted against the fraction of time spent in the subsequent sleep-like state (high evoked response amplitude). The resulting scattergram shows a regression near unity ( $1.3 \pm 0.2$ ) and a correlation of  $0.54 \pm 0.21$  ( $P < 0.01$ ), suggesting that the sleep-like behavior of localized brain regions can be dependent on prior use.

while others are functionally asleep. While this manuscript is focused on local NREM sleep states, many REM sleep-like phenomena are not addressed in this manuscript, but the same principles may apply. Localized REM sleep may also appear as REM intrusion, or other REM-like state mixed with another behavioral state.

These in vivo experiments help in demonstrating how the brain could be organized to produce sleep and provide insights in to the mechanism of local sleep and even of sleep function. We have established a set of observable parameters that allow us to assess sleep state based on the characteristics of SEPs to whisker and auditory stimulation. Periodic fluctuations in SEP amplitude, which is different across different regions, support the hypothesis that neural groups can fluctuate in and out of sleep-like states independently of organism sleep state. Since the circuitry responsible for generating both the post-synaptic and high-frequency burst response can be influenced at the local level (e.g., cortical columns), the SEP patterns observed provide indicators for assessing the sleep/wake-like states of individual neural groups.

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