State-dependent effects of light-dark cycle on somatosensory and visual cortex EEG in rats

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Yasuda, Tadanobu, Kyo Yasuda, Richard A. Brown, and James M. Krueger. State-dependent effects of light-dark cycle on somatosensory and visual cortex EEG in rats. Am J Physiol Regul Integr Comp Physiol 289: R1083–R1089, 2005; doi:10.1152/ajpregu.00112.2005.—Somatosensory (SSctx) and visual cortex (Vctx) EEG were evaluated in rats under a 12:12-h light-dark (LD) cycle and under constant light (LL) or constant dark (DD) in each sleep or wake state. Under LD conditions during light period, relative Vctx EEG slow-wave activity (SWA) was higher than that of the SSctx, whereas during dark period, relative Vctx EEG SWA was lower than in the SSctx. These effects were state specific, occurring only during non-rapid eye movement sleep (NREMS). Under LL conditions, the duration of REMS and NREMS during the period that would have been dark if the LD cycle had continued (subjective dark period) was greater than under LD conditions. DD conditions had little effect on the duration of NREMS and REMS. SSctx and Vctx EEG SWA were suppressed by LL during the subjective dark period; however, the degree of Vctx SWA suppression was smaller than that of the SSctx. DD conditions during the subjective light period enhanced SSctx SWA, whereas Vctx SWA was suppressed. Under LL conditions during the subjective dark period, Vctx EEG power was higher than that of the SSctx across a broad frequency range during NREMS, REMS, and wakefulness. During DD, SSctx EEG power during NREMS was higher than that of the Vctx in the delta wave band, whereas SSctx power during REMS and wakefulness was higher than that of the Vctx in frequencies higher than 8 Hz. We concluded that the SSctx and Vctx EEGs are differentially affected by light during subsequent sleep. Results provide support for the notion that regional sleep intensity is dependent on prior regional afferent input.

slow-wave activity; electroencephalogram power; fast Fourier transform analyses; primary cortex

SLEEP IS USUALLY CONSIDERED a property of the whole animal/human, in part because quiescent behavior is often a defining criterion of sleep. However, over the past 10–20 years, data from a variety of approaches have suggested that sleep and/or sleep intensity can be localized and vary independently from whole animal behavior. Marine mammals do not have deep non-rapid eye movement sleep (NREMS) on both sides of the cortex simultaneously, and if only one side of the brain is deprived of sleep, only that side shows sleep rebound during recovery (33, 35). Neurology patients can express symptoms of wakefulness and sleep simultaneously (29). Sleep intensity, as determined by the power of electroencephalogram (EEG) slow waves (0.5–4 Hz) during NREM sleep, is enhanced in the somatosensory cortex (SSctx) during NREM sleep after prolonged stimulation of the SSctx during prior waking in humans (20) and rodents (48). Brain imaging studies of humans indicate that blood flow/metabolism is greater in areas disproportionately used during prior waking (30). Similarly, EEG delta wave activity in specific areas of the human cortex is dependent on prior waking activity (15). Developmental studies also support the notion that afferent neural activity is a determining factor in EEG delta wave activity in specific cortical areas (17, 31, 32). EEG slow-wave activity (SWA) during NREMS after a motor learning task is enhanced in Brodmans areas 7 and 40, the ones involved in the motor learning tasks. These results are interpreted as a manifestation of local use-dependent sleep (19). Finally, application of sleep regulatory substances unilaterally to the surface of the cortex induces localized state-dependent enhancement of EEG delta waves (49, 50). Theoretical approaches to brain organization of sleep also suggest that sleep is a distributed process being a fundamental property of neural assemblies (4, 21, 24). Collectively, these data and the theoretical approaches are consistent with the idea that sleep and sleep intensity are regional properties of the brain and that sleep is a distributed process dependent on prior afferent input (24, 25).

Rats are nocturnal; therefore, their motor activity and tactile activity during the dark period are greater than during the light period. Rats spend most of their time sleeping during the light period. Thus, during the dark period, the visual cortex (Vctx) receives reduced visual input and the SSctx receives disproportionately more somatosensory stimulation via whiskers for spatial orientation. Because regional sleep/sleep intensity are posited to be dependent on prior afferent input, we investigated 1) whether SSctx EEG power differs from that of the Vctx under a 12:12-h light-dark condition (LD) and 2) the effects of constant light (LL) or constant dark (DD) on EEG power of the SSctx and the Vctx.

MATERIALS AND METHODS

Animals and surgery. Male Sprague-Dawley rats (n = 6) weighing 300–350 g were obtained from Taconic (Germantown, NY). The use of rats in these experiments was in accordance with Washington State University guidelines and was approved by the Animal Care and Use Committee. The rats were kept on a 12:12-h LD cycle (lights on at 0900, ∼300 lx) at 23 ± 2°C ambient temperature. Water and food were available ad libitum throughout the experiment. Surgeries were performed using ketamine-xylazine (87 and 13 mg/kg, respectively) anesthesia. The rats were provided four stainless steel jewelry screw EEG electrodes placed epidurally through a burr hole in the skull bilaterally over the SSctx and primary Vctx. The stereotaxic coordinates for the electrodes were 2.5 mm posterior to the bregma and ±5.5 mm bilaterally to the midline for the SSctx and 8 mm posterior to the...
RESULTS

SSctx and Vctx relative EEG power during NREMS under LD conditions. The differences of absolute EEG power values between the SSctx and the Vctx in individual rats were variable. Thus, to compare the changes of SSctx and Vctx EEG SWA during NREMS, we normalized the averages of SSctx or Vctx EEG SWA throughout the entire 23-h control recording period to 100% for each animal, respectively. EEG SWA during NREMS of both the SSctx and the Vctx showed a typical diurnal rhythm (Fig. 1, left). During the light period, relative EEG SWA during NREMS of the Vctx from 4 h to 11 h after light onset (clock time 13 to 20 h) was significantly higher than that of the SSctx. In contrast, during the dark period, SSctx EEG SWA during NREMS was higher than that of the Vctx, especially from 6 h to 11 h after dark onset (clock time 3 to 7 h) [ANOVA, interaction: F(11, 44) = 5.228, P < 0.001]. Delta power during REMS and the waking period was lower than that observed during NREMS. Its diurnal rhythm was attenuated compared with that shown for NREMS in Fig. 1, and relative power in the Vctx and SSctx did not vary across the recording period (data not shown).

The pattern of change in EEG power in the 8- to 35-Hz frequency band during NREMS was distinct from that of the 0- to 4-Hz band. Thus, during daylight hours, relative EEG power increased in both the Vctx and SSctx and peaked during the first 2 h of the dark period for both areas of the brain (Fig. 1, right). Regardless of this distinct pattern of 8- to 35-Hz power, similar differences between the Vctx and SSctx were observed...
[ANOVA, interaction: \( F(11,44) = 15.641, P < 0.001 \)] with power in the Vctx being greater during daylight hours and power in the SSctx being greater during dark hours.

**Duration of NREMS and REMS under LL and DD conditions.** Constant light during the subjective dark period enhanced both NREMS and REMS (Fig. 2). On the baseline day (LD), the duration of NREMS and REMS showed a typical diurnal pattern with higher values during light hours. Under LL conditions, the durations of NREMS significantly increased during the subjective dark period (Fig. 2, left) [ANOVA, main effect: \( F(1,5) = 34.211, P = 0.002 \)]. Similarly, the duration of REMS under LL increased during the subjective dark period [ANOVA, main effect: \( F(1,5) = 31.564, P = 0.002 \); interaction: \( F(5,25) = 4.333, P = 0.006 \)]. In contrast, under DD conditions, the duration of NREMS significantly decreased [ANOVA, main effect: \( F(1,5) = 7.845, P = 0.038 \)] during the first 2 h of the subjective light period (Fig. 2, right). The duration of REMS under DD conditions tended to be higher than that observed during DL conditions, but this effect was not significant.

**SSctx and Vctx EEG SWA during NREMS under LL conditions.** Constant light during the subjective dark period suppressed EEG SWA during NREMS in both the SSctx and the Vctx (Fig. 3). On the baseline day, the course of EEG SWA during NREMS in both the SSctx and the Vctx showed the typical diurnal pattern (compare Figs. 1 and 3). With LL conditions, SSctx EEG SWA during NREMS was significantly lower than that observed during LD conditions (Fig. 3, left) [ANOVA, main effect: \( F(1,5) = 34.350, P = 0.002 \)]. Similarly, Vctx EEG SWA during NREMS decreased during the subjective dark period in LL conditions (Fig. 3, right) [ANOVA, main effect: \( F(1,5) = 9.260, P = 0.029 \)]. However, the degree of EEG SWA suppression of the Vctx during NREMS was smaller than that observed in the SSctx (compare Fig. 3, left and right). LL conditions did not affect EEG SWA of either the SSctx or the Vctx during REMS or wakefulness (data not shown).

**SSctx and Vctx EEG SWA during NREMS under DD conditions.** On the baseline day, the time course of EEG SWA during NREMS from both the SSctx and the Vctx showed a typical diurnal pattern. Under DD conditions, during the sub-

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**Fig. 2.** Effects of constant light (LL; left) and constant dark (DD; right) (filled symbols) on NREMS and rapid eye movement sleep (REMS). Open symbols indicate data obtained from the same rats during LD conditions. Data shown are averages (means ± SE) obtained from 2-h time blocks (n = 6). Hatched bars indicate dark hours. *P < 0.05, LD vs. LL (left) or DL vs. DD (right).

**Fig. 3.** Effects of constant light on EEG SWA from the SSctx (left) and the Vctx (right). Percent SWA values are EEG delta wave power during NREMS. Average EEG power in the 0.5- to 4-Hz band from the SSctx and the Vctx throughout the 23-h control-recording period (LD condition) was normalized to 100% for each rat, and then all EEG SWA data were converted to relative percentage values. Data shown are averages (means ± SE) obtained from 2-h time blocks (n = 6). Hatched bars indicate dark hours. *P < 0.05, LD vs. LL.
jective light period, SSctx EEG SWA during NREMS significantly increased (Fig. 4, left) [ANOVA, main effect: $F(1,5) = 12.741, P = 0.016$]. In contrast, Vctx EEG SWA during NREMS decreased during the subjective light period in DD conditions in first 2 h after subjective light onset (clock time 9 h) (Fig. 4, right) [ANOVA, interaction: $F(5,25) = 12.017$, $P < 0.001$]. DD conditions did not affect EEG SWA of either the SSctx or the Vctx during REMS or wakefulness (data not shown).

**Effect of light on EEG power spectrum in each vigilance state.** The 2-h time block (6 and 7 h after dark onset in the subjective dark period; clock time 3 to 5 h) (Fig. 1) was chosen for power spectrum analyses because the differences of EEG SWA during NREMS between the SSctx and Vctx under LL conditions compared with LD conditions were largest in that period. The ratio of EEG power under the LL condition to that of the LD condition in each 1-Hz frequency bandwidth during each vigilance state is shown in Fig. 5, top. LL conditions had a significant suppressive effect in a wide frequency range (0.5–11 Hz) in the SSctx compared with the Vctx during NREMS. The relative EEG power values in the 1.5- to 10.5-Hz frequency band of the Vctx were significantly greater than those of the SSctx during LL (Fig. 5, top left) [ANOVA, main effect: $F(1,5) = 14.920, P = 0.012$]. Under LL conditions during REMS, power in the theta band (8.5–10.5 Hz) was greater in the Vctx than in the SSctx (Fig. 5, top center) [ANOVA, interaction: $F(24,120) = 1.949, P = 0.01$]. During wakefulness under LL conditions, the relative Vctx spectral values in 5.5- to 6.5-, 11.5- to 12.5-, and 20.5- to 25-Hz bands during wakefulness were significantly higher than those of the SSctx (Fig. 5, top right) [ANOVA, interaction: $F(24,120) = 3.458, P < 0.001$].

**Effect of DD conditions on EEG power spectrum in each vigilance state.** The 2-h time block (6 and 7 h; clock time 15 to 17 h, Fig. 1) after light onset in the subjective light period was chosen for power spectrum analysis. The ratios of EEG power under DD conditions compared with those obtained during DL conditions in each 1-Hz frequency bandwidth during each vigilance state are shown in Fig. 5, bottom. During NREMS, the relative SSctx EEG power compared with the Vctx in the 0.5- to 5.5- and 6.5- to 8.5-Hz bands were significantly higher (Fig. 5, bottom left) [ANOVA, interaction: $F(24,120) = 1.699$, $P = 0.033$]. During REMS and wakefulness, the relative Vctx spectral values were suppressed across a broader frequency range. Thus, during REMS, the relative SSctx spectral values in the 7.5- to 12.5-, 13.5- to 16.5-, and 19.5- to 25-Hz bands were significantly higher than those of the Vctx (Fig. 5, bottom center) [ANOVA, main effect: $F(1,5) = 20.151, P = 0.006$; interaction: $F(24,120) = 2.118, P = 0.004$]. During wakefulness, the relative SSctx spectra values in the 4.5- to 6.5-, 8.5- to 11.5-, and 14.5- to 25-Hz bands were significantly higher than those of the Vctx (Fig. 5, bottom right) [ANOVA, main effect: $F(1,5) = 18.026, P = 0.008$].

**DISCUSSION**

Our first finding reported is that analyses of regional differences of EEG indicate that site-specific, state-specific, and frequency-specific topographic changes occur during spontaneous sleep. This finding is consistent with several previous findings. Thus Vyazovskiy et al. (48) also reported that EEG slow-wave power from the SSctx in rats varies across the day. As mentioned in the Introduction, dolphins clearly demonstrate state-dependent EEG asymmetries (33). In humans, power in the 11- to 15-Hz frequency range during NREMS dominates in the left hemisphere. In contrast, in the centroparietal EEG 4- to 8-Hz band, the right hemisphere has predominance during NREMS and the left hemisphere has predominance during REMS (39). Lateralization of theta and beta activities in the right frontal region and of delta activity in the left occipital region occurs during REMS in humans (7). Furthermore, the number of delta waves in the right frontal and central regions during all-night sleep was greater than that in the left regions in humans (42). Similarly, frontal EEG power in the 10.25- to 16.0-Hz band during NREMS and REM is larger than that of the occipital region, whereas occipital power in the 6.25- to 9.0-Hz band in REMS is larger than that of the frontal region in rats (40). The mechanisms inducing such EEG asymmetries remain unknown, although some ideas have been posited. Thus functional and structural asymmetry of the brain could cause regional changes of the EEG. Gender- and age-dependent structural brain asymmetries occur in humans (34). EEG power is dependent in part on regional cerebral blood flow, and there are state-dependent changes in regional blood flow (22).
glucose metabolism would affect regional blood flow, and there are state-specific regional differences of glucose utilization (23).

A second major finding of this study was that EEG power during sleep also is dependent on afferent input. Thus the regional differences described in the studies mentioned above could in part be the result of waking activity differences, as well. The finding that regional EEG power is dependent on afferent activity also is consistent with prior reports. SWA is thought to reflect sleep intensity during NREMS. SWA during NREMS is enhanced after sleep deprivation in animals (14, 28, 37), and arousal thresholds correlate with EEG SWA (36). Furthermore, several sleep regulatory substances, such as IL-1β (26) and adenosine (4, 5), enhance EEG SWA during NREMS. In addition, sleep deprivation or local activation of a particular brain region induces EEG SWA asymmetry during NREMS. Frontal EEG power in the 2- to 4-Hz frequency band is larger than that of the occipital region, whereas frontal EEG power in the 10.25- to 16.0-Hz band is more attenuated in NREMS after sleep deprivation in rats (40). Forty hours of sleep deprivation enhance the anterior predominance of delta activity in the left, but not in the right, hemisphere in humans (42). Prolonged and excessive stimulation of the right hand of human subjects during wakefulness increases EEG SWA during subsequent sleep in the left cortex (20). Similar results were obtained from the rat SStx after unilateral facial whisker removal and sleep deprivation; thus the side ipsilateral to the cut whiskers received disproportionate sensory stimulation and exhibited enhanced EEG delta power in subsequent sleep (47, 48). Results of the current study show that similar changes occur spontaneously in untreated rats and can be manipulated by changing the LD schedule.

The asymmetries of SWA during NREMS reported in the present study suggest that sleep intensity is not spread uniformly in the brain. Under LD condition, the relative Vctx SWA during NREMS was higher than that of the SSctx in the light period. On the other hand, the relative Vctx SWA during NREMS was lower than that of the SSctx in the dark period. These results indicate that each part of the brain has its own diurnal pattern of SWA during NREMS and that the power of EEG SWA is dependent on afferent input.

We also report changes in the duration of sleep in response to acute LL and DD conditions. Light is an important environmental factor regulating sleep. There are several previous reports that the light-dark cycle affects sleep. In those reports, four methods for changing the light-dark (LD) cycle conditions...
were used: 1) constant light (LL) (6, 46) or constant dark (DD) (3, 6, 45, 46); 2) long-light and short-dark, or long-dark and short-light (2, 9); 3) short intervals of LD cycle (8, 13, 18, 43); and 4) 8-h advance of the LD cycle (41). These reports demonstrated that various types of LD cycles strongly affect sleep propensity. In the current study, the duration of NREMS in subjective dark period under LL was significantly longer than that observed under LD. Similarly, the duration of REMS in subjective dark period under LL increased. These findings are consistent with previous findings obtained in rats (3, 45). In rabbits, the duration of NREMS increases, however, and the duration of REMS decreases under LL (46). In pigeons, the LL conditions suppress both NREMS and REMS (6). The different reactions to constant light in rats, rabbits, and pigeons are likely due to their living habits; rats are nocturnal, rabbits are crepuscular, and pigeons are diurnally active.

Under DD conditions, the duration of NREMS in the subjective light period significantly decreased during the first 4 h and the duration of REMS increased slightly but not significantly. Similarly, Tobler and colleagues (3, 45) demonstrated that the duration of REMS increased under DD conditions, whereas NREMS did not significantly increase in the corresponding subjective light period in rats. The reasons for these discrepancies are not known.

Under DD conditions, SSctx SWA during NREMS increased in the subjective light period, whereas Vctx SWA during NREMS decreased significantly. Tobler et al. (45) reported that SWA during NREMS, which was recorded from the midcortical region under the same lighting conditions as ours, increased significantly. Under LL conditions, the SSctx SWA during NREMS decreased significantly in the subjective dark period. Although the Vctx SWA during NREMS decreased, the degree of the decrease was smaller than that of the SSctx. There are few studies about SWA under constant light, although in pigeons, SWA did not show any consistent changes under LL conditions (6). Collectively, by comparing data in the SSctx to those in the Vctx, our results suggest that light during the subjective dark period decreases SWA during NREMS, whereas dark during the subjective light period had the opposite effects on SWA during NREMS.

We have proposed a mechanistic model for neuronal assembly sleep (24, 25). Briefly, we posited that as synapses and circuits are used, sleep regulatory substances such as tumor necrosis factor-α (TNF-α), nerve growth factor, brain-derived neurotrophic factor (BDNF), and IL-1β, are released. In an autocrine fashion, these activity-dependent substances alter synaptic efficacy of the specific synapses that were activated. These activity-dependent substances also act in paracrine/juxtacrine fashions to affect the electrical properties of nearby neurons such that a given input results in a different output. This action alters synaptic usage within the neuronal assembly and thereby, via activity-dependent mechanisms, helps to preserve synaptic efficacy of synapses not activated by the original environmental input. Activity-dependent driven changes in neural connectivity and the necessity for the preservation of microcircuitry sculpted by past events are both served by such mechanisms, and we consider this a function of sleep. In current study, we clearly demonstrated state-dependent differences of EEG SWA between the SSctx and the Vctx under various LD cycles. According to our theory, the above activity-dependent sleep regulatory substances accumulate in the cortex during the active period (during dark period in rats); several prior observations support this idea. TNF-α mRNA levels in the cortex at light onset are higher than at 6 h after light onset in rats (11). Brain TNF-α levels in the cortex peak at light onset in rats, suggesting an accumulation during the prior dark period (16). Furthermore, IL-1β mRNA in the cortex peaks just before or after light onset in rats (12, 44). BDNF mRNA and BDNF protein levels in the Vctx, but not in the SSctx, increase during the circadian light period, whereas those levels are suppressed by temporal or continuous darkness (38). Furthermore, NGF immunoreactivity in SSctx pyramidal neurons and GAD-67 mRNA in the SSctx depend on both sleep and afferent input into the SSctx (10). Collectively, such data support the notion that changing levels of activity-dependent sleep regulatory substances in various parts of the brain result in region-specific changes in EEG SWA and support the hypothesis that sleep is a property of neuronal assemblies.

**REFERENCES**

18. Franken P, Tobler I, and Borbély AA. Varying photoperiod in the laboratory rat: profound effect on 24-h sleep pattern but no effect on sleep...


