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Interhemispheric EEG asymmetries during unilateral bright-light exposure and subsequent sleep in humans

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Cajochen C, Di Biase R, Imai M. Interhemispheric EEG asymmetries during unilateral bright-light exposure and subsequent sleep in humans. *Am J Physiol Regul Integr Comp Physiol* 294: R1053–R1060, 2008. First published January 23, 2008; doi:10.1152/ajpregu.00747.2007.—We tested whether evening exposure to unilateral photic stimulation has repercussions on interhemispheric EEG asymmetries during wakefulness and later sleep. Because light exerts an alerting response in humans, which correlates with a decrease in waking EEG theta/alpha-activity and a reduction in sleep EEG delta activity, we hypothesized that EEG activity in these frequency bands show interhemispheric asymmetries after unilateral bright light (1,500 lux) exposure. A 2-h hemi-field light exposure acutely suppressed occipital EEG alpha activity in the ipsilateral hemisphere activated by light. Subjects felt more alert during bright light than dim light, an effect that was significantly more pronounced during activation of the right than the left visual cortex. During subsequent sleep, occipital EEG activity in the delta and theta range was significantly reduced after activation of the right visual cortex but not after stimulation of the left visual cortex. Furthermore, hemivisual field light exposure was able to shift the left predominance in occipital spindle EEG activity toward the stimulated hemisphere. Time course analysis revealed that this spindle shift remained significant during the first two sleep cycles. Our results reflect rather a hemispheric asymmetry in the alerting action of light than a use-dependent recovery function of sleep in response to the visual stimulation during prior waking. However, the observed shift in the spindle hemispheric dominance in the occipital cortex may still represent subtle local use-dependent recovery functions during sleep in a frequency range different from the delta range.

use-dependent sleep; spectral analysis; photic stimulation

IN HUMANS, THE GROSS ANATOMY and functional layout of the brain are organized asymmetrically, with hemispheric specialization for key aspects of language and motor function (for a review, see Ref. 39). Whether there is an unequal distribution of sleep-related functions between the hemispheres during human sleep is not known. Unlike in marine mammals and birds, sleep captures the entire human brain and is thus considered primarily a global brain phenomenon. Yet, several studies have reported small hemispheric asymmetries in the EEG during human sleep (2, 16, 32, 36), which could arise from structural and functional asymmetries of brain regions involved in the generation of the sleep EEG. Indeed, neuroanatomical differences between the hemispheres have been reported for regional blood flow (20), and the regional distribution of cerebral glucose during wakefulness (3, 19) and also during REM and non-REM sleep (3). Whether subcortical areas like the thalamus that modulates various brain functions such as incoming sensory and motor information routed to higher brain centers show hemispheric asymmetry is not clear (see Ref. 13, and references therein). There is, however, a strong neurochemical asymmetry in the thalamus such that noradrenergic neurons are strongly lateralized (29), which may be related to the reported asymmetry of human sleep spindles (32), which are generated in the thalamocortical system. Another frequency range of the human sleep EEG, which exhibited a distinct state-related asymmetry (right hemispheric dominance in non-REM sleep and left hemispheric dominance in REM sleep), corresponds to the high delta/theta band (4–8 Hz) (32). Supporting this, Sekimoto et al. (36) found a greater delta count per hour over the right hemisphere during non-REM sleep.

In addition to observations of these naturally occurring EEG asymmetries during sleep, there have been several efforts to challenge hemispheric sleep asymmetries via experimental manipulation, such as unilateral somatosensory stimulation (11, 24) or monaural auditory stimulation prior to sleep (7). So far, the results are ambiguous. Kattler et al. (24) showed that unilateral stimulation of the left somatosensory cortex during 6 h of wakefulness resulted in a small, but significant, shift of the interhemispheric asymmetry over a central region for the 0.75–4.5 frequency range during the first hour of non-REM sleep relative to baseline. On the other hand, Huber et al. (23) were able to show that arm immobilization during wakefulness for 12 h causes local decreases in slow-wave activity during the subsequent sleep episode. Thus, these studies clearly support the idea of a use-dependent recovery function of sleep. In contrast, after 6 h of monaural acoustic stimulation, no significant effects of regional scalp EEG asymmetries were found either in slow-wave or REM sleep (7). This is not surprising, since the auditory system is bilaterally organized (42). Thus, unilateral inputs should affect homologous subcortical and cortical auditory structures in a similar way, although left-hemispheric auditory processing advantages have been reported in a dichotic listening study (25). In contrast to Kattler et al. (24), Cantero et al. (7) found EEG increases in frequency ranges different from the delta range, namely, in the alpha and spindle frequency range during slow-wave sleep in both brain hemispheres (7). This indicates that besides delta activity, also EEG alpha and spindle activity respond to intensive activation of specific neural inputs during wakefulness. Surprisingly, there was no evidence that unilateral somatosensory stimulation during slow-wave sleep induced asymmetrical EEG

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changes and disrupted sleep in the contralateral hemisphere (11), which rather supports the idea that the human brain is capable of monitoring the environment without compromising slow-wave sleep or EEG delta activity (11). Thus, except for evidence from the somatosensory system, it is not clear whether there is a simple relationship between a use dependency of neurons during wakefulness and the recovery function of sleep in humans.

Exposure to polychromatic bright light in the evening (>1,000 lux) suppresses EEG delta activity in the subsequent sleep episode and sometimes also leads to an increase in sleep latency (4–6, 12). Very recently, we could show that theses effects are wavelength and topographically dependent such that only short-wave length light at 460 nm (blue light) was particularly efficient in suppressing EEG delta activity in occipital brain regions (28). In contrast to the reported increase in EEG delta activity during subsequent sleep after somatosensory stimulation (24), EEG delta activity after light exposure was reduced. These findings are less related to the use-dependent aspect of sleep function but rather reflect an alerting effect of light, which continues into the initial part of the sleep episode.

In the present study, we took advantage of the facts that human visual perception is retinotopic [i.e., in lower visual areas (e.g., V1), the neurons are organized in an orderly fashion in the sense that they form a two-dimensional representation of the visual image formed on the retina] and light from the right visual world strikes the temporal retina of the left eye and the nasal retina of the right eye, activating the contralateral visual primary cortex (i.e., left hemisphere) and vice versa. In other words, it is possible to activate the left visual cortex by light coming from the right side and vice versa (i.e., hemivisual light exposure). We predicted that waking EEG alpha activity during unilateral light exposure would be attenuated in the occipital cortex contralateral to the position of the light source. Furthermore, we hypothesized that hemifield light exposure prior to sleep elicits hemispheric EEG asymmetries during subsequent non-REM sleep, particularly in the delta and spindle EEG range. Because exposure to evening light exposure has alerting properties in humans, we expected that the hemivisual field stimulation by light would decrease EEG delta and spindle activity predominantly in the occipital cortex contralateral to the source of the light, that is, in the activated hemisphere.

MATERIALS AND METHODS

Study participants. Eight young healthy male volunteers (mean age 26.6 yr ± 6.5 SD) completed the study. All were nonsmokers, free from medical, psychiatric, and sleep disorders, as assessed by a physical examination and questionnaires. One week before the study, the volunteers were asked to abstain from excessive alcohol and caffeine consumption (i.e., at most, five alcoholic beverages per week, and 1 cup of coffee or 1 caffeine-containing beverage per day). Furthermore, they were instructed to sleep 8 h per night and to keep a regular sleep-wake schedule (with bed and wake times within ±30 min of self-selected target times between 10:00 PM and 1:00 AM). The actual range of bedtimes for the eight volunteers was between 10:30 PM and 0:30 AM. The outpatient segment of the study was verified using a wrist actigraph (Cambridge Neurotechnology, Cambridge, UK), questionnaires, and self-reported sleep logs. All volunteers confirmed their compliance by written informed consent. The protocol, questionnaires, and consent form were approved by the local ethical committee and conformed to the Declaration of Helsinki.

Study protocol and light exposure. The study consisted of three light conditions (i.e., left side light, right side light, no light), which were carried out in weekly intervals in a balanced cross-over design with intrasubject comparisons. All volunteers maintained their self-selected bedtimes virtually the same prior to each of the three treatments. Furthermore, they were requested to avoid direct exposure to sunshine as much as possible before reporting at 10:00 AM to the laboratory on the recording day. After preparation for polysomnographical sleep recordings, they sat in a comfortable chair in dim light (8 lux at eye level; polychromatic white light) from 2 PM to 8 PM (i.e., 6-h light deprivation episode) and were not allowed to nap. This dim light episode was followed by 2 h of hemivisual field bright-light exposure. During the light exposure, subjects were instructed to gaze at a fixation point that was placed 80 cm in front of the subject. A light box [Philips HF3305 Bright Light Box (L×W×H): 18 × 33 × 57 cm, full daylight spectrum, with an UV-filtering screen, Koninklijke Philips Electronics N.V., The Netherlands] was positioned at 80 cm in front and 20 cm to the left or right side, corresponding to a visual angle of 14.3–43.0 left or right relative to the subjects' direction of gaze (Fig. 1), to deliver light to the contralateral visual cortex. The eye opposite of the light box was covered with a special goggle to prevent

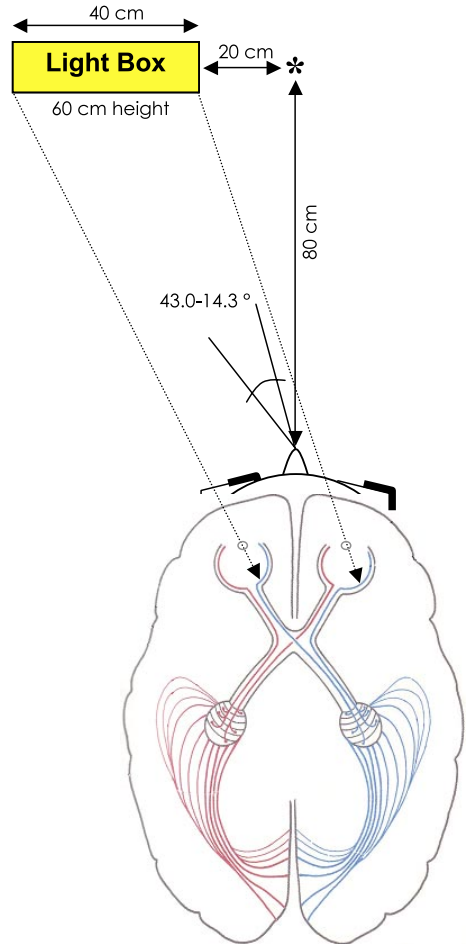

Fig. 1. Experimental lighting setup for the right hemifield light condition. The subjects were asked to fixate a point at a distance of 80 cm. The light box was placed either 20 cm left or right to the fixation point, resulting in a visual angle of 14.3–43.0 left or right relative to the direction of gaze of the subject. The eye opposite to the light box was covered with a special goggle (dark bars) to prevent stimuli by stray light. The light intensity was 1,500 lux measured at eye level. During the 2-h exposure time, bright light was delivered six times from the left side or right side, respectively, for a 15-min episode followed by a 5-min resting episode in dim light.

stimuli by stray light. The light intensity was 1,500 lux measured at eye level. During the 2-h exposure time, bright light was delivered six times from the left side or right side, respectively, in 15-min episodes followed by a 5-min resting episode in dim light. During the no-light condition, subjects were asked to sit in dim light and to gaze at a fixation point similarly as during the light conditions. After light exposure, subjects sat again in dim light for 1 h before they were allowed to go to bed and sleep in complete darkness (0 lux). To monitor the subject's vigilance level, the EEG and the electrooculogram (EOG) were continuously inspected on a computer display during the entire experimental protocol prior to sleep. At the same time, a technician sat in the subject's room controlling his gaze and delivering the bright light six times from the left side or right side, respectively, in 15-min episodes followed by a 5-min resting episode in dim light. If changes in alertness were recognized on the monitor, the subjects were asked to continue to gaze at the point. Subjective sleepiness was assessed with the Karolinska sleepiness scale (KSS) (1) and with the Karolinska drowsiness test (KDT) (1, 18), which was scheduled once during the first dim light episode, twice during the light exposure episode, and once during the second dim light episode before sleep.

Waking and sleep EEG recording and analysis. EEG signals were recorded from gold electrodes placed at the locations F3, F4, C3, C4, P3, P4, O1, O2, referred to linked-mastoids using the Vitaport digital ambulatory system (Vitaport-3 digital recorder; TEMEC Instruments, Kerkrade, The Netherlands). Ocular movements were recorded with a pair of electrodes placed 1 cm above and below and 1 cm outside from the outer canthi of each eye. In addition, submental electromyogram (EMG) and the ECG were recorded. All signals were low-pass filtered at 30 Hz (4th-order Bessel antialiasing, total 24 dB/Oct) at a time constant of 1 s before online digitization (range: 610 μV, 12-bit analog-to-digital converter, 0.15 V/bit) with a sampling rate of 128 Hz (for the EEG). The raw signals were stored online on a Flash RAM card (Viking) and downloaded off-line to a personal computer hard drive. Sleep stages were visually scored according to standard criteria (31) based on the C4 lead. Visually scored sleep stages were expressed as percentages of total sleep time or in minutes (sleep onset latencies, REM sleep onset latencies, total sleep time). All EEGs were subjected to spectral analysis using a fast Fourier transformation with a 10% cosine 4-s window during sleep resulting in a 0.25-Hz bin resolution and a 10% cosine 2-s window during wakefulness prior to sleep resulting in a 0.5-Hz bin resolution. EEG artifacts were automatically detected (CASA, 2000 PhyVision, Gemert, The Netherlands). EEG data collected during the 3-min KDT were visually scored for artifacts before they were subjected to a fast Fourier transform routine. For data reduction, artifact-free, 2-s epochs were averaged over 20-s epochs. Next, the 20-s epochs were further reduced by averaging them over each 3-min KDT. Here, we only report waking EEG data collected during KDTs, to compare artifact-free EEG samples between the three conditions. Because of too many eye blink artifacts, one subject was excluded from the waking EEG analyses. During sleep, EEG power density was calculated during non-REM sleep (stages 2, 3, and 4) in the frequency range from 0.25 to 25 Hz. Sleep EEG power density after light coming from the left- and right-hand side was expressed relative to EEG power density after the no-light condition (log ratios). After averaging across subjects, relative all-night sleep EEG spectra were retransformed as percentages of the no-light condition for graphical illustration. For time course analyses, non REM-REM sleep cycles were defined according to Feinberg and Floyd (14), with the exception that for the last sleep cycle, no minimum REM sleep duration was required. Thereafter, each sleep cycle was subdivided into 10 time intervals of equal length during non-REM and into 4 time intervals during REM sleep. Hemispheric asymmetries (i.e., laterality index, LI) were investigated by computing the log ratio of EEG spectra from homologous derivations of the left and right hemisphere (frontal: F3/F4, central: C3/C4, parietal; P3/P4, occipital: O1/O2). Then the difference between the ratio from the light conditions (left and right) and the no-light condition was calculated for each subject and light condition. Before computing means across subjects, spectral ratios were individually mean-adjusted. For the mean adjustment, the mean value was calculated for each subject across the frequency range of 0.75–25 Hz from the all-night spectrum of non-REM sleep.

Statistics. The statistical packages SAS (ver. 6.12; SAS Institute, Cary, NC) and Statistica (ver. 6.1; StatSoft, Tulsa, OK) were used. ANOVA for repeated measures (rANOVA) with the factors "condition" (light left, light right, no-light), "hemisphere" (left, right), "antero-posterior gradient" (frontal, central, parietal, occipital) and

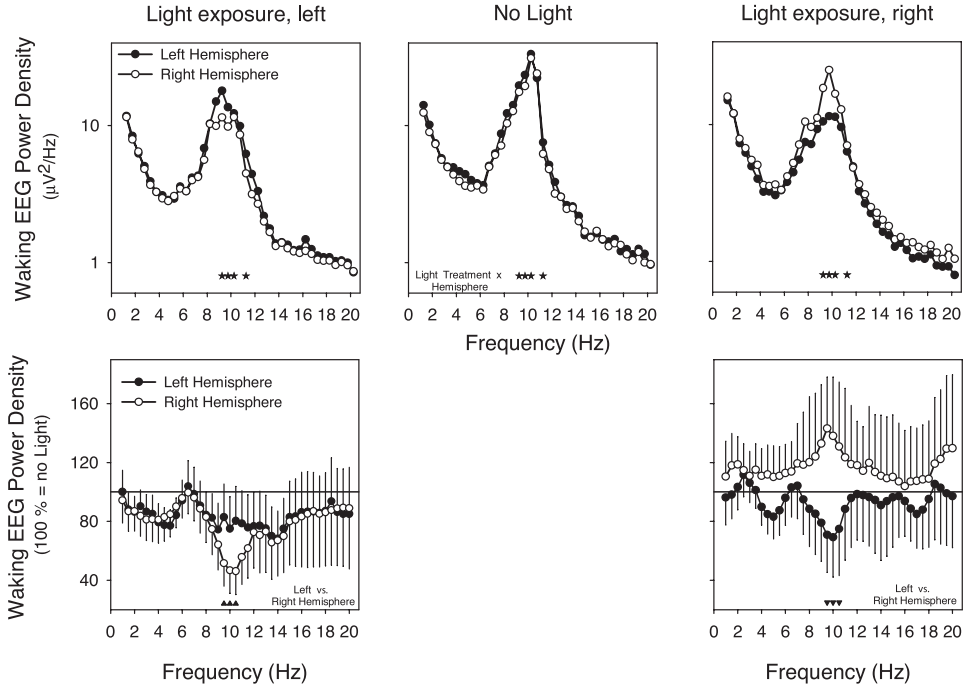

Fig. 2. *Top*: absolute waking EEG power density between 1 and 20 Hz (per 0.5-Hz bin) during light exposure from the left-hand side, dim light control (no-light), and light exposure from the right-hand side for the left and right hemispheres in the occipital derivations (O1 and O2). Asterisks near the abscissa indicate frequency bins for which the interaction "light treatment" (left vs. right) and "hemisphere" (left vs. right) yielded significance (for statistics, see text). *Bottom*: relative waking EEG power density in the range of 1–20 Hz (100% = no-light condition) for the left and right occipital hemisphere after left and right light exposure. Triangles near the abscissa indicate frequency bins for which the factor "hemisphere" (left vs. right) was significant (for statistics, see text). Values are expressed as means ± SE; $n = 7$.

Table 1. *Visually scored sleep stages (percentages of total sleep time), sleep onset latency, REM sleep onset latency, and total sleep time in minutes*

Sleep Parameter	Light, Left		No-Light		Light, Right		
Total sleep time	424.4	10.1	421.4	12.6	423.4	6.7	n.s
Sleep efficiency	90.0	2.2	90.7	2.2	91.6	0.7	n.s
Sleep onset latency	12.8	4.1	17.1	6.4	16.3	4.1	n.s
REM sleep onset latency	89.8	4.1	96.5	10.3	103.8	13.0	n.s
Waking after sleep onset	5.3	2.8	2.2	1.4	1.5	1.5	n.s
Stage one	9.4	1.5	11.9	2.5	11.8	2.4	n.s
Stage two	57.6	2.5	56.8	3.1	55.1	2.4	n.s
Stage three	7.1	2.1	6.6	1.6	7.8	1.9	n.s
Stage four	1.6	0.8	0.8	0.4	1.8	0.9	n.s
Slow-wave sleep	8.7	2.8	7.4	1.9	9.7	2.5	n.s
REM sleep	24.2	2.5	24.0	3.2	23.4	3.1	n.s

Values are expressed as means ± SE; $n = 8$. REM, rapid eye movement; n.s., nonsignificant.

"cycle" (sleep cycle 1, 2, 3) were used on either log-transformed absolute values, on log ratios or on LIs. All P values from rANOVAs were based on Huynh-Feldt's corrected degrees of freedom, but the original degrees of freedom are reported. If not otherwise stated, the Duncan's multiple-range test was used to locate significant post hoc differences. Effect size was calculated to define the size of significant effects [0.3, small; 0.5, medium; 0.8, large; according to Cohen (10)].

RESULTS

Subjective sleepiness and EEG power density during wakefulness. Evening light exposure to both the left and right hemivisual field elicited a significant alerting response (significant interaction "light condition" × "time": $F_{4,28} = 3.0$; $P < 0.05$, on prelight exposure adjusted sleepiness values). Significant lower subjective sleepiness ratings were found after both light exposure conditions than during the dim light condition (two post hoc tests, $P < 0.006$, for both light treatments, effect size = 0.38 for right light and 0.42 for left light). The left-side light showed a stronger alerting response during the second hour of light exposure than the right-side light (left vs. right light $P < 0.02$, effect size = 0.47).

Unilateral light exposure induced a significant reduction of EEG alpha activity in the occipital EEG leads (O1 and O2) of the respective activated brain hemisphere. A two-way rANOVA with the factors light condition and hemisphere yielded significant interactions between these factors in the frequency bins between 9 and 10.5 Hz and between 11.0 and 11.5 Hz (Fig. 2, *top*, $F_{2,12}$ at least 4.6; P at least 0.03, on log-transformed absolute values). Post hoc comparisons for

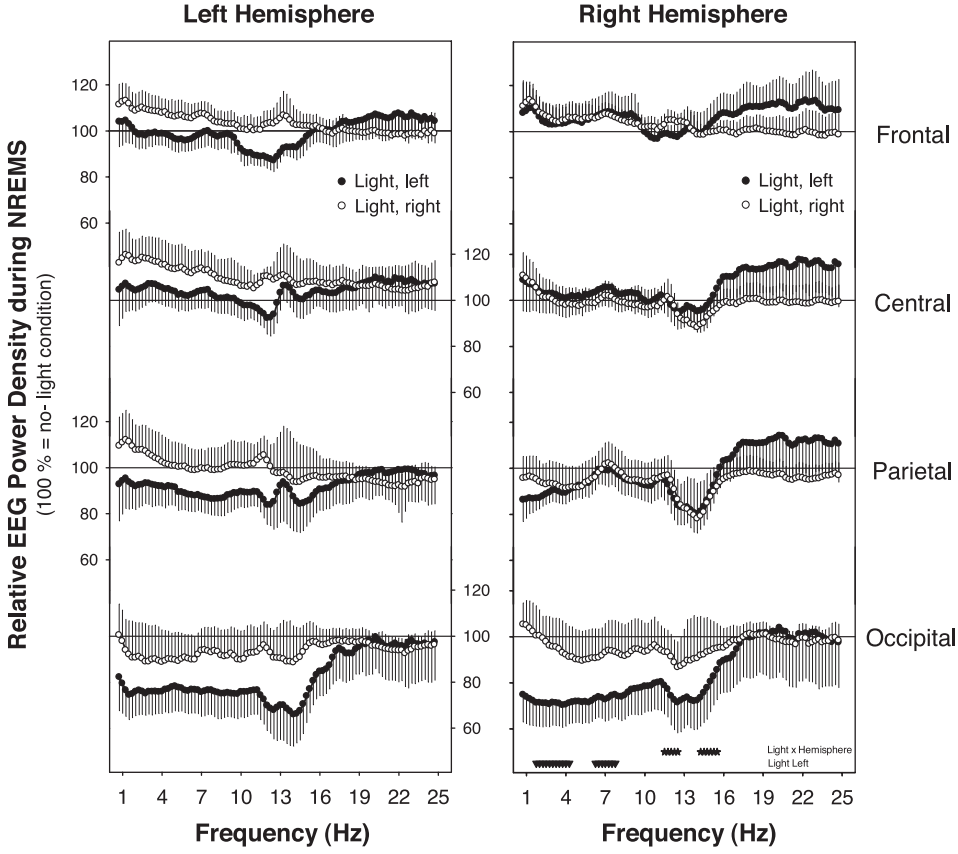

Fig. 3. All-night relative EEG power spectra (0.75–25 Hz, per 0.25-Hz bin) during non-REM sleep in the left and right hemisphere along the antero-posterior axis after light coming from the left- and right-hand side (values are expressed as percentages of the no-light condition). Asterisks near the abscissa delineate frequency bins for which the interaction "light condition" and "hemisphere" yielded significance [repeated-measures ANOVA (rANOVA) with the factors light condition, hemisphere, and antero-posterior gradient for more statistics, see text]. Significant post hoc comparisons between the light and the no-light condition are indicated with triangles. Post hoc tests were performed for the frequency bins for which the rANOVA (for each hemisphere separately) revealed significant interactions between light condition × antero-posterior gradient (for more statistics, see text). Values are expressed as means ± SE; $n = 8$.

these frequency ranges yielded significant reductions in left hemispheric EEG power density in the range of 9–10.5 Hz after the right-side light exposure compared with right hemispheric EEG power density in this range (Fig. 2, *bottom*, post hoc comparisons on relative EEG power density, 100% = no light condition, 3 tests, $P < 0.05$, effect size at least 0.65). On the other hand, right hemispheric EEG power density in the range of 9–10.5 Hz bin after left-side light exposure was significantly reduced compared with left hemispheric EEG power density in this range (Fig. 2, *bottom*, post hoc comparisons on relative EEG power density, 100% = no light condition, 3 tests, $P < 0.05$, effect size at least 0.66). Waking EEG power density derived from other EEG derivations than from occipital brain sites did not reveal any significant changes (data not shown).

Visual sleep scoring. We did not find any significant changes in any of the visually assessed sleep parameters between the three light conditions (Table 1; one-way rANOVA with the factor light condition highest $F_{2,14} = 1.4$; all P values >0.2).

All-night relative EEG spectra during non-REM sleep. Relative EEG power density (1–25 Hz) expressed as a percentage of the no-light condition is illustrated in Fig. 3 for the left and right brain hemisphere separately along the antero-posterior axis after left- and right-side light exposure. A three-way rANOVA with the factors light condition, hemisphere, and antero-posterior gradient revealed significant interactions between light condition and hemisphere for bins in the following frequency ranges: 11.5–12.75 Hz and 14.25–15.75 Hz ($F_{1,7}$ at least 3.4; $P < 0.05$, on relative values). There was no significant main effect of light condition or interactions between light condition and the antero-posterior gradient (on relative values, data not shown). Computing a two-way rANOVA for each hemifield light condition (left and right) separately, however, yielded a significant effect of light condition (light coming from the left side) and antero-posterior gradient in the following frequency bins in range of 0.75–4.5 Hz, 6.25–9.25 Hz, 12.25–12.5 Hz, and 14.5–15.75 Hz ($F_{3,21}$ at least 3.8, $P < 0.05$). Post hoc comparisons revealed a significant decrease in occipital EEG power density in the range of 1.75–4.5 and 6.25–8 Hz in the right hemisphere after left-side light activating the right hemisphere (Fig. 3, *bottom*, *right*, 18 tests, effect size at least 0.63). For the light coming from the right-hand side, no significant changes were observed.

Laterality index of EEG power density during non-REM sleep. Statistics on the relative laterality index of EEG power density in the frequency bins between 0.75 and 25 Hz yielded a significant interaction between light condition and the antero-posterior gradient in the spindle frequency range between 12.25 and 15.25 Hz (Fig. 4; rANOVA, $F_{6,42}$ at least 3.7, $P < 0.03$). Thus, the laterality index in this spindle range (12.25–15.25 Hz) was collapsed for further analyses. A two-way rANOVA revealed a significant effect for the antero-posterior gradient ($F_{3,24} = 3.9$, $P < 0.04$) and a significant interaction between light condition and the antero-posterior gradient (Fig. 5; $F_{3,24} = 6.8$; $P < 0.004$) for the laterality index of spindle EEG activity during non-REM sleep (Fig. 5). Light coming from the right-hand side shifted the index to the left occipital hemisphere, while light coming from the left-hand side and thus activating the right occipital hemisphere shifted the index to the right side compared with the no-light condition (Fig. 5, four post hoc tests $P < 0.001$, effect size = 0.64 for the occipital derivation).

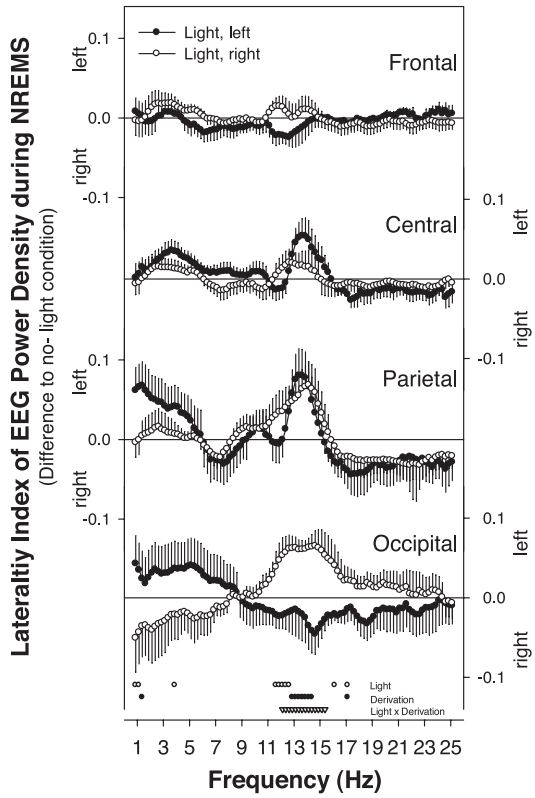

Fig. 4. Laterality index of EEG power density (0.75–25 Hz) during non-REM sleep along the antero-posterior axis after light from the left and right hand side (for the calculation of the laterality index, see MATERIALS AND METHODS section). Symbols near the abscissa delineate frequency bins for which the factor "light treatment" (left vs. right), "derivation" (frontal, central, parietal, occipital), and the interaction of these two factors yielded significance. Values are expressed as means ± SE; $n = 8$.

Time course of the spindle laterality index. The time course of the relative laterality index of EEG spindle activity across sleep cycles is illustrated in Fig. 6. A two-way rANOVA (light condition × sleep cycle) performed for each derivation separately yielded significance in the occipital derivations ($F_{2,14} = 4.3$; $P < 0.03$). Other main factors or interactions did not yield significance in either the frontal, central, parietal, and occipital derivation. A significantly more left-oriented spindle laterality index after light activating the left hemisphere compared with light activating the right hemisphere during the first two sleep cycles was observed in the occipital EEG derivations (3 post hoc tests, $P < 0.01$, effect size at least 0.43 for the first two sleep cycles).

DISCUSSION

We provide evidence that unilateral photic stimulation of the visual system prior to nocturnal sleep leads to shifts in hemispheric EEG asymmetries in the poststimulation sleep episode. These shifts are found in the sleep spindle range in brain areas comprising the primary visual cortex. Ipsilateral to the hemisphere stimulated by light, spindle activity during non-REM sleep increased compared with the contralateral side and the no-light condition. Since visual stimulation elicits an increase in metabolism in the visual cortex that is reflected in a greater

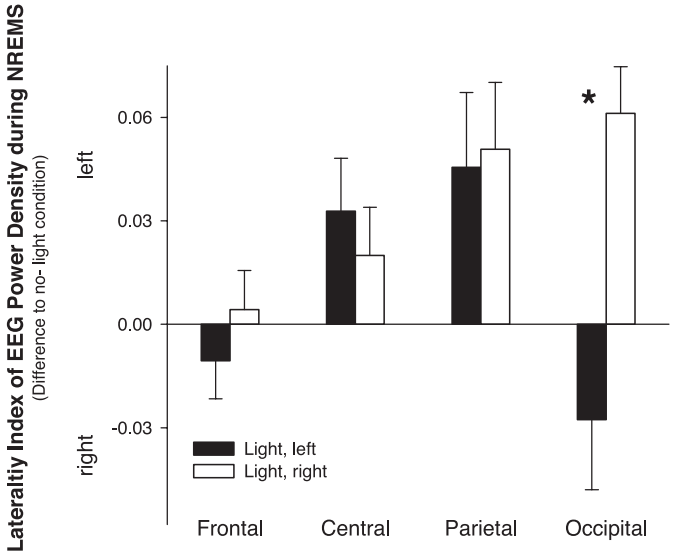

Fig. 5. Laterality index of spindle EEG activity in the range of 12.25–15.25 Hz along the antero-posterior axis after light coming from the left- and right-hand side. The asterisk indicates a significant difference between left- and right-hand side light in the occipital derivations (O1 and O2). Values are expressed as means ± SE; $n = 8$.

proportional increase in regional cerebral blood flow compared with oxygen consumption (15), it is possible that the observed light effects on the sleep EEG represent a correlate of a persistent increase of regional cerebral blood flow or, alternatively, a physiological change that had been induced by the neural activity during photic stimulation prior to sleep.

Our aim was to show that unilateral light exposure stimulating either the right or left primary visual cortex evokes an alerting effect concomitant with an attenuation of waking EEG alpha activity and with a decrease in EEG delta activity during subsequent sleep in the ipsilateral occipital hemisphere. Waking EEG alpha activity was indeed reduced in the ipsilaterally activated occipital hemisphere contralateral to the direction of the light source. We consider this as a proof of principle that we were able to successfully stimulate the respective hemivisual field in our subjects with our experimental setup, both with light coming from the left- and right-hand side. This effect is somewhat reminiscent of the observation by Rattenborg et al. (30) who showed reductions of EEG delta activity in ducks (where the optic chiasm is almost completely crossed) when they slept with one eye open in the hemisphere contralateral to the opened eye (30).

Although both light stimuli attenuated the evening increase in subjective sleepiness as rated on the KSS, this alerting response was more pronounced after left-side light stimulating the right visual cortex. Also during subsequent sleep, only light stimulating the right occipital hemisphere led to a significant reduction in EEG delta and theta activity in the right occipital hemisphere. It could be that there is a dominating hemisphere for the integration of visual information arriving via either the left or right hemivisual field. At least for the metabolic activation of somatosensory information, such predominance has been observed. Metabolic activation of the contralateral somatosensory cortex in response to an active sensorimotor task was larger after right-hand stimulation than after left-hand stimulation in right-handed subjects (43). This could also explain why Kattler et al. (24) did not observe any sleep EEG changes after somatosensory stimulation of the left hand (24). Another explanation could arise from lesion studies in stroke patients that revealed an important role of the right hemisphere for intrinsic alertness; several studies (see Ref. 38, and references therein) have reported a dramatic increase in simple visual and auditory reaction time after right hemispheric lesions.

Arguments against use-dependent recovery during sleep. Contrary to the prediction that a higher metabolic activity during wakefulness leads to an increase in EEG delta activity during subsequent sleep, we found that evening bright light exposure elicits a "decrease" in EEG delta activity, which is consistent with several other studies (4–6, 12). If sleep is regarded not only as a global but also as a local brain phenomenon, the amount of delta activity in a given brain region during sleep depends on how much it was "used" while awake (i.e., delta increases in those brain regions that were more strongly activated during prior wakefulness). Thus the concept of use dependency does not appear appropriate for visual stimulation by bright light. The reduction in EEG delta activity in occipital brain regions rather reflects a reduced hyperpolarization, suggesting a diminished cortical deactivation in the visually stimulated occipital brain regions. Interestingly, this effect seems to be hemispheric dependent such that left side light activating the right hemisphere was most efficient in EEG

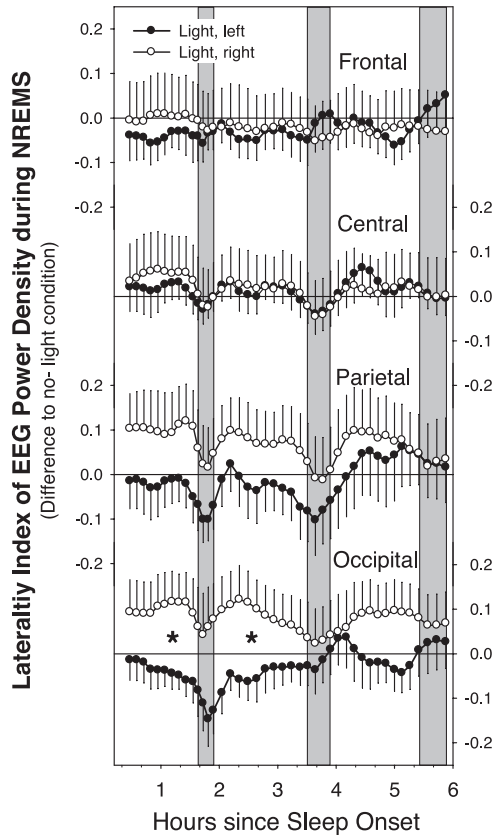

Fig. 6. Dynamics of the spindle laterality index per NREM-REM sleep cycles 1–3 after sleep onset along the antero-posterior axis for light coming from the left and right hand side. Values are plotted against relative clock time. Values are expressed as means ± SE; $n = 8$. Asterisks indicate sleep cycles for which a significant difference between the left vs. right light treatment was observed.

delta attenuation during sleep and in its alerting response prior to sleep. This is consistent with the results of Heilman and Van Den Abell (21) who have shown a right-hemisphere dominance in arousal to lateralized visual stimuli during wakefulness. If one follows the hypothesis of Tucker and Williamson (40), who argued that the right hemisphere became organized around a noradrenergic arousal system that maintains alertness, one could speculate that the right hemisphere is especially prone to the alerting action of light. Thus, our results rather reflect a hemispheric asymmetry in the alerting action of light than a use-dependent recovery function of sleep in response to the visual stimulation during prior waking.

Arguments for use-dependent recovery during sleep. We obtained evidence that unilateral photic stimulation leads to local increases in sleep spindle activity in the previously stimulated occipital hemisphere. The discrimination of whether this increase was caused by a change in the amplitude or the number of sleep spindles or a combination of them is not possible based on spectral EEG data. From our previous analyses, based on a spindle detection algorithm, however, we know that increases in sleep spindle power density are rather related to increases in spindle density than increases in its amplitude, particularly in parietal brain regions (26). If not only synchronized EEG activity in the delta but also in the spindle range is considered to be dependent on the nature of prior wakefulness, one could interpret our finding as an argument in favor of a use dependency. At the cellular level, spindles are associated with substantial neuronal activity. Spindles arise from cyclic inhibition of thalamo-cortical neurons by reticular thalamic neurons, and postinhibitory rebound spike bursts in thalamo-cortical cells entrain cortical populations in spindle oscillations (37). Hemodynamic cerebral correlates of human sleep spindles are associated with an activation pattern in the left and right thalamus, the anterior cingulate cortex, the left anterior insula, and, bilaterally, the superior temporal gyrus (33). On the level of the EEG, a naturally occurring left-hemispheric dominance in spindle activity in parieto-occipital brain regions has been found (32). Whether this is related to left but not right insula activation during sleep spindles (33) remains to be elucidated. The left insula is known to be involved in the cortical organization of speech processing (for a review, see Ref. 22), and its activation has been suggested as a marker for language attainment in bilinguals (8). Furthermore, brain responses to a complex cognitive task are modulated by light exposure in structures typically involved in executive functions, mostly located in the left hemisphere, in keeping with the left lateralization of verbal working memory (41). Because speech processing and several aspects of verbal working memory are major tasks in everyday life, brain regions involved in such tasks probably need intense recovery during sleep, which could explain the naturally occurring left dominance in human sleep spindle activity. If so, unilateral overstimulation of the left hemisphere by light exaggerated the left spindle dominance while overstimulation of the right hemisphere by light significantly reduced it (Fig. 5).

Local increases in spindle activity and spindle density have also been found after hippocampal dependent declarative tasks (9, 17, 34, 35) and after procedural motor learning tasks (27) prior to sleep. Interestingly, significant correlations between spindle activity in the left hemisphere and postsleep performance were reported for the declarative word learning tasks (9, 35), while the correlation between sleep spindle activity and postsleep motor performance was not hemispheric dependent (27). This suggests that sleep spindles are not only involved in use-dependent aspects of sleep regulation but in the consolidation of recently acquired memories in humans.

Taken together, we have further evidence that the alerting action of evening light exposure continues into the sleep episode and that it is more pronounced after stimulation of the right hemisphere. Because light led to a decrease in EEG delta activity and therefore "masked" the originally proposed use-dependent increase in EEG delta activity, the use-dependent aspect may have manifested itself in the spindle frequency range. Thus, the observed shift in the spindle hemispheric dominance in the occipital cortex (O1 and O2) may represent subtle local use-dependent recovery functions during sleep.

Perspectives and Significance

Challenging hemispheric sleep asymmetries via unilateral photic stimulation prior to sleep elicits reductions in delta EEG activity and interhemispheric EEG differences in the sleep spindle frequency range. This suggests that the human brain is capable of responding to prior light history during later sleep. Because both light and sleep are important modulators of subjective sleepiness and mood levels, our results further suggest the possibility that careful attention of prior light history is considered necessary when treating sleepiness/mood disturbances that are related to sleep problems.

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