
REVIEW ARTICLE

Electroencephalographic activity during wakefulness, rapid eye movement and non-rapid eye movement sleep in humans: Comparison of their circadian and homeostatic modulation

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Abstract

Electroencephalographic (EEG) activity is a key indicator of a vigilance state, and quantitative analyses of the EEG have revealed profound differences both between and within vigilance states in humans. We summarize recent studies that investigated how the spectral composition of the EEG during the three vigilance states, that is, wakefulness, rapid eye movement (REM) and non-REM sleep, is modulated by a circadian oscillator, which is independent of sleep–wake behavior, and by the sleep–wake oscillation itself, that is, elapsed time awake and elapsed time asleep. The data collected in sleep deprivation experiments and in protocols in which the sleep–wake cycle was desynchronized from endogenous circadian rhythmicity show that both factors contribute to this variation in a frequency- and state-specific manner. Low frequency EEG activity, including slow waves and theta frequencies, during both wakefulness and non-REM sleep, gradually increases with elapsed time awake and progressively declines with elapsed time asleep. The EEG activity in this 0.75–8 Hz frequency range is not markedly affected by circadian phase. In contrast, alpha activity (8–12 Hz) during wakefulness and REM sleep, as well as sleep spindle activity (12–15 Hz) during non-REM sleep, show a robust circadian regulation. Circadian and sleep–wake dependent regulation of EEG activity within the vigilance states also exhibits topographical variation such that frontal brain areas are more susceptible to the effects of the sleep homeostat than more parietal brain regions. It will be challenging to identify the functional correlates of these different spectral EEG patterns and relate them to neurobehavioral performance and recovery functions of sleep.

Key words: forced desynchrony protocol, frontal low electroencephalogram activity, homeostasis, plasma melatonin, spectral analysis, spindle activity.

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INTRODUCTION

Since the discovery of electrical brain wave activity by Berger in 1929,¹ the electroencephalogram (EEG) has become one of the most important electrophysiological measures in human clinical and basic research. Key

advantages of the EEG are its high temporal resolution, low cost, and ease of implementation. These advantages make the EEG an attractive monitoring tool, even though imaging techniques such as Positron Emission Tomography (PET) and functional Magnetic Resonance Imaging (fMRI) have a better spatial resolution. In this review, a summary of the studies that aimed at quantifying long-term temporal changes of the EEG within the three main vigilance states: wakefulness, rapid eye movement (REM) sleep and non-REM sleep are presented.

The EEG reflects electrical activity of a multitude of neural populations in the brain. This signal is complex because the EEG emerges from a superposition of different simultaneously acting dynamical systems. The oscillatory activity of neuronal pools, reflected in characteristic EEG rhythms, constitutes a mechanism by which the brain can regulate state changes in selected neuronal networks that lead to a qualitative transition between modes of information processing.² The complex character of EEG and its significance in brain research and clinical practice brought the early introduction of signal analysis methods to EEG studies. Quantitative methods of EEG processing in the frequency domain can be traced back to the first attempt of Fourier analysis application to the EEG in 1932.³ The Fast Fourier transform (FFT) was applied to the EEG soon after its introduction, and spectral analysis remains the most widespread signal processing method in this field. The Fourier transform, in essence, decomposes or separates a waveform (e.g. EEG waves) into sinusoids of different frequency and phase, which sum to the original waveform. It identifies or distinguishes the different frequency sinusoids and their respective amplitudes. In this review, EEG changes in a frequency range between 0.5 and 25 Hz, which comprises frequencies of the classical EEG bands, that is, delta, theta, alpha and beta band, are reported.

Two facets of 'time' are emphasized: the effect of 'internal biological time' and 'time spent within a vigilance state', which play an important role in the modulation of human EEG power spectra. 'Internal time' is driven by the endogenous circadian pacemaker (circadian clock-like process), which requires daily synchronization with 'external time.' The other dimension, 'elapsed time', spent into one of three vigilance states, reflects a homeostatic hourglass process, which is continuously depleted or replenished, depending on the vigilance state. A summary of the importance of circadian and homeostatic aspects as an integral part of the regulation of brainwave activity within the three vigi-

lance states: wakefulness, REM sleep and non-REM sleep, is presented.

EFFECTS OF SLEEP DEPRIVATION ON THE EEG DURING WAKEFULNESS, REM SLEEP AND NON-REM SLEEP

The concept of sleep homeostasis implies that compensation for loss of sleep is achieved either by variations in the duration of sleep or by variations in the intensity of sleep.⁴ Homeostatic mechanisms augment sleep propensity when sleep is curtailed or absent, and they reduce sleep propensity in response to an excess of sleep.

Sleep deprivation protocols are classical tools used to activate homeostatic sleep regulatory mechanisms. Increasing sleep pressure leads to an enhancement of low-frequency EEG activity in the range of 0.75–8 Hz during non-REM sleep and also during REM sleep episodes.^{5–8} A nap study demonstrated that these low EEG components increase when wakefulness preceding sleep is varied from 2 to 20 h in a dose-dependent manner.⁹ In the course of the sleep deprivation episode itself, low-frequency components in the EEG during wakefulness progressively increase.^{10–14} This increase can be significantly attenuated by short intermittent nap episodes (Fig. 1).¹⁵ During both sleep and wakefulness, the homeostatic increase in low-EEG components is most prominent in frontal brain areas (Fig. 2).^{8,14} Activity in the sleep spindle range (12–15 Hz) also changes with increasing sleep pressure during non-REM sleep, such that high spindle frequency activity (>13.5 Hz) decreases and low spindle activity (<13.5 Hz) increases.^{7,16} Taken together, the application of quantitative EEG analyses in sleep-deprivation protocols has revealed that low EEG components during wakefulness, REM sleep and non-REM sleep, as well as sleep-spindle activity during non-REM sleep, respond to variations in the duration of prior wakefulness and sleep, and are thus correlates of the homeostatic sleep regulatory process. Whether the changes in the EEG during wakefulness solely depends on the duration of wakefulness or also the quality of wakefulness is not yet clear. There are indications, at least in the animal literature, that stressful events such as social conflict during waking can alter the homeostatic process and speed up the accumulation of sleep pressure.¹⁷ However, a recent study in humans failed to support the proposition that low EEG components reflect a need for sleep that accumulates at a rate depending on mental activity during prior

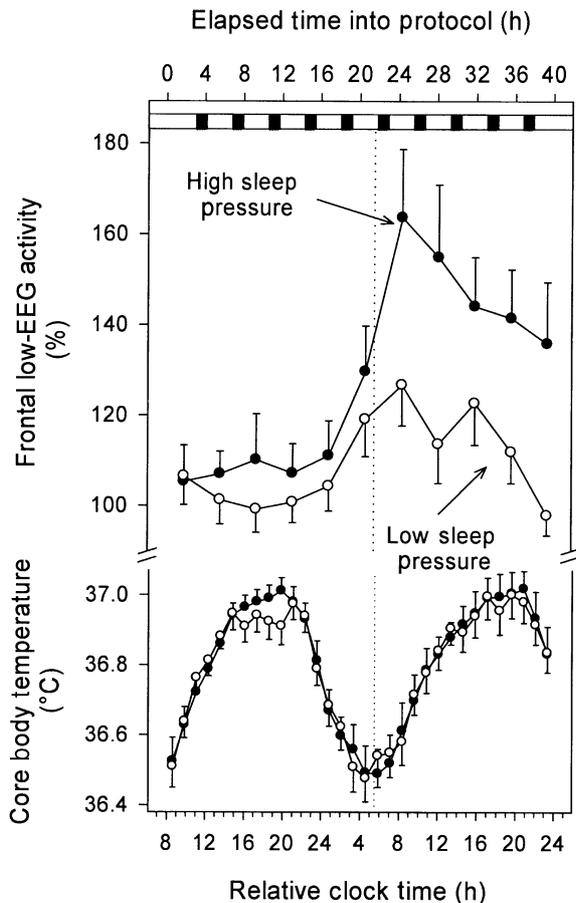


Figure 1 Dynamics of frontal low electroencephalogram (EEG) activity (EEG power density in the 1–7 Hz band) and core body temperature during wakefulness across a 40-h sleep deprivation (high sleep pressure) and Nap protocol (low sleep pressure). The upper two panels indicate the timing of the naps (■) and scheduled episodes of wakefulness (□), respectively, for the sleep deprivation and Nap protocol. Data were collapsed into 3.75-h time intervals for the EEG and into 1.25-h time intervals for core body temperature (mean values, ± 1 SEM, $n = 10$). Data are plotted against the midpoint of the time intervals. Relative clock time represents the average clock time at which the time intervals occurred. Note that the increase in low frequency EEG activity during wakefulness is markedly attenuated in the presence of naps. Adapted with permission.¹⁵

wakefulness.¹⁸ The decay rate of the homeostatic process during sleep is considered to depend on the sleep stage such that it is more rapid during slow-wave sleep than during REM sleep.⁴ Most of the aforementioned studies did not allow separation and quantification of the influence of the circadian and homeostatic process, because in the acute sleep deprivation experiments, not

all combinations of circadian phase and elapsed-time-awake were achieved.

CIRCADIAN AND HOMEOSTATIC PROCESS AND THEIR INTERACTION

Early studies indicated that sleep homeostasis, the sleep-wake dependent regulation of sleep, cannot solely account for changes in sleep propensity. Early reports suggested that total sleep loss is only compensated by a $\sim 20\%$ increase in sleep duration during the following recovery night in humans (Patrick and Gilbert, 1896 in¹⁹). This led to the assumption that, besides the homeostatic process, at least one other process must be involved in the regulation of sleep duration. In fact, it was realized that such variations in sleep duration occur in a consistent and predictable manner that depend on when subjects go to sleep (i.e. time of day^{20–22}). The role of ‘time of day’, referred to as the circadian process *C*, and the homeostatic process *S*, have been conceptualized in the two process model of sleep regulation in order to predict sleep propensity in humans.^{23,24} According to this model, the timing of sleep and wakefulness is determined by the interaction of the circadian process *C*, generated by an endogenous circadian clock, and the homeostatic process *S*.

Brain structures and/or neurochemical processes, governing the homeostatic process *S*, have not been conclusively identified. In contrast, circadian rhythms are thought to be generated and driven by a specific brain structure, the master circadian pacemaker, located in the suprachiasmatic nuclei (SCN) of the anterior hypothalamus (for a review see²⁵). Recent progress in molecular biology has unraveled canonical clockwork genes and how these genes encode circadian time such that clock outputs are converted into temporal programs for the whole organism (for a review see^{26,27}). On a behavioral level, clock outputs can be assessed by measuring rhythms such as the circadian rhythm of core body temperature, plasma melatonin, or cortisol concentration, etc. These variables, when assessed under appropriate conditions in which the confounding evoked effects of variations in behavior and the environment are controlled for, represent markers of circadian phase, period and amplitude; all parameters of ‘internal time’. The classical marker of the homeostatic process *S*, is slow-wave or delta activity (SWA) during non-REM sleep.^{6,23,28} In fact, all model simulations of the two process model of sleep regulation were initially based on SWA during non-REM sleep in humans and animals.^{29,30}

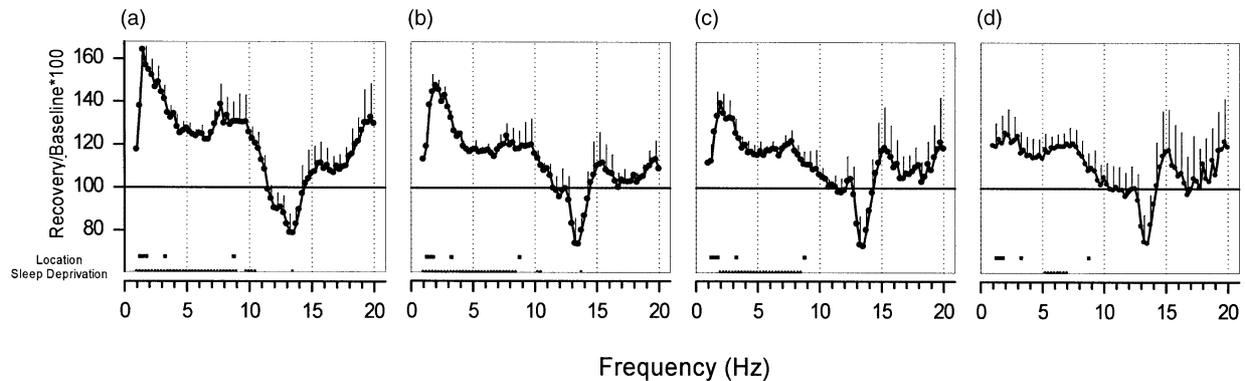


Figure 2 Effects of sleep deprivation on the power spectrum in non-rapid eye movement (REM) sleep (stages 2, 3, and 4). Data were averaged over the first 7.5 h of recovery sleep and were expressed as a percentage (mean values, ± 1 SEM, $n=6$) of the corresponding value in baseline sleep. Horizontal symbols indicate frequency bins for which the value in recovery sleep was significantly different from the baseline value (paired t -test on log transformed values $P < 0.05$). Note the frontal predominance of the relative increase of low frequency components in non-REM sleep. (a) Frontal, (b) central, (c) parietal, (d) occipital. Adapted with permission.⁸

How the circadian and the homeostatic process interact has not been firmly established. It is not clear at which level, that is, where in the central nervous system this interaction occurs and whether the central circadian oscillator in the SCN directly or indirectly interacts with brain centers responsible for sleep homeostatic processes. Studies in SCN-lesioned animals have shown that the homeostatic process is still operative and not altered substantially in these animals.^{31,32} This indicates that the two processes are, at least at this level of analysis, independent from each other. Another possibility is that C and S interact more downstream in the cascade or that the output variables we measure do not reflect a 'real' interaction, but are biased by our metrics (for a discussion see^{33,34}). To conclusively show how circadian and homeostatic processes interact with each other, and in order to quantify their strength in the control of sleep and wakefulness, protocols must be applied that allow for a separation of the two processes.

DESYNCHRONIZATION OF THE CIRCADIAN AND HOMEOSTATIC PROCESS

It has been recognized early on, that for a better understanding of the mechanisms underlying the timing of the sleep-wake cycle, a distinction should be made between internal and environmental factors that both contribute to variations in the propensity to initiate and terminate sleep. Nathaniel Kleitman was the first to conduct an experiment in which human beings were stud-

ied in the absence of periodic cues in the external environment.³⁵ He realized that in order to prove the existence of internal time or the existence of endogenous self-sustained rhythms, paradigms must be applied in which it is possible to desynchronize internal time from external time. In the Mammoth Cave, in Kentucky USA, in 1938, he scheduled subjects to live on artificial day-lengths, which deviated from 24 h. Under such conditions, near 24-h rhythms (circadian) were not able to entrain to the newly imposed day length, but they continued to oscillate with their endogenous period. It was possible to separate the influence of the timing of the sleep-wake schedule from that of the circadian pacemaker. This imposed desynchrony between the sleep-wake schedule and the output of the circadian pacemaker occurs only under conditions in which the non-24-h sleep-wake schedule is outside the range of entrainment or range of capture of the circadian system. This protocol has been termed the forced desynchrony protocol. In 1967, Aschoff convincingly demonstrated that the human sleep-wake cycle can also spontaneously desynchronize from the core body temperature cycle.³⁶ Aschoff's protocol has been termed the spontaneous internal desynchrony protocol. The period of core body temperature remains rather stable during spontaneous desynchronization. The sleep-wake cycle, however, is unstable and may vary within a subject, being close to the period of the temperature rhythm to close to twice the period of the core body temperature rhythm. One key observation in the spontaneous desynchrony protocol has been that sleep is rarely initiated on

the latter part of the rising portion of the core body temperature rhythm. This window has been called the wake maintenance zone.³⁷ To further quantify the interactions between the sleep–wake cycle and circadian processes in the regulation of sleep, EEG, neurobehavioral and physiological variables, forced desynchronization protocols have been implemented.³⁸ In these protocols, scheduled sleep and wake episodes occur at virtually all circadian phases, and when light intensities during scheduled waking episodes are kept low, the pacemaker freeruns with a stable period in the range of 23.9–24.5 h.³⁹ Furthermore, as subjects are scheduled to stay in bed in darkness, the variation in the amount of wakefulness preceding each sleep episode is minimized. It is thus possible to average data either over successive circadian cycles or over successive sleep or wake episodes and to thereby separate these two components. This averaging serves to isolate the circadian profile of the variable of interest by removing the contribution of the confounding sleep–wake dependent contribution or vice versa in the averaging process (i.e. subtracting background noise, which is not temporally related to the evoked component). The efficacy of the forced desynchrony protocol in removing or uniformly distributing several driving factors is demonstrated by the observation that the observed period of the pacemaker was nearly identical in forced desynchrony protocols with markedly different cycle lengths, for example: 11, 20, 28, or 42.85 h and with markedly different levels of physical activity.^{39–41}

Here we summarize previously published data from two forced desynchrony (FD) protocols with different sleep–wake schedules. Data on waking EEG spectra were gathered in a 42.85-h FD protocol (28.57 h wakefulness and 14.28 h sleep), whereas data on EEG spectra during sleep were collected in a 28-h FD protocol (18.67 h wakefulness and 09.34 h sleep).

STRENGTH OF THE CIRCADIAN AND HOMEOSTATIC INFLUENCE ON EEG POWER DENSITY DURING WAKEFULNESS, REM SLEEP AND NON-REM SLEEP

In the course of the forced desynchrony protocol in which the period of the sleep–wake cycle was either 28 or 42.85 h, the circadian rhythm of plasma melatonin oscillated with a period that was, in all subjects, close to 24 h and similar to the period of the circadian rhythm of core body temperature. Thus, a complete desynchro-

nization between the imposed sleep–wake schedule and the endogenous circadian system occurred. During scheduled waking and sleep episodes, the EEG was continuously measured. In order to gather artifact-free EEG samples during scheduled wakefulness, the subjects were asked, every 2 h, to sit down and fixate on a dot for a 5-min episode (KDT, Karolinska Drowsiness Test).⁴² The EEG epochs were visually scored for containing no signs of sleep and movement artifacts, and later subjected to spectral analysis. During scheduled sleep episodes, the entire data train was subjected to spectral analysis, and the resulting average power spectra per 30-s epoch were aligned with the corresponding sleep stage in that 30-s epoch.

Power spectra during wakefulness, REM sleep and non-REM exhibited the typical wake- and sleep stage-specific characteristics (Fig. 3): high alpha power during wakefulness, an EEG predominance at low frequencies and in the spindle range during non-REM sleep, and lower values in the same frequency ranges during REM sleep. The relative contribution of the circadian and homeostatic process to the variation in power spectra exhibited a frequency specific modulation. During wakefulness, REM sleep and non-REM sleep, low EEG components were predominantly modulated by the homeostatic factor. In addition, beta frequencies (>15 Hz) during wakefulness were also under strong homeostatic influence. The circadian modulation of the EEG differed between wakefulness, REM sleep and non-REM sleep such that for wakefulness, and to a lesser extent also for REM sleep alpha activity and for non-REM sleep spindle frequency activity, the greatest circadian variance was shown (Fig. 3).

SLEEP SPINDLE ACTIVITY AND THE PLASMA MELATONIN SECRETORY PHASE

Circadian changes in EEG power spectra during non-REM sleep are not directly associated with the circadian variation in the duration of these sleep stages. When sleep coincides with the circadian phase of melatonin secretion and when sleep is highly consolidated, the EEG in non-REM sleep is characterized by very moderate reductions in the frequency range of slow waves and theta activity, and in profound changes in the frequency range of sleep spindle activity.^{43,44} In particular, low frequency sleep spindle activity (12.25–13 Hz) exhibits a prominent circadian modulation, such that during the circadian phase of melatonin secretion, low frequency

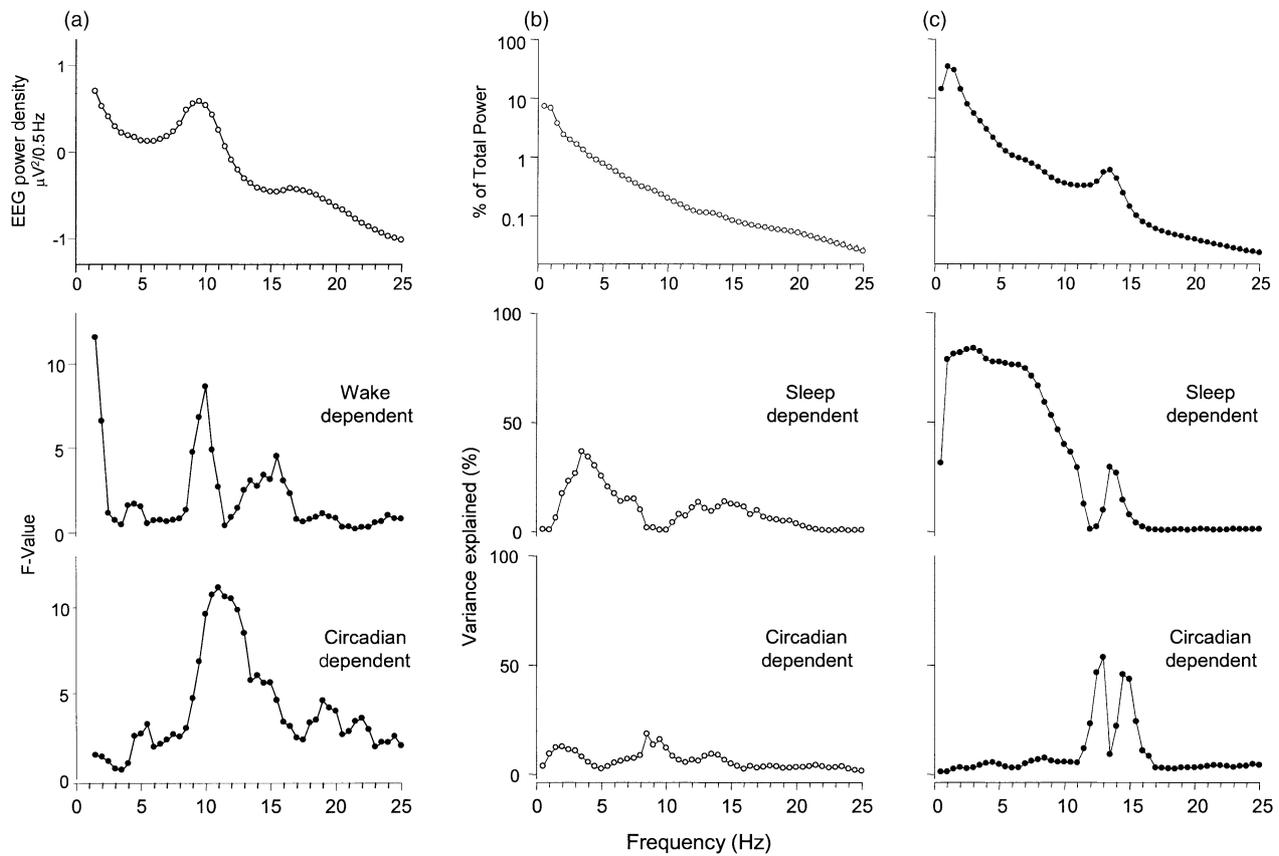


Figure 3 (a) Effect of circadian phase and time elapsed since the start of the wake episode on electroencephalogram (EEG) power density spectra in the range of 1–25 Hz. The EEG data were acquired while subjects were awake with their eyes open and staring at a dot during the Karolinska Drowsiness Test. (i) Grand average of log transformed EEG power spectra and its standard deviation are plotted at the upper limit of the 0.5-Hz bins. (ii, iii) F values resulting from a repeated measures ANOVA (rANOVA) with the factor circadian phase (circadian dependent) and elapsed time awake (wake dependent; mean values, $n=7$). (b,c) (i) Effect of circadian phase and time elapsed since the start of a sleep episode on EEG power spectra in rapid eye movement (REM) sleep (b) and non-REM sleep (c). Average EEG power spectra values are plotted at the upper limit of the 0.5-Hz bins. Data above 25 Hz are not shown (mean values, $n=7$). Note the logarithmic scale on the ordinate. (ii) Percentage of variance of power spectra in non-REM and REM sleep explained by the factor time elapsed since the start of the sleep episode. (iii) Percentage of variance of power spectra in non-REM and REM sleep explained by the factor circadian phase. (a) Wakefulness, (b) REM sleep, (c) non-REM sleep. Adapted with permission.⁴⁴

spindle activity is abundant (Fig. 4).⁴⁴ During this phase, EEG power density in the frequency range of 12.75–13.0 Hz is at 157.5% relative to the EEG power values collected outside the phase of melatonin secretion.⁴⁴ These results have been confirmed by analyses of the EEG with spindle detection algorithms, which demonstrate that characteristics of sleep spindles, such as their average frequency, amplitude, duration and incidence, all vary with circadian phase.⁴⁵ During the melatonin secretory phase, lower spindle frequencies were promoted: peak frequencies shifted towards the lower end of the spindle frequency range, and the spindle

amplitude was enhanced in the low-frequency range (up to ~14.25 Hz) and reduced in the high-frequency range (~14.5–16 Hz).⁴⁶ These data have been interpreted as evidence for either a circadian modulation of the frequency of sleep spindles or a circadian modulation of two types of sleep spindles. In addition, recent data indicate that the circadian modulation of sleep spindle characteristics varies with brain location.⁴⁶ The most marked difference in the extent of circadian modulation is between frontal and parietal spindle frequency activity. Frequency differences in frontal and parietal spindles during nocturnal sleep have been

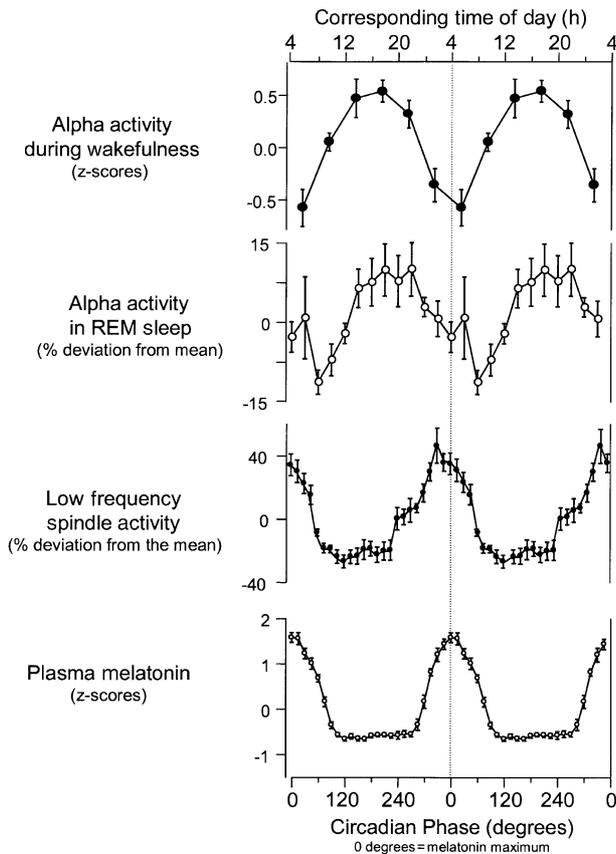


Figure 4 Phase relationships between the circadian rhythms of plasma melatonin and alpha electroencephalographic (EEG) activity during wakefulness and in rapid eye movement (REM) sleep, and low frequency sleep spindle activity during non-REM sleep (mean values, ± 1 SEM, $n=7$). Data are plotted against the circadian phase of the plasma melatonin rhythm (0° corresponds to the fitted maximum, bottom x-axis). To facilitate a comparison with the situation in which the circadian system is entrained to the 24 h day, the top x-axis indicates the average clock time of the circadian melatonin rhythm during the first day of the forced desynchronization protocol, that is, immediately upon release from entrainment. Plasma melatonin data and alpha activity during wakefulness were expressed as z-scores to correct for interindividual differences in mean values. Low-frequency sleep spindle activity in non-REM sleep and alpha-activity in REM sleep are expressed as a percentage deviation from the mean. Data are double plotted, that is, all data plotted left from the dashed vertical line are repeated to the right of this vertical line. Adapted with permission.^{44,68}

demonstrated before.^{47–52} Frontal spindles were found to have a lower frequency (approximately 12 Hz) than parietal spindles (approximately 14 Hz), and these findings were interpreted as an indication for the existence

of two separate types of sleep spindles. It is, however, still not clear whether frontally and parietally scalp-recorded sleep spindles originate from two functionally distinct thalamic sources, or whether it represents a topography-dependent frequency modulation of one single spindle type. In fact, sleep spindles arise from distant sites in the thalamus.⁵³ The spindle-generating network includes various reciprocal connections between the thalamus and the cortex. The prefrontal cortex (slow spindles) is connected mainly to the dorsomedial thalamic nucleus, whereas parietal parts of the cortex (fast spindles) are mainly connected with the lateroposterior and the pulvinar thalamic nucleus.⁵⁴ Therefore, the cortical distribution of sleep spindles may reflect activities of corresponding nuclei within the dorsal thalamus, controlled by the reticular thalamic nucleus,^{55,56} which is thought to play a key role in the regulation of thalamocortical transmission and to be the initial site in the sleep spindle generating network.⁵⁷ It remains to be elucidated whether such topographical differences are related to distinct functional roles of sleep spindles such as memory consolidation and/or sleep protection, because there is increasing evidence for an involvement of sleep spindles in synaptic plasticity and memory processes^{58,59} (for a review see⁶⁰).

ALERTNESS AND PERFORMANCE, AND THE EEG DURING WAKEFULNESS

Waking EEG data may provide us with electrophysiological correlates of circadian phase and elapsed-time-awake effects on performance. The circadian waveform of EEG alpha activity (Fig. 4) resembled the circadian modulation of subjective alertness and neurobehavioral performance measures described in other forced desynchrony protocols.⁶¹ The decrease in alpha activity across the waking day⁶⁸ also parallels the wake-dependent drop reported for alertness and cognitive performance.^{41,61} Therefore, high levels of EEG alpha activity during an eyes open condition may be indicative of high levels of alertness. The weak circadian modulation of slower oscillations in the waking EEG only partially parallels the circadian rhythm in alertness and performance. The progressive increase of low EEG activity in the 1–4.5 Hz range across the waking episode is somewhat reminiscent of the deterioration of performance with elapsed-time-awake, although details of their time-courses may differ. A detailed analysis of the association between EEG characteristics during wakefulness and performance at many combinations of circadian phases and elapsed-time-awake is needed to further under-

stand the functional consequences of these circadian- and wake duration-dependent variations in the waking EEG.^{10,62}

SPECTRAL EEG CHANGES DURING WAKEFULNESS: COMPARISON TO SLEEP

Low frequency components, that is, SWA and theta activity during non-REM sleep, are primarily dependent on elapsed-time since sleep onset. This is very similar to the wake-dependent modulation of low frequency components in the waking EEG in frontal derivations (Fig. 5). Furthermore, SWA during non-REM sleep can be reduced by a nap preceding the nocturnal sleep episode.⁶³ Similarly, the wake-dependent increase in frontal low EEG activity during wakefulness can also be significantly attenuated by short-nap episodes.¹⁵ Taken together, these data suggest that low frequency activity during both non-REM sleep and wakefulness depends to a large extent on 'how long we have been awake' and 'how long we have been asleep'. Delineation of the frequency ranges most responsive to elapsed-time-awake may vary between the type of study. During forced desynchrony protocols, waking EEG activity in the theta range did not show a prominent and robust homeostatic component for all circadian phases. This contrasts with the robust increase in theta activity observed in sleep deprivation studies that did not cover all combinations of circadian phase and elapsed-time-awake.^{10-13,64} From

the data collected at many different circadian phases, it appears that waking EEG activity in the 1–4.5 Hz band exhibits the most robust response to elapsed-time-awake. Some of the minor discrepancies in the magnitude of the response and the frequency range affected by time awake are likely to be caused by the use of bipolar versus referential EEG derivations. The increase of low-frequency EEG activity (1–4.5 Hz) during wakefulness with increasing elapsed-time-awake was nearly linear. A near-linear increase has been reported recently in humans¹⁴ and in mice.⁶⁵

Analyses of sleep EEG during a forced desynchrony protocol yielded a circadian modulation of the sleep EEG, which was limited to sleep spindle activity in non-REM sleep and alpha activity in REM sleep.^{43,44} Interestingly, the circadian rhythm of alpha activity during REM sleep^{43,44} resembled the circadian rhythm of alpha activity during wakefulness (Fig. 4). This underscores the similarities in EEG characteristic during REM sleep and the awake state, and suggests that the circadian pacemaker modulates the EEG during both states in a similar way.

CONCLUDING REMARKS

Spectral hallmarks of EEG activity during wakefulness and sleep show a frequency-specific homeostatic and circadian regulation. These two processes represent an integral part of the regulation of brain activation during wakefulness and sleep, which is likely to be related

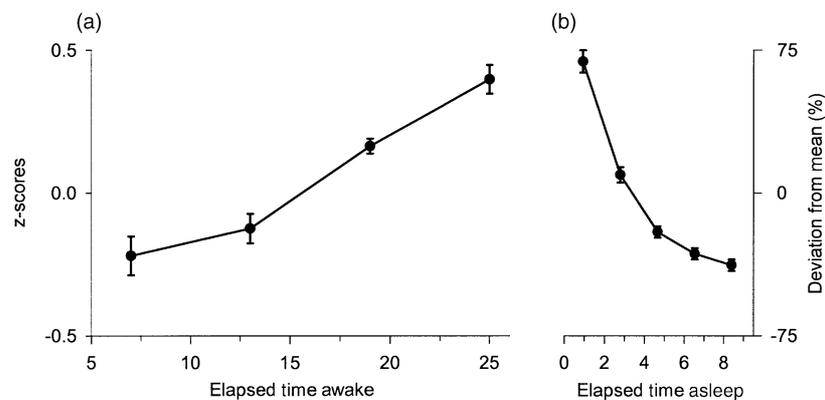


Figure 5 Wake- and sleep-dependent variation in power density in wakefulness (a) and non-rapid eye movement (REM) sleep (b, mean values, ± 1 SEM, $n=7$). For each band and each subject, the wake- and sleep-dependent effect was first calculated per 0.5 Hz and expressed as a percentage deviation from the mean (non-REM sleep) or z-scores (wakefulness). Next, these values were averaged over bins to form the bands shown, and then averaged over subjects. Data are plotted at the midpoints of the time intervals (360 min for wakefulness and 112 min for non-REM sleep). The electroencephalogram power density is in the 0.75–4.5 Hz range. Adapted with permission.^{44,68}

to the processing of external sensory stimuli and behavioral responses. It will be important to demonstrate the variations in responsiveness to external stimuli and the recovery functions of sleep are indeed related to these variations in the spectral composition of the EEG.^{66,67}

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