Subjective sleepiness correlates negatively with global alpha (8–12 Hz) and positively with central frontal theta (4–8 Hz) frequencies in the human resting awake electroencephalogram

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Abstract

Subjective sleepiness is part of the system controlling the decision to go to sleep in humans. Extended periods of waking lead to increased sleepiness, as well as to changes in cortical electroencephalogram (EEG) during waking. We investigated the association of sleepiness and awake EEG spectra during 40 h of wakefulness using multi-electrode EEG recordings for full coverage of the scalp. We found: (1) strong negative correlations of alpha (8–12 Hz) power with subjective sleepiness at all scalp locations, suggesting a negative association between sleepiness and general cortical activation; and (2) positive correlations of theta (4–8 Hz) power with subjective sleepiness with a focus on frontal locations, suggesting additional location specific associations between sleepiness and cortical activation. These findings support the notion that sleepiness is directly represented in the awake EEG.

Keywords: Spectral analysis; Electroencephalogram localization; Sleep deprivation

Prolonged wakefulness results in deeper sleep in humans [5, 10]. Feelings of sleepiness, however, do not simply increase with a prior awake duration. There is a pronounced influence of time of day dictated by the endogenous biological clock [2,11]. Additionally, sleepiness can also be influenced by environmental light [8] and by psychological factors [9,16].

The electroencephalogram (EEG) distinguishes between states of vigilance, i.e., wakefulness and sleep [17], and to some extent between the ‘levels’ of vigilance within a state. The EEG frequency spectrum is subdivided in delta (1–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (15–30 Hz) and gamma (30– > 40 Hz) frequency ranges. Within NREM sleep, delta power (slow wave power) indicates the intensity of sleep and represents the need for sleep [4]. During wakefulness, alpha and theta frequencies in the awake EEG are of particular interest for research on sleepiness. During active wakefulness (with eyes open), alpha power is usually low, unless the subject is severely fatigued [9,15,16]. However, in resting conditions (with eyes closed), alpha power is high also when the subject is fully rested. During the transition from resting conditions with eyes closed to sleeping, a gradual reduction of alpha power and a gradual increase in theta power occurs [20]. Reduced alpha power and increased theta power during resting awake periods with eyes closed may thus indicate a high motivation for sleeping. Indeed, it was found that subjective sleepiness during awake periods correlates negatively with alpha power and positively with theta power in the awake EEG [11] during prolonged wakefulness. However, in that study EEG was recorded at central locations, covering effects in the EEG of the somatosensory cortex only. It is unclear whether such an association is specific for central locations or applies to the cortex in general. The location of EEG changes may be crucial to understand the cortical systems involved in sleepiness.

The ten participating healthy young subjects (20–35 years, four males, six females) did not smoke or use drugs, and abstained from alcohol and coffee throughout the experiment. They did not rate as extreme morning or evening types [14]. Subjects signed an informed consent form. The experiment was approved by the Medical Ethics Committee of the University of Groningen.

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Subjects were awake for 40 h, from 8:00 h in the morning of day 1 to 24:00 h on the evening of day 2. At predetermined times between 8:30 h on day 1 to 23:30 h on day 2, subjects performed 21 test series, during which sleepiness was scored and awake EEG was recorded. Sleepiness was scored by means of the Karolinska sleepiness score (KSS), a 9-unit rating scale, ranging between 'very alert' and 'very sleepy, fighting sleep' [3]. During awake EEG recordings, subjects were sitting for 3 min in a chair with their eyes closed.

EEGs were recorded using a cap system with Ag/AgCl electrodes (Electro-Cap International, Inc., Eaton, Ohio, U.S.A.), on 28 positions on the scalp (10–20 system; Fp1, Fp2, F7, F3, Fz, F4, F8, FC5, FC1, FC2, FC6, T3, C3, Cz, C4, T4, CP5, CP1 CP2, CP6, T5, P3, Pz, P4, T6, O1, Oz, O2). The left earlobe was used as reference, and the inion was used as ground. Data were sampled at 100 Hz, and band pass filtered between 0.16–40 Hz. EEG was recalculated to average reference before fast Fourier transformation was applied to artifact-free 5 s intervals. EEG power was calculated per 0.2 Hz frequency bin. For some calculations, EEG power was averaged over the theta (4–8 Hz) and alpha (8–12 Hz) ranges.

For each subject, the data of the 21 recording sessions were normalized to standard normal distributions (mean = 0, standard deviation = 1) to correct for inter-individual variation (z-transformation). Within subject Pearson correlations were combined to average correlation coefficients [13], of which the z-statistic was used for statistical evaluation.

Fig. 1A shows the pattern of normalized sleepiness (KSS; black line), theta power (red line) and alpha power (blue line) over 21 recordings during 40 h of wakefulness (z-values, mean ± SEM, n = 10). Theta and alpha power was averaged over all 28 recorded scalp locations. KSS shows a general increasing trend with a superimposed daily oscillation, consistent with earlier findings [1]. Alpha power shows a mirror image to the KSS pattern. The average individual correlation was calculated by averaging z-transformed individual correlation coefficients [13]. The average correlation coefficient of alpha power and KSS was −0.65 (z-statistic = −10.3, P < 0.00001). Theta power increased over the 40 h awake period, also in line with earlier findings [1]. The average correlation coefficient between theta power and KSS was 0.29 (z-statistic = 4.11, P = 0.00004).

Fig. 1B,C show the average correlation coefficients (n = 10) of the associations of theta power (Fig. 1B, red dots) and alpha power (Fig. 1C, blue dots) with KSS for all recorded scalp locations. Highly negative correlations with KSS were found for alpha power at all scalp locations. Highly positive correlations between KSS and theta power were found on the central, frontal and temporal locations.

The highest correlation coefficient was found on Fz, indicating prominent central frontal theta.

Fig. 1D depicts the z-statistic values of the average correlation (n = 10) of KSS and awake EEG power per 0.2 Hz frequency bin as a function of the anterior to posterior location on the scalp. Average EEG power of the EEG derivations closest to the midline (derivations used: Fp1, Fp2; F3, Fz, F4; FC1, FC2; C3, Cz, C4; CP1, CP2; P3, Pz, P4; O1, Oz, O2). Dotted line: P = 0.05, solid line: P = 0.0003 (Bonferroni correction)
Pz, P4; occipital: O1, Oz, O2). Sign and size of the z-statistic is indicated by colors ranging from dark blue (z-statistic $=-8$) to orange (z-statistic $=+6$, see Fig. 1 legend). Significance of the correlation is reached at a z-statistic of $\pm 1.96$ ($P = 0.05$, dotted contour line), or a z-statistic of $\pm 3.62$ when correcting for multiple testing was applied (Bonferroni correction, $P = 0.00033$, solid contour line). Highly significant negative correlations occurred around 10 Hz, ranging over all anterior to posterior locations, and on posterior locations between 15–22 Hz (beta-1 range). It was verified if the negative correlation of alpha power and KSS at frontal locations was caused by the use of an average reference. Re-analyzing the correlations at Fz and Oz using the left earlobe as common reference yielded negative correlations of similar magnitude. Positive correlations were found below 0.5 Hz, between 3–8 Hz and between 23–29 Hz (beta-2 range), with a focus at frontal locations.

The positive correlation between beta-2 power and KSS may be counter-intuitive, since high beta-2 power is mostly interpreted as an index of effort or activation. A speculative interpretation may be that this beta-2 power resembles processes underlying an increasing effort to maintain wakefulness, e.g., the motivation to stay awake, which coincides with increased feelings of sleepiness. The negative correlation between alpha power and KSS appears general for all scalp locations, whereas the positive relation of theta power and KSS showed particularly high correlations at frontal-central locations.

Recent data on the underlying basis for changes in awake EEG variables, i.e., whether these changes are related to homeostatic or circadian aspects of sleep regulation [7], show converging evidence. Alpha power (8–12 Hz) showed a gradual decrease with time awake, whereas theta (4–8 Hz) and beta (20–32 Hz) power increased at frontal-central locations. The alpha power decrease was also present occipito-parietally, whereas changes in theta and beta power were absent there. Besides that, all frequencies showed marked circadian fluctuations.

The detailed picture of the relationship between sleepiness and awake EEG power in all EEG frequencies recorded from various scalp locations (Fig. 1D) incites a speculative interpretation of the interactions between sleepiness, wakefulness and sleep. Sleepiness is a subjective measure reflecting the human motivational system serving sleep homeostasis. In terms of awake EEG power, the inverse of resting (eyes closed) alpha power may well represent the level of sleepiness during prolonged wakefulness. It shows a strong correlation with sleepiness for all derivations throughout the awake period (see Fig. 1A), and was observed earlier at a single central location [1]. This correlation may represent a high motivation to sleep since it mimics the alpha power decrease during sleep entry [20].

Relations between alpha power and performance have mostly been studied in activating task situations, and thus are not comparable to our resting conditions. However, the co-occurrence of reduced alpha activity with reduced performance as a result of effects of aging and pathologies [15] are well described, and indicates that low alpha activity can predict low performance. Associations of both low frequency (8–10 Hz) alpha power and high frequency (10–12 Hz) alpha power with sleepiness appear global, suggesting that both attention related aspects [15] and working memory related aspects [15] of alpha are associated globally with sleepiness.

The reduction in alpha power may be related to a reduction of activation in sub-cortical brain structures with general cortical activation properties, e.g., brain stem, midbrain, hypothalamus and other parts of the limbic system, since these structures show a positive relation between regional cerebral blood flow and cortical alpha power in resting conditions [18].

The awake EEG showed a positive correlation between theta power and sleepiness. High theta power may indicate a high motivation for sleep, because it follows the alpha power decrease during sleep entry [20]. Increased theta power during awake periods co-occurs with decreased performance. The frontal focus of the relationship is of interest, because frontal areas display most intense sleep after prolonged sleep deprivation [6]. Additionally, the increase in awake EEG theta power over 24 h of sleep deprivation correlates best with the increase in slow wave power (e.g. the intensity of sleep) during subsequent sleep at frontal locations [12]. Furthermore, thalamic glucose metabolism is negatively correlated with frontal theta power [19], and reduction in frontal and thalamic regional cerebral glucose metabolism has been observed during prolonged wakefulness [21]. Thus, theta activity may relate to low frontal cortical activity during resting wakefulness.

In conclusion, subjective sleepiness during prolonged wakefulness is associated with: (1) increased resting EEG theta power with a specific frontal focus; and with (2) a general decrease in resting EEG alpha power. Possibly, the processes underlying (1) and (2) reflect subjective feelings of sleepiness, which guide humans in their decision to go to sleep.

References


