EEG Analysis Applied to Sleep*

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Summary

The electroencephalogram (EEG) is a complex signal and an important brain state indicator (e.g. waking, sleep, seizure). Modern brain research is intimately linked to the feasibility to record the EEG and to its quantitative analysis. EEG spectral analysis (decomposing a signal into its constituent frequency components) is an important method to investigate brain activity. Basic principals of signal analysis (filtering, sampling, and spectral analysis) are reviewed and illustrated with applications to the sleep EEG.

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Key words: Electroencephalogram, power density spectrum, power, spectral analysis

EEG-Analyse am Beispiel des Schlafes

Das Elektroenzephalogramm (EEG) ist ein komplexes Signal und liefert wichtige Hinweise über die Zustände des Gehirns wie zum Beispiel Wachsein, Schlaf oder Anfallsaktivität. Die moderne Hirnforschung ist eng verbunden mit der Möglichkeit, das EEG zu registrieren und zu quantifizieren. Die Spektralanalyse (Zerlegung eines Signals in die zugrundeliegenden Frequenzanteile) ist eine wichtige Methode zur Untersuchung der Hirnaktivität. Die Grundlagen dieser Auswertung (Filtern, Abtastfrequenz, Spektralanalyse) werden zusammengefasst und am Beispiel des Schlaf-EEGs erläutert.

Schlüsselwörter: Elektroenzephalogramm, Leistungsdichtespektrum, Leistung, Spektralanalyse

L'analyse de l'EEG appliquée pour l'étude du sommeil

L'électroencéphalogramme (EEG) est un signal complexe qui reflète et permet d'identifier les différents états de l'activité cérébrale (e.g, éveil, sommeil, attaque cérébrale). La recherche sur le cerveau est intimement liée à la capacité d'enregistrer l'EEG ainsi qu'à son analyse quantitative. L'analyse spectrale consiste à décomposer le signal en fréquences le composant. C'est une importante méthode pour étudier l'activité cérébrale. Les principes de ce type d'analyse sont exposés dans cette revue et illustrés pour ces applications dans l'étude de l'EEG au cours du sommeil.

Mots clés : Electroencéphalogramme, densité spectrale de puissance, analyse spectrale

Introduction

The electroencephalogram (EEG; brain waves) can be recorded by electrodes placed on the scalp. It is a complex signal resulting from postsynaptic potentials of cortical pyramidal cells. The EEG is an important brain state indicator (e.g. waking, sleep, seizure) with specific state dependent features. Crucial aspects of the signal might not be recognized by visual inspection of the EEG. Therefore, additional quantitative analysis is fundamental to investigate the EEG in more detail. Hans Berger, the German psychiatrist and pioneer in human EEG recordings, had already recognized this need in the 1930's. At his suggestion, Dietsch performed the first Fourier analysis of short EEG segments in 1932 [1]. Dietsch enlarged EEG curves and then measured manually the data points and calculated the harmonic components using mathematical tables.

Some brain waves such as for example "alpha activity" (encompassing frequencies between 8 and 12 Hz) in the resting EEG during relaxed wakefulness and sleep spindles in the nonREM sleep EEG are rhythmic. Thus, spectral analysis, which decomposes a signal into its constituent frequency components, is an important method to investigate brain activity. The focus of this paper will be on theory and application of spectral analysis on the sleep EEG. Sleep stages and sleep structure will be briefly introduced in order to provide the background for the analyses that follow.

Sleep states and structure

Characteristic features of the EEG, in conjunction with the electrooculogram (EOG) and the electromyogram (EMG), serve to discriminate sleep and waking. Since the classic EEG studies performed in the 1920's and 1930's, it has been known that human brain waves become slower and increase in amplitude during the transition from waking to sleep and even more so in deep sleep (see [2] for a review). A night of sleep is typically divided into two states, rapid eye movement (REM) and non-REM sleep, based on visual inspection of the EEG, EOG and EMG. REM sleep (**Figures 1A and 2A**) occupies 20 - 25 % of sleep in human adults, and is characterized by rapid eye movements, which occur phasically under closed eyelids, in conjunction with a loss of muscle tone. In addition, autonomic nervous activity shows increased variations that are manifested as fluctuations in heart rate, blood pressure and respiration. Non-REM sleep is traditionally subdivided into stages 1 to 4 [3], with stages 3 and 4 referred to as slow wave sleep (N3 according to new scoring rules [4a]); see companion article [4b] for more details. Slow waves (defined as waves encompassing frequencies below 4.5 Hz) during non-REM sleep have proven to be valuable markers of sleep intensity, and indirectly, of sleep need. The cyclic alternation of the two basic sleep states (non-REM sleep and REM sleep; **Figures 1A and 2A**) is one of the hallmarks of sleep. In the human adult the non-REM-REM sleep cycle exhibits a periodicity of 90 - 100 min.

The conventional method of sleep scoring which is used to differentiate sleep stages is inadequate for quantitative EEG analysis because the definition of sleep stages is based on rather general and arbitrary criteria. Assessment of EEG variables by computer-aided methods of signal analysis, such as spectral analysis, provides complementary information to sleep stages.

Spectral analysis of the sleep EEG: theoretical background

Spectral analysis is a mathematical approach to quantify the EEG. It does not provide a biophysical model of EEG generation. Its purpose is the decomposition of signals such as the EEG, into its constituting frequency components. The fast Fourier transform (FFT; [5]) is a widely applied method for obtaining the EEG spectrum.

Analog-to-digital (A/D) conversion, anti-aliasing filtering and calibration. EEG signals are electrical potential differences that vary continuously over time. For data processing with a digital computer, signals need to be digitized. Analog-to-digital (A/D) conversion involves
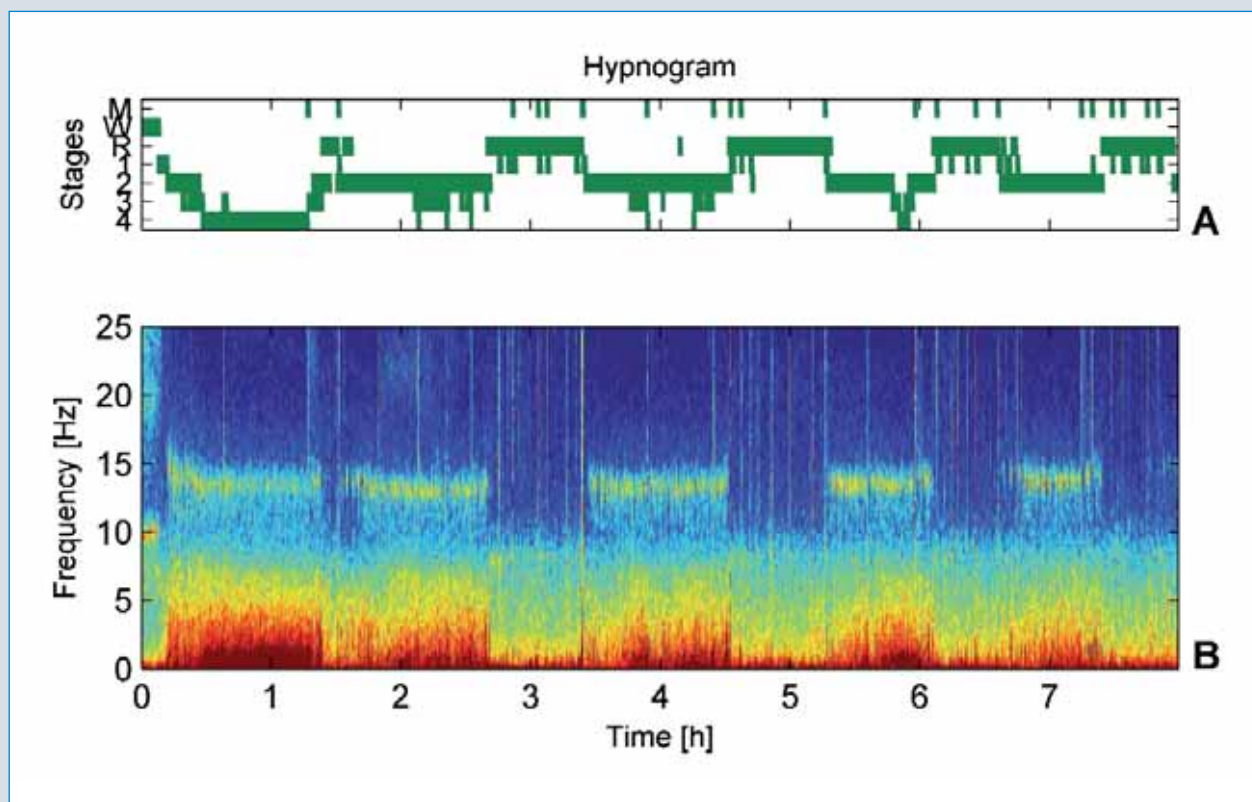

Figure 1: **A** Sleep profile (hypnogram) and **B** color-coded power spectra of consecutive 20-s epochs (average of 5 spectra calculated for 4-s epochs; Hanning window). Data were sampled with 256 Hz. Spectra (derivation C3A2) are color coded on a logarithmic scale (0 dB = 1 μV^2/Hz; -10 dB [color bar] 20 dB). Sleep stages were visually scored for 20-s epochs (W: waking; M: movement time; R: REM sleep; 1 to 4: non-REM sleep stages 1 to 4).
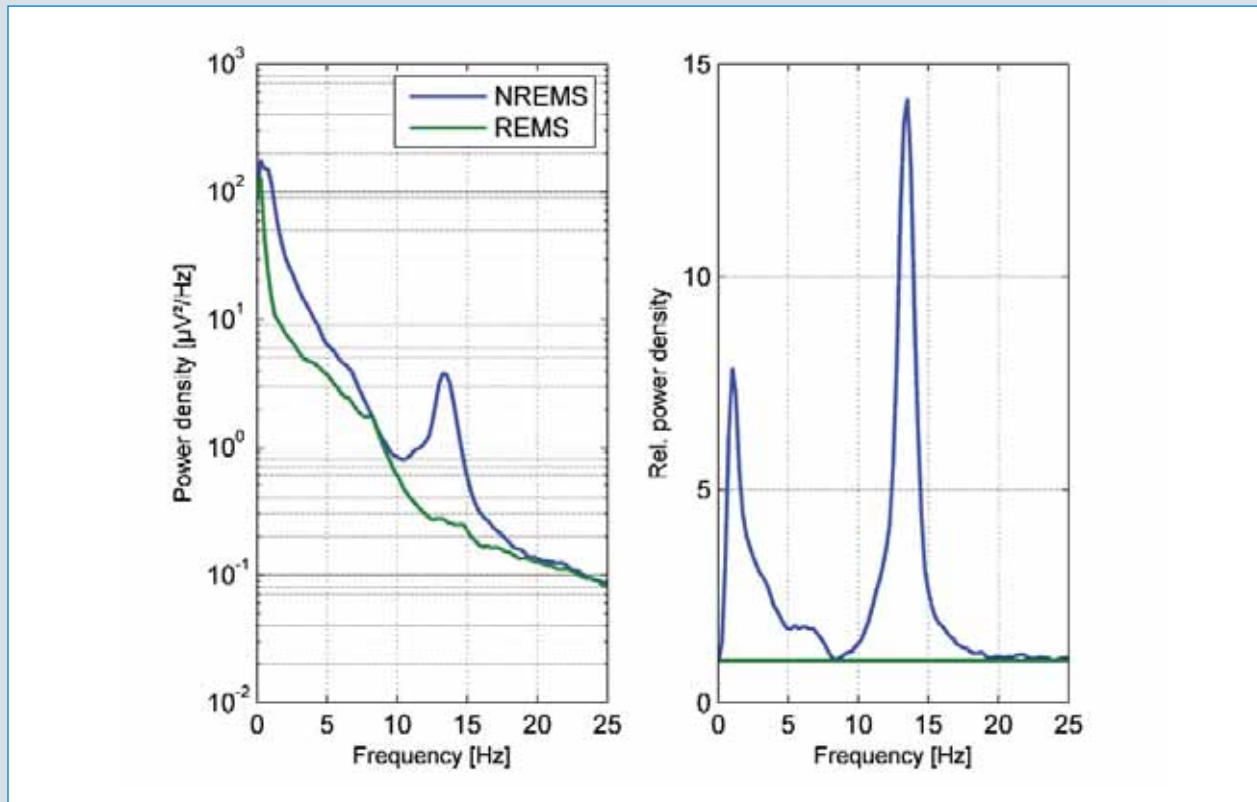
Figure 2: Left: Average spectra of non-REM sleep (stages 2, 3, and 4) and REM sleep. **Right:** Non-REM sleep spectrum plotted relative to the REM sleep spectrum. Only 20-s epochs without artifacts were included in the average spectra. Same recording as in Figure 1.

sampling and quantization of the signals. The sampling frequency must respect the sampling theorem to avoid aliasing, i.e. mirroring of fast frequency components onto the low frequency range. This means that the sampling frequency must be equal to or higher than twice the frequency of the highest component present in the signal. In practice, adequate low-pass filtering is necessary prior to sampling to avoid aliasing. As a rule of thumb, the cut-off frequency of a low-pass anti-aliasing filter should be set at approximately 1/5 of the sampling rate. It should be kept in mind that after A/D conversion, aliasing effects can not be recognized or eliminated. The problem of aliasing is independent of the method used for further processing of the signal.

Prior to each recording, calibration of the recording equipment is highly recommended. One approach is to record a calibration signal (e.g. a 10 Hz sine wave with an amplitude of 50 ºV) of 20-s duration or longer. By doing so, the gain can easily be calculated and the spectra scaled properly.

Spectral analysis. Spectral analysis seeks to describe the frequency content of a signal based on a finite set of data. The literature on spectral estimation and time series is extensive. For a sound mathematical background see e.g. [6 - 8]; for tutorial texts on spectral analysis of the EEG see e.g. [9 - 11].

The *power density spectrum or power spectrum* displays the distribution of power or variance over the frequency components of a signal. It is defined as the Fourier transform of the autocorrelation function.

In practical applications, spectra are estimated by the discrete Fourier transformation based on data of finite length. Power density spectra can be estimated by the "periodogram method" [12]. To this effect, the signal is divided into segments, which may overlap. These segments are weighted (multiplied) by a non-rectangular window function to reduce edge effects (leakage) prior to the FFT. The FFT results in a complex spectrum. The absolute values are squared to obtain power density values. To estimate the power density spectrum it is advisable to average over several segments or smooth over frequency bins in order to reduce the variance of the estimate.

The frequency resolution is given by the inverse of the length of the segment in time. For example, with a segment length of 4 s the frequency resolution is 0.25 Hz; averaging over 5 segments will then provide a power density spectrum for a 20-s epoch, a commonly used time interval for scoring sleep stages. A further constraint in some FFT routines is that the number of data points used has to be a power of 2 (i.e. 64, 128, 256, 512, etc). Therefore, the segment length may also depend on the sampling rate, e.g. with a rate of 100 Hz possible segment lengths are 1.28 s, 2.56 s, 5.12 s, etc.

The units of power density values are expressed either in V^2/Hz or μV^2/Hz. When looking at broad bands, e.g. the delta band (0.7 - 4.5 Hz; **Figure 3B**), one must integrate (sum) over the appropriate frequency range

while taking into account the frequency resolution (bin width). The resulting units of power are V^2 or μV^2.

A requirement of the Fourier transform is that the signal is stationary in the time window over which the transform is applied. The EEG, and in particular the sleep EEG, however, is a non-stationary signal with typical changes in total power as a function of the non-

EEG signal. The major problem is the dependency of measures in higher frequency bands on those in lower frequency bands. Particularly, incidence measures of higher frequencies are a mirror image of low frequency activity and thus may lead to misinterpretations [15]. Therefore, PAA should be applied only to band-pass filtered signals. Signal distortion through filtering can be
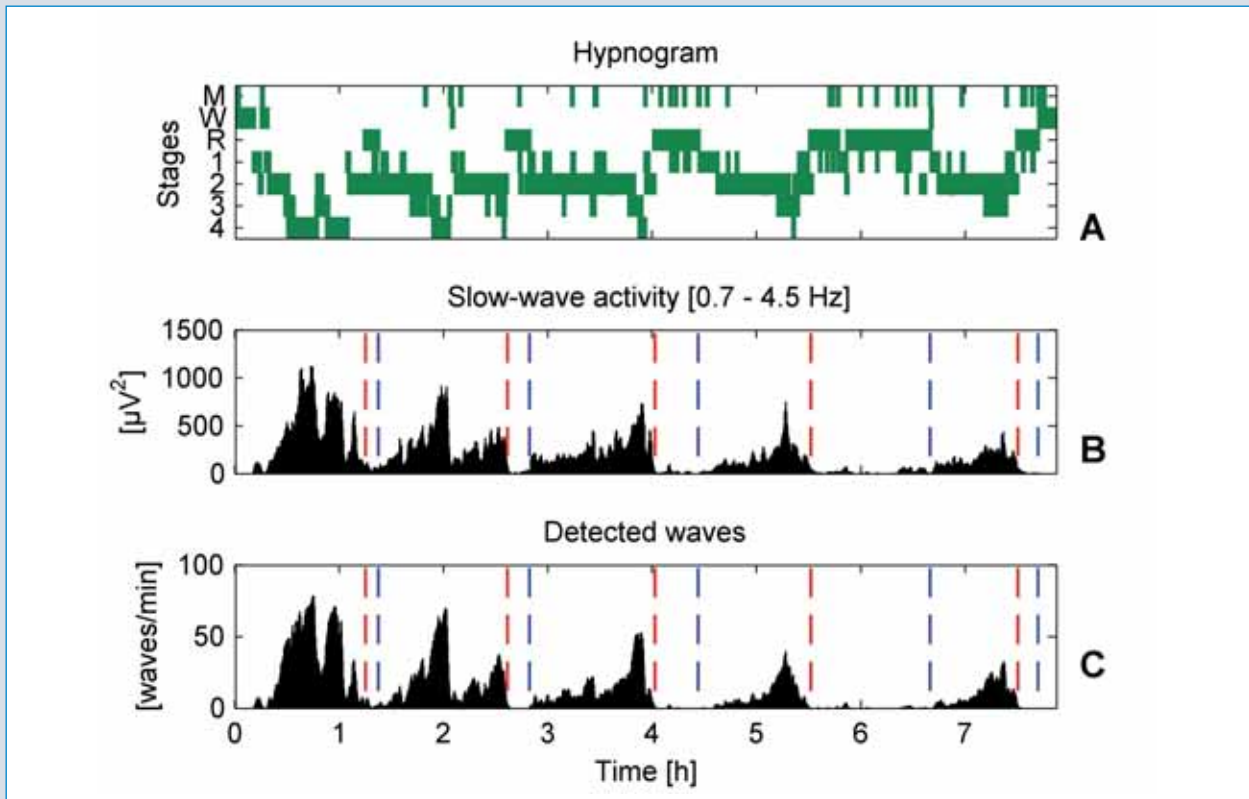

Figure 3: Sleep profile (hypnogram), slow-wave activity and number of detected waves of a single individual during baseline sleep. A Hypnogram (M: movement time; W: wake; R: REM sleep; 1-4: NREM sleep stages 1-4). B Slow-wave activity (spectral power in the range of 0.7-4.5 Hz). C Number of half-waves per min detected with an absolute threshold of 37.5 μV. Dashed lines delimit the beginning (red) and end (blue) of REM sleep episodes. Data were sampled with 128 Hz.

REM-REM sleep cycle (**Figure 3B**). Nevertheless, by selecting short epochs in which the parameters of interest vary minimally, the requirements for stationarity may be fulfilled (quasi stationarity). The choice of the epoch length is a compromise between frequency resolution and stationarity. For spectral analysis of the sleep EEG, epochs of 2 to 10 s are most often used.

Period-amplitude analysis (PAA). An alternative approach to spectral analysis is analyzing signals in the time domain. Salzberg et al. [13] introduced period analysis of the EEG by classifying intervals between zero crossings into various frequency bands. Feinberg et al. [14] published a detailed description of an algorithm for period-amplitude analysis (PAA), which promoted its application in sleep research. PAA appears to be an attractive method because (1) its concept is straightforward and easy to understand and (2) it provides separate measures for the incidence and amplitude of waves. Problems arise, however, if PAA is applied to the raw

avoided by using digital filters with zero or linear phase-shifts. PAA after band-pass filtering can be useful to analyze phasic events.

Spectral analysis of the sleep EEG: applications

Figure 1 illustrates color-coded power spectra of an entire nights' sleep. Spectral activity is markedly modulated by the non-REM-REM sleep cycle. Delta activity (<4.5 Hz) and spindle frequency activity (12 - 14 Hz) are distinct features of non-REM sleep. They can be identified in the color plot by the presence of warm colors. The absence of activity in these frequency bands is a marker of REM sleep. Alpha activity (approx. 10 Hz) is present during waking prior to sleep onset. This quantitative analysis provides a clear overview of the structure of a sleep recording even if sleep stages have not yet been visually scored.

All-night average EEG power spectra in non-REM and REM sleep are depicted in **Figure 2**. In the non-REM sleep spectrum the greatest power is observed in the delta range and a clear peak is present in the spindle frequency range (around 13 Hz). To visualize the differences between non-REM and REM sleep spectra, their ratios were calculated (**Figure 2**, right). The relative spectrum revealed peaks in the delta and spindle range that are typical of non-REM sleep. Below 15 Hz, power in non-REM sleep usually exceeds power in REM sleep.

One of the most important functional EEG variables is referred to as "slow-wave activity". It is equivalent to "delta activity" and encompasses components of the EEG signal in the frequency range of approximately 0.5 to 4.5 Hz as obtained by spectral analysis (**Figure 3B**) or other methods of EEG analysis (**Figure 3C**). It is modulated by the non-REM-REM sleep cycle and exhibits a declining trend in the course of the night. Slow-wave activity in the first non-REM sleep episode increases proportional to the duration of prior wakefulness and is enhanced after prolonged wakefulness compared to the corresponding baseline sleep period.

An example of PAA is illustrated in **Figure 3**. Half-waves were determined as negative or positive deflections between two consecutive zero crossings in the band-pass filtered signal (0.5 - 2 Hz) and an amplitude threshold of $\pm$ 37.5 μV was applied, corresponding to the scoring rules of slow waves (75 μV peak-to-peak; [3]). The frequency of the half-waves was calculated as the inverse of the period, i.e. twice the time interval between the two zero crossings characterizing the half-wave. Data of a single individual during baseline sleep are illustrated in **Figure 3**. Slow-wave activity showed the typical decline in the course of sleep and is markedly modulated by the non-REM-REM sleep cycle (**Figure 3A**, B). The number of waves per min with an absolute amplitude larger than 37.5 μV (**Figure 3C**) closely resembled the profile of slow-wave activity (Pearson's correlation coefficient r=0.724).

EEG topography: Global versus local aspects of sleep

The increasing ease of recording the sleep EEG from multiple derivations combined with the availability of computer programs to analyse and visualize the data, have made it possible to explore the sleep process as a function of brain region. A number of researchers have investigated whether sleep represents a global or a local brain process (see [2] for an overview). The observations that dolphins do not exhibit "deep" slow wave sleep in both hemispheres simultaneously, and that the selective deprivation of slow wave sleep in one hemisphere gives rise to a unihemispheric slow wave sleep rebound in the hemisphere kept awake [16, 17] showed that the sleep process does not necessarily encompass the entire brain. Hypotheses have been advanced im-

plying that regional increases in neuronal activity and metabolic demand during wakefulness may result in selective changes in EEG synchronization of these neuronal populations during NREM sleep [18, 19]. There is recent experimental support for a local, use-dependent facet of sleep regulation. In humans and rodents selective regional cerebral activation during waking was shown to give rise to a predominant increase of sleep intensity in the previously activated brain region as reflected by enhancement of slow-wave activity [20-22].

Furthermore, topographical analyses of the sleep EEG have revealed regional differences. In particular, a sleep-dependent hyperfrontality of slow-wave activity was observed, both in baseline and recovery sleep after 40 h of sustained wakefulness (**Figure 4**, middle panels). Moreover, sleep deprivation was associated with an accentuation of the frontal predominance of the low-frequency EEG activity (**Figure 4**, right). It was hypothesized that the predominant increase of low frequency power in frontal areas after sleep deprivation may be due to a high 'recovery need' of the frontal heteromodal association areas of the cortex [23]. This is supported by PET studies showing a selective deactivation of frontal areas in non-REM sleep compared to waking [24] as well as during prolonged waking [25].

Further topographical aspects and their functional relevance are addressed and discussed in [23, 26] and functional aspects of sleep in a companion article within this issue [4b].

Concluding remarks

The basic steps of data acquisition and processing with a focus on spectral analysis have been discussed with an emphasis on sleep EEG data.

There is no standard representation of spectral EEG data. Spectra may be plotted in absolute units (μV^2/Hz) or in relative units (%). Many standardization methods are possible: Each bin expressed as a percentage of the total power accentuates the predominance of certain frequency ranges; when expressed relative to the first non-REM sleep episode temporal changes are illustrated; if spectra of an experimental condition are expressed with respect to a baseline or placebo condition, treatment effects can be demonstrated.

If adequate attention and prudence are applied to the proper collection of EEG data, there are many interesting ways to analyze the data using quantitative methods. Further methods include wavelet analysis, independent component analysis, time-frequency and nonlinear approaches.

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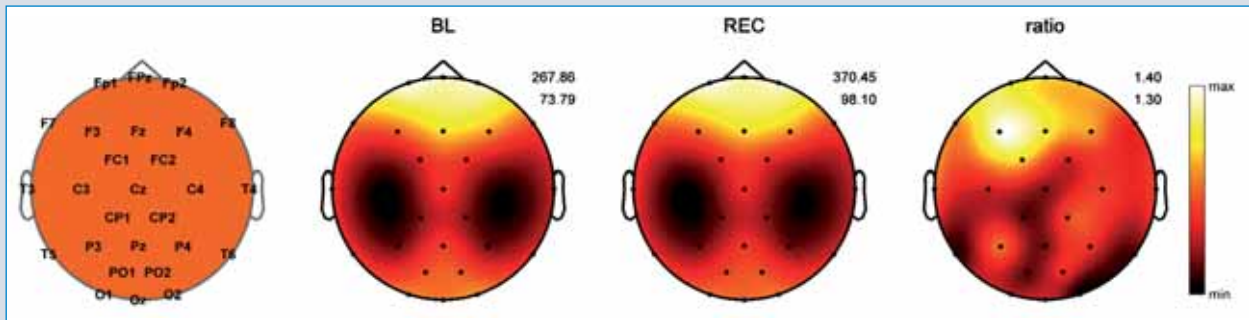
Figure 4: Functional topography of non-REM sleep EEG power in the delta (0.75 - 4.5 Hz; slow-wave activity) band. **Left to right:** electrode placement according to the extended 10-20 system; slow-wave activity during baseline (BL); slow-wave activity during recovery sleep (REC) after 40 h of sustained wakefulness; ratio (recovery/baseline). Average data of 8 subjects are illustrated. Maps are based on 27 EEG derivations (average reference). Values are color coded and plotted at the corresponding position on the planar projection of the hemispheric scalp model. Values between electrodes were interpolated (biharmonic spline interpolation). Power and ratio maps were scaled separately to optimize contrast by using the full color range. Minima (min) and maxima (max) are indicated next to each map.

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