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Comparison of the Properties of EEG Spindles in Sleep and Propofol Anesthesia

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Abstract— **Electroencephalogram spindle patterns corresponding to two different phenomena—natural sleep and propofol anesthesia—are compared. The spindles are extracted from 5 overnight sleep recordings and 10 recordings of deep propofol anesthesia. Mean frequency, angle of the trend in instant frequency as well as 3 nonlinear parameters—spectral entropy, approximate entropy, and Higuchi fractal dimension—are calculated to characterize the spindle waveforms. Using the Wilcoxon rank sum test with significance level of 0.01, all the mentioned features, except approximate entropy, differ significantly for the two types of EEG spindles.**

I. Introduction

Spindles in the EEG signal are generally defined as waxing and waning oscillations of 12–14 Hz, lasting from 0.5 sec. to several seconds. In sleep electroencephalography spindles are important waveforms marking the onset of sleep stage 2 and differentiating between REM and non-REM sleep [1]. It has been suggested that sleep spindles originate from the hyperpolarization-rebound sequence of the thalamocortical neurons and that spindle frequency depends on the hyperpolarization length of these cells [2], [3]. Spindle frequency has been found to form a U-shape during the first NREM sleep episode in the course of the night [4]. The average spindle frequency tends to increase towards the end of the night in healthy subjects while in the case of obstructive sleep apnea it remains at a lower level [5].

Another neurophysiological state that induces EEG spindles is anesthesia. Spindles can be seen, for example, in deep propofol anesthesia in humans [6], [7]. Most anesthetic agents, however, do not induce spindles, neither have spindles been detected in animals in propofol anesthesia. Propofol spindles can most clearly be seen during the burst-suppression pattern in deep anesthesia, however, our earlier study showed that synchronous EEG activity corresponding to spindles actually starts before burst-suppression (in the course of deepening anesthesia) at a higher frequency (about 20 Hz) [8]. The frequency of this activity gradually decreases becoming stable (at about 13 Hz) after the onset of burst-suppression. While sleep spindles have been studied intensively, EEG spindles in anesthesia have only recently gained the attention of researchers. It has been suggested that propofol spindles have the same origin as sleep spindles, however, there is too little evidence to confirm these suggestions.

The aim of this paper is to compare the spindles induced by propofol with those occurring during natural sleep. We first present some observations based on visual inspection of the two types of EEG spindles. In the analysis, two approaches have been taken. Firstly, the average frequency as well as the change in instantaneous frequency during individual spindles are studied. Instantaneous frequency is estimated using the Choi-Williams time-frequency distribution. In the second part of the analysis we compare three nonlinear measures—spectral entropy, approximate entropy and Higuchi fractal dimension—of the two spindle phenomena. By analyzing the complexity of the spindle patterns we aim to detect possible differences in the complexity of the neural generators underlying spindles in sleep and propofol anesthesia. These measures have previously been suggested as indicators of anesthetic depth (see [9] and references therein).

It is well known that the frequency of sleep spindles varies during the night, according to the age of the subject, and in different areas of the cortex. Spindles induced by anesthesia are too weakly studied to decide about similar variations. In this study we have intentionally discarded these variations as our intention is to compare the general waveforms of the spindles of the two types.

II. Material

Sleep spindles were extracted from 5 overnight sleep recordings. EEG signal, sampled at 200 Hz, was measured from the electrode locations Fp1-M2, Fp2-M1, C3-M2, C4-M1, O1-M2 and O2-M1, according to the standard 10-20 electrode system with M1 and M2 referring to corresponding mastoid electrodes. Spindles were marked by experienced neurophysiologist. We then visually inspected the EEG recordings, leaving out short and noisy spindles, choosing the EEG channel were the spindle was best presented and marking the start- and endpoints for the analysis. Our aim in scoring was to obtain as good samples of the sleep spindle waveform as possible.

Propofol spindles were extracted from 10 EEG recordings, performed to study the evoked EEG patterns during burst-suppression anesthesia. The signals were originally sampled

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at 5 kHz. The analysis was performed on the signal recorded from channel Pz-FCz. Detailed description of the course of anesthesia as well as the recording setup can be found in [6]. Propofol spindles were marked visually—these patterns are easy to detect as the level of the background activity during suppression is low.

Minimum length of the spindles incorporated into the study was 0.75 seconds. The number of sleep and propofol spindles satisfying our selection criteria was 248 and 192, respectively. Before the analysis, the EEG from the propofol recordings was decimated to 200 Hz and all the signals were digitally filtered using equiripple bandpass FIR filter of 2. . .47 Hz bandwidth and maximum error of 0.01.

III. Methods

A. Frequency analysis

EEG spindles are rhythmic patterns and therefore usually described by their peak frequency. We were interested in the peak frequency as well as the dynamics of the instantaneous peak frequency during individual spindles. The best time-frequency resolution can be achieved using time-frequency distributions. For the analysis of the spindles we chose Choi-Williams distribution, described by the equation:

$$C(t,\omega) = \frac{1}{2\pi}\iint \phi(\xi,\tau)AF(\xi,\tau)e^{-j(\xi t+\omega\tau)}d\xi d\tau, \quad (1)$$

where the ambiguity function $AF(\xi,\tau)$ is:

$$AF(\xi,\tau) = \int x(t+\frac{\tau}{2})x^*(t-\frac{\tau}{2})e^{j\xi t}dt, \quad (2)$$

and the kernel function $\phi(\xi,\tau)$ is:

$$\phi(\xi,\tau) = e^{-\frac{(\xi\tau)^2}{\sigma}}. \quad (3)$$

σ is the parameter of the kernel function and is given the value 1 in our analysis.

The maximum of the obtained time-frequency representation was found for each time instant, and a time series of peak frequencies $f_{peak}(t)$ was formed. To eliminate the influence of noise and artifacts, the relative power in the narrow frequency band of 2 Hz around the peak frequency was calculated for every time instant and the obtained series was smoothed using a time window of 11 samples. The series $f_{peak}(t)$ was then fitted by a straight line in the time segment where the average power of the frequency peak exceeded a predefined threshold. $f_{spindle}$ was then calculated as the mean of the values of the fitted line at the points where the average peak power crossed the threshold value. f_{slope} was obtained as the slope of the fitted line. The estimation of the frequency parameters is illustrated in figure 1.

B. Nonlinear analysis

In order to quantify the spindle waveforms, nonlinear parameters like spectral entropy ($SpEn$), approximate entropy ($ApEn$), and Higuchi fractal dimension (HFD) were calculated. $SpEn$ is fully based on the second order statistics of the signal, quantifying the peakiness of the power spectrum [10]. $ApEn$ is a measure of randomness or unpredictability of the signal, calculated in phase space [11]. HFD constitutes an algorithm for fractal dimension estimation, operating in time domain and giving reliable parameter values for short signal segments [12]. The detailed description of the algorithms are presented in [9] and [13]. All algorithms were implemented as custom written Matlab routines.

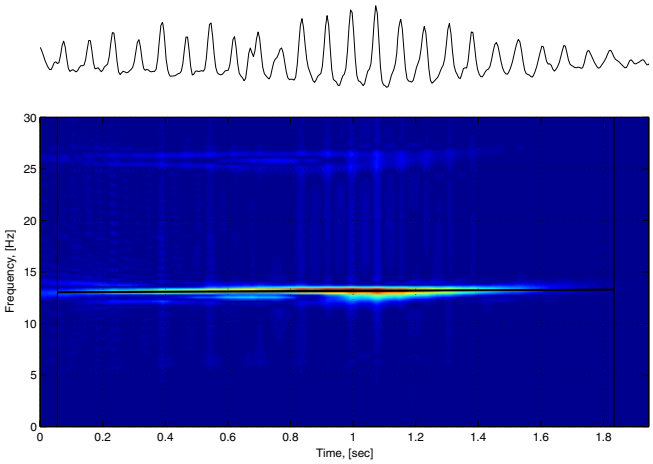

Fig. 1. Estimation of the parameters $f_{spindle}$ and f_{slope}. The upper and lower plots show the spindle waveform and its Choi-Williams distribution, respectively. The vertical black lines denote the points where the average power crosses the threshold and the horizontal black line denotes the linear approximation of $f_{peak}(t)$

C. Statistical analysis

In order to determine whether the medians of the calculated measures for sleep- and propofol spindles are statistically different the Wilcoxon rank sum test was applied. The test was performed at the 0.01 significance level.

IV. Results

A. Visual comparison of EEG spindles in sleep and propofol anesthesia

Figure 2 presents a typical pattern seen during burst-suppression level propofol anesthesia (upper curve) as well as a typical sleep spindle (lower curve). Although spindles in propofol anesthesia can be seen either in the middle of longer suppression segments, superimposed on bursts, or even during continuous EEG before burst-suppression, they most often occur immediately after bursts. The combination of burst and a spindle in propofol anesthesia resembles that of a K-complex and a spindle in sleep (figure 2).

By visual inspection, several features of propofol spindles can be observed. Firstly, the deviation of the signal from the baseline during the spindle is often one-sided. Secondly, propofol spindles sometimes occur as a sequence of two or even three waxing and waning oscillations (see figure 2). Thirdly, the waves constituting the spindles "break" in some cases so that another, higher frequency component appears in the signal (figure 3).

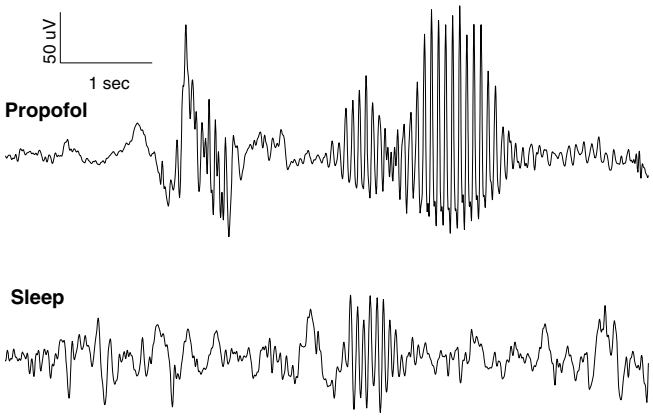

Fig. 2. An example of a spindle following a burst in deep propofol anesthesia (upper curve) and a sequence of K-complex and a spindle in natural sleep (lower curve)

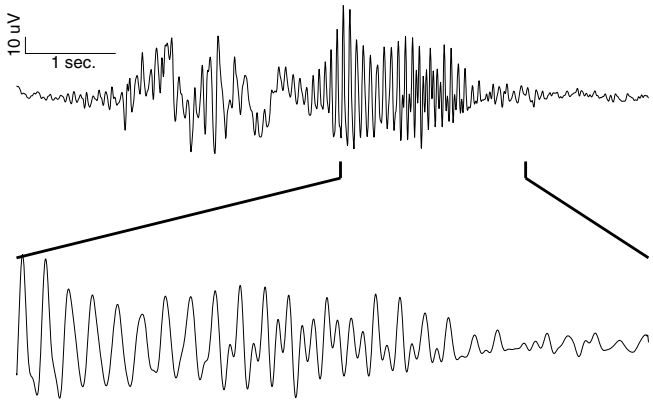

Fig. 3. An example of a propofol spindle with 'breaking' waveform

B. Comparison of the parameters of EEG spindles in sleep and anesthesia

Statistical analysis of the calculated measures is presented in figure 4. The corresponding p-values obtained using the Wilcoxon rank sum test are given in table I. With significance level of 0.01 all the measures except $ApEn$ indicate significant difference between sleep and propofol spindles. The most discriminative parameter appears to be HFD.

TABLE I
RESULTS OF THE WILCOXON RANK SUM TEST, $\alpha = 0.01$

	$f_{spindle}$	f_{slope}	$SpEn$	$ApEn$	HFD
p	0.0000	0.0000	0.0030	0.5013	0.0000
Significance	Sign.	Sign.	Sign.	Not Sign.	Sign.

V. DISCUSSION AND CONCLUSIONS

Visual inspection of the spindle patterns of natural sleep and deep propofol anesthesia has revealed several differences in these waveforms. The envelope of propofol spindles is often asymmetric, indicating a baseline shift or a slow wave underlying the spindle. Also, propofol spindles often contain two or three waxing and waning oscillations. An interesting property of propofol spindle waveforms is the appearance of a higher frequency component at twice the principal frequency of the spindle. It is known that spindles during sleep as well as propofol anesthesia occasionally become "spiky", resembling the μ rhythm, also called sensorimotor rhythm of central brain areas in human subjects awake (see, e.g., the spindle in figure 1). In spectral analysis of spindles this yields peaks at harmonic frequencies, often up to four times the frequency of the basic rhythm. In propofol anaesthesia, on the other hand, spindles occasionally transform to another rhythm of first harmonic frequency as shown in fig. 3. It remains to be investigated if these two harmonic-producing phenomena have the same origin.

Frequency analysis of the spindles originating from natural sleep and deep propofol anesthesia shows that both the mean frequency and the trend in the instantaneous frequency differ significantly for the two classes. However, although the mean frequency of propofol spindles tends to be higher than that of sleep spindles, it still fits into the frequency range considered typical to sleep spindles in general. The angle of the trend in the instantaneous frequency is very small for either type of spindles. Among the nonlinear measures, the Higuchi fractal dimension shows the largest difference between the two types of spindles.

The study presented in this paper has several deficiencies, the most important of which concerns the different recording setup underlying the acquisition of the two compared data sets. Propofol data were sampled at 5000 Hz while the sampling frequency of the sleep EEG was 200 Hz. Downsampling of the propofol data to 200 Hz was performed using digital filters to remove the alias components and the results were visually verified, however, the nonlinear measures can still be sensitive to the differences in preprocessing. Also, the differences in the recording environments may have some influence on the signal properties in terms of noise and disturbances. This might have impact on Higuchi fractal dimension, for example, as this measure is especially sensitive to high frequencies.

The neural mechanisms underlying EEG spindle generation during sleep are relatively well known. Clinically more interesting, however, is the impact of various disorders like sleep apnea, for example, on these mechanisms and thus on the properties of spindle waveforms. It can easily be argued that the spindles during deep propofol anesthesia have similar origin to sleep spindles. Our results show, however, that important differences can be noticed in the waveforms of sleep and propofol spindles. The results should be confirmed based on data acquired with more homogenous recording setup.

Our future work will concentrate on more detailed analysis of propofol spindles and classification of these patterns. Also, sleep spindles should not be treated as a homogenous pattern class but should be classified according to location and frequency. We believe that the features of the EEG spindles can be a valuable modality in sleep research as well as in anesthesia monitoring.

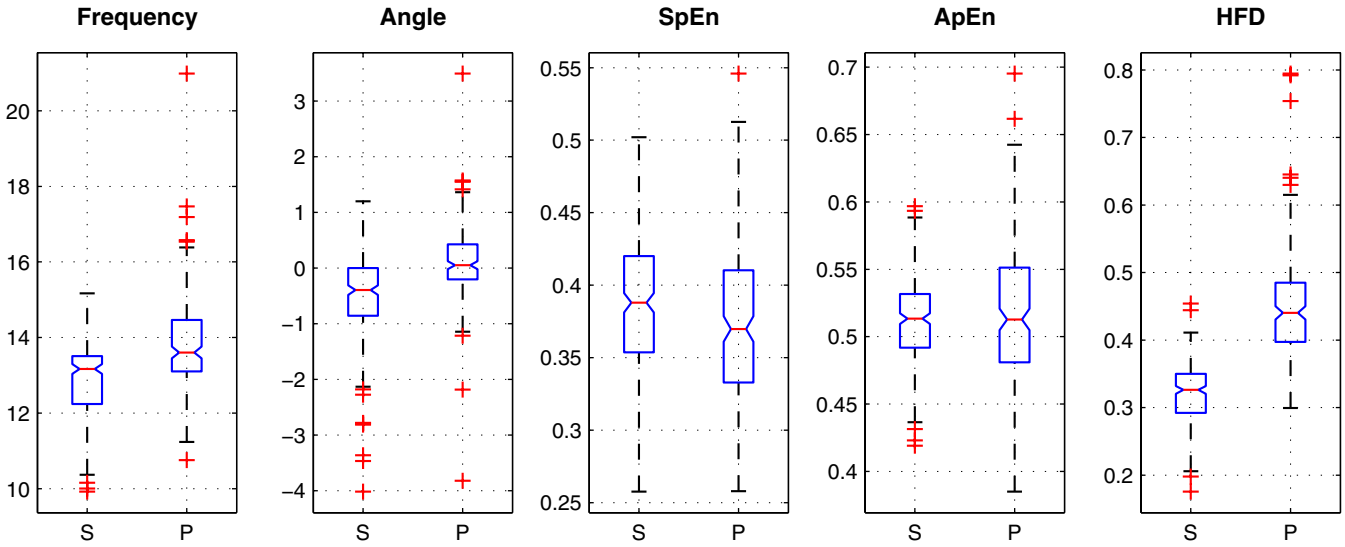

Fig. 4. Comparison of the calculated measures for sleep ("S") and propofol ("P") spindles. The boxes mark the lower quartile, median and the upper quartile of the data. Notches around the median indicate the uncertainty of the estimate of the median. The whiskers indicate the range of the data and outliers are marked as "+"-signs.

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