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Model-related analysis of EEG burst patterns in sedated patients

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Abstract— **A model-related analysis approach was introduced to study amplitude-frequency dependencies within and between EEG frequency components. An oscillator network was used to model EEG burst patterns of sedated patients during encephalographic burst-suppression periods (BSP). The parameter set of the oscillator network was determined for a set of bursts during BSP. In this way, these burst-related parameter sets were used to investigate (i) the dynamics of interrelation of the amplitude and frequency within and between the frequency components during the occurrence of burst patterns and (ii) changes of signal properties (burst-by-burst) during the BSP. Representative results are demonstrated for one patient (group of 7 patients).**

I. INTRODUCTION

The electroencephalographic burst-suppression-pattern (BSP) in sedated patients is an indicator for a maximally reduced cerebral metabolic rate of the brain (brain protection), and a further increasing the dosage of hypnotics is useless. Therefore, BSP can be seen as a defined “reference point” within the stream of changes in EEG properties during the cerebro-protective treatment. The BSP is characterized by alternating periods of high-voltage burst activity and periods of nearly total amplitude-depression (suppression). As shown in previous studies, two dominant oscillatory components of EEG burst patterns during BSP exist [1, 2]. A low-frequency oscillation (<5Hz), which starts with an initial negative wave, is superimposed by a delayed spindle-like high-frequency oscillation (>8 Hz; high-frequency). It can be assumed that the low-frequency component is related to the cortex and that the high-frequency component originates from the thalamus. The interrelation between both components is characterized by a transient but strong quadratic phase coupling (QPC) [3, 4]. The QPC is demonstrable between the frequency ranges 0-2.5Hz and 8-12Hz (3-7.5Hz) which is initiated 0.25sec after the burst onset and reaches maximum between 0.75 and 1.25sec. The most probable cause for the QPC has been identified as an amplitude modulation, i.e. the low-frequency oscillation modulates the amplitude of the high-frequency oscillation. But not all coupling properties can be explained by amplitude modulation. The model may be beneficially expanded by adding a frequency modulation of both oscillatory components because it has been shown by time-variant spectral analysis [2] that the frequency of the high-frequency component changes from 10 to 15 Hz during propofol induced bursts. In thiopental bursts the frequency increase of the high-frequency component is not so strong.

The fundamental idea of this study is to adapt the parameter set of a coupled oscillator network to consecutive bursts that are directly subsequent to a suppression period of the BSP. The oscillator network is expressed by an ordinary differential equation system (ODES). Each of the oscillators (each differential equation) represents a model for one frequency component of the burst signal. In this way, burst-related parameter sets of the ODES can be used to investigate (i) the dynamics of interrelation of the amplitude and frequency within and between the frequency components during the occurrence of burst patterns and (ii) changes of signal properties (burst-by-burst) during the BSP.

The dynamics of interrelation can be studied in the following way. The solution of a burst-related ODES results in a corresponding model-burst. If all signal properties of interest can be extracted by the determination of the burst-related ODES then the model-burst can be analysed instead of the real burst, e.g. by means of time-variant spectral analysis (time-frequency representation TFR) and demodulation techniques. Additionally, the parameter set of the burst-related ODES is available which characterises the whole burst. Therefore, the first goal of the study was to find an appropriate oscillator type and to test the corresponding oscillator network with the aim of evaluating the signal properties of model-bursts in comparison to real bursts. If the results prove satisfactory then it can be assumed that the burst-related ODES models the essential signal properties (burst morphology), including properties of interrelation between the frequency components.

To investigate the changes of signal properties (burst-by-burst) during the BSP the parameter sets can be used. Each parameter set represents a burst and therefore the sequence of bursts can be described as a sequence of corresponding parameter sets.

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The study is focused on the high-frequency component because this component is related to thalamic activity, which is associated with the triggering of the burst onset and the maintenance of the burst pattern [5]. Additionally, the frequency modulation of this component is more interesting because amplitude modulation characteristics have been investigated by previous studies.

II. SUBJECTS

The investigations were carried out on seven sedated patients (M=7) with various neurosurgical diseases, a subgroup (thiopental group) of a group of patients who have already been described in detail (clinical characteristics, medication, and EEG recording conditions) in our previous study [1]. All were given an individualized basic sedation to ensure controlled mechanical ventilation and safe nursing. A rising intracranial pressure, which cannot be influenced by a conventional therapy (ventricular drainage - if available, hyperventilation to a $PaCO_2$ of below 4.6 kPa and an administration of mannitol®), was the indicator used for increasing the basic sedation by adding i.v.-hypnotics (thiopental in our group). The EEG was recorded by an eight channel analogous EEG (Neurofax 5610G, Nihon Kohden, Japan); the electrodes were placed in superior lengthwise positions according to the international 10-20 system with Cz as the reference. This method is the favored recording mode in important clinical studies [6]. The sampling frequency was 256 Hz. A down-sampling to a rate of 128 Hz was performed after a digital low pass filtering with an upper cut-off frequency of 64 Hz. Only the first 2 sec of the EEG patterns were used for analysis (256 sampling points after down sampling).

The burst onset positions were automatically detected by the pattern detection unit developed by Leistritz et. al. [7] on the basis of Fp1 vs. Cz. Thereby, we restricted ourselves to the analysis of bursts that are directly subsequent to a suppression period.

III. METHODS

A. *Time-frequency representation and demodulation*

A Gabor filter technique was used for time-frequency analysis. This approach was applied in our previous studies with regard to burst analysis ($\gamma = 1$ and deg = 2) [4].

The demodulation (extraction of the instantaneous amplitude *IA* and frequency *IF*) was carried out under the following hypothesis. The main power of the two signal components can be modeled using a piecewise continuous amplitude and frequency modulated function fitted to the main ridge in the time-frequency representation *(TFR)* [8]. To find an appropriate frequency demodulation, we used a so called snake algorithm [9], that is usually used as active contour model in 2D image processing. A frequency $\omega(t)$ should be determined at each time t with an amplitude that is as large as possible from a given time-frequency representation $S = S(t,\omega)$. In order to avoid large fluctuations of the function ω, the integral of the squared second derivative should be as small as possible. Consequently, we defined the total energy of ω by

$$E(\omega) = \lambda \sum_{i=0}^{255} \ddot{\omega}^2(t_i) - (1-\lambda) \sum_{i=0}^{255} S\big(t_i, \omega(t_i)\big), \tag{1}$$

that has to be minimized with respect to ω. Thereby the parameter λ controls the compromise between the inner (smoothness) and outer energy (large amplitudes of S) of the snake. Basically, the snake algorithm is an iterative approach that needs an initial contour or function ω_0, respectively. Choosing a constant function in the middle of the frequency band we are interested in, a local frequency demodulation may be determined if an amplitude depression between different frequency bands may be assumed over the time. This approach generalizes the piecewise linear method described in [8].

B. *Duffing oscillator network*

It was found that coupled Duffing oscillators can be used to explain these coupling characteristics and the time courses of amplitude and frequency modulation [10]. A suitable model for the low-frequency cortical oscillatory activity is the damped Duffing oscillator given by the ordinary differential equation *ODE #1*

$$\ddot{x} = -(2\pi\omega_L)^2 x - \mu\dot{x} - \beta_L x^3,\; x(0) = x_0,\; \dot{x}(0) = \chi_0 . \tag{2}$$

Furthermore, the *ODE #2*

$$\ddot{y} = -\left((2\pi\omega_H)^2 + \frac{2}{\tau} + 4\left(\frac{(t-t_0)^2}{\tau}\right)\right) y - \frac{t-t_0}{\tau}\dot{y} \tag{3}$$

has the solution

$$y(t) = a \cdot \cos(2\pi\omega_H t + \varphi) \cdot e^{-\frac{(t-t_o)^2}{\tau}}, \tag{4}$$

which is a suitable model for the high-frequency component. Adding the nonlinear term $-\beta_H y^3$ to the right hand side, an amplitude-dependent frequency may be realized by the *ODE #2*

$$\ddot{y} = -\left((2\pi\omega_H)^2 + \frac{2}{\tau} + 4\left(\frac{(t-t_0)^2}{\tau}\right)\right) y - \frac{t-t_0}{\tau}\dot{y} - \beta_H y^3, \tag{5}$$
$$y(0) = y_0,\; \dot{y}(0) = \nu_0 .$$

A mutual coupling of both components yields a network of two nodes.

$$\begin{aligned}
\ddot{x} &= -(2\pi\omega_L)^2 x - \mu\dot{x} - \beta_L x^3 - \varepsilon_{xy} y \\
\ddot{y} &= -\left((2\pi\omega_H)^2 + \frac{2}{\tau} + 4\left(\frac{(t-t_0)^2}{\tau}\right)\right) y \\
&\quad - \frac{t-t_0}{\tau}\dot{y} - \beta_H y^3 - \varepsilon_{yx} x, \\
x(0) &= x_0,\ \dot{x}(0) = \chi,\ y(0) = y_0,\ \dot{y}(0) = \nu_0
\end{aligned} \quad . \qquad (6)$$

That is, the model is determined by a set of 9 parameters $(\omega_L, \omega_H, \mu, \beta_L, \beta_H, \tau, t_0, \varepsilon_{xy}, \varepsilon_{yx})$ and 4 initial values. The model was fitted to 91 burst pattern with a duration of 2 seconds using the least square deviation from the model to the measured data points as error criterion. Thereby, x was fitted to the original burst data, and y was fitted to a band pass filtered signal (FIR filter, order 256, pass band 11.5 Hz – 15.5 Hz).

IV. RESULTS

In a first step the methodology was tested by means of simulated burst patterns and their corresponding model-bursts (solution of the ODES). The simulated burst consists of the two oscillatory components mentioned above, where each component is amplitude and frequency modulated according to $x(t) = A(t)\sin(\omega(t)t)$.

Figure 1A shows the burst simulation and the corresponding model-burst (solution of the ODES). The extracted spindle-like high-frequency components (Figure 1B) demonstrate the quality of modeling and the degree of amplitude modulation. The IF course of the high-frequency components of both signals as well as the corresponding modulation signal ("true" IF) are depicted in Figure 1C. For the frequency demodulation the snake method applied to the TFR was used. It can be shown that the Duffing oscillator network enables an adequate modeling of the burst, especially for the spindle-like high frequency component. A transient frequency alteration of 1.5-2Hz during a simultaneously existing amplitude modulation can be modeled. The amplitude-dependent frequency characteristic of the Duffing oscillator ODE #2 enables modeling of this type of dependency between amplitude and frequency. Figure 2 exemplarily depicts the result of a model fit of a real burst. All in all, the ODES was adapted for each burst (*N*=91) of the BSP in one patient, i.e. a sequence of 91 burst-models can be derived. The averaged TFR was computed for both real bursts and model-bursts. Additionally, the averaged IF of the high-frequency component was computed. It can be noticed that the essential signal characteristics can be modeled (see Figure 3), whereas a frequency modulation cannot be observed in the majority of cases.

The time evolution of a selection of ODES parameters is illustrated in Figure 4. Such parameters were used which show a significant trend during the BSP (according to the dynamics of sedation depth during BSP [1]).

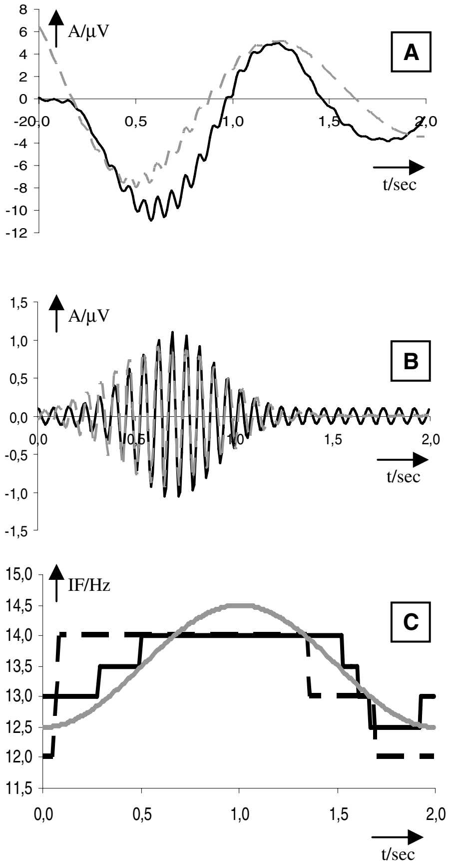

Figure 1: (A) The simulated burst pattern (solid line), where both frequency components are amplitude and frequency modulated, and the corresponding model burst (dashed gray line). (B) Spindle-like high-frequency components of the simulated burst (solid, black line) and of the model-burst (dashed, gray line). (C) The IF course of the simulated burst (solid line) and the model-burst (dashed line). The modulation signal ("true" IF) is depicted as grey line.

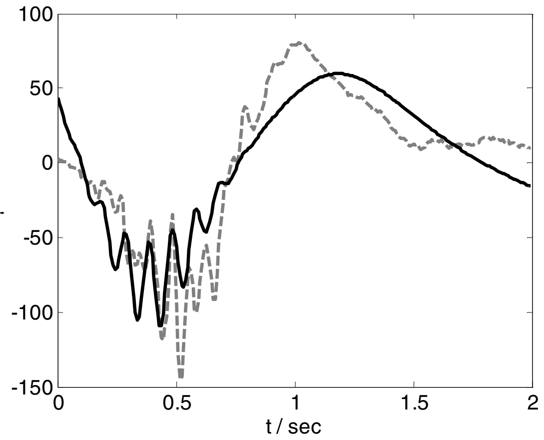

Figure 2: A real burst (gray, dashed) and the fitted model (solid line)

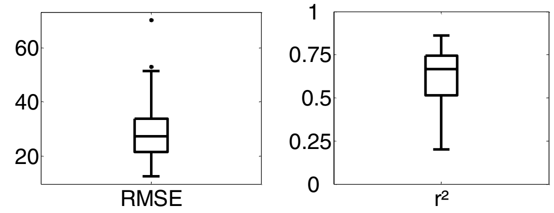

Figure 3: Two goodness of fit measures for the 91 burst signals. The left subplot depicts the distribution of the root mean squared error (RMSE), where the mean squared error was used as optimization criterion. On the right hand side, the corresponding R-square (r²) is given.

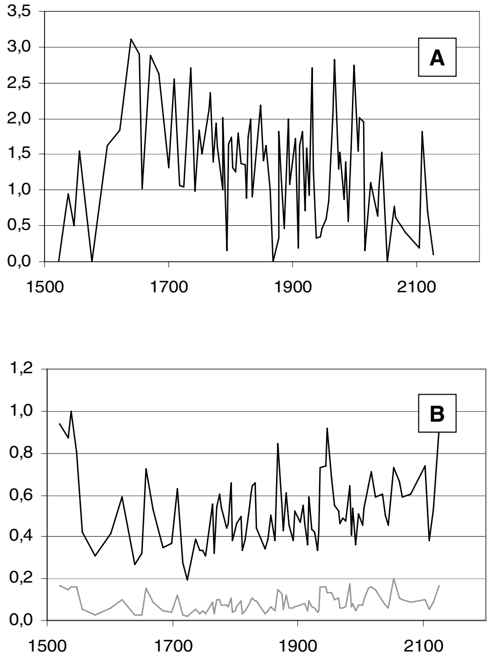

Figure 4: (A) Time course of the damping parameter ω during the BSP. (B) Time courses of the spindle parameters t_0 (black line) and ω (gray line). The time-scale ranges from the onset to the end of the BSP. The BSP is a time-segment (1500-2100 sec) of the whole recording.

V. DISCUSSION

Oscillatory phenomena in electrical brain activity can be understood within the framework of coupled oscillator theory. Here a methodology is demonstrated which not only contributes to the improvement of the interpretation of results [10], but also enhances the analysis methods themselves. Amplitude-dependent frequency characteristics within one frequency band can be explained by the autoresonance phenomenon which can be observed in periodically driven Duffing oscillators i.e. when such an oscillator is driven by a , e.g., sinusoidal signal, the oscillator's amplitude will automatically adjust itself so that the frequency of the oscillator matches the frequency of the driving signal. Our oscillator network consists of two bi-directionally coupled oscillators and both are Duffing-like oscillators with amplitude dependent frequency characteristics. Therefore, more complex amplitude-frequency dependencies can be modeled.

Limitations should be noted however. The modeling is time consuming and the parameters of the ODES are difficult to interpret. These limitations are possibly due to the fact that the model is too simplistic. On the other hand, the identified parameters may be considered as features, where some of them are probably dependent on the depth of sedation. The methodology of this study is part of a strategy in which the changes of coupling properties of so-called burst-like patterns of the EEG before entering the BSP are used to forecast the depth of sedation. It is assumed that these changes may be continuously interpreted within the properties of the burst patterns, i.e. QPC, amplitude as well as frequency modulation characteristics.

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