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Increase of Slow Periodic Modulation of EEG in a Patient with Alzheimer's Disease

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Summary

The recently described slow oscillations of amplitude of theta and alpha waves of the EEG (with a frequency below 0.08 Hz) in healthy subjects are attributed to the autonomic nervous system with control at the brain stem level. In the present pilot study, the slow brain rhythms were analyzed in a patient with Alzheimer's disease and were compared to a healthy subject. Dynamic analysis of the EEG was performed using time-frequency mapping which gives simultaneous time and frequency representation of the brain signal. This method comprises a transform of the filtered EEG signal into its analytic form and application of the Wigner distribution modified by time and frequency smoothing. It has been shown that the envelope of both theta and alpha activities oscillates at 0.04 Hz and 0.07 Hz in the healthy subject and at 0.03 Hz and 0.06 Hz in a patient with Alzheimer's disease. The amplitude of the slow oscillations of theta activity was substantially higher in the patient with Alzheimer's disease as compared with the healthy subject. It is being proposed that the increase of slow brain rhythms in the patient with Alzheimer's disease reflects an abnormal activity of the autonomic nervous system. However, the underlying pathophysiological mechanisms need to be further studied.

Key words

EEG – Time-frequency mapping – Slow brain wave – Alzheimer's disease – Wigner distribution

Introduction

We have recently described the presence of slow rhythms of EEG in healthy subjects (Novák and Lepičovská 1992a, Novák *et al.* 1992b). This slow activity is superimposed on the background EEG and manifests itself as periodic oscillations of amplitude of theta and alpha waves. Typically, two rhythms are present in healthy subjects – a rhythm with a frequency of 0.02 Hz (period 50 s) and a faster rhythm with a frequency at 0.06 Hz (period 16.6 s). Hyperventilation significantly increases the amplitude of the slower 0.02 Hz rhythm. Rhythms with similar frequencies were found in brain stem neurones responsible for cardiovascular and respiratory regulations (Langhorst *et al.* 1980). Therefore, the origin of slow (< 0.08 Hz) activity of EEG is attributed to the brain stem level and it is thought to reflect the activity of the autonomic nervous system (Novák and Lepičovská 1992a). (Hereafter we refer to slow rhythms as the amplitude modulation of EEG with a frequency below 0.08 Hz).

The aim of this pilot study was to compare the slow rhythms of a healthy subject and of a patient with Alzheimer's disease using time-frequency mapping. This novel method is based on the modified Wigner distribution of the analytic EEG signal (Novák and Lepičovská 1992c) and was applied directly in the present paper for the first time to the digitized EEG data.

Theoretical Considerations

The concept of the Wigner distribution (WD) was introduced by Wigner (1932) and incorporated into signal analysis by Ville (1948). The WD decomposes the time function into the function of time and frequency. Properties of the WD have been extensively studied by Claasen and Mecklenbrauker (1980).

For two discrete complex signals z and x the smoothed discrete cross WD is defined (Novák and Lepičovská 1992c) by the following equation:

$$W_{zx}(n,m) = \frac{1}{2N} \sum_{k=-N+1}^{N-1} |h(k)|^2 \left[\sum_{p=-M+1}^{M-1} g(p)\, z(n+p+k)\, x^*(n+p-k)\right] e^{-2i\pi km/N}, \quad (1)$$

where n = time index,
m = frequency index,
h(k) = window function with the length 2N-1,
g(p) = window function with the length 2M-1,
and the asterisk denotes a complex conjugate.
The effect of h(k) is in frequency smoothing while g(p) applies for time smoothing. The auto WD is computed with z=x. The time smoothing employed in the WD algorithm leads to a reduction of noise and enhances the underlying signal structure. For stationary signals the Wigner spectrum reduces to the ordinary Fourier spectrum. However, the Wigner spectrum differs from the Fourier spectrum when applied to nonstationary signals proportionally to the level of nonstationarity of the analyzing process.

Methods

Data from a 52-year-old man without a neurological history and from a 55-year-old man with Alzheimer's disease were analyzed. Resting EEG was recorded for 5 min in the supine position with eyes closed. EEG was obtained using the Brain Imager IIs system with a standard ten-twenty system and monopolar recording. Linked ears served as a reference point. Silver-silver chloride electrodes were filled with EEG gel and the maximum impedance level was kept under 4.8 kOhm.

The EEG signal was filtered with a bandpass 0.3 Hz–40 Hz and digitized at a sampling frequency of 200 Hz with 12 bit resolution per channel. The mean and baseline trend were removed by the third order moving polynomial with 65 samples window length.

The EEG signal from the lead O2 was converted into an analytic signal by Hilbert transform (Oppenheim and Schafer 1975). The analytic signal has a real component which is simply the original data and an imaginary component that is a version of the original real sequence with a 90 degree phase shift. The analytical signal has the same amplitude and frequency content as the original real data. However, because the analytical signal does not have negative frequencies, the undesirable interference between negative and positive frequencies on the WD is removed.

For computation of the WD, we set N=128, M=9, g(p)=1. The Gaussian function with parameter alpha = 2.8 was used for h(k) (Harris 1978). Further computational details can be found in Novák and Lepičovská (1992c).

The WD was then divided into standard frequency bands delta, theta, alpha, beta1 and beta2. The maximum in each band was detected for each time index and these values were stored for further analysis. The WD in time direction is compatible with the original time-domain signal and this process can therefore be viewed as time varying filtering of the EEG signal within the preselected frequency bands. In other words, the square envelope of refined alpha activity is extracted without interfering with the theta, delta or other activity. An analogical approach can be applied for delta and theta waves. The oscillations of the extracted envelope were analyzed by computing the Fourier spectra.

Results

Visual inspection of EEG of the healthy subject revealed dominant alpha activity without any abnormalities (Fig. 1a). On the corresponding Wigner distribution, the dominant frequency energy is concentrated within the alpha band (Fig. 2a). The delta/theta frequency contents were increased only sporadically.

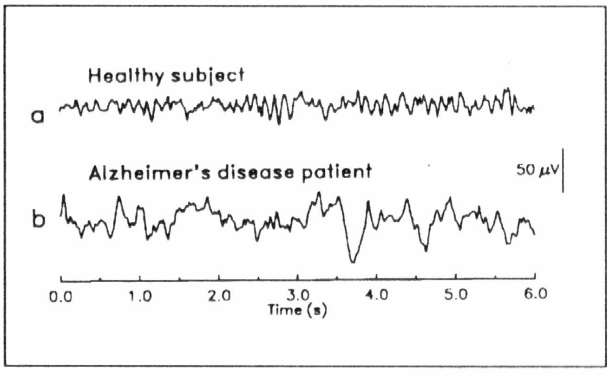

Fig. 1
EEG from a healthy subject does not show any abnormalities (a) while nonspecific slowing is seen in the EEG of the patient with Alzheimer's disease (b).

The EEG of the patient with Alzheimer's disease exhibited nonspecific slowing of background activity with irregular delta/theta waves (Fig. 1b). This corresponds to concentration of the frequency energy on the Wigner distribution within the delta and theta bands (Fig. 2b). Alpha activity was at a similar level as in the healthy subject

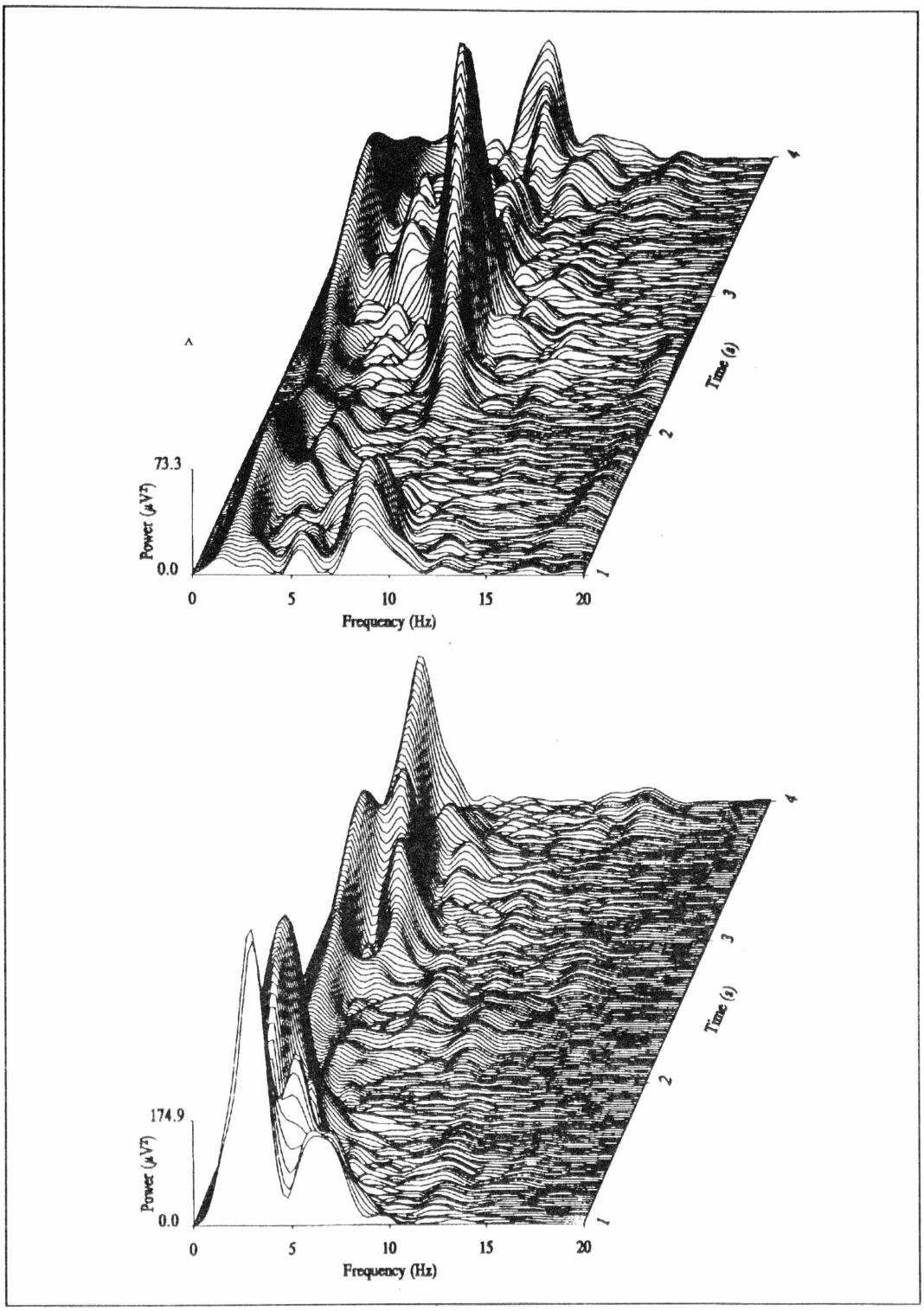

Fig. 2

The Wigner distribution of the healthy subject exhibit a concentration of the frequency content within the alpha band (above). The frequency content of the WD obtained from the Alzheimer's disease patient is concentrated below 7 Hz (below). The frequency content within the alpha band is on a similar level as that of the healthy subject (Note different scale and see Fig. 3).

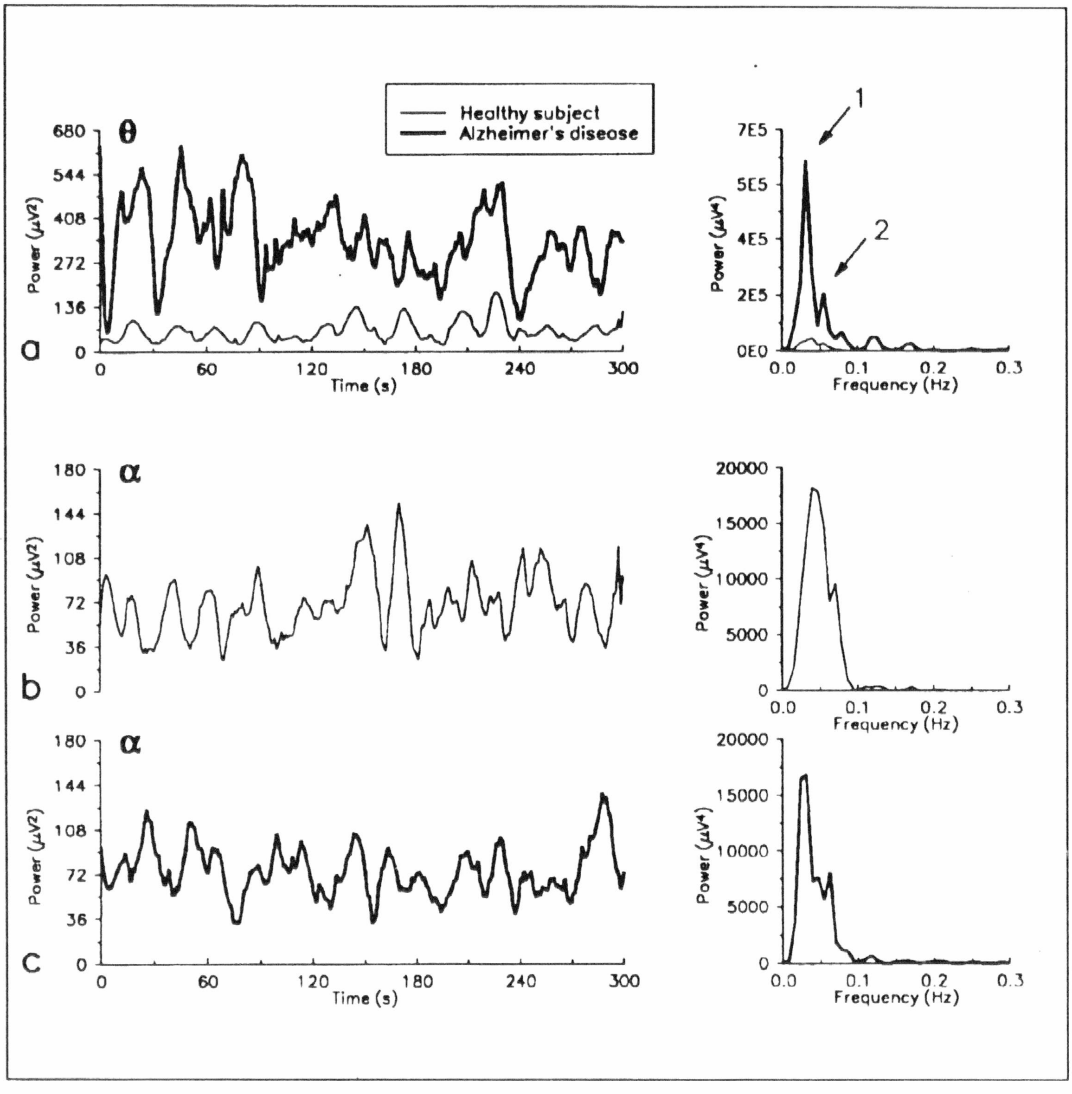

Fig. 3

Extracted envelope of the theta (a) and alpha (b,c) activities of both the healthy subject and the patient with Alzheimer's disease shows remarkable periodic fluctuations. These oscillations result in two peaks in the corresponding Fourier spectra (designated by arrows in the right panel).

Envelopes of the theta and alpha bands were extracted from the Wigner distribution in both subjects (Fig. 3). The Fourier spectra of the alpha and theta envelope revealed a dominant peak at 0.04 Hz in the normal subject and at 0.03 Hz in the patient with Alzheimer's disease. The absolute power of this peak was 6000 times higher in the patient with Alzheimer's disease than that of the healthy subject. The second peak, smaller in amplitude, was detected at 0.03 Hz and 0.06 Hz in the healthy subject and in the Alzheimer's patient, respectively.

Discussion

The time-frequency mapping confirmed our previous results, i.e. periodic oscillations of brain activity with a frequency below 0.08 Hz.

Slowing of the background EEG activity accompanied by an increase of absolute delta and theta power has been reported in patients with Alzheimer's disease (Leuchter *et al.* 1991, Giannitrapani *et al.* 1991). Similarly, delta/theta activity also dominated in our patient. Moreover, this patient exhibited a substantially higher amplitude of slow modulation than the normal subject. It should be stressed that these slow brain rhythms are not due to the baseline fluctuations of EEG. The mean and baseline fluctuations (<0.01 Hz) of the EEG as well as the mean of envelopes of the

theta/alpha activity were removed before computing the frequency characteristics.

In spite of the fact that this study is limited to two subjects, a high level of slow modulation in the patient with Alzheimer's disease is considered as an abnormal pattern. We have analyzed altogether slow rhythms in more than 150 healthy subjects in the age range of 20-65 years (Novák and Lepičovská 1992a, Novák *al.* 1992b, Novák *et al.* 1992, unpublished results) and we never observed such a high level of modulation of the resting EEG.

The assumption that the increase of slow rhythms can be a marker of a pathological process is supported by the report of Babloyantz (1991) who observed a non-baseline periodic pattern of EEG of the order of 58 s in a patient in the terminal stage of the Creutzfeldt-Jakob disease.

Whether the increased slow rhythms in the Alzheimer's disease patient can be attributed to the activation of the autonomic nervous system similar to that found in healthy subjects during hyperventilation (Novák and Lepičovská 1992a), or whether it appears as a result of structural changes of the central nervous system, such as degeneration of vagal neurones in the brain stem, which are observed in patients with Alzheimer's disease (Leuchter *et al.* 1991), should be clarified in subsequent studies.

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