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Spectral and Coherence Analysis of EEG during Intermittent Photic Stimulation in Patients with Photosensitive Epilepsy

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Abstract.

Objective: The aim of this study is to assess changes in the EEG dynamics preceding the transition to the photo-paroxismal response (PPR) in photosensitive patients
Methods: Occipital EEG derivations were considered in 10 photosensitive patients and 10 controls, both at rest and during intermittent photic stimulation (IPS) at 14, 3, 5, 10, 20 and 40 Hz. The two EEG signals were analysed by means of an autoregressive (AR) bivariate parametric model, and the correspondent autospectra and coherence function were qualitatively and quantitatively assessed.
Results: At rest, the coherence function showed an higher number of peaks in the patients compare with the controls, mostly in the gamma band. Also, during IPS at 14 at 10 Hz, where stimulus was more effective in producing PPR, high frequency iper-synchronization in the patients group was enhanced before the appearance of the paroxysmal response. The same did not happen at those frequencies not able to bring about to PPR
Conclusion: Results indicate an increased synchronization, mostly in beta and gamma bands, present at those frequencies able to sustain paroxysmal responses.

Keywords: photosensitive epilepsy, photic stimulation, autoregressive analysis, coherence, multichannel EEG.

1. Introduction

Photosensitive epilepsy (PSE) is the most common form of reflex epilepsy in humans. The prevalence of photosensitivity in patients with epilepsy ranges from 2 to 20%, and it is also possible to find it in non-epileptic individuals. PSE does not constitute an epilepsy syndrome on its own, because it can be found in all the main categories of epileptic disorders, but it offers a highly reproducible model to investigate whether changes in neuronal activity occurs before the transition to an epileptic response.
Photosensitivity is manifest in the EEG in the form of paroxysmal discharge, the so-called photoparoxysmal response (PPR), and it can be assessed in laboratory conditions with intermittent photic stimulation (IPS).
Though photosensitive EEG features have been known for a long time, the current understanding of the generation mechanisms is still limited, in particular concerning the relationship between the physiological and pathological responses during IPS. Previous studies suggest that the PPR originates in the cortex and involves the synchronization of large neuronal networks (Wilkins et al., 1979; Binnie et al., 1985; Harding and Fylan, 1999). It is believed that photosensitive individuals have lacking or impaired cortical mechanisms of contrast gain control which, for certain visual patterns of relatively low frequency and high luminance contrast, produce an abnormal excitatory response (Porciatti et al., 2000).
Recently, Parra et al.(2003), analysing MEG recordings, showed that an enhancement of synchrony, harmonically related to the frequency of the photic stimulation, occurs in the gamma band (30-120) preceded the stimulation trials that evolved into PPRs. This can be due to a failure of a control mechanism that normally operates to counteract the initial increase in synchrony brought about by visual stimulation.
The aim of this study is to assess spectral and coherence changes in the EEG preceding the transition to PPR, in order to understand how a normal steady-state evoked activity can degenerate into a PPR response. We performed the analysis using autoregressive methods that are known to be appropriate for

estimating the spectral properties of brief single EEG segments, lasting from a few hundred ms to several seconds (Gersch and Yonemoto, 1977)

2. Material and Methods

2.1 Patients

Among patients with known idiopathic generalized epilepsy (IGE) showing a paroxysmal response to photic stimulation during their EEG examination at the Department of Neurophysiology of the Foundation C. Besta Neurological Institute, we selected ten consecutive subjects (3 men and 7 women; mean age: 19.3±10 years) on condition that they had a sufficiently delayed onset of the PPR with respect to that of the photic stimulus train at 14 Hz allowing an adequate time window for the analysis. All patients had a normal neurological picture and normal MRI findings. Control population included 10 healthy volunteers (4 men and 6 women; mean age 19.3±6.1 years). Informed consent was obtained from all adult patients and subjects and from the parents of subjects' younger than 18 years.

2.2 EEG recording

EEG was recorded by means of Ag/AgCl surface electrodes placed on the scalp, according to the 10-20 International System. All the EEG signals were recorded using montages with a common reference electrode, using a Micromed computerised system (sampling frequency 256 Hz; band pass filter 1-70 Hz).
The recordings were obtained alternating rest and photic stimulation. IPS was performed at 14, 3, 5, 10, 20, 40 Hz (10 s for each frequency), with eyes closed; the time interval between each session was 10 s.

2.3 Data analysis

EEG signals recorded from occipital derivations were analysed. Before undergoing to spectral analysis, EEG signals were off-line reformatted via the laplacian reference (Perrin et al.1989). For each stimulation frequency, power spectra and coherence analysis was estimated on the 1.5 s epoch immediately preceding the stimulation and 1.5 s epoch after the IPS onset. At 14 and 10 Hz we also analysed an 1.5 s epoch immediately preceding the PPR in the patients group and a 1.5 s epoch starting 2.5 s after the IPS onset in the control group. Auto-spectra and inter-hemispheric coherence were calculated by means of a blockwise bivariate autoregressive model.
In particular, the power spectral density matrix , is given by:

$$S(f) = H(f) R \overline{H}(f)^T \tag{1}$$

where the matrix $H(f)$ is

$$H(f) = \left(I - \sum_{k=1}^{p} A_k e^{-j2\pi f k \Delta T} \right)^{-1} \tag{2}$$

with

p = model order

$A_1, A_2, \ldots A_p$ = 2x2 matrices of the bivariate AR model coefficients

R = covariance matrix of the input noise having a null mean value

I = 2x2 identity matrix

ΔT = sampling interval

the apical symbol 'T' denotes matrix transposition, while $\overline{H}$ stands for the complex conjugate of H.
The optimum model order p was determined using the multichannel version of the Final Prediction Error (FPE) criterion (Marple, 1987), after having verified the goodness of the identification with the Anderson's test on the residuals (Box and Jenkins,1971). Peak power and frequency were estimated by a spectral decomposition based on the residual method, taking into account for the analysis only peaks whose amplitude was higher than 5% of the total power.
The coherence spectrum is defined as the modulus of the normalised cross-spectrum

$$C_{xy}(f) = \frac{|S_{xy}(f)|}{\sqrt{S_{xx}(f) S_{yy}(f)}} \tag{3}$$

Where S_{xx} and S_{yy} are taken from the diagonal of the matrix S in eq.(1) and represent the power spectral density of the two EEG signals (x(t) and y(t) under study. S_{xy} is the off-diagonal element of S and represents the cross-spectrum.

According to Halliday et al (1995) the critical value for the null hypothesis of zero coherence is defined as

$$1 - \left(1 - \frac{\alpha}{100}\right)^{1/(L-1)} \tag{4}$$

where α is the significance level and L the degree of freedom of AR model, given by N/p (with N number of samples and p model order) (Jenkins and Watts, 1968).
For the evaluation of the number of coherence peaks, only the peaks whose amplitude was higher than the critical values with α=5% were considered.

All of the data analyses were performed using custom routines written in Matlab R2008b (Mathworks Inc., Natick, MA, USA). Results were statistically analysed by means of the two-sample t test.

3. Results

The effectiveness of the different stimulus frequencies in inducing a paroxysmal response in the analyzed patients is shown in Table 1. The 14 Hz stimulus was the most provocative one and the results here presented are mainly related to this frequency.

Table 1 *Percentage of patients who had PPR during IPS at different frequency stimulation*

	14 Hz	3 Hz	5 Hz	10 Hz	20 Hz	40 Hz
PPR	100 %	0 %	0 %	70 %	10 %	0 %

3.1 Basal EEG

In basal condition the autospectra of both groups were characterized by a dominant alpha peak and a peak in the beta band at double frequency. However, no difference between patient and control groups was found.
The coherence spectrum revealed a higher number of peaks in patients compared with the healthy subjects ($p<0.05$), difference mainly present in the gamma band where peaks number grew from a mean value of 2,3±0,7 in the control to a significantly higher value of 3±0,6 in the patients ($p<0.01$), as shown in Fig. 1.

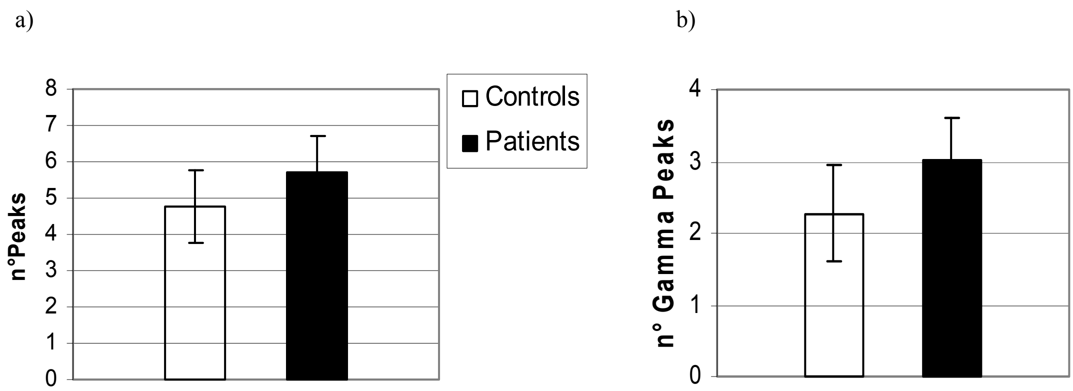

Fig. 1 mean value with standard deviation superimposed of the total number of peaks (a) and the number of peaks in the gamma band (b).

3.2 14 Hz IPS

During 14 Hz photic stimulation, in the spectra of both groups, power peaks appeared at IPS and twice IPS frequency, in some cases coexisting with alpha peaks, in others completely substituting it.
The coherence analysis revealed an higher peaks number in patients than in controls, mainly caused by an increased gamma band coherent activity. This difference is present both at the IPS onset, where the mean number of gamma band peaks grew from 5.7±1.3 in the controls group to 6.9±1.2 in the patients one, and in the epoch preceding the PPR, where the number of peaks rose from 6.1±1.5 to 7.6±1.4 ($p<0.05$).
At the IPS onset, beta peaks amplitude significantly rose compared with the basal condition, for both controls and patients but, interestingly, in the controls immediately afterwards it decreased to basal value, whereas in the patients high beta band coherence persisted for the entire stimulus train.
Another meaningful result is that the main peak of the coherence spectra, which was centered at IPS frequency in the controls, shifted to higher harmonics in the patients group, mainly in the gamma range (42-56 Hz) (Fig. 2). All these evidences indicate an increased synchrony preceding the PPR in the PSE patients.

3.3 10-3-5-20-40 Hz IPS

At 10 Hz stimulus, where 70% of patients had PPR, enhancement of coherent activity in the gamma band in the patients group were found; at the IPS onset, indeed, the mean number of gamma band peaks grew from 2.3±1.6 of the controls to 3.5±1.4 of the patients.
On the contrary, at the other frequencies, where IPS did not bring about a paroxysmal response, no significant differences in coherence between patient and controls appeared during IPS.

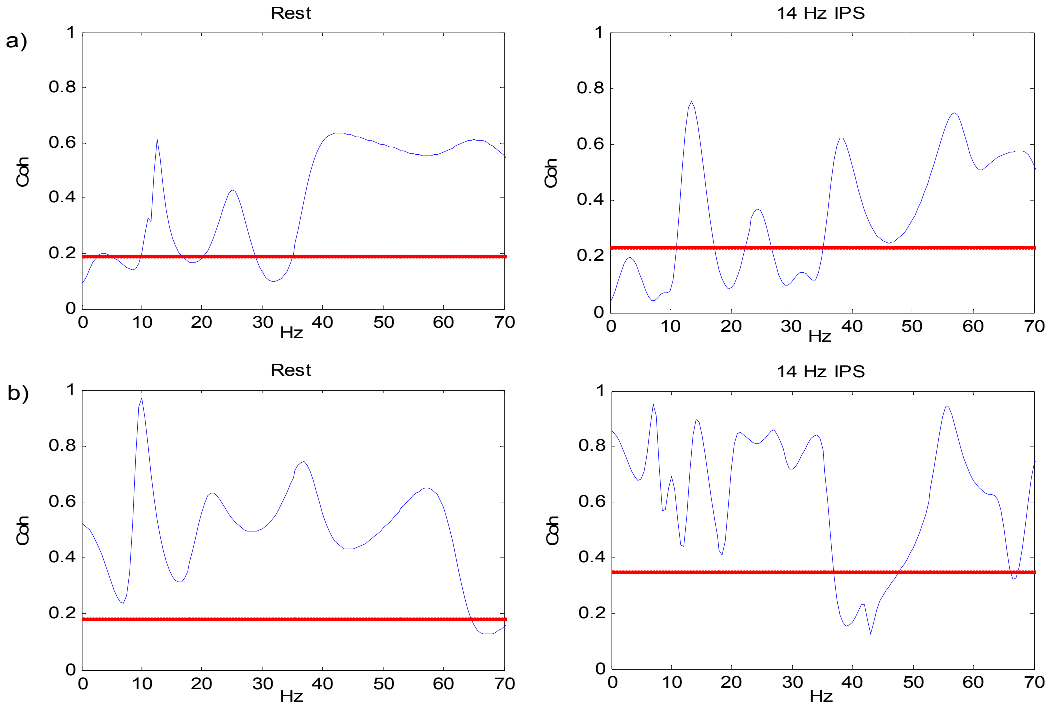

Fig. 2 Coherence spectra from occipital derivations at rest an during 14 Hz stimulus for a) controls group and b) patients group

4. Discussion and conclusion

Our results indicate that PSE subjects, compared with controls, show an enhancement of synchronization, mainly in the beta and gamma range, provided that the photic stimulation induces an aberrant response.

These results substantially confirm and extend the findings of Parra et al. (2003) obtained by using the Phase Clustering Index (PCI) . However our data differs from those of Parra as far as resting condition, where we found that a greater coherent activity at high frequencies was already present in patients with respect to controls. This difference was enhanced during IPS, when it led to PPR.
At the frequency of 14 Hz, which is well know in clinical practice as one of the most effective frequency in inducing PPR, coherent gamma activity is significantly greater in the PSE-patients, mainly in the epoch immediately preceding the photo-paroxysmal response, according with the idea that fast synchronized activity is often linked with the appearance of various form of epileptic seizures (Allen et al.,1992; Fisher et al., 1992; Alarcon et al.,1995; Traub at al.,2001). Moreover, high coherence values were found at the onset of IPS in all subjects but, while in controls the coherence values immediately came back to the basal one, they persisted until the beginning of the paroxysmal response. This confirms the idea that, in physiological condition, there is a control mechanism able to counteract the increase in synchrony due to the stimulus, but this control is ineffective in PSE-patients when IPS leads to PPR.

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