DISCRIMINATING OCD PATIENTS FROM HEALTHY CONTROLS USING PATTERN RECOGNITION METHODS ON THE P600 COMPONENT OF ERP SIGNALS

I. Kalatzis*, E. Ventouras*, N. Piliouras*, D. Glotsos**, C. Papageorgiou***/****, A. Rabavilas****, C. Soldatos***, D. Cavouras*

* Department of Medical Instrumentation Technology, Technological Educational Institution of Athens, Athens, Greece
** Department of Medical Physics, University of Patras, Patras, Greece
*** Department of Psychiatry, Eginition Hospital, Medical School, University of Athens, Athens, Greece
**** University Mental Health Research Institute, Athens, Greece

cavouras@teiath.gr

Abstract: A series of inverted Event-Related Potential (ERP) signals were analyzed with pattern recognition methods using new morphological features and powerful classifiers, in an attempt to develop a computer-aided discrimination system of OCD patients from controls. Eighteen OCD patients and twenty controls were examined. All subjects were evaluated by a computerized version of the digit span subtest of the Wechsler Adult Intelligence Scale. EEGs were recorded from 15 scalp leads, and they were inverted to intracranial current sources using the BET-ART method. 60 source locations were positioned on a spherical shell corresponding to the outer layers of the cortex. From the P600 component of each signal nineteen waveform-features were calculated. The Probabilistic Neural Network (PNN) classifier was developed, and it was fed with feature combinations from all source locations. Highest overall accuracy (84.2%) was found at the right frontal brain region indicating that OCD patients may present deficits related to working memory mechanisms corresponding to that region.

Introduction

Event-realted potentials (ERPs) are neuronal signals occuring as small voltage fluctuations in Electroencephalogram (EEG) recordings. ERPs reflect the electric respone of the central nervous system activity, which is evoked by visual or audio stimuli. The P600 component of the ERPs, that appears between 500 and 800ms poststimulus, has been associated with the function of the hippocampus [1-3], which is related to working memory (WM) operation [4-6]. Recent neuropsychological studies have implicated WM-deficits in the manifestation of obsessive-compulsive disorders (OCD), even though brain mechanisms underlying WM-deficits are still a subject of ongoing investigation [7]. In the present study, a pattern recognition system was developed for discriminating OCD patients from healthy controls, using the P600 component of the ERP signals, in an attempt to locate brain areas that may be related to WM deficits.

Material and Methods

Subjects: Eighteen OCD patients and twenty age and gender-matched healthy controls were examined. The controls were recruited from hospital staff and local volunteer groups. Both patients and controls had no history of any neurological or hearing problems and they were right-handed as assessed by the Edinburgh Inventory [8]. Written informed consent was obtained from all subjects.

Recordings: All participants were evaluated by a computerized version of the digit span Wechsler test [9,10]. The EEG activity was recorded from 15 scalp leads (Fp1, Fp2, F3, F4, C3, C4, C5, C6, P3, P4, O1, O2, Pz, Cz, and Fz [11], see Fig. 1a). ERPs were inverted to intracranial current sources by means of the Brain Electromagnetic Tomography method using Algebraic Reconstruction Techniques (BET-ART) (see Fig. 1b) [12].

Features generation: Nineteen (19) features related to the time window between 500 and 800 msec of the waveform of the intracranial current signal were generated, by means of custom-developed software for the purposes of the present study (see Fig. 2). Features with highest discriminatory power that were employed in the design of the classification system are described in the following relations (1-7):

1. Latency (LAT) is the time interval to maximum signal value:

$$LAT = tsmax = \{t \mid s(t) = smax\} \quad (1)$$

where $s(t)$ is the signal value at time t after stimulus.

2. Positive area (PAR) is the sum of the positive signal values:

ISSN: 1727-1983

$$PAR = A_p = \sum_{t=500ms}^{800ms} \left\{0.5 \cdot \left(s(t) + \left|s(t)\right|\right)\right\} \qquad (2)$$

3. Absolute negative area (ANAR) is the absolute value of the sum of the negative signal values:

$$ANAR = \left|A_n\right| = \left| \sum_{t=500ms}^{800ms} \left\{0.5 \cdot \left(s(t) - \left|s(t)\right|\right)\right\} \right| \qquad (3)$$

4. Average absolute signal slope (TAAS) is the mean of consecutive signal-values slopes:

$$\overline{|\dot{s}|} = \frac{1}{n} \cdot \sum_{t=500ms}^{800ms-\tau} \left(\frac{1}{\tau} \cdot \left| s(t+\tau) - s(t) \right| \right) \qquad (4)$$

where τ is the sampling interval of the signal (τ =2ms, for the sampling rate of 500Hz), n is the number of samples of the digital signal (actual n = (800ms -500ms) / 2ms = 150), and $s(t)$ the signal value of the *t-th* sample.

5. Peak-to-peak slope (PPS) is the slope of the line connecting the maximum and the minimum signal points:

$$\dot{s}_{pp} = \frac{pp}{t_{pp}} \qquad (5)$$

where $pp = s_{max} - s_{min}$, $s_{max} = \max\{s(t)\}$ and $s_{min} = \min\{s(t)\}$ are the maximum and the minimum signal values respectively, and $t_{pp} = t_{s_{max}} - t_{s_{min}}$.

6. Zero crossings (ZC) is the number of times where the signal is equal to zero:

$$ZC = \sum_{t=500ms}^{800ms-\tau} \delta_s \qquad (6)$$

where δ_s=1 if $s(t)$=0, 0 otherwise.

7. Slope sign alterations (SSA) is the number of slope sign alterations of two adjacent points of the ERP signal:

$$\mathrm{SSA} = \sum_{t=500ms+\tau}^{800ms-\tau} 0.5 \cdot \left| \frac{s(t-\tau) - s(t)}{\left|s(t-\tau) - s(t)\right|} + \frac{s(t+\tau) - s(t)}{\left|s(t+\tau) - s(t)\right|} \right| \qquad (7)$$

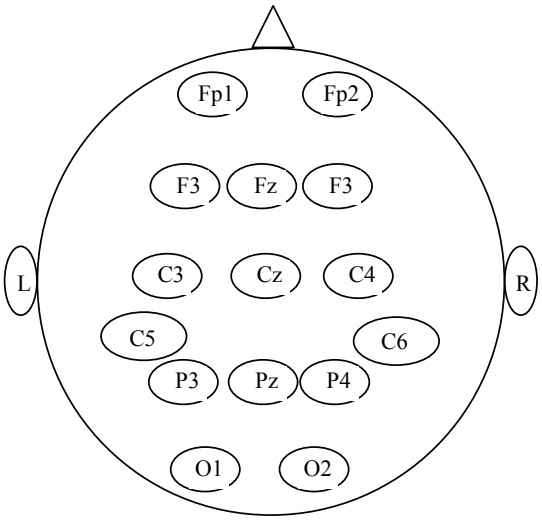

Figure 1a: Schematic diagram of lead distribution.

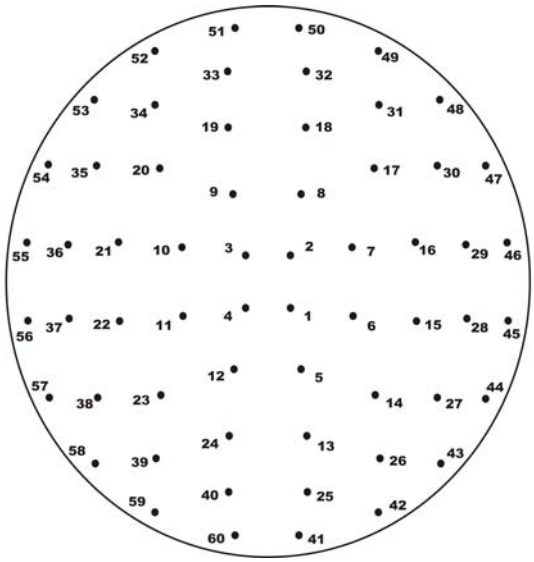

Figure 1b: Intracranial current source positions.

Classification: The Probabilistic Neural Network (PNN) [13] was implemented by a feed-forward and one-pass structure and encapsulates the Bayes' decision rule together with the use of Parzen estimators of data's probability distribution function (PDF). The PNN classifier was chosen due to its non-parametric nature and because its training is easy and instantaneous [13], especially in comparison with the back-propagation neural network and the support vector machine classifiers. Also, the small number of cases in both group requires a non-parametric classifier, as PNN, which do not depends from the data's PDF. Features were combined in pairs of all possible combinations to form pattern vectors at each intracranial source for the two classes (OCD patients and controls). The pattern vectors fed a PNN with a Gaussian kernel-based discriminant function given in equation (8):

$$g_k(\mathbf{x}) = \frac{1}{(2\pi)^{d/2} \prod_{j=1}^{d} \sigma_j} \frac{1}{N_k} \sum_{i=1}^{N_k} \exp\left[-\frac{1}{2} \sum_{j=1}^{d} \left(\frac{x_j - x_{ij}}{\sigma_j} \right)^2 \right] \qquad (8)$$

where $\mathbf{x} = [x_1\ x_2\ \ldots\ x_d]^T$ is the test pattern vector to be classified, $\mathbf{x}_i$ is the i-th training pattern vector, N_k is the number of patterns in class k, σ_j are the standard deviations of the distributions of the pattern vector element variables, and d is the feature space dimensionality. The test pattern $\mathbf{x}$ is classified to the class with the higher discriminant function value.

The performance of the classification system was evaluated by means of the leave-one-out method and results were presented in truth tables that revealed the classifier's discriminatory ability.

Results and Discussion

In the present study, the goal was to investigate whether a number of features, that were extracted from the waveform of inverted ERP signals, may distinguish

ISSN: 1727-1983

OCD patients from normal controls. This distinction is not evident, as may be realized in Figure 3, which shows a scatter diagram of the latency and the amplitude of the P600 component, of an intracranial current source lying at the right frontal brain area (source 32, see Fig. 1b).

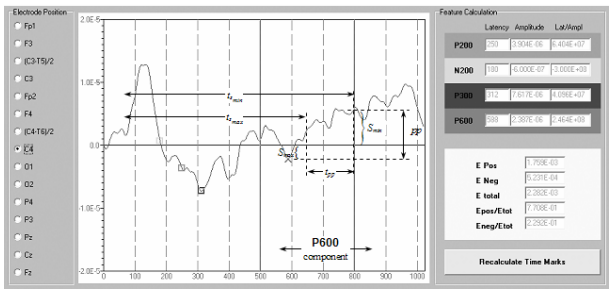

Figure 2: Interface of the custom-made software system designed to read ERP signals and for feature extraction.

It is worthy of noticing that the *amplitude* and the *latency* of the ERP components are features commonly employed by psychiatrists in assessing ERP signals. However, the quantitative assessment of these features has shown a significant overlap between OCDs and controls, as can be observed from Figure 3. This actually means that the most usual clinically investigated features, which are also relatively easy to evaluate by visual inspection, may lead to no conclusive evidence of differences between the two groups of subjects.

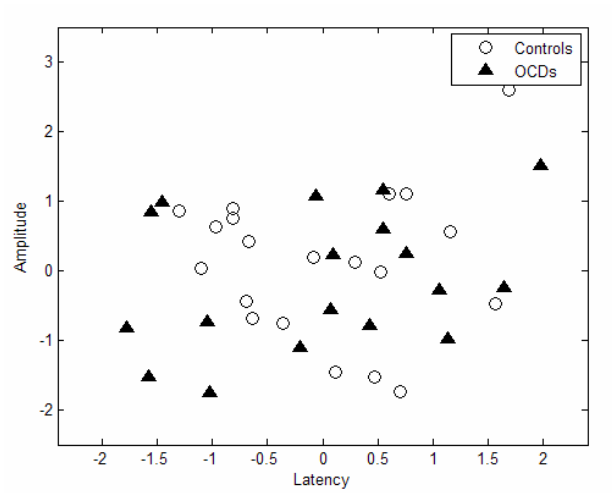

Figure 3: Amplitude-Latency scatter diagram of an intracranial current source lying at the right frontal brain area.

Higher classification accuracy was 84.2% achieved for a source located in the right frontal brain region, using the feature combination "total signal area" and "peak-to-peak signal slope". As it may be observed from Table 1, one OCD patient and five healthy controls were misclassified, resulting in 94.4% sensitivity and 75.0% specificity. A graphical representation of the discrimination result is shown in Figure 4.

Table 1: Truth table of OCDs vs. Controls classification (source located in the right frontal brain region)

	Classification		
Subjects	**Controls**	**OCDs**	
Controls	15	5	75.0% (Specificity)
OCDs	1	17	94.4% (Sensitivity)
	93.7% (NPV*)	72.3% (PPV**)	84.2% (Overall)

* NPV: Negative predictive value
** PPV: Positive predictive value

The differences between OCD patients and normal controls in right frontal brain region are important since ERPs from the temporo-central region have been previously associated with the subject's effort to respond to evoked stimuli [14].

Conclusions

Intracranial current sources combined by pattern recognition methods on the P600 component indicate that right frontal brain regions may be implicated in the mechanisms responsible for the manifestation of WM deficits characterizing the OCDs' behaviour.

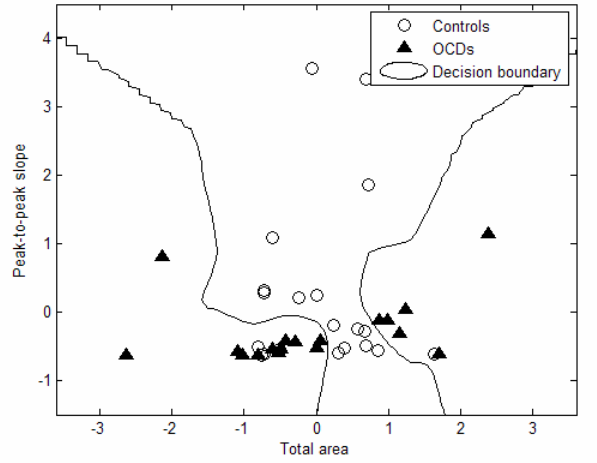

Figure 4: Scatter diagram for best feature combination of an intracranial current source lying at the right frontal brain area.

Acknowledgment

The present research was carried for the project "Development of an Evoked Potentials and Intracranial Current Classification System using Support Vector Machines (SVM) and Probabilistic Neural Networks (PNN)" co-funded by 75% from the European Union and 25% from the Greek Government under the framework of the Education and Initial Vocational Training Program – Archimedes.

ISSN: 1727-1983

References

[1] POLICH J. (1998): 'P300 Clinical Utility and Control of Variability', *J. Clin. Neurophysiol.*, Vol. 15, pp. 14-33.

[2] GUILLEM F., N'KAOUA B., ROUGIER A., and CLAVERIE B. (1998): 'Location of the Epileptic Zone and its Physiopathological Effects on Memory-Related Activity of the Temporal Lobe Structures: A Study with Intracranial Event-Related Potentials', *Epilepsia*, Vol. 39, pp. 928-941.

[3] GRUNWALD T., BECK H., LEHNERTZ K., BLUMCKE I., PEZER N., KUTAS M., KURTHEN M., KARAKAS H.M., VAN ROOST D., WIESTLER O.D., and ELGER C.E. (1999): 'Limbic P300s in Temporal Lobe Epilepsy with and without Ammon's Horn Sclerosis', *Eur. J. Neurosci.*, Vol. 11, pp. 1899-1906.

[4] GARCIA-LARREA L. and CEZANNE-Bert G. (1998): 'P3, Positive Slow Wave and Working Memory Load: A Study on the Functional Correlates of Slow Wave Activity', *Electroencephalography and Clinical Neurophysiology*, Vol. 108, pp. 260 – 273.

[5] GUILLEM F., ROUGIER A., and CLAVERIE B. (1999): 'Short- and Long-Delay Intracranial ERP Repetition Effects Dissociate Memory Systems in the Human Brain', *J. Cogn. Neurosci.*, Vol. 11, pp. 437-458.

[6] FRISCH S., KOTZ S., VON CRAMON D., and FRIEDERICI A. (2003): 'Why the P600 is not just a P300: the Role of the Basal Ganglia', *Clinical Neurophysiology*, Vol. 114, pp. 336–340.

[7] PAPAGEORGIOU C. and RABAVILAS A. (2003): 'Abnormal P600 in Obsessive–Compulsive Disorder. A Comparison with Healthy Controls', *Psychiatry Research* 119:133–143.

[8] OLDFIELD R.C. (1971): 'The Assessment and Analysis of Handedness: The Edinburgh Inventory', *Neuropsychologia*, vol. 9, pp. 97-113, 1971.

[9] WECHSLER, D. (1955): 'Manual for the Wechsler Adult Intelligence Scale', (Psychological Corporation, New York).

[10] PAPAGEORGIOU C., VENTOURAS E., UZUNOGLU N., RABAVILAS A., and STEFANIS C. (2002): 'Changes of P300 Elicited during a Working Memory Test in Individuals with Depersonalization-Derealization Experiences', *Neuropsychobiology*, vol. 46, pp. 70-75.

[11] JASPER H. (1958): 'The Ten-Twenty Electrode System of the International Federation', *Electroenceph. Clin. Neurophysiol*, vol. 10, pp. 371-375.

[12] VENTOURAS E., PAPAGEORGIOU C., RABAVILAS A., UZUNOGLU N., STEFANIS C. (1999): 'Brain Electrical Tomography using Algebraic Reconstruction Techniques', *Biotechnol. Biotechnol. Eq*. 13:113-118.

[13] SPECHT D. F. (1990): 'Probabilistic Neural Networks', *Neural Networks* 3:109-118.

[14] PAPAGEORGIOU, C., RABAVILAS, A., LIAPPAS, I., STEFANIS, C. (2003): 'Do Obsessive-Compulsive Patients and Abstinent Heroin Addicts Share a Common Psychophysiological Mechanism?', *Neuropsychobiology* Vol. 47, pp. 1-11.

ISSN: 1727-1983