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Identifying Differences in the P600 Component of ERP-Signals between OCD Patients and Controls Employing a PNN-based Majority Vote Classification Scheme

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Abstract–**In the present study an attempt was made to focus in the differences between Obsessive-Compulsive Disorder (OCD) patients and healthy controls, as reflected by the P600 component of event-related potential (ERP) signals, to locate brain areas that may be related to Working Memory (WM) deficits. Neuropsychological research has yielded contradicting results regarding WM in OCD. Eighteen patients with OCD symptomatology and 20 normal controls (age and sex matched) were subjected to a computerized version of the digit span Wechsler test. EEG activity was recorded from 15 scalp electrodes (leads). A dedicated computer software was developed to read the ERP signals and to calculate features related to the ERP P600 component (500-800 ms). Nineteen features were generated, from each ERP-signal and each lead, and were employed in the design of the Probabilistic Neural Network (PNN) classifier. Highest single-lead precision (86.8%) was found at the Fp2 and C6 leads. When the output from all single-lead PNN classifiers fed a Majority Vote Engine (MVE), the system classified correctly all subjects, providing a powerful classification scheme. Findings indicated that OCD patients differed from normal controls at the prefrontal and temporo-central brain regions.**

Keywords–**Obsessive-compulsive disorder, event-related potential, pattern recognition, probabilistic neural network**

I. Introduction

Event-related potentials (ERPs) are specific EEG signals, that are recorded after audio or visual stimuli, and consist of a series of electrical potentials (ERP components). The P600 is a late positive component, elicited between 500 and 800ms after stimulus presentation, and it has been linked to hippocampal function [1-3], having much in common with working memory (WM) operation [4-6].

Obsessive-Compulsive Disorder (OCD) patients have been previously examined for WM disorders using standard neuropsychological tests and/or experimental behavioural tests, but their results are contradicting; some studies have detect dysfunctions of WM in OCD patients [11-14], while others have found no impairments [15-17]. Recently, however, OCD patients have been examined employing ERP-signals, detecting differences at right temporoparietal and parietal regions in the P600 component [18].

In the present study a probabilistic neural network-based majority-vote classification scheme is proposed, in an attempt to achieve high discrimination between OCD patients and healthy controls, using characteristics extracted from the P600 ERP-signals.

II. Materials and Methods

In this study, 18 patients with OCD symptomatology and 20 age and sex matched healthy controls were examined. The controls were recruited from hospital staff and local volunteer groups and they were free of physical illness. All participants had no history of any neurological or hearing problems. All participants were right-handed as assessed by the

Edinburgh Inventory [19]. Written informed consent was obtained from both patients and controls. OCD patients and controls were evaluated by a computerized version of the digit span Wechsler test [20,21]. ERP signals were recorded from 15 scalp electrodes; abductions set at Fp1, Fp2, F3, F4, C3, C4, C5, C6, P3, P4, O1, O2, Pz, Cz, and Fz [22], as shown at Fig. 1.

Features related to the P600 component of the ERP signals were calculated using a dedicated computer software. Feature values are normalized to zero mean and unit standard deviation [23]. A total of 19 features were extracted from each ERP-signal; the features with highest discriminatory power that were employed in the design of the design of the classification system are described in the following equations (1-7):

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

$$\mathrm{LAT} = t_{s_{max}} = \{t \mid s(t) = s_{max}\} \quad (1)$$

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

2. Absolute Amplitude (AAMP) is the absolute value of maximum signal value:

$$\mathrm{AAMP} = |s_{max}| \quad (2)$$

3. Absolute Latency/Amplitude ratio (ALAR):

$$\mathrm{ALAR} = |t_{s_{max}}/s_{max}| \quad (3)$$

4. Peak-to-peak time window (PPT) is the time interval between moments where maximum and minimum signal values appear:

$$\mathrm{PPT} = t_{s_{max}} - t_{s_{min}} \quad (4)$$

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

$$\mathrm{ZC} = \sum_{t=500ms}^{800ms-\tau} \delta_s \quad (5)$$

where δ_s=1 if $s(t)$=0, 0 otherwise.

6. Zero crossings density in peak-to-peak time (ZCDPP) is the frequency of zero crossings in peak-to-peak time window:

$$\mathrm{ZCDPP} = \frac{n_{zc}}{t_{pp}} \quad (6)$$

where n_{zc} are the zero crossings and t_{pp} is the peak-to-peak time window.

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

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

where τ is the sampling interval of the signal (τ =2ms, for the sampling rate of 500Hz).

The Probabilistic Neural Network (PNN) [24] was implemented by a feed-forward and one-pass structure and encapsulate the Bayes' decision rule together with the use of Parzen estimators of data's probability distribution function. The discriminant function of a PNN classifier for class k is given by the following equation:

$$g_k(\mathbf{x}) = \frac{1}{(2\pi)^{d/2}\sigma^d N_k} \sum_{i=1}^{N_K} \exp\left(-\frac{(\mathbf{x}-\mathbf{x}_{ki})^T(\mathbf{x}-\mathbf{x}_{ki})}{2\sigma^2} \right) \quad (8)$$

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 is a smoothing parameter, and d is the feature space dimensionality. The test pattern $\mathbf{x}$ is classified to the class with the larger discriminant function value.

For classifying a subject as belonging to either the "OCDs" or "controls" category, a classification system was developed based on our previous work [25] as shown in Fig. 1. At each lead there is a PNN classifier working, designed to use the lead's particular best P600 features and to assign the P600 component to one of two classes. The outcome of each lead (either "OCD" or "control") is collected by a Majority-Vote Engine (MVE), which decides on the class by a majority-vote rule.

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.

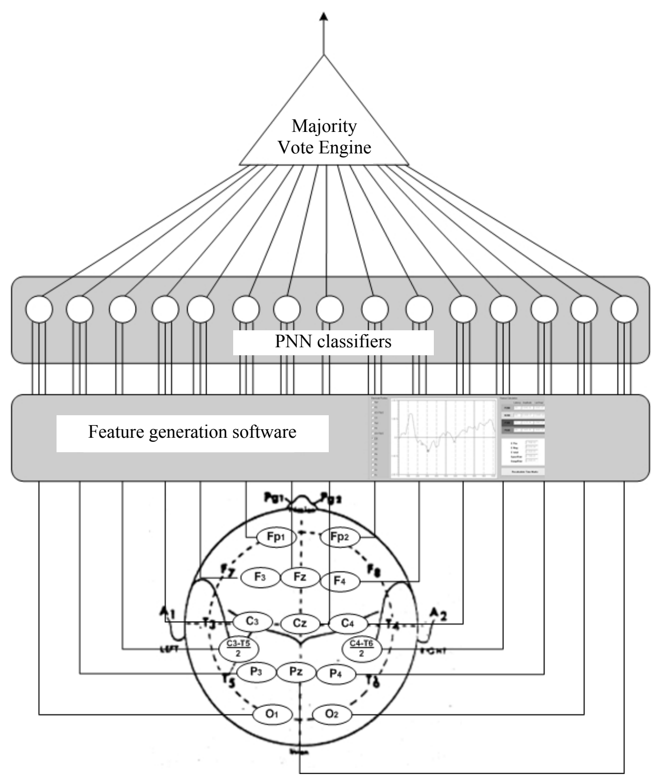

Fig. 1: Schematic diagram of lead distribution and network of PNN classifiers with the Majority-Vote Engine.

III. RESULTS AND DISCUSSION

Highest single-lead precision (86.8%) was found at the Fp2 and C6 leads. When the classification result of all single-lead PNN classifiers passed through a Majority Vote Engine (MVE), the system classified correctly all subjects. Tables I and II show best results and best feature combinations obtained at the Fp2 and C6 abductions by the PNN classifier employing the leave-one-out method. Fig. 2 illustrates the best 2-features combination at lead C6 with the PNN decision boundary. Outliers (see Fig.2 and Tables I and II) may be due to noise in the ERP signals caused by the recording procedure.

In a previous study by our group [25], a similar classification scheme was employed to discriminate between depressive patients and healthy controls and it was found that the use of the SVM classifier at each electrode gave higher classification accuracies than the PNN, while in the present study the opposite is true. This may imply that the choice of classifier is application specific, although the majority vote end-stage in both classification schemes gave best results.

The differences between OCD patients and normal controls at Fp2 and C6 abduction are important since ERPs from the temporo-central region have been previously associated with the subject's effort to respond to evoked stimuli [26]. In addition, in a recent MRI study differences between OCD patients and normal controls were found at the posterior orbitofrontal and right parietal regions [27] and, in a recent study employing PET, differences were found at the right parietal region, which was associated with the severity of OCD symptoms [28].

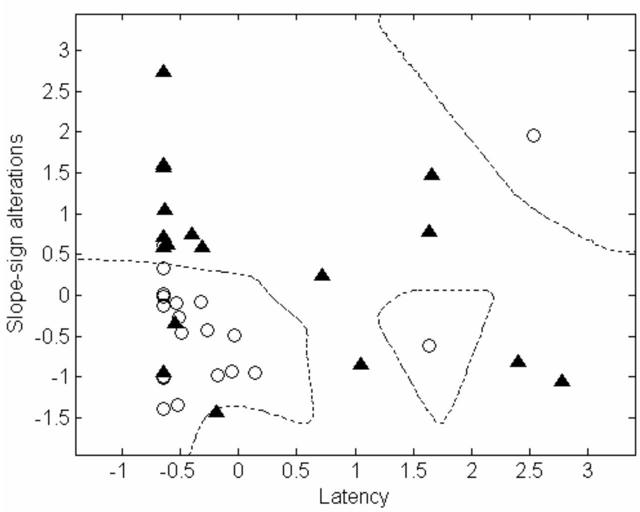

Fig. 2: Best 2-feature/lead C6 combination diagram with PNN decision boundary (triangles: OCDs, circles: controls). Feature values are normalized [23].

TABLE I
BEST FEATURE COMBINATION AT LEAD FP2 (LAT, ALAR, ZCDPP, SSA), EMPLOYING THE PNN CLASSIFIER WITH THE LEAVE-ONE-OUT METHOD.

Fp2 lead PNN classification

Groups	OCDs	Controls	Accuracy	
OCDs	14	4	77.8%	(Sens.*)
Control	1	19	95.0%	(Spec.*)
Accuracy	93.3%	82.6 %	86.8%	
	(PPV*)	(NPV*)	(Overall)	

* Spec. =Specificity
Sens. =Sensitivity
PPV = Positive Predictive Value
NPV = Negative Predictive Value

TABLE II
BEST FEATURE COMBINATION AT LEAD C6 (AAMP, PPT, ZC, ZCDPP), EMPLOYING THE PNN CLASSIFIER WITH THE LEAVE-ONE-OUT METHOD.

C6 lead PNN classification

Groups	OCDs	Controls	Accuracy	
OCDs	16	2	88.9%	(Sens.*)
Control	3	17	85.0%	(Spec.*)
Accuracy	84.2%	89.5 %	86.8%	
	(PPV*)	(NPV*)	(Overall)	

* Spec. =Specificity
Sens. =Sensitivity
PPV = Positive Predictive Value
NPV = Negative Predictive Value

In conclusion, these findings may be indicative that OCD patients present deficits related to WM mechanisms, corresponding to prefrontal and temporo-central regions, as reflected by the P600 component.

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REFERENCES

[1] J. Polich, "P300 clinical utility and control of variability," *J. Clin. Neurophysiol.*, vol. 15, pp. 14-33, 1998.

[2] F. Guillem, B. N'Kaoua, A. Rougier, and B. Claverie, "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, 1998.

[3] T. Grunwald, H. Beck, K. Lehnertz, I. Blumcke, N. Pezer, M. Kutas, M. Kurthen, H.M. Karakas, D. Van

Roost, O.D. Wiestler, and C.E. Elger, "Limbic P300s in temporal lobe epilepsy with and without Ammon's horn sclerosis", *Eur. J. Neurosci.*, vol. 11, pp. 1899-1906, 1999.

[4] L. Garcia-Larrea and G. Cezanne-Bert, "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, 1998.

[5] F. Guillem, A. Rougier, and B. Claverie, "Short- and long-delay intracranial ERP repetition effects dissociate memory systems in the human brain," *J. Cogn. Neurosci.*, vol. 11, pp. 437-458, 1999.

[6] S. Frisch, S. Kotz, D. von Cramon, and A. Friederici, "Why the P600 is not just a P300: the role of the basal ganglia," *Clinical Neurophysiology*, vol. 114, pp. 336–340, 2003.

[10] C.M. Zielinski, M.A. Taylor, and K.R. Juzwin, "Neuropsychological deficits in obsessive-compulsive disorder," *Neuropsychiatry, Neuropsychology and Behavioral Neurology*, vol. 4, pp. 110-126, 1991.

[11] K.B. Boone, J. Anath, L. Philot, A. Kauer, and A. Djenderedjian, "Neuropsychological characteristics of nondepressed adults with obsessive-compulsive disorder," *Neuropsychiatry, Neuropsychology and Behavioral Neurology*, vol. 4, pp. 96-109, 1991.

[12] K.J. Christensen, S.W. Kim, M.W. Dysken, and K.M. Hoover, "Neuropsychological performance in obsessive-compulsive disorder," *Biological Psychiatry*, vol. 31, pp. 4-18. 1992.

[13] R. Purcell, P. Maruff, M. Kyrios, and C. Pantelis, "Neuropsychological deficits in obsessive-compulsive disorder. A comparison wth unipolar depression, panic disorder, and normal controls," *Archives of General Psychiatry*, vol. 55, pp. 415-423, 1998.

[14] R. Barnett, P. Maruff, R. Purcell, K. Wainwright, M. Kyrios, W. Brewer, and C. Pantelis, "Impairment of olfactory identification in obsessive-compulsive disorder," *Psychological Medicine*, vol. 29, pp. 1227-1233, 1999.

[15] S. Galderisi, A. Mucci, F. Catapano, A.C. D'Anato, and M. Maj, "Neurophysical slowness in obsessive-compulsive patients. Is it confined to test involving the frontal-subcortical systems?" *British Journal of Psychiatry*, vol. 167, pp. 394-398, 1995.

[16] A. Martin, C.L. Wiggs, M. Altemus, C. Rubenstein, and D. Murphy, "Working memory as assessed by subject-ordered tasks in patients with obsessive-compulsive disorder," *Journal of Clinical and Experimental Neuropsychology*, vol. 17, pp. 786-792, 1995.

[17] R. Gross-Isseroff, Y. Sasson, H. Voet, T. Hendler, K. Luca-Halimovici, H. Kandel-Sussman, and J. Zohar, "Alternation learning in obsessive-compulsive disorder," *Biological Psychiatry*, vol. 39, pp. 733-738, 1996.

[18] C.C. Papageorgiou and A.D. Rabavilas, "Abnormal P600 in obsessive–compulsive disorder. A comparison with healthy controls,", *Psychiatry Research*, vol. 119, pp. 133-143, 2003.

[19] R.C. Oldfield, "The Assessment and Analysis of Handedness: The Edinburgh Inventory", *Neuropsychologia*, vol. 9, pp. 97-113, 1971.

[20] D. Wechsler, *Manual for the Wechsler Adult Intelligence Scale*. New York, NY: Psychological Corporation, 1955.

[21] C. Papageorgiou, E. Ventouras, N. Uzunoglu, A. Rabavilas, and C. Stefanis, "Changes of P300 Elicited During a Working Memory Test in Individuals with Depersonalization-Derealization Experiences," *Neuropsychobiology*, vol. 46, pp. 70-75, 2002.

[22] H. Jasper, "The Ten-Twenty Electrode System of the International Federation", *Electroenceph. Clin. Neurophysiol*, vol. 10, pp. 371-375, 1958.

[23] S. Theodoridis and K. Koutroumbas, *Pattern Recognition*, San Diego, CA: Academic Press, 1998

[24] D.F. Specht, 'Probabilistic Neural Networks', *Neural Networks*, vol. 3, pp. 109–118, 1990.

[25] I. Kalatzis, N. Piliouras, E. Ventouras, C.C. Papageorgiou, A.D. Rabavilas, and D. Cavouras, "Design and Implementation of an SVM-based Computer Classification System for Discriminating Depressive Patients from Healthy Controls using the P600 Component of ERP Signals", *Computer Methods and Programs in Biomedicine*, vol. 75, pp. 11-22, 2004.

[26] C. Papageorgiou, A. Rabavilas, I. Liappas, C. Stefanis, "Do obsessive-compulsive patients and abstinent heroin addicts share a common psychophysiological mechanism?" *Neuropsychobiology*, vol. 47, pp. 1-11, 2003.

[27] A. A. Valente Jr., E. C. Miguel, C. C. Castro, E. Amaro Jr., F. L.S. Duran, C. A. Buchpiguel, X. Chitnis, P. K. McGuire, and G. F. Busatto, "Regional Gray Matter Abnormalities in Obsessive-Compulsive Disorder: A Voxel-Based Morphometry Study," *Biological Psychiatry*, in press.

[28] N. J. A. van der Wee, N. F. Ramsey, J. M. Jansma, D. A. Denys, H. J. G. M. van Megen, H. M.G. Westenberg, and R. S. Kahn, "Spatial working memory deficits in obsessive compulsive disorder are associated with excessive engagement of the medial frontal cortex," *NeuroImage*, vol. 20, pp. 2271–2280, 2003.