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SIGNAL ANALYSIS METHODS TO DISCRIMINATE BETWEEN OBSESSIVE-COMPULSIVE DISORDER (OCD) PATIENTS AND HEALTHY CONTROLS

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Abstract. *A series of 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. From the P600 component of each signal nineteen waveform-features were calculated. The 3rd-degree Least Squares - Minimum Distance classifier (LSMD^{3}C) and the Support Vector Machines classifier (SVMC) were developed. The LSMD^{3}C was fed with features from all leads and the best feature combinations were inputted into the SVMC to improve the classification results. Highest overall accuracy (89.5%) was found at the C6 lead indicating that OCD patients may present deficits related to working memory mechanisms corresponding to the right temporocentral region.*

1 INTRODUCTION

Specific EEG signals, called event-related potentials (ERPs), consist of a series of electrical potentials (ERP components) that are recorded after visual or audio stimuli. The P600 is the ERP component that lies between 500 and 800ms after stimulus appearance, and it has been associated with the function of the hippocampus[1-3], which is related to working memory (WM) operation[4-6].

In recent years contradicting results have been obtained concerning the inspection of WM dysfunction in obsessive-compulsive disorder (OCD) patients, using behavioral and psychological tests. Particularly, some studies have found no impairments[7-9], while others have detected disorders of WM in OCD patients[10-13]. Recently, however, differences at right temporoparietal and parietal regions were detected at the P600 component of ERP signals in OCD patients[14].

In the present study a support vector machines-based classification system is proposed, in an attempt to achieve high discrimination between OCD patients and healthy controls, using characteristics extracted from the P600 ERP-signals.

2 MATERIALS AND METHODS

2.1 Subjects

Eighteen patients with OCD clinical symptoms and twenty normal controls were examined. All subjects had no history of any neurological or hearing problems, and they were right-handed, as assessed by the Edinburgh Inventory[15]. The participants were evaluated by a computerized version of the digit span Wechsler test[16,17].

Event-related potential signals were recorded from 15 scalp electrodes (leads), based on the International 10-20 system of Electroencephalography[18], referred to both earlobes (abductions set at Fp1, Fp2, F3, F4, C3, C4, C5, C6, P3, P4, O1, O2, Pz, Cz, and Fz, see Fig. 1).

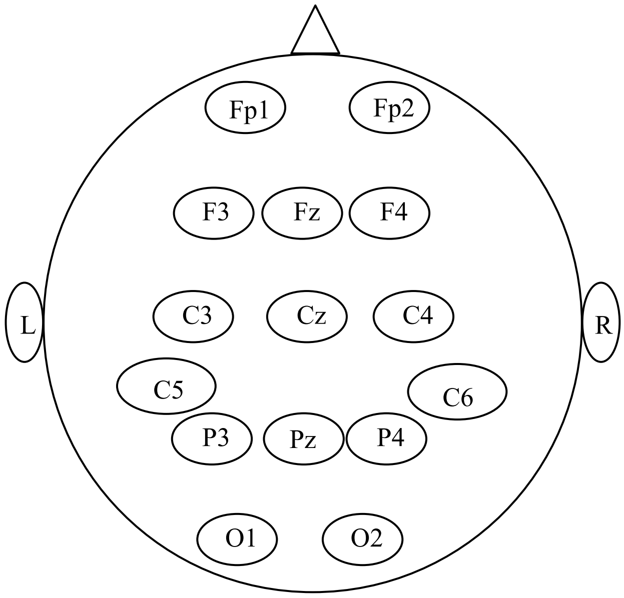

Figure 1. Schematic diagram of lead distribution

2.2 Feature extraction

A total of 19 features related to the waveform of the P600 component of the ERP signals were calculated using dedicated computer software. Feature values were normalized to zero mean and unit standard deviation[19]. The features are described by the following set of equations (1-19):

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

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

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

2. Amplitude (AMP) is the maximum signal value:

   $$\text{AMP} = \max\{s(t)\} \quad (2)$$

3. Latency/Amplitude ratio (LAR) is the ration of of features Latency and Amplitude:

   $$\text{LAR} = t_{s_{max}}/s_{max} \quad (3)$$

4. Absolute Amplitude (AAMP) is the absolute value of feature Amplitude:

   $$\text{AAMP} = |s_{max}| \quad (4)$$

5. Absolute Latency/Amplitude ratio (ALAR) is the absolute value of feature Latency/Amplitude ratio:

   $$\text{ALAR} = |t_{s_{max}}/s_{max}| \quad (5)$$

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

   $$\text{PAR} = \sum_{t=500ms}^{800ms} \left\{0.5 \cdot \left(s(t) + |s(t)|\right)\right\} \quad (6)$$

7. Negative area (NAR) is the sum of the negative signal values:

   $$\text{NAR} = \sum_{t=500ms}^{800ms} \left\{0.5 \cdot \left(s(t) - |s(t)|\right)\right\} \quad (7)$$

8. Absolute Negative area (ANAR) is the absolute value of feature Negative area:

$$\text{ANAR} = |A_n| \tag{8}$$

9. Total area (TAR) is the sum of all signal values:

$$\text{TAR} = A_{pn} = A_p + A_n \tag{9}$$

10. Absolute Total area (ATAR) is the absolute value of feature Total area:

$$\text{ATAR} = |A_{pn}| \tag{10}$$

11. Total Absolute area (TAAR) is the sum of absolute signal values:

$$\text{TAAR} = A_{p|n|} = A_p + |A_n| \tag{11}$$

12. Average absolute signal slope (AASS) is the mean of consecutive signal values slope:

$$\text{AASS} = \frac{1}{n} \cdot \sum_{t=500ms}^{800ms-\tau} \left(\frac{1}{\tau} \cdot \left| s(t+\tau) - s(t) \right| \right) \tag{12}$$

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.

13. Peak-to-peak (PP) is the difference between maximum and minimum signal values:

$$\text{PP} = s_{max} - s_{min}, \tag{13}$$

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

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

$$\text{PPT} = t_{s_{max}} - t_{s_{min}} \tag{14}$$

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

$$\text{PPS} = \frac{pp}{t_{pp}} \tag{15}$$

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

$$\text{ZC} = \sum_{t=500ms}^{800ms-\tau} \delta_s \tag{16}$$

where δ_s=1 if $s(t)$=0, 0 otherwise.

17. Zero crossings in peak-to-peak time (ZCPP) is the number of times where the signal is equal to zero, into the peak-to-peak time window:

$$\text{ZCDPP} = \sum_{t=t_{S_{\min}}}^{t_{S_{\max}}} \delta_s \tag{17}$$

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

$$\text{ZCDPP} = \frac{n_{zc}}{t_{pp}} \tag{18}$$

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

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

$$\text{SSA} = \sum_{t=500ms+\tau}^{800ms-\tau} 0.5 \cdot \left| \frac{s(t-\tau)-s(t)}{|s(t-\tau)-s(t)|} + \frac{s(t+\tau)-s(t)}{|s(t+\tau)-s(t)|} \right| \quad (19)$$

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

All features were normalized to zero mean and unit standard deviation [19], according to relation:

$$x_i' = (x_i - \mu) / \sigma \quad (20)$$

where x_i and x_i' are the i-th feature values before and after the normalization respectively, and μ and σ are the mean value and standard deviation respectively of feature x over all the subjects (OCDs and controls).

2.2 Best feature selection

Best feature selection was based on the exhaustive search method[19], using the reliable and fast 3rd-degree Least Squares - Minimum Distance classifier (LSMD^{3}C), prior to applying more powerful but time-consuming classification algorithms. The LSMD^{3}C was developed in MATLAB environment and it was fed with features from all leads. All possible 2, 3 and 4 feature combinations at each one of the 15 leads were exhaustively examined, in order to find the best feature combination that provides the highest classification accuracy at each lead.

The LSMD^{3}C is designed in two phases: During the first phase, the pattern vectors are augmented with elements till the third degree, i.e. quadratic terms of the form x_i^2 and $x_i x_j$, where i,j=1,2…d and $i \neq j$, and cubic terms of the form x_i^3, $x_i^2 x_j$ and $x_i x_j^2$, where i,j,k=1,2…d and $i \neq j \neq k$, where $\mathbf{x} = [x_1\, x_2\, \ldots\, x_d]$ is a pattern vector and d is the input space dimensionality. By considering all the quadratic and cubic terms, as well as a constant term (of zero-th degree), the augmented pattern vectors dimensionality[19] is equal to:

$$d' = (d+3)!/(3!d!) \quad (21)$$

During the second phase, the augmented patterns are mapped into the "decision" space, where the patterns of each class are clustered around pre-selected representative points, such that the mapping error is minimized[20]. Thus, the discriminant function of the LSMD^{3}C for class C may be described by the following relation:

$$g_c(\mathbf{x}) = \sum_{i=1}^{d} a_{ciii} x_i^3 + \sum_{i=1}^{d-1} \sum_{j=i+1}^{d} a_{ciij} x_i^2 x_j + \sum_{i=1}^{d-1} \sum_{j=i+1}^{d} a_{cijj} x_i x_j^2 + \sum_{i=1}^{d-2} \sum_{j=i+1}^{d-1} \sum_{k=j+1}^{d} a_{cijk} x_i x_j x_k + \sum_{i=1}^{d} a_{cii} x_i^2 + \sum_{i=1}^{d-1} \sum_{j=i+1}^{d} a_{cij} x_i x_j + \sum_{i=1}^{d} a_{ci} x_i - b_c \quad (22)$$

where $\mathbf{x}$ is the vector to be classified, d is the number of features, α_c and b_c are parameters determined during the mapping procedure[20], and x_j are the pattern vector elements.

2.3 Classification

The best feature combinations, provided in the feature selection step, fed the Support Vector Machines classifier (SVMC). The discriminant equation of the SVMC [21,22] is given by:

$$g(\mathbf{x}) = \text{sign}\left(\sum_{i=1}^{N_S} \alpha_i y_i k(\mathbf{x}_i, \mathbf{x}) + b \right) \quad (23)$$

where $k(\mathbf{x}_i,\mathbf{x})$ is the kernel function, a_i and b are parameters[21], $\mathbf{x}_i$ are the support vectors (i.e. the pattern vectors for which $a_i \neq 0$), N_S is the number of support vectors, and $y_i \in \{-1, +1\}$ depending on the class.

In the present study, the 3rd-degree non-homogeneous polynomial function kernel was used as in relation (24):

$$k(\mathbf{x},\mathbf{x}_i) = (\mathbf{x}\cdot\mathbf{x}_i + \theta)^d \quad (d=3,\ \theta=1.0) \quad (24)$$

Finally, substituting equation (24) in (23) the following discriminant function for the SVM classifier is obtained:

$$g(\mathbf{x}) = \text{sign}\left(\sum_{i=1}^{N_S} \alpha_i y_i (\mathbf{x}_i \cdot \mathbf{x} + 1)^3 + b\right) \quad (25)$$

2.4 Evaluation

The performance of the classification system was evaluated by means of the leave-one-out method. Accordingly, one pattern was left out, and the classifier was designed by the rest of the pattern. In this way, the left-out sample was considered by the system as unknown. The procedure was repeated for all samples and results were presented in truth tables[19].

3 RESULTS AND DISCUSSION

Highest single-lead precision (89.5%) was found at the C6 lead employing a 3-features combination consisting of LAT, AAMP and SSA. All controls were classified correctly (specificity 100%) and 4 OCD patients were misclassified as normal controls (sensitivity 77.8%). Regarding 2-features combinations, the best combination consisted of the LAT and AAMP features that resulted in an overall accuracy equal to 81.6%, classifying correctly all normal controls (specificity 100%) but misclassifying 7 OCD patients (sensitivity 61.1%).

Tables 1 and 2 show the best 2- and 3-feature combination classification accuracies at the C6 abduction, using the SVMC and employing the leave-one-out method. Correspondingly, Figures 2 and 3 illustrate the best 2-feature and 3-feature combinations at the C6 lead with the SVMC decision boundaries and, in the case of the 2-dimension diagram, with class margins and support vectors.

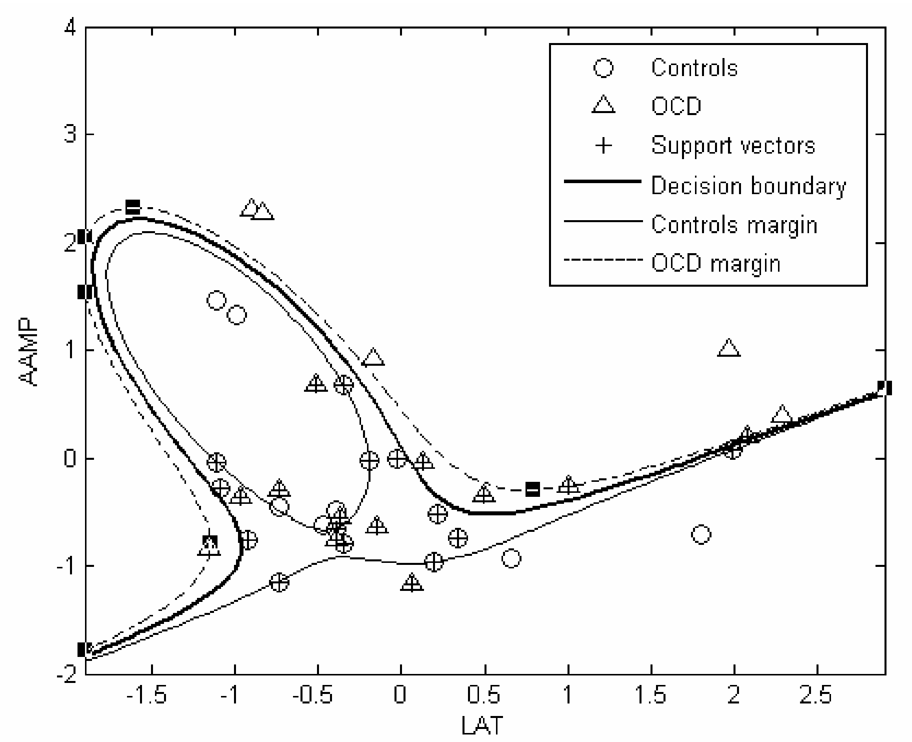

Figure 2. Best 2-feature combination at the C6 lead employing the SVM classifier.

SVM classification at C6 lead (features LAT, AAMP)				
Groups	**OCDs**	**Controls**	**Accuracy**	
OCDs	11	7	61.1%	(Sens.*)
Control	0	20	100%	(Spec.*)
Accuracy	100%	74.1%	81.6%	
	(PPV*)	(NPV*)	(Overall)	

Table 1
Best 2-feature combination (LAT, AAMP) at the C6 lead, employing the SVM classifier with the leave-one-out method.
* Sens. / Spec. = Sensitivity / Specificity
PPV / NPV = Positive Predictive Value / Negative Predictive Value

SVM classification at C6 lead (features LAT, AAMP, SSA)				
Groups	**OCDs**	**Controls**	**Accuracy**	
OCDs	14	4	77.8%	(Sens.*)
Control	0	20	100%	(Spec.*)
Accuracy	100%	83.3%	89.5%	
	(PPV*)	(NPV*)	(Overall)	

Table 2
Best 3-feature combination (LAT, AAMP, SSA) at the C6 lead, employing the SVM classifier with the leave-one-out method.
* Sens. / Spec. = Sensitivity / Specificity
PPV / NPV = Positive Predictive Value / Negative Predictive Value

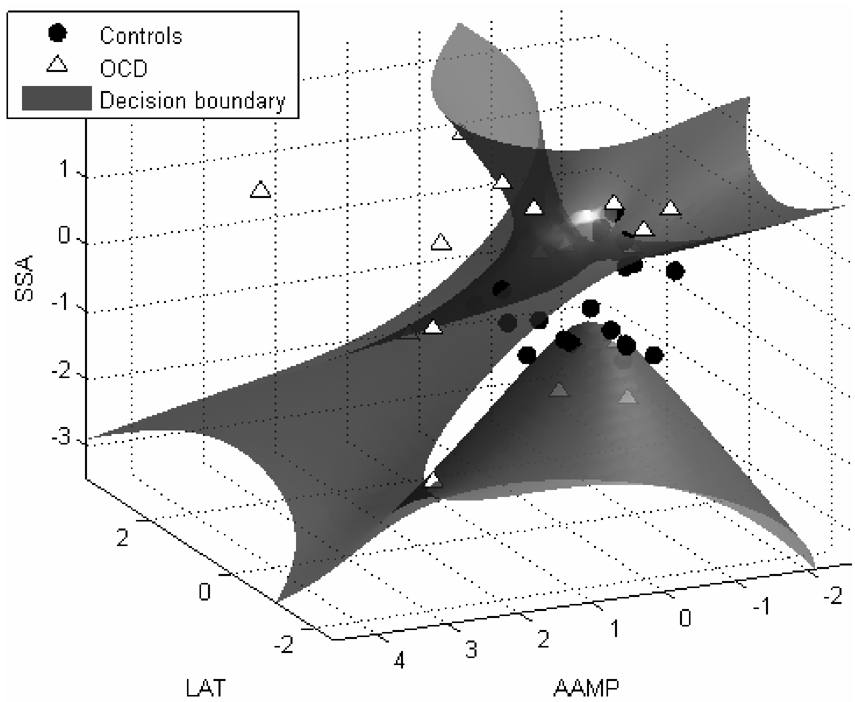

Figure 3. Best 3-feature combination at the C6 lead employing the SVM classifier.

Our results indicate that the proposed pattern recognition system could classify with highest accuracy the normal controls and with an acceptable high accuracy the OCD patients. This was achieved by employing features related to the amplitude and latency of the P600 ERP signals at a lead positioned at the right temporocentral brain region. Similar indications have been also obtained by previous studies[14,23] on OCDs employing the P600 component, however, using different data analysis methods.

4 CONCLUSION

The findings of the present study show that OCD patients may present deficits related to WM mechanisms, corresponding to the right temporocentral region, as reflected by the P600 component.

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