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Detecting Brain Responsivity in Disorders of Consciousness: a Brain-Computer Interface-Based Methodology

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Abstract. A method to evaluate the performances of different Brain-Computer Interface (BCI) protocols is proposed. This methodology, besides representing a first step toward the standardization of the evaluation of BCI protocols, provides details on the statistical significance of classification accuracy thus addressing the investigation of the discriminability of different brain responses elicited by means of specific protocols. Results deriving from the application of the method on data from patients diagnosed with disorders of consciouseness (DOC) indicate the value of this BCI-based methodology in supporting the objectifiable detection of brain residual responses indicative of awareness in such severe conditions. Thanks to the integration into a multi-purpose platform for the analysis of physiological signals and to the easiness of use, this methodology paves the way for a systematic detection of *mental states* in non-responsive/non-communicative patients, who represent the challenge of BCI applications.

Keywords: BCI, DOC, Performance Evaluation, ECM, chi-square test

1. Introduction

Recently the Brain-Computer Interface (BCI) technology has been proposed as a possible communication mean for patients clinically diagnosed with disorder of consciousness (DOC), such as vegetative states (VS) or minimally conscious states (MCS) [Lulè et al., 2013]. In this case, BCI technology might capture the brain responses correlated with residual awareness and funnel them outside as overt sign of voluntary communication. This specific application of BCIs demands not only a high level of accuracy in detecting the brain responses but, even more, that brain responses are reliably discriminated from the chance level (i.e. low probability errors).

Here we present a standard methodology, developed within the NPXLab suite (www.braininterface.com) which relies on confusion matrices and on a statistical test to evaluate classification performance and its significance. It is independent from the protocol implemented to elicit the brain responses, a property that boosts the standardization of the evaluation process and it can be applied to the single-subject level. This latter is essential feature when due to the variability of the patients' brain signals, a grand-average analysis might fail in highlight the significant individual responses. The availability of a semi-automated evaluation of brain responsiveness and its integration in a user-friendly and features-reach software application facilitates the translation of the BCI-based technology into clinical practice to support diagnosis of non-behaviorally responsive patients.

2. Material and Methods

3.1. The Extended Confusion Matrix (ECM) and the chi-square test: statistical evaluation of classification

Classification performance can be stored into an ECM, a table where the number of times the brain responses to be classified (classification classes) were correctly classified, misclassified or not recognized [Bianchi et al., 2007], are saved. From an ECM, different performance metrics can be calculated (accuracy, bit rate, mutual information, etc). Also, a statistical test (chi-square test) can be associated to each class to evaluate if the classification results significantly differ from the chance level. This strictly depends on the number of trials (the number of times each brain response is classified) which determines the confidence interval of the chance level. In this way it is possible to validate results by adding information on the accuracy significance. The p-value associated to the accuracy assesses how much significant the classifications are.

3.2. EEG recording and data analysis

To show the method, data from 4 DOC patients were used. They were administered a classical acoustic oddball P300-based paradigm, during which they were asked to mentally count the deviant tones (targets, T=60) against the standard *(non-targets*, NT=420). The ISI was set to 850ms. EEG potentials were recorded from 32 active electrodes, with a sampling rate of 512 Hz. For classification purposes, data were sub-sampled to 256Hz, ocular and muscular artifacts were identified and 60 NT were randomly selected. A subset of electrodes (F3, Fz, F4, C3, Cz, C4, P3, Pz, P4) was chosen. A post-stimulus period of interest (50 ms to 650 ms) was selected and a leave-one-out validation was applied on the artifacts-free single trials belonging to each class to test the classifier (SWLDA).

3. Results

Results of the classification validation are reported in Table 1. In S1 diagnosed as VS, at significance threshold of 5%, classifications were random for all the trials belonging to both T and NT class ($p > 0.05$). In the second VS case S2, the average accuracy for all the trials was 72.32% and both T and NT class were significantly classified ($p_T=0.027$, $p_{NT}=0$). For the two patients diagnosed as MCS, total accuracies were slightly better, 64.46% and 72.73% for S3 and S4, respectively. Both T and NT classes were significantly discriminated from chance ($p < 0.05$).

Table 1. *Classification validation results. The following values are listed: subject, clinical diagnosis, total number of trials, total accuracy, target (T) accuracy and p value, non target (NT) accuracy and p value.* ***Bold values= p<0.05***.

Subj	*Diagn.*	*Trials*	*Total Acc[%]*	*T Acc[%]*	*p*	*NT Acc[%]*	*p*
S1	VS	109	55.05	49.06	0.891	60.71	0.109
S2	VS	112	72.32	65.38	**0.027**	78.33	**0**
S3	MCS	121	64.46	65	**0.02**	63.93	**0.03**
S4	MCS	110	72.73	67.31	**0.013**	77.59	**0**

4. Discussion

The proposed methodology unveiled that in one VS case (S2) single trial brain evoked responses were classified with a highly significant p-values, thus suggesting the preservation of a command following ability otherwise not detectable by the patient behavioral clinical assessment. The classification validation results obtained for the two MCS patients confirmed, at the level of single trial, the clinical assessment indicating the ability for these 2 patients to discriminate between two different types of stimulations.

It is mandatory to stress that the absence of a positive result in our test (as in the S1 case) could be ascribed to many factors independent from the diagnosis of VS thus, preventing any definitive conclusions on the clinical diagnosis reliability. False negative inducing factors may be: vigilance status at the time of the recording (patient was sleeping), cognitive dysfunction masked by the consciousness disorder that affects the auditory task accomplishment, high signal to noise ratio, the classifier was not the best to extract relevant features. One recommended solution is to obtain patient's multiple recordings at different times and/or to test different translation algorithms to identity the best appropriated for the relevant features. On the other hand, a possible occurrence of false positives (statement on the presence/intactness of patient's cognitive processing ability) has to be considered. In this case, one source of errors might be the capture of brain response components not directly related to a voluntary shifting of attention between T and NT class (in our auditory paradigm) that interfere with the algorithm classification output. A careful stimulation protocol design is the first step to prevent such error source.

This BCI-based methodology implemented in a practical tool offers an effective instrument for a standard evaluation of performance accuracy and for the assessment of the reliability of such accuracy.

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