International Journal of Psychophysiology 93 (2014) 162–166

Contents lists available at ScienceDirect

International Journal of Psychophysiology

journal homepage: www.elsevier.com/locate/ijpsycho

Machine learning approach for classification of ADHD adults

Aleksandar Tenev [a,*], Silvana Markovska-Simoska [b], Ljupco Kocarev [b], Jordan Pop-Jordanov [b], Andreas Müller [c], Gian Candrian [c]

[a] Faculty for Computer Science and Engineering, University of Skopje, Former Yugoslav Republic of Macedonia
[b] Macedonian Academy of Sciences and Arts, Skopje, Former Yugoslav Republic of Macedonia
[c] Brain and Trauma Foundation Grison/Switzerland, Poststrasse 22, 7000 Chur, Switzerland

ARTICLE INFO

Article history:
Received 7 September 2012
Received in revised form 17 October 2012
Accepted 21 January 2013
Available online 27 January 2013

Keywords:
ADHD
EEG power spectra
Support vector machines
Karnaugh map

ABSTRACT

Machine learning techniques that combine multiple classifiers are introduced for classifying adult attention deficit hyperactivity disorder (ADHD) subtypes based on power spectra of EEG measurements. The analyzed sample includes 117 adults (67 ADHD, 50 controls). The measurements are taken for four different conditions: two resting conditions (eyes open and eyes closed) and two neuropsychological tasks (visual continuous performance test and emotional continuous performance test). We divide the sample into four data sets, one for each condition. Each data set is used for training of four different support vector machine classifiers, while the output of classifiers is combined using logical expression derived from the Karnaugh map. The results show that this approach improves the discrimination between ADHD and control groups, as well as between ADHD subtypes.

1. Introduction

Attention deficit hyperactivity disorder (ADHD) is heterogeneous neurobehavioral disorder that is most frequently diagnosed in children and adolescents and it has more recently been documented to continue into adulthood. According to DSM-IV (American Psychiatric Association, 1994), the disorder is characterized by inattention, hyperactivity and impulsivity symptoms. The ICD-10 (World Health Organization, 1993), although using different name, hyperkinetic disorder (HD), lists similar criteria for the disorder. The prevalence of the disorder in childhood is estimated between 5 and 9% (Polanczyk et al., 2007; American Academy of Pediatrics, 2000). The ADHD symptoms may decline over time, however more than one half of the ADHD children continue to manifest clinically significant symptoms after reaching adulthood. That means that nearly 5% of the adults worldwide are affected (Wender, 1995).

Most of the EEG studies concern the ADHD children and they summarize indicators such as lower alpha and beta bands, and higher theta and delta bands to discriminate the ADHD children from healthy control groups (Barry et al., 2003; Clarke et al., 1998, 2001a, 2001b, 2002; Lubar, 1991; Monastra et al., 1999; Pop-Jordanova et al., 2005). However, the results from the few EEG studies in which ADHD adults are involved are very divergent (Bresnahan and Barry, 2002; Bresnahan et al., 2006; Clarke et al., 2008; Koehler et al., 2009; Markovska-Simoska and Pop-Jordanova, 2010). Reason for this may be the nature of the quantitative EEG parameters that are analyzed, as well as the developmental nature of the disorder itself. This is why diagnosis of the disorder in the adult population remains dependent of the skills and the knowledge of the doctor.

Most of the methods for finding some relevant discriminators between ADHD and control groups include standard statistical techniques, such as ANOVA test that are run on the data obtained from the EEG measurements. These methods have led to consistent results between the researchers in the studies of ADHD children and adolescents, but that is not the case in the studies of ADHD adults.

A very few studies have been carried out on discriminating the ADHD from the control groups that use machine learning techniques. There have been studies that discriminate ADHD from control groups by using linear classifiers with moderate accuracy (Barry et al., 2003; Buchsbaum and Wender, 1973; Robaey et al., 1992; Satterfield and Braley, 1977; Smith et al., 2003). Non-linear classifiers such as support vector machines and artificial neural networks have emerged that can find non-linear relationship in the data. Mueller et al. (2010, 2011) have introduced a machine learning system that uses support vector machine classifier to discriminate the ADHD adults from control groups on the base of the event related potentials that are generated from the EEG measurements.

In this paper, we introduce a model for classification of adults ADHD and control groups on the basis of EEG power spectra obtained from different measurement conditions. The EEG power spectrum is generated from the EEG signals recorded from the scalp electrodes, and it represents the distribution of the squared amplitude of the signal along all frequency bands of the signal. The EEG signals are

* Corresponding author at: Institute of Software Engineering, Faculty of Computer Science and Engineering, Ss. Cyril and Methodius University — Skopje, Rudjer Boskovikj 16, 1000 Skopje, Former Yugoslav Republic of Macedonia. Tel.: +389 2 3099154, +389 78 308428.
E-mail address: aleksandar.tenev@finki.ukim.mk (A. Tenev).

0167-8760/$ – see front matter
http://dx.doi.org/10.1016/j.ijpsycho.2013.01.008

generated inside the brain as a result to the brain neuronal activity (Sanei and Chambers, 2007). According to the frequency band at which they are recorded they can be divided into four bands (delta, theta, alpha and beta). Signal detection at each of these bands corresponds to a specific behavior of the person. ADHD is viewed as a disorder of the executive system of the brain which is responsible for the executive functions which are defined as the patient's ability to plan, regulate and monitor his or her cognitive, emotional and motor skills in order to achieve certain goals (Kropotov, 2008). The data we had for analysis is obtained from four different conditions under which the EEG measurements are taken. The conditions were visual continuous performance test and emotional continuous performance test, which give us insight into the properties of the executive system of the patient's brain, as well as eyes open and eyes closed conditions. The goal of our study was to build a machine learning model for discriminating adults ADHD and control groups that use information from all of the conditions under which the measurements are taken. We want to show that we acquire more useful information by combining parameter values from each condition and in that way we can improve the discrimination between ADHD and control groups. With four different support vector machine classifiers (one for the data from each condition) and a simple voter that makes a final output decision with combining the outputs from each of the classifiers by voting, we present an exhaustive analysis of EEG power spectra data and the conditions under which the data is obtained.

2. Methods

2.1. Subjects

Our analyses were made on 117 adult patients from which 67 were diagnosed as ADHD and 50 were controls. 67 adults (between 18 and 50 years of age) diagnosed with ADHD with 50 age-matched control subjects, participated in the study. Each group consisted of almost equal number of females and males: the ADHD group consisted of 33 females and 34 males (the gender imbalance noted in children has not been established in adults with ADHD) and gender distribution in control group was 25 females and 25 males. The groups were matched on age, with the mean age being 33.4, S.D. = 8.39 years for ADHD subjects, and 32.8, S.D. = 8.22 years for the control group.

ADHD subjects were patients collected during the ADHD Project of EU-Cost Action B27, from 2007 to 2009 until the target number was obtained. The diagnosis was made by a psychiatrist and a psychologist, and both had to agree on the diagnosis for the subject to be included in the study. All subjects met the DSM-IV criteria for ADHD. In order to ensure diagnostic validity, additional information was collected from parents, partners, relatives and friends. According to DSM-IV criteria, the assessment resulted in 26 ADHD subjects being diagnosed with the inattentive type, 4 with hyperactive-impulsive type and 37 with combined type.

The control group was recruited through professional colleagues and community organization from Skopje, Macedonia. Inclusion criteria required the control group to be free of history of ADHD or other psychopathological or neurological symptomatology, assessed through personal interview, self-report, and the DSM-IV symptom checklist for ADHD. All subjects had normal or corrected to normal vision.

2.2. Procedure

All participants were individually assessed with neurophysiological testing in an environment free from distractions, in a single session that lasted approximately 1.5 h, during office hours (8:00–15:00 h). The study was approved by the local ethics committee and written informed consent was obtained from all participants after an explanation of the procedure.

Subjects were not allowed to take any medication in the 48-hour-period prior to testing and were asked not to use caffeine or tobacco on the morning of their testing. All subjects were seated in a comfortable chair with a backrest and were instructed not to move their eyes during the recording. Recording was suspended for a short period if the subject was found to be experiencing drowsiness or becoming restless. The EEG was recorded using a Mitsar 19-channel QEEG system in the following conditions:

1. 5 min eyes closed (EC) resting condition;
2. 5 min eyes open (EO) resting condition (sufficient for 2 min artifact-free data EC and EO);
3. Visual continuous performance test — VCPT from Psytask (two-stimulus Go/NoGo paradigm) with 20 min duration;
4. Emotional continuous performance test — ECPT from Psytask (two-stimulus Go/NoGo paradigm) with 20 min duration.

EEG electrode placement was in accordance with the international 10/20 system using an electrocap produced by Electrocap international. Activity in 19 derivations was recorded from Fp1, Fp2, F3, F4, F7, F8, Fz, C3, C4, Cz, T3, T4, T5, T6, P3, P4, Pz, O1 and O2, referenced to linked ears. The ground electrode was placed between Fpz and Fz. To control eye movement artifacts, the electrooculogram (EOG) was recorded, using two 9 mm tin electrodes, above and under the right eye, referenced to Fpz and Oz. The EOG rejection was set at 50 μV. The bandwidth of the amplifiers was set at 0.53 Hz for low frequency filter, 50 Hz for high frequency filter and 45–55 Hz notch filter. The EEG digitization frequency was 256 Hz. The impedance levels for all electrodes were set to 5 kΩ. EEG was continuously recorded on the hard disc for off-line analysis. The VCPT and ECPT were administered using the standard protocol. The authors also visually appraised every epoch and decided to accept or reject it, based on the absence or presence of artifact. EEG data was processed with the WinEEG software version 2.82.32 (St. Petersburg, Russia). Spectral analysis using fast Fourier transform was carried out for four frequency bands, Delta (0.5–4 Hz), Theta (4–8 Hz), Alpha (8–12Hz), Beta (12–30 Hz), for absolute power (μV^2). The transformed data were analyzed separately for each subject, frequency band, and measurement condition. Also, all individual spectra's of ADHD subjects were analyzed by the second author and were compared with the HBI (Human Brain Index) database. According to the Kropotov's classification (Kropotov, 2008), ADHD subjects were divided in four subtypes: QEEG subtype I — 13 patients (19.4%), QEEG subtype II — 14 patients (20.9%), QEEG subtype III — 16 patients (23.9%) and QEEG subtype IV — 24 patients (35.8%).

2.3. VCPT and ECPT tasks

We used the two-stimulus CPT tasks (GO/NOGO tasks) developed specifically for the Psytask software of Mitsar system. In this study we used these tasks to assess the power spectra during a mental task, compared to the resting states in EC and EO conditions.

The task consisted of 400 trials. The duration of the stimuli is equal to 100 ms. Trials consisted of presentation of a pair of stimuli with inter stimulus interval of 1.1 s. The interval between the trials is equal to 3100 ms and the response interval from 100 to 1000 ms. Subjects were instructed to press a button with index finger of their right hand as fast as possible every time when animal or angry face was followed by an animal or angry face (Go-condition), respectively, and to withhold the suppressing on the other three trials (No-Go condition). Pictures were presented in a pseudo randomized order in the center of a computer monitor placed 100 cm from the subjects' eyes. Before each session, the test was explained to the subject in details and 10–20 training tasks were performed. Accuracy and speed were encouraged.

More detailed explanation of the VCPT and ECPT tasks can be found in the study of Markovska-Simoska and Pop-Jordanova (2009).

2.4. Support vector machine (SVM)

Support vector machine is a method for supervised learning that is used for classification or regression analysis. That means, given an input data sample, in which each data point is marked as belonging to one of the two possible groups or classes, the SVM builds a model which is then used for classifying new data points to one of the two classes. This approach is non-probabilistic because instead of using the probability distribution of data points for discrimination, it uses the spatial and geometric properties of the data points. The SVM model represents the data points in space so that the points that belong to separate classes are divided by a gap that is as wide as possible. This gap, also called margin, is modeled with the boundaries of a hyperplane in the multidimensional space in which the points are distributed. The positioning of the hyperplane depends on the closest data points which are called support vectors. The only problem here is that this is true for linearly separable data. Most of the time, input data is not linearly separable in its original input space. To overcome this problem, SVM algorithm uses kernel functions. The trick with the kernel functions is that these functions are nonlinear functions which map the data points to another, higher dimensional space in which these points can be linearly separable. This makes the SVM classifier a nonlinear classifier. There are different types of kernels. In our analysis we used the radial basis function kernel.

In our study, the input data sample represents the patients. Each data point in the data sample represents a patient who belongs to one of the two classes (ADHD or normal). The dimension of the input space depends on the attributes or features associated with each data point (for example, if we have potentials from 19 electrodes, the dimension of our input space is 19). Using the kernel function, we map our input space to higher dimensional space where the data can be linearly separable and SVM algorithm can be implemented.

2.5. Model

The model we applied is shown on Fig. 1. We divided the data from the EEG measurements for each of the four conditions separately. Note that with splitting the data, we do not reduce the number of patients in the original data set. The number of patients in all data sets is equal. With splitting the data, we mean splitting the attributes that correspond to each condition. In the original data set, each patient has the attributes (electrode values) from the measurements taken in all conditions. In the ECPT data set, the patient has only the attributes that are obtained from the ECPT condition, and the same is for the others data sets shown in Fig. 1. We did this because it is reasonable to think that during different tasks or conditions under which the measurements are taken, the arousal level is different and the propagation of EEG activity changes. Therefore, the EEG measures differ in topography, as well as in power levels (Barry et al., 2007). With this approach, the results we get are based on the combined knowledge that we get from the condition-dependent EEG information.

2.5.1. Preprocessing

Each of the classifiers is trained with the corresponding data set. Because the set of features we obtained from the EEG measurements is large (values from all 19 electrodes in all bands), it is good practice to reduce this set and feed the classifier with the most appropriate subset of these features, therefore reducing complexity and dimensionality (part A from Fig. 1). For each SVM classifier (shown in Fig. 1), we applied the forward selection scheme to choose the best attributes or features that correspond to the selected classifier. Forward selection scheme is an algorithm that iteratively selects subset of features from a set of features, such that the subset of features it chooses is most relevant to the discrimination of the data. Applying this technique to each classifier that corresponds to a different condition, we obtain the features that represent the most relevant discrimination of the data in the corresponding condition.

2.5.2. Classifier training

After selecting the relevant features for each data set, the data sets are feed to the SVM classifiers and the models are built. For generalization of each classifier model we used 10 fold cross-validations. Cross-validation is technique that tells us how the classifier model we have chosen will generalize to an independent data set that is different than the one we have trained the model with (Arlot and Celisse, 2010). It partitions the data into n complementary subsets and uses $n-1$ of the subsets for training the model, and the remaining set for testing the model. This procedure is repeated n times so that each of the subsets is used exactly once as a testing set. The results are than averaged over the rounds to get the final estimation.

2.5.3. Voter

The next part of our model is the voter (part B from Fig. 1). The voter is defined as a logical or Boolean algebra expression and it depends on four input variables. As it can be seen from the Fig. 1, these input variables are the classifiers outputs. Note that the outputs

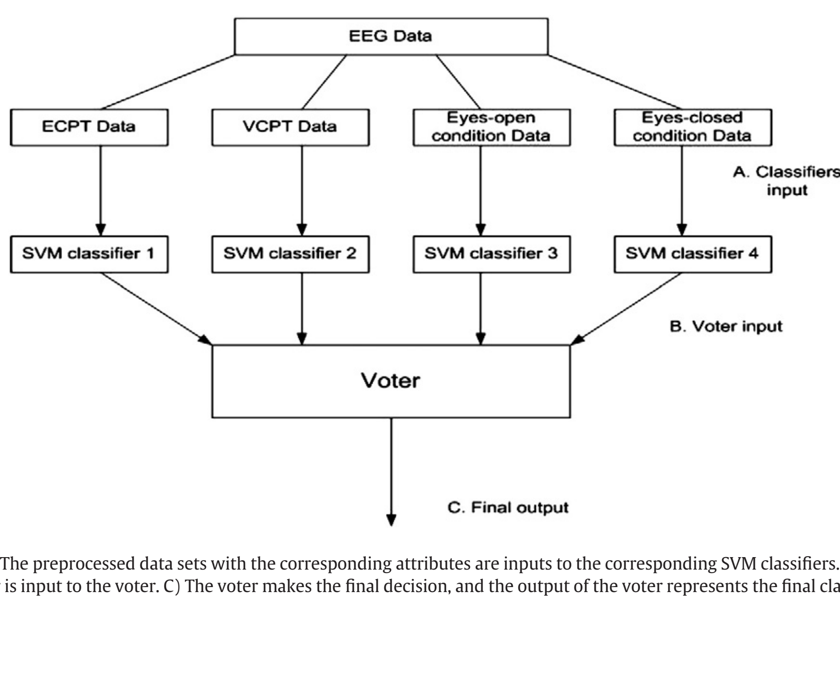

Fig. 1. Illustration of the model. A) The preprocessed data sets with the corresponding attributes are inputs to the corresponding SVM classifiers. B) Then, SVM classifiers are trained, and the output from each classifier is input to the voter. C) The voter makes the final decision, and the output of the voter represents the final class which is given to the corresponding patient.

of the classifiers are binary values because we have binary classification problem. Namely, 1 represents the ADHD group and 0 represents the Normal group. Because of this fact, we define our voter as a logical expression, otherwise it is pointless. We analytically derived the expression from Karnaugh map that represents the voter function. The Karnaugh map is a method for simplifying Boolean algebra or logical expressions, which takes advantage of the human capability of pattern recognition, instead of performing extensive calculation using the Boolean algebra axiom laws and theorems (Karnaugh, 1953).

If we have the following Boolean equation:

$$f(A,B,C,D) = (A'BC'D') + (A'BC'D) + (A'BCD) + (ABC'D') + (ABC'D) + (ABCD). \quad (1)$$

The notation $\overline{A}$ represents the complement of A. For example, if A = 0, then $\overline{A} = 1$ and if A = 1, then $\overline{A} = 0$. The same is for other variables. Note that in the previous equation the sign '+' represents the logical OR operator, and the multiplication represents the logical AND operator. This function is not simplified and to simplify it, one can use the Karnough map method as mentioned before. It is worth mentioning here that we do not reduce complexity with simplifying the logical expression. For the previous unsimplified logical expression, the simplified expression is:

$$f(A,B,C,D) = BC' + BD. \quad (2)$$

As it can be seen, the simplified expression has less logical operations than the original unsimplified expression, but still produces that same final result for the given combination of input variables. What is significant here is that we can see the impact each of the variables has on the final result. In our example, after the simplification of the expression, we can see that variable A does not have impact on the result. The result depends only on variables B, C and D. This information we get from our voter is crucial because the input variables in our voter are the classifiers for each condition and we can see which condition has impact in our discrimination and which has not.

The idea behind the standard voter function of four variables is simple. The function output is 1 if there are more ones in the input variables (three or four input variables have the value 1), and the output is 0 if the zeros dominate among the input variables. When the number of ones and zeros is equal, the output is undefined.

In our model, the input variables represent the classifiers output. We can use the knowledge we have to replace the undefined outputs from our function with 1 or 0. We do this by using the information we have about the performance of each classifier. So, instead of counting the ones and zeros, we can compute the average performance of the classifiers and assign the voter function value of 1, if the average performance of the classifiers that have output of 1 is bigger than the average performance of the classifiers that have output of 0, or assign value of 0 when the performance of classifiers that have output of 1 is less than the performance of classifiers that have output of 0.

3. Results and discussion

The results we got from applying our model to power spectra data are shown in Table 1.

Table 1
Results from the power spectra. Percent of correctly classified instances is shown.

Condition	ADHD II vs. ADHD III	ADHD III vs. ADHD IV	Normal vs. ADHD
Eyes open	90%	95%	70.9%
Eyes closed	90%	87.5%	72.6%
VCPT	90%	92.5%	69.2%
ECPT	93.3%	95%	71.7%
Voter	96.7%	100%	82.3%

From the results we can see that the voter improves the classification, therefore we truly acquire more information with combining conditions, then analyzing each condition separately. We also applied the model to discriminate between ADHD II and ADHD III subgroups, and ADHD III and ADHD IV. We choose this combination, because the number of patients in these groups is almost equal. It can be seen that the classification between the subgroups is much better compared to the classification of ADHD and normal groups. This is because of ADHD subgroups being more homogeneous than ADHD and normal groups. If someone has breathing problems, it can be because he or she has weak heart, or lungs problem. The symptom is the same, but the problem that caused the symptom is different and should be treated different. The ADHD subtypes should be seen as different aspects of ADHD. Each of the subtypes has different characteristics that are represented by corresponding brain activity. Therefore, the EEG power spectrum is more homogeneous for the subtypes.

In conclusion, in this paper we have presented a novel model for discriminating adults ADHD and control groups based on machine learning techniques. The voter, which has been implemented as a logical expression, improves the classification performance by combining the knowledge from the different conditions under which the EEG measurements were obtained. In this way, the final result depends on the impact that different conditions have on the patient data. For future research, the model presented in this work can be expanded by exploring other, in particular non-spectral characteristics of EEG data for analyzing neurophysiological disorders. Using simple logical expression, we can inference results that not only contain the knowledge from the different conditions, but also from different QEEG parameters. This approach could be very useful from medical point of view, because such models can be applied to any neurophysiological disease or disorder, and for every disorder and disease we can find the combinations of QEEG parameters and conditions with the largest impact on the results.

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