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RESEARCH ARTICLE

An EEG-based machine learning method to screen alcohol use disorder

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Abstract Screening alcohol use disorder (AUD) patients has been challenging due to the subjectivity involved in the process. Hence, robust and objective methods are needed to automate the screening of AUD patients. In this paper, a machine learning method is proposed that utilized resting-state electroencephalography (EEG)-derived features as input data to classify the AUD patients and healthy controls and to perform automatic screening of AUD patients. In this context, the EEG data were recorded during 5 min of eyes closed and 5 min of eyes open conditions. For this purpose, 30 AUD patients and 15 aged-matched healthy controls were recruited. After preprocessing the EEG data, EEG features such as inter-hemispheric coherences and spectral power for EEG delta, theta, alpha, beta and gamma bands were computed involving 19 scalp locations. The selection of most discriminant features was performed with a rank-based feature selection method assigning a weight value to each feature according to a criterion, i.e., receiver operating characteristics curve. For example, a feature with large weight was considered more relevant to the target labels than a feature with less weight. Therefore, a reduced set of most discriminant features was identified and further be utilized during classification of AUD patients and healthy controls. As results, the inter-hemispheric coherences between the brain regions were found significantly different between the study groups and provided high classification efficiency (*Accuracy* = 80.8, *sensitivity* = 82.5, *and specificity* = 80, *F-Measure* = 0.78). In addition, the power computed in different EEG bands were found significant and provided an overall classification efficiency as (*Accuracy* = 86.6, *sensitivity* = 95, *specificity* = 82.5, *and F-Measure* = 0.88). Further, the integration of these EEG feature resulted into even higher results (*Accuracy* = 89.3 %, *sensitivity* = 88.5 %, *specificity* = 91 %, *and F-Measure* = 0.90). Based on the results, it is concluded that the EEG data (integration of the theta, beta, and gamma power and inter-hemispheric coherence) could be utilized as objective markers to screen the AUD patients and healthy controls.

Keywords Alcohol use disorder (AUD) · Alcohol abuse (AA) · Alcohol dependence (AD) · Electroencephalography (EEG) · Resting-state EEG (REEG) · Inter-hemispheric coherence · Spectral powers of EEG data

Introduction

A severe alcohol intake is normally diagnosed as alcohol use disorder (AUD) (Association 2013). According to the Institute of Alcohol Abuse and Alcoholism (IAAA), approximately 7.2 % or 17 million adults in United States aged 18 and older had an AUD in 2012 (Alcoholism 2012). According to the definition, alcohol consumption less than 48 grams per day or 144 grams per week is characterized as safe (Parsons and Nixon 1998). In contrary, chronic heavy drinking eventually leads to AUD, alcohol abuse (AA), or alcohol dependence (AD). More specifically, the AD is a

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more severe form of AA. Unfortunately, heavy consumption of alcohol and its cumulative toxic effects may lead to medical, neurological, psychiatric and social problems. According to the Diagnostic and Statistical Manual of Mental Disorders V (DSM V), people with AA keep drinking despite social and personal problems (Association 2013). In addition, people with AD not only fulfill the criteria of AA, but also develop increased tolerance and withdrawal symptoms once abandoned drinking, also termed as alcoholics (Moss et al. 2007).

Conventionally, the screening and assessment of AUD patients involves questionnaire-based techniques such as AUDIT (alcohol use disorder identification test) (Maisto and Saitz 2003). However, the subjective feedbacks observed from AUD patients may confound the screening process. For example, a large number of AUD patients are less candid and unable to quantify their alcohol intake (Popham and Schmidt 1981; Solomon et al. 1980; Watson et al. 1984). Hence, assessments with questionnaire-based techniques could be confounded due to misjudgments during screening and assessing actual quantity of alcohol consumption unless supported with neuroimaging modalities such as electroencephalography (EEG) (Alhassoon et al. 2015; Son et al. 2015). The EEG is a standard modality and has been utilized for various applications such as monitoring depth of anesthesia (Shalbaf et al. 2015), assessment of spontaneous perceptual switching (Ozaki et al. 2012), assessing learning processes (Gutiérrez and Ramírez-Moreno 2016), and modeling purposes (Fründ et al. 2008; Kiebel et al. 2008).

In the literature, various EEG features are reported showing clinical relevance with the AUD, e.g., inter-hemispheric coherences, phase delay and synchronization likelihood have been proposed to explore functional influences among different brain regions (Herrera-Díaz et al. 2015). The inter-hemispheric coherence can quantify the functional coupling between two spatially located EEG sensors representing distinct brain regions. However, contradictory findings have been reported regarding the changes in the inter-hemispheric coherence. For example, Tcheslavski and Gonen (2012) highlighted significant reduction of EEG power, inter-hemispheric coherence and phase synchronization in alcoholics as compared with controls. In contrary, higher inter-hemispheric coherence in first degree male relative (parents, full siblings, or children) of alcoholics was found in the frontal and cento-parietal regions than in controls without a family history of AUD (Michael et al. 1993). Moreover, studies based on resting-state EEG (REEG) data have identified differences of neuronal activities among different brain regions in alcoholics and healthy controls (Campanella et al. 2009; Parvaz et al. 2011; Porjesz et al. 2005).

Spectral power analysis to discriminate alcoholics and control groups has been the most popular EEG analysis method. For example, higher theta power has been reported in alcoholics when compared with healthy subjects (Bauer 2001; de Bruin et al. 2004; de Bruin et al. 2006; Rangaswamy et al. 2003; Winterer et al. 1998). This abnormal increase may inhibit the ability to encode new information (Klimesch 1999). Similarly, an increase of theta power at all scalp loci, prominent at central and parietal in males and at the parietal for females was observed (Rangaswamy et al. 2003). In addition, significant changes in theta power were associated with cortical atrophy (Coutin-Churchman et al. 2006; Saletu-Zyhlarz et al. 2004). A higher low-voltage alpha (LVA) (<10 μV) has been reported in alcoholics than healthy controls (Ehlers and Phillips 2007; Ehlers et al. 2004). However, the observed difference was not statistically significant. In a study, increased beta power is reported as a primary characteristic feature found in alcoholics and high risk subjects, and it was associated with benzodiazepines intake, that were mainly used for alcohol detoxification (Bauer 2001; Rangaswamy et al. 2002). Therefore, beta power needs to be considered when used for alcohol treatment. In contrary, theta and delta bands were found significantly increased in alcoholics than controls. In addition, these bands were not affected by medication or found in people with family history of AA. However, the findings based on alpha and gamma bands are not matured and yet considered as active research areas.

In the context of clinical applications of EEG-based methods to solve issues related with screening alcoholic subjects from healthy controls, machine learning (ML) techniques have shown promising results (Acharya et al. 2012; Bajaj et al. 2016; Mumtaz et al. 2016; Sinha 2016). However, the requirements for clinical application are tougher and require more evidences that the EEG could be utilized to classify the AUD patients and healthy controls (Huys et al. 2016). As revealed in the literature, the EEG bands such as delta, theta, alpha, and beta show relevance with the AUD. Moreover, this study sought to perform *t* test to investigate statistically significant differences between the two groups, i.e., MDD patients and healthy controls. Hence, most useful data that can be used as input features for the classification purpose was identified. Therefore, the inter-hemispheric coherences and power of different bands were investigated to be suitable to discriminate the MDD patients and healthy controls. In addition, the secondary objective is to develop a less complex ML method than the ones presented in the literature (Mumtaz et al. 2016) that show high efficiencies based on the EEG data acquired from the AUD patients and healthy controls. The proposed ML method involved a general methodology of feature extraction, selection, and classification validated with tenfold cross validation (10-

CV). Finally, to validate the proposed method, it is compared with the methods reported in the literature.

Method

Study participants

The study participants: thirty (30) AUD patients (mean 55.4 ± 12.87 years) and fifteen (15) healthy controls (mean 42.67 ± 15.90 years) were recruited from clinic Bingkor, Sabah, East Malaysia. The experimental data acquisition was performed according to the experiment design that was approved by the ethics committee of Universiti Malaya, Malaysia. According to the inclusion criteria, only those participants were recruited that were able to sign the consent of participation and met the diagnostic criteria defined by the alcohol use disorders identification test (AUDIT) (Babor et al. 2001). Moreover, the study participants with AUDIT score greater than seven were categorized as AUD patients (Bush et al. 1998). All participants were volunteers and had signed the consent forms of participation and were well-informed about the experimental procedure. The healthy participants were assessed for any neurological disorder and were found naïve.

Electrophysiological data recordings

In this study, resting-state EEG recordings and clinical assessment scores were used as experimental data. As shown in Fig. 1, the EEG data were recorded with Discovery 24E EEG system involving 19 EEG channels located according to international 10–20 system (Klem et al. 1999). The brain signals were digitized at a sampling rate of 256 samples per second. Furthermore, the EEG data were filtered at a frequency bandwidth of 0–70 Hz with an additional 50 Hz notch filter to supress the line noises. The resting-state EEG data were recorded during two physiological conditions: (1) 5 min of eyes-closed (EC), and (2) 5 min of eyes-open (EO). During EEG recordings, the participants were instructed to sit relaxed in a semi-recumbent position. In addition, the EO session included recordings with less eye movements to reduce the artifacts. Finally, the EEG data were then transferred to a PC through an optically and magnetically isolated USB cable. REEG data are of composite nature and normally analyzed by decomposing into frequency bands such as delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (12–30 Hz) and gamma (>30 Hz).

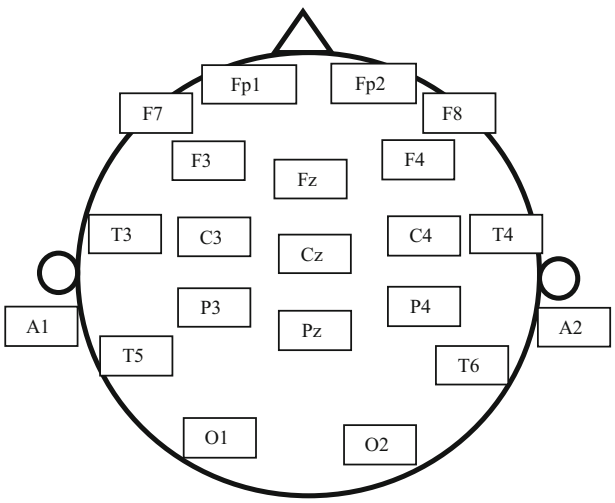

Fig. 1 Topomap showing EEG sensors locations on the scalp

EEG noise removal

Generally, the EEG data were confounded with different types of noises due to eye movements, blinks, or muscle activity and drowsiness. In this study, the noise from the EEG data was removed by visual inspection, semi-automatically, using specialized software named as NeuroGuide (R. Thatcher 2008). Semi-automatic means both user-defined and machine selected the artifact in the recorded EEG data. In order to improve the noise removal process, the selected templates should be at-least of 60 s of artifact free epochs from the raw data. In the software, the selected EEG segments were estimated for reliability using the Split-Half reliability score (SHR score). SHR is the ratio of variance between the odd and even time points of the time series from the selected EEG (Eisinga et al. 2013). The selection was performed with SHR score >0.90. Hence, the noise in the EEG data was removed and the clean EEG data were used for data analysis and building ML models.

The proposed ML method

Figure 2 shows a block level representation of the proposed ML methodology including feature extraction, selection, classification and tenfold cross validation (10-CV). In this study, the extracted EEG features such as the power computed from different bands and the inter-hemispheric coherence values were saved in a data matrix termed as the EEG data matrix. In the matrix, the rows correspond to the study participants during eyes closed (EC) and eyes open (EO) recordings, whereas the features were arranged column-wise. Further, the EEG data matrix was subjected to feature reduction via selecting the most significant features. The reduced set of most discriminant features were fed into the classifier to classify the study participants into their respective groups, i.e., either AUD patients or healthy controls.

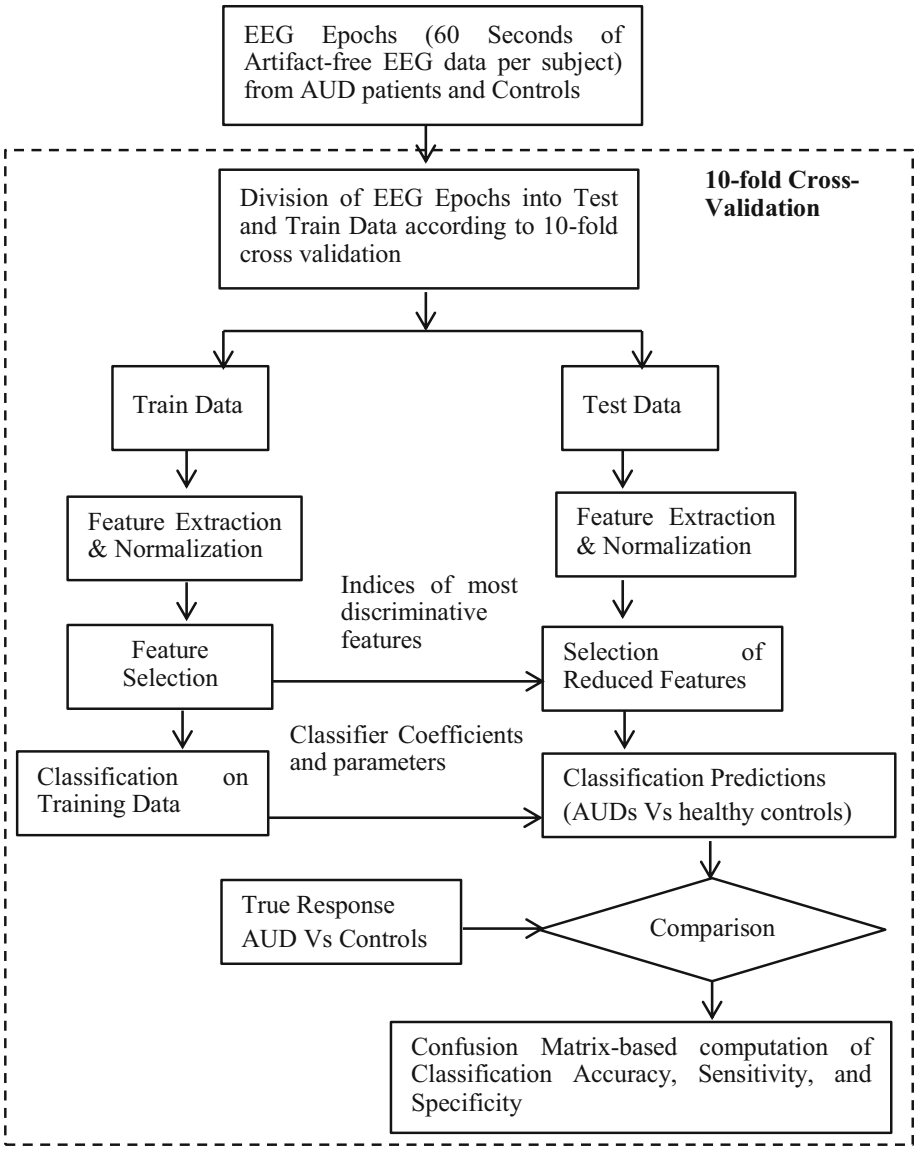

Fig. 2 Proposed ML method to classify the AUD patients and healthy controls

The input data to the proposed ML method was segmented into two groups (the train and test datasets) according to the 10-CV which ensures the independence between the test and train sets. The train dataset was involved to train the classification model including the sub processes such as the feature extraction, feature selection, and classification. On the other hand, the test dataset was included to compute the classifier performance such as accuracy, sensitivity, specificity, and the F1 measure.

Feature extraction

The spectral powers and inter-hemispheric coherences were computed from REEG data acquired to investigate the differences of these quantities between the AUD patients and controls. EEG-based features such as the spectral or absolute power (AP) were computed for each of 19 electrodes with 7 frequency bands: delta (0–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (12–25 Hz), high beta (25–30 Hz), gamma (30–40 Hz) and high gamma (40–50 Hz). Moreover, the relative power (RP) was computed as a ratio of each frequency band power over the total power (sum of AP of all frequency bands).

In addition to the power computations, the inter-hemispheric coherences were computed during EC and EO conditions. The associations between the brain regions were also evaluated for the detection of alcohol-related alterations in AUD using coherence. Inter-hemispheric coherence was calculated for all intra-hemispheric and inter-hemispheric pairwise combinations of electrodes. It was calculated based on the coupling degree of frequency spectral between two different time series (Thatcher et al. 2004). In this study, the inter-hemispheric coherence was computed pair-wise between two different EEG electrodes

and can be expressed by the following mathematical formula mentioned in Eq. (1). According to the formula, the magnitude squared of the cross spectrum of two EEG sensors was computing and divided by a product of the power spectral densities (PSD) of each of the signals:

$$C_{xy}(f) = \frac{|S_{xy}|^2(f)}{S_x(f)S_y(f)} \quad (1)$$

where f is the frequency, S_x is the PSD of x, S_y is the PSD of y, and S_{xy} is the cross-spectral density of the two EEG sensors of interest. The coherence was computed for each channel pair involving frontal (Fp1, Fp2, F3, F4, F7, F8, Fpz), temporal (T3, T4, T5, T6), parietal (P3, P4, P7, P8), occipital (O1, O2), and central (C3, C4). For example, EEG alpha asymmetry computed for Fp1 included channel pairs such as Fp1-Fp2; Fp1-F4; Fp1-F8; Fp1-T4; Fp1-T6; Fp1-P4; Fp1-P8; Fp1-O2; Fp1-C4. The extracted features were subjected to z-score normalization for the train and test matrices, separately.

Feature selection

To improve the classification accuracy and to reduce the risk of over-fitting the learned classifier model, it was mandatory to perform the feature selection (Guyon and Elisseeff 2003). In this study, the selection of features was performed based on the method of feature weighting according to the ROC curves of individual features (Mamitsuka 2006). According to the method, the Area under the ROC curve (AUC) was computed for each feature that reflected its ability to discriminate the target classes. The resulting values of AUC ranged from 0 to 0.5 that implicated bad to good classification ability. The features were assigned with weights and were arranged in descending order accordingly. For example, a features with lager weight was top-listed than a feature with a lesser weight. Now the top-listed features were considered as most relevant to the target labels. Moreover, the ranked-ordered features might be correlated with each other and could be redundant. Hence, the correlated features were identified and discarded. Hence, only the most relevant features were selected and employed for classification purposes.

The integration of features included concatenation of top ranked features from each feature set such as spectral powers of different bands and inter-hemispheric coherences. More specifically, top 5 features from delta power + top 5 features from theta power + top 5 features from alpha power + top 5 features from beta power + top 5 features from coherence. The integration of features was performed to determine the best feature patterns that corresponds highest classification of the AUD and healthy controls.

Classification

In this study, the classification was performed after selecting the most discriminant features. The feature selection was based on individual features such as power in different frequency bands and also based on their integration such as power and inter-hemispheric coherences. After selection of most discriminant feature, they were employed as input data to logistic regression (LR) classifier (Hosmer Jr and Lemeshow 2004). In this study, the LR classifier was used to model the relationship between the reduced set of features and the corresponding treatment outcomes (AUD patients and healthy controls) $y = [AUD, Controls]$, according to Eq. (4) (Hosmer Jr and Lemeshow 2004). The LR classifier was utilized in various epidemiological studies mainly for binary classification problems such as classification of cancer cases as malignant or benign and classification of microarray data (Liao and Chin 2007; Timmerman et al. 2005; Zhu and Hastie 2004).

The LR model coefficients were estimated based on maximum likelihood method and resulted into a likelihood value $l(x)$, where $0 \leq l(x) \leq 1$, which was an indication of a study participant's association either to AUD patients group or healthy controls group. If $l(x)$ was greater than a $threshold = 0.5$, the study participant was declared as associated with AUD patients group, and otherwise declared as associated with healthy control group, as mentioned in Eq. (2):

$$F(z) = E(Y/x) = \frac{1}{1 + e^{-z}} \quad (2)$$

where Y indicates the class labels and assigned a value either 'ADU' or 'Controls'. In addition, x represents a combination of different EEG features, i.e., the spectral power of different frequency bands and inter-hemispheric coherences. To obtain the LR model from the logistic function, we used Eq. (3):

$$z = \alpha + \beta_1 X_1 + \beta_2 X_2 + \cdots + \beta_k X_k \quad (3)$$

where z is a linear combination of α plus β_1 multiplied with X_1, plus β_2 multiplied with X_2, and plus β_k multiplied with X_k, where the X_k are the independent variables and α, and β_i are constant terms representing unknown parameters. Furthermore, by replacing the value of z from Eq. (3) to Eq. (2), the following Eq. (4) represents the logistic function:

$$F(z) = E(Y/x) = \frac{1}{1 + e^{-(\alpha + \sum \beta_i X_i)}} \quad (4)$$

In terms of response and non-response, the risk of a person to be non-responder or a responder is estimated and represented by Y or $l(x)$. The LR classifier resulted into a likelihood value $l(x)$, where $0 \leq l(x) \leq 1$, which was an indication of subjects, associated either with AUDs or healthy controls. If $l(x)$ was greater than the *threshold* $= 0.5$, the subject was declared as AUD, and otherwise as a healthy control. In summary, the LR classifier generated probability values to classify the study participants as either AUD patients or healthy controls.

Validation

The validation of the proposed ML method was important and based on computing values such as the classification accuracies, sensitivities, and specificities and F-measures. In this study, the values of classifier performances were computed during iterations of the 10-CV and were finally averaged. The true positive (TP) means the number of patients that were identified as patients and directly proportional to the classification sensitivity (Eq. 5). In addition, true negative (TN) means the number of healthy controls that were identified by the proposed method as healthy and directly proportional to the classification specificity (Eq. 6). The classification accuracy was computed as a ratio of sum of TP and TN divided by the sum of all possible cases during a classification process (Eq. 7). On the other hand, the false positives (FP) and negatives (FN) were considered as errors during classification and erroneously identified as either AUD patients or healthy controls.

F-scores as defined in Eq. (8), was applied to compare two classification models. F-score could be interpreted as a weighted harmonic average of precision and recall values (Van Rijsbergen 2004). The precision was defined as the probability that a (randomly selected) patient analyzed to be AUD was really AUDs. On the other hand, the recall was defined as the probability that an (randomly selected) AUD patient was correctly identified as AUDs. F-score was calculated using harmonic averaging because it preferred the balance between precision and recall so it would determine better for the optimal pair in highly unbalanced datasets. Due to an absence of prior information to either precision or recall, the beta value was set to 1 and the F-score was also named F1 score:

$$Sensitivity = \frac{TP}{TP + FN} \tag{5}$$

$$Specificity = \frac{TN}{TN + FP} \tag{6}$$

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN} \tag{7}$$

$$F = (1 + \beta^2) \times \frac{precision \times recall}{\beta \times precision + recall} \tag{8}$$

Results

Table 1 summarizes the alteration of brain activities based on AP, RP, standard deviation (SD) and the group comparison p value. During EC condition, the group comparison between AUD and controls exhibited an increase in total AP involving whole brain of AUD as compared with controls (53.90 vs. 106.88 μV^2; $AP_{AUD} \approx 1/2AP_{control}$). The AP increase was observed in most of frequency bands except for EC high beta and EO delta, which showed slight decrease ($p > 0.05$). Only theta and high gamma band presented significant increase of AP in AUD as compared with controls ($p < 0.01$ and $p < 0.05$ respectively). High gamma also showed a significant increase ($p < 0.05$) of AP in occipital and left temporal region. To summarize, as compared with controls, the AP of AUDs increased significantly in Theta and High Gamma frequency bands, and was larger but not significantly different in most other frequency bands..

Table 2 provides classification results for the two study groups involving the AUD patients and healthy controls. As shown in the table, among the EEG frequency bands the theta and delta, and high gamma bands showed highest classification performance such as accuracy $= \sim 85$ %. Moreover, the integration of all power bands resulted into an accuracy of 86.6 %. The inter-hemispheric coherence has shown accuracy of 80.8 % and combined with theta and hi-gamma features resulted into 89.3 %.

Discussion

In this paper, a ML method is proposed that utilizes EEG-based features as input data to discriminate the AUD patients from healthy controls. In this paper, the primary finding is that the EEG features such as the EEG powers and interhemispheric coherences computed from theta, delta, and high gamma bands can be used as physiological markers for the screening of AUD patients. In addition, these features are used as input data for the proposed ML models to classify the AUD patients and healthy controls. In contrary, the conventional methods for screening require subjective feedbacks from the AUD patients that may confound the screening process due to the human errors because quantification of the AUD intake is a tedious task.

In Table 1, the theta and high gamma bands show a significant difference between the groups which is in accordance with literatures (Porjesz and Begleiter 2003;

Table 1 EEG's mean AP in the whole brain of different frequency bands

Variable	AUD		Controls		Group comparison p value
	Mean	SD	Mean	SD	
EC					
Delta	9.88 (9 %)	1.64	8.73 (16 %)	1.5	0.480 (0.004)
Theta	**52.53 (49 %)**	**18.7**	**18.45 (34 %)**	**4.7**	**0.003 (0.044)**
Alpha	13.48 (13 %)	4.87	13.18 (24 %)	4.2	0.906 (0.001)
Beta	8.42 (8 %)	1.52	8.17 (15 %)	1.5	0.845 (0.000)
High beta	1.43 (1 %)	0.43	1.52 (3 %)	0.4	0.735 (0.001)
Gamma	2.99 (3 %)	0.96	2.02 (4 %)	0.9	0.055 (0.086)
High gamma	**18.16 (17 %)**	**7.16**	**1.83 (3 %)**	**0.5**	**0.018 (0.005)**
Total	106.88 (100 %)		53.90 (100 %)		
EO					
Delta	8.38 (9 %)	1.26	8.59 (18 %)	2.0	0.867 (0.001)
Theta	**45.87 (51 %)**	**15.5**	**17.34 (36 %)**	**4.8**	**0.012 (0.046)**
Alpha	6.89 (8 %)	1.41	6.32 (13 %)	1.2	0.586 (0.000)
Beta	8.91 (10 %)	2.32	8.28 (17 %)	1.5	0.679 (0.000)
High beta	2.28 (3 %)	1.22	2.58 (5 %)	1.7	0.677 (0.004)
Gamma	4.05 (5 %)	2.08	2.97 (6 %)	1.8	0.183 (0.037)
High gamma	**13.44 (15 %)**	**5.41**	**2.25 (5 %)**	**0.9**	**0.010 (0.015)**
Total	89.81 (100 %)		48.34 (100 %)		

Numbers without parentheses refer to AP, numbers with parentheses refer to RP

Bold values indicates $p < 0.01$

Table 2 Classifying AUD and healthy controls based on LR classification

QEEG feature	Accuracy (%)	Sensitivity (%)	Specificity (%)	F-measure
Delta power	79.1	82.5	80	0.80
Theta power	**85**	**82.5**	**87.5**	**0.84**
Alpha power	75.4	90	75	0.78
Beta power	85	85	87.5	0.84
Hi-gamma band	**85.8**	**85**	**87.5**	**0.87**
Integration of theta and hi-gamma	**87.8**	**87**	**89.5**	**0.89**
Integration of alpha, beta and delta	86	86	88.5	0.85
Inter-hemispheric coherence	80.8	82.5	80	0.78
Integration of theta, alpha, beta and hi-gamma bands	86.6	95	82.5	0.88
Integration of theta, high gamma and coherence	**89.3**	**88.5**	**91**	**0.90**

Bold values indicates $p < 0.01$

Rangaswamy et al. 2002, 2003). These findings implicate that the theta, beta and high gamma bands are most significant while analyzing the AUD patients and healthy controls. In Table 1, spectral power shows their ability in analyzing and discriminating AUD patients from healthy controls. Spectral power shows overall differences between AUD patients and controls but show insignificance at every electrode location. Using spectral power would help to explain the alteration of brain activities of AUD patients. In comparison, AP and RP show more discrimination between the two groups. Especially, theta power has proved its potential by outperforming other frequency bands with a remarkable power increase exhibited in AUD patients. Theta power changes, observed in alcoholics, were also reported in literature as a consistent indication for alcoholics screening. In addition, power of gamma band shows significant differences between AUD patients and controls. However, its potential has not received adequate attention. On the other hand, the inter-hemispheric coherence exhibits associations between different brain regions and their variation under the effect of alcohol in AUD patients.

The classification results presented in Table 2 reveal the significance of the theta, and high gamma bands and their integration have revealed classification accuracy nearly ~87 %. This implicates the robustness of the proposed method. Since the results are based on the logistic

Table 3 Related studies about EEG application and their limitations

Objective	EEG brain dynamics	Algorithm	Authors	Results (%)
Predicting relapse	Spectral power	Logistic regression	Bauer (2001)	75
	Spectral power with Hjorth's features	Discriminant analysis and ANN	Winterer et al. (1998)	83–85
	P300	Discriminant function analysis	Wan et al. (2010)	63.9
Screening alcoholics	Spectral power and coherence	Locally weight regression	Guntaka and Tcheslavski (2013)	66.45
	ERP's components	ANN	Lopes et al. (2004)	71
	ERP's components	Learning vector quantization	Lopes et al. (2005)	80
	Gamma visual evoked potential (VEP) power	Least square support vector machine (SVM)	Shooshtari and Setarehdan (2010)	82.98
	Raw EEG in F4 and P8	Hidden Markov model	Zhong and Ghosh (2002)	90.50
	Gamma VEP	MLP–BP with elliptic filter	Kanna et al. (2005)	91
	Approximate entropy (ApEn), Sample entropy (SampEn), Largest Lyapunov exponent (LLE), (high order spectra) HOS	SVM	Acharya et al. (2012)	91.70
	HOS	Fuzzy Sugeno classifier	Faust et al. (2013a)	92.40
	ERP's components	Random forest	Kuncheva and Rodríguez (2013)	94.50
	Multi gamma band VEP	MLP	Palaniappan (2007)	94.55
	Yule Walker coefficient	Artificial NN	Ek et al. (2013)	95.00
	Wavelet relative power	K-nearest neighbor	Faust et al. (2013b)	95.80
	Horizontal visibility graph entropy	K-nearest neighbor	Zhu et al. (2014)	95.80
	Gamma VEP	PCA	Ong et al. (2005)	95.83
	Gamma VEP	MLP	Palaniappan et al. (2002)	96.10
	Gamma VEP	LDA	Palaniappan (2005)	97.40
	Gamma VEP	KNN	Palaniappan (2003)	98.71
	Spectral power using Haar wavelet	Multilayer perceptron network (MLP)	Kousarrizi et al. (2009)	98.83
	Spectral entropy	Probabilistic neural network	Padmanabhapillai et al. (2006)	99.00
	VEP energy in occipital	KNN OR support vector data description	Zúquete et al. (2010)	99.20
	Mean and variance of signals	Bayes with KNN and PCA (claim to classify AA)	Yazdani and Setarehdan (2007)	100
Classify epileptic and alcoholic	Recurrence quantification analysis (RQA)	Gaussian mixture model (GMM)	Ng et al. (2012)	98.6

regression classifier which is considered as a simple classifier when compared with the SVM. Hence, the proposed ML classifier model is simple in complexity. EEG may be utilized to screen AUD patients, to predict relapse and to evaluate medication effects. As summarized in Table 3, in spite of the rapid development in physiological studies of alcoholic brains, few reports discuss application of EEG for early relapse detection and medication evaluation, because low accuracy made it impossible for EEG clinical applicability for AUD patients. Besides that, in review article about clinical and neuropsychiatric application for alcohol addiction treatment (Ritsner 2009; Tavakoli et al. 2011), EEG was not mentioned in primary health care. In addition, few studies have applied EEG for AUD treatment. For relapse prediction, there are few studies using spectral power and nonlinear features, e.g., extracting Hjorth features from REEG. Unfortunately, their accuracy is not efficient enough for clinical practice because of either low sensitivity (Bauer 2001) or low specificity (Winterer et al. 1998).

Regarding AUD screening, various studies have utilized different electrophysiological features and classification algorithms with high accuracy (>90 %) for the classification between alcoholics and controls. These results have

confirmed the difference between AUD and controls, and provide evidence that EEG may be a potential screening tool for AUD. However, there is no discussion or analysis about the features and algorithms used in most of those studies. In this study, integration of EEG features such as theta power, high gamma power and inter-hemispheric coherence are proposed as markers that can classify the AUD patients with an accuracy of $\sim$89 %.

Studies based on EEG observation in patients with alcoholism had resulted into seizures like patterns similar to the ones happened during epilepsy. Ping et al. (Ng et al. 2012) has implemented an automatic method to differentiate epileptic, controls and alcoholics using EEG with accuracy of 98.6 %. However, the validity of data was doubtful because the datasets were acquired from different sources and experiment designs such as visual oddball stimulus versus eye closed. The data were recorded with different equipment having 64 and 128 channels, and references systems (Cz vs. common average reference) without any indication about the synchronization between two datasets. Moreover, the dataset of alcoholism in the study contained not only alcoholics but also control subjects (Zhang et al. 1997). There were no standard procedures to categorize study populations during clinical evaluation. In addition, factors such as sociodemographic characteristics and family drinking history need to be considered and controlled.

There is a possibility that our proposed ML models are confounded with some outliers other than the relevant patterns extracted from the brain activities. We have ruled out this concern by (1) properly adopting artifact removal techniques, (2) standardizing preprocessed data based on z-scores, (3) during classifier's testing and training, selecting random data points so that each data point in the feature space can be used. Based on all these precautions, we may conclude that the results shown here are un-biased and true representation of the information from the recorded pretreatment EEG data.

Conclusion

In this study, a ML method was proposed to classify the AUD patients from healthy controls base on resting-state EEG data. While comparing with the healthy controls, the AUD patients have shown a significant increase in theta, high gamma powers and inter-hemispheric coherences. The classification results implicate that qEEG features such as theta, gamma power and inter-hemispheric coherence could be utilized as characteristic features to automatically learn the disease-specific patterns in the resting-state EEG data acquired from the study groups. In addition, it has been concluded that the integration of qEEG features could reach a highly accurate method. Furthermore, the proposed ML method implicate that EEG-based CAD tool can be developed and help in making the AUD screening an automated and a standard procedure.

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