ORIGINAL ARTICLE

Depression Identification Using Asymmetry Matrix and Machine Learning Algorithms

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Abstract

Purpose: Developing an efficient and reliable method for the identification of depression is highly important. This paper aims to propose an approach for depression diagnosis using an interhemispheric asymmetry matrix and machine learning algorithms.

Materials and Methods: First, an EEG signal was acquired from 24 depressed patients and 24 healthy subjects. The EEG signal was acquired from participants for 5 minutes in Eyes-Closed (EC) and 5 minutes in Eyes-Open (EO) condition. After preprocessing data, interhemispheric asymmetry for absolute and relative powers of theta and beta frequency bands, theta-to-alpha power ratio, and Individual Alpha Frequency (IAF) features were computed. Then, the proposed asymmetry matrix is used as a feature for statistical and classification analysis. In this paper, the classification was performed using a Support Vector Machine (SVM), logistic regression, and Multi-Layer Perceptron (MLP).

Results: The results demonstrated that central and temporal theta absolute power, central and temporal IAF asymmetries in the EC condition and occipital beta absolute power, temporal theta relative power, temporal theta-to-alpha power ratio, and temporal IAF asymmetries in the EO condition have significant differences between depressed and healthy groups. Findings show that beta absolute power asymmetry in the occipital region and EO condition is a good biomarker for depression identification with 77.1% accuracy using the Gaussian SVM classifier.

Conclusion: The results of this study show performance of proposed asymmetry matrix features in depression detection. Findings show that beta absolute power asymmetry in the occipital region and EO condition is a good biomarker for depression identification.

Keywords: Depression; Electroencephalogram; Asymmetry Matrix; Machine Learning Algorithms.

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1. Introduction

Major Depressive Disorder (MDD) is a mental illness that includes symptoms such as hopelessness, lack of motivation, loss of interest, feeling of sadness, and even suicidal thoughts. According to the World Health Organization (WHO), all over the world, approximately 800,000 people die due to this disorder every year [1]. Depression is associated with a stressful condition, genetic vulnerability, and an imbalance in hormones and neurotransmitters [2]. Approximately, half of MDD patients are unaware of their illness or their illness is misdiagnosed. Traditionally, depression diagnosis depends on subjective evaluation using interview sessions and psychiatric scales. These methods are useful but time-consuming and may lead to misdiagnosis due to environmental and human factors. Therefore, it is crucial to develop an accurate method for classifying depressed and healthy subjects. For this aim, the brain activity of the patients can be monitored objectively using imaging techniques. Among various imaging modalities, EEG has gained attention as it is non-invasive and cost-effective with high temporal resolution [3]. Nowadays, EEG-based depression diagnosis using machine learning algorithms is of great interest. In [4] absolute and relative beta power bands have been analyzed with separate three-way multivariate analysis (ANOVA). The results of this study indicate that relative beta power was greater in depressed patients than in healthy subjects at all electrode locations and absolute power has the same manner for some of the electrode locations. This paper does not use any classification method to separate depressed and normal groups using these features. The authors in [5] find increased activity in theta and alpha bands in the occipital and parietal regions of the brain in depressed subjects. A study conducted by Hosseinifard *et al.* [6] with 90 subjects presented evidence that alpha and theta bands are good discriminators between depressed and healthy controls. They used K-Nearest Neighbors (KNN), linear discriminant analysis, and Logistic Regression (LR) for discriminating the two groups. In [7], the classification of normal subjects from depressed patients was identified by using the power spectrum of EEG signals and Support Vector Machine (SVM) classifier. The experimental results of this study are carried out with the help of 13 depressed patients and 12 normal subjects. Authors in [8] and [9] conducted experiments with 176 and 170 subjects, respectively. Only 3 electrodes (Fp1, Fp2, and Fz) were used in these studies. The results show that beta frequency band activity achieved the best results between MDD and healthy group classifications. In these studies, KNN, SVM, Artificial Neural Network (ANN), and Deep Belief Network (DBN) were used to analyze the data. Mumtaz *et al.* [10] used LR, SVM, and Naïve Bayesian (NB) methods for classifying 33 MDD and 30 healthy controls. They used band power and alpha interhemispheric asymmetry as linear characteristics of EEG signals. Saeedi *et al.* [11] employed Discrete Wavelet Transform (DWT) to decompose EEG signals into detailed and approximate coefficients. Then, the delta, theta, alpha, beta, and gamma frequency bands of the EEG signals were used as linear features. They utilized KNN, and SVM machine learning algorithms, and also Multi-Layer Perceptron (MLP) as a deep learning method to identify depressive cases. Most of the studies [3, 10, 12] show that interhemispheric frontal alpha asymmetry is a key marker of the human brain in depression detection. Except for the alpha frequency band, asymmetry activities in other brain regions and frequency bands may also be associated with depression. This paper investigates the absolute and relative power of theta and beta frequency bands, Individual Alpha peak Frequency (IAF), and theta-to-alpha power ratio features asymmetries capability in depression detection using statistical analysis and machine learning algorithms.

The rest of the paper is organized as follows: In the "Materials and Methods" section, participants, EEG recording and preprocessing, asymmetry matrix extraction, statistical analysis, and classification methods are described. In the "Results" section, the output of the statistical analysis and classification of the proposed features are investigated. In the last section, the discussion and conclusion are presented.

2. Materials and Methods

2.1. Subject

This study includes 24 MDD and 24 normal subjects that were referred to the Asayesh rehabilitation clinic, Tabriz, Iran.

The MDD diagnosis was made based on DSM-V criteria by an expert psychiatrist. All of the subjects were medication-free and expressed their consent to participate in this research. The demographic information of the subjects is illustrated in Table 1.

Table 1. Demographic information of participants

	Gender			Age		
	Male	Female	Total	Male	Female	Total
Depression	12 (50%)	12 (50%)	24	35.66±11.39	38.25±14.40	36.95±12.77
Healthy	12 (50%)	12 (50%)	24	32.58±7.11	33.16±8.03	32.99±7.73

Based on this table, there are no significant differences between MDD and normal subjects in age and gender.

2.2. EEG Recording and Preprocessing

First, the resting state EEG signal was acquired from subjects for 5 minutes in Eyes-Closed (EC) and 5 minutes in Eyes-Open (EO) conditions according to the 10-20 system using Mitsar 19 channel device. Then, recorded signals passed through the low-pass filter with a 50 Hz cut-off frequency and the high-pass filter with a 0.1 Hz cut-off frequency. Also, a notch filter with 45 and 55 Hz cut-off frequencies was used to remove the electrical noise (Gamma and high gamma bands were analyzed in simulations. However, the results of these frequency bands are not mentioned in this paper. For this aim, 50 Hz was used for lowpass filter's cut-off frequency, and for removing line power artifact notch filter was used). For removing eye movement artifacts such as saccades and blinking the Infomax Independent Component Analysis (ICA) was used [13]. Recordings were further cleaned with an automated z-score-based method using the FASTER plugin [14].

2.3. Asymmetry Matrix Computation

After preprocessing EEG signals, interhemispheric asymmetry of theta (4-8 Hz) absolute power, theta relative power, beta (13-30 Hz) absolute power, beta relative power, theta-to-beta power ratio, and IAF were computed based on Equation 1:

$$A(ch1, ch2) = \frac{F_{ch1} - F_{ch2}}{F_{ch1} + F_{ch2}} \tag{1}$$

Where *ch1* is a channel in the left hemisphere and *ch2* is the analogous channel of *ch1* in the right hemisphere. F_{ch} defines the specific feature value in channel *ch*.

Figure 1 shows a schematic of EEG asymmetry calculation. Using Equation 1, it is possible to calculate the difference between the features of two channels for each channel pair, and hence the difference in activity corresponding to each part of the brain can be identified [15].

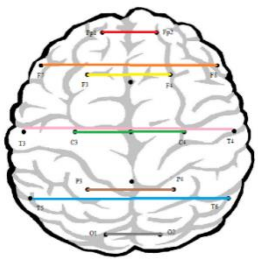

Figure 1. Schematic of EEG asymmetry calculation. For example, the red line shows asymmetry calculated between Fp1 and Fp2

After calculating asymmetry values for each pair of electrodes, an asymmetry matrix according to Table 2 is proposed to express the asymmetry values of each feature. This matrix is used as a feature for statistical and classification analysis.

Table 2. Asymmetry matrix. Orange, yellow, blue, green, and gray cells define frontal, central, temporal, parietal, and occipital regions asymmetry

A(Fp1,Fp2)	*A*(T3,T4)
A(F3,F4)	*A*(T5,T6)
A(F7,F8)	*A*(P3,P4)
A(C3,C4)	*A*(O1,O2)

2.3.1. IAF Calculation

IAF is defined as a frequency associated with the strongest EEG power within the alpha frequency band. For IAF calculation, the Fast Fourier Transform (FFT) based power spectrum analysis (Welch method) was obtained for each subject. The frequency within the extended alpha range (8-13 Hz) showing a power peak in the power spectrum was considered as the IAF [16].

2.4. Statistical Analysis

In this study, to investigate asymmetry features' ability in depression detection statistical analysis was performed to measure the level of statistically significant differences between various groups. Due to the non-normal distribution of asymmetry features, the Mann-Whitney U-test ($\alpha \leq 0.05$) was applied to asymmetry matrixes. This test takes a value of two groups as input. For prepare inputs, first 4×2 asymmetry matrixes are reshaped into 8×1 vectors resulting in 24 vectors with a size of 8×1 per group. By accumulating these vectors in one vector, a suitable input with a size of 192×1 was generated for each group (see Appendix). Then, Mann-Whitney U-test was applied to them. Since the Mann-Whitney test is a non-parametric test the length of each input vector indicates the degree of freedom. To investigate brain regions' effects on depression detection, statistical analysis was also performed at the level of the region. For this aim, the asymmetry matrix of each feature was divided into 5 brain regions according to Table 3. Then, the Mann-Whitney test was applied to these electrodes for investigating the related brain region's role in depression detection.

Table 3. Channel clustering for each brain region

Frontal	A(Fp1, Fp2), A(F3, F4), A(F7, F8)
Central	A(C3, C4)
Parietal	A(P3, P4)
Temporal	A(T3, T4), A(T5, T6)
Occipital	A(O1, O2)

2.5. Classification

A classifier utilizes features as input to predict the corresponding label of each input by training a number of parameters from the training dataset. A trained classifier can recognize a new instance in an unseen testing dataset [17]. In this study, three types of classifiers, including SVM, LR, and MLP were used to categorize normal and depressed subjects. SVM has been widely used for the classification of EEG signals for the diagnosis of neural disorders [18]. This method transforms input data into higher dimensional space using a kernel trick. Then, it segregates the data via a hyperplane with maximal margins. LR is a classification algorithm used to find the best-fitting to describe the relationship between features and labels. This method transforms its output using the logistic sigmoid function to return aprobability value [19]. In 1958, Rosenblatt [20] introduced the first neural network called perceptron which is the basic unit of deep learning. When perceptron is combined

with other components, it can solve complex problems. When several perceptrons combine in layers, an artificial neural network named MLP is created that comprises three sequential layers: input, hidden, and output.

3. Results

3.1. Statistical Analysis

The results of the comparison of healthy and MDD groups using different asymmetry matrixes in EC and EO conditions are illustrated in Table 4. According to this table, features extracted from all 19 channels do not show any significant differences between the two groups. But, in region-based analysis, theta absolute power asymmetry and IAF asymmetry in the central and temporal regions in the EC condition are statistically significant between healthy and MDD groups. In the EO condition, beta absolute power asymmetry in the occipital region, and theta relative power asymmetry, theta-to-alpha power ratio asymmetry, and IAF asymmetry in the temporal region have significant differences between the two groups.

Figure 2 shows box plots of significant features. According to this figure, in the EC condition, theta absolute power asymmetry in the central and temporal regions has greater values in MDD patients than in normal subjects. But, IAF asymmetry in the central and temporal regions has larger values in normal subjects than in MDD patients. In the EO condition, MDD patients have large theta relative power asymmetry, theta-to-alpha power ratio asymmetry, and IAF asymmetry in the temporal region, and healthy subjects have large beta absolute power asymmetry in the occipital region.

3.2. Classification

In this section, the classification ability of statistically significant features was investigated using

Table 4. Results of the statistical analysis between two groups of depressed and healthy by Mann-Whitney test. P, U, Z, and DF indicates the p-value, U-value, Z-value, and degree of freedom respectively. F, C, P, T, and O indicates frontal, central, parietal, temporal. and occipital regions of the brain

Features		EC						EO					
		All	F	C	P	T	O	All	F	C	P	T	O
Theta absolute power asymmetry	P	0.43	0.24	**0.01**	0.65	**0.005**	0.15	0.26	0.42	0.42	0.26	0.40	0.50
	U	19280	2883	164	266	1531	218	17229	2393	249	234	1266	255
	Z	0.78	1.16	-2.54	-0.44	2.77	-1.43	-1.11	-0.79	-0.79	0.83	-1.10	-0.67
	DF	192	72	24	24	48	24	192	72	24	24	72	24
Beta absolute power asymmetry	P	0.88	0.99	0.28	0.79	0.09	0.08	0.14	0.20	0.54	0.47	0.96	**0.01**
	U	18590	2594	236	301	1381	205	16840	2276	318	253	1158	165
	Z	0.14	0.00	-1.06	0.26	1.67	-1.70	-1.46	-1.26	0.61	-0.71	0.04	-2.53
	DF	192	72	24	24	48	24	192	72	24	24	48	24
Theta relative power asymmetry	P	0.74	0.75	0.58	0.95	0.63	0.70	0.16	0.88	0.17	0.94	**0.003**	0.38
	U	18790	2671	261	258	1217	307	19959	2629	222	292	1547	331
	Z	0.32	0.31	-0.54	-0.05	0.47	46	1.40	0.15	-1.35	0.07	2.89	0.88
	DF	192	72	24	24	48	24	192	72	24	24	48	24
Beta relative power asymmetry	P	0.16	0.16	0.30	0.78	0.17	0.46	0.62	0.53	0.94	0.57	0.92	0.48
	U	16919	2241	338	302	965	252	17899	2437	292	316	1165	254
	Z	-1.39	-1.40	1.02	0.28	-1.37	-0.73	-0.49	-0.62	0.07	0.57	0.09	-0.69
	DF	192	72	24	24	48	24	192	72	24	24	48	24
Theta-to-alpha power ratio asymmetry	P	0.73	0.61	0.47	0.87	0.35	0.71	0.14	0.19	0.38	0.54	**0.001**	0.12
	U	18804	2719	253	280	1280	270	20010	2266	245	318	1594	362
	Z	0.34	0.51	-0.71	-0.15	0.93	-0.36	1.45	-1.30	-0.87	0.61	3.24	1.52
	DF	192	72	24	24	48	24	192	72	24	24	48	24
IAF asymmetry	P	0.29	0.27	**0.01**	0.55	**0.03**	0.73	0.78	0.55	0.17	0.94	**0.05**	0.78
	U	17283	2319	402	863	259	305	18135	2741	354	284	889	274
	Z	-1.06	-1.09	2.34	-2.11	-0.59	0.34	-0.27	0.59	1.35	-0.07	-1.92	-0.28
	DF	192	72	24	24	48	24	192	72	24	24	48	24

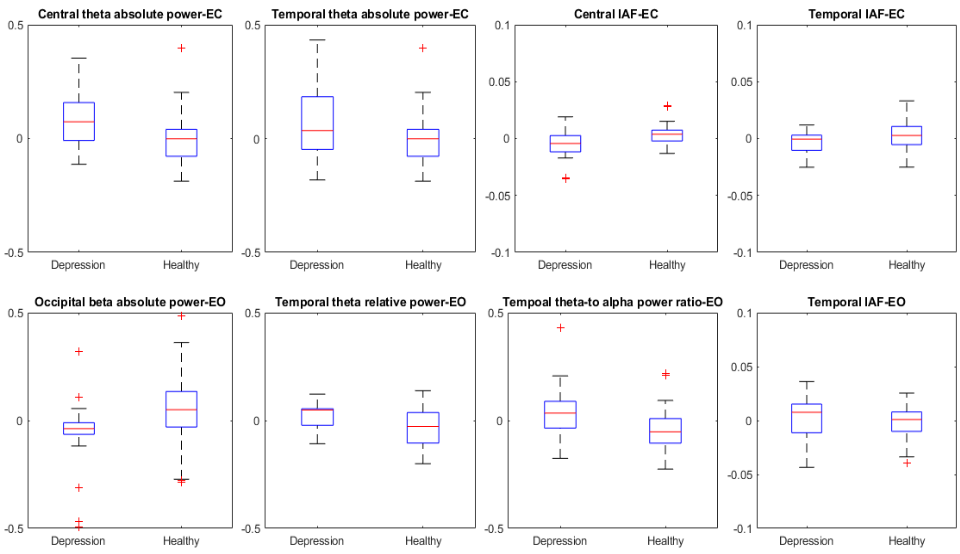

Figure 2. Mean value of significant features in depressed and healthy groups

SVM with the quadratic kernel, LR, and MLP neural network. The MLP used in this paper has one hidden layer with 20 neurons and the sigmoid function was used as activation of neurons. For this aim, 70% of the dataset was used in the training phase and 30% was used in the testing phase. Also, a 5-fold cross-validation method was used in the training of classifiers, and the evaluation criteria are reported as mean ± standard deviation of folds. The criterion applied for classification evaluation is accuracy. Based on Equation 2, the classification accuracy is the number of correctly predicted data points out of all the data points.

$$ACC = \frac{TP + TN}{TP + TN + FP + FN} \quad (2)$$

In this equation, TN, FN, TP, and FP are respectively true negative, false negative, true positive, and false positive values.

Figure 3 shows MDD and healthy subjects' classification mean accuracy using different asymmetry features and various classifiers. Based on this figure, occipital beta absolute power in the EO condition achieves the best classification result with 77.1% accuracy using the SVM classifier. Also, this feature shows good classification performance with 72.7% accuracy using MLP as a classifier. Temporal theta absolute power asymmetry in the EC condition has good classification performance with 74.2% and 70.8% accuracy using MLP and SVM classifiers, respectively.

4. Discussion and Conclusion

According to previous studies, interhemispheric frontal alpha asymmetry is a key marker for depression detection. This paper investigates other frequency bands and brain regions' abilities in this field. For this aim, interhemispheric asymmetry for theta and beta absolute power, theta and beta relative power, theta-to-beta power ratio, and IAF features were computed. Then, the asymmetry matrix was calculated from the asymmetry values of pair electrodes for each feature. This matrix was used as a feature for statistical and classification analysis. The results showed that, in the EC EEGs, theta absolute power and IAF asymmetries in the central and temporal regions have significant differences between MDD and healthy groups. In the EO EEGs, beta absolute power asymmetry in the occipital region, theta relative power, theta-to-alpha power ratio, and IAF asymmetries in the temporal region show significant differences between the two groups.

Structural MRI studies in adult samples show differences in shape and volume between depressed and healthy groups in the temporal region [18]. In line with this finding, in current research, the asymmetry matrix of different features mostly shows significant differences between MDD and healthy groups in the temporal region.

Each EEG frequency band is associated with some mechanisms in the brain. The beta band is related to expectancy and theta band is related to emotion processing [19]. Analysis of this paper shows that beta absolute power asymmetry in the occipital region is significantly lower in MDD patients. In support of our finding, a recent work [20] reports reduced beta waves in the left side of the brain for depression. Furthermore, authors in [8, 9] indicate that beta band features had good depression prediction ability. In the present study, the best classification result was achieved by occipital beta absolute power asymmetry. The authors in [5] found increased activity in theta, alpha, and beta bands in the occipital and parietal areas of the brain of depressed subjects. In line with this

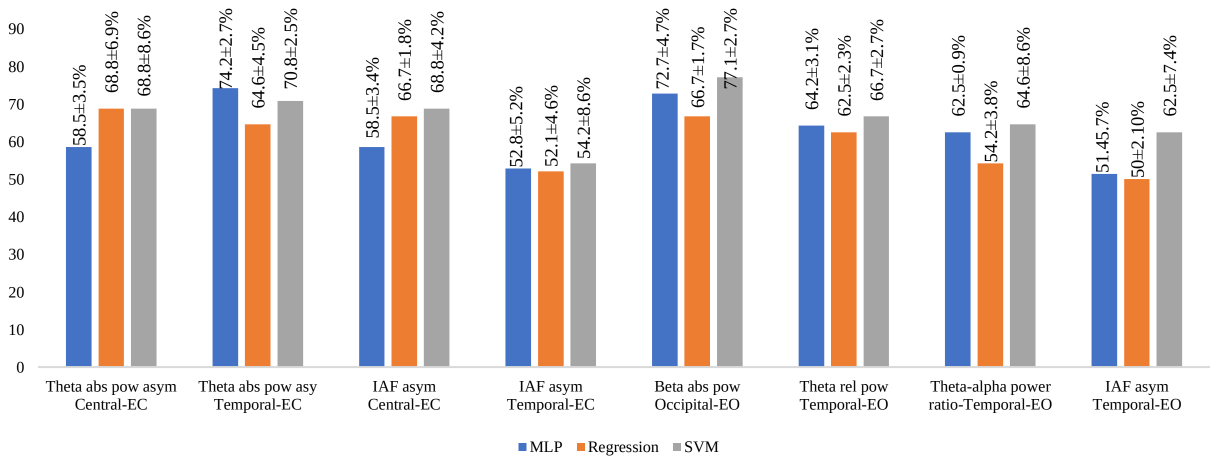

Figure 3. Classification accuracy of healthy and depressed subjects using significant features and SVM, MLP, and regression methods. The results were reported based on the mean ± standard deviation of folds

research, asymmetry matrix features of theta frequency band are greater in MDD patients. But in contrast with [5], asymmetry matrix features are significant in the temporal and central brain areas. Using the accuracy of a classifier, Hosseinifard *et al.* [6] find that theta band especially in the left hemisphere is a good feature to discriminate depressed from healthy subjects. Our classification results show good performance using theta absolute power asymmetry of the temporal region, too. The authors could not find any article that used theta-to-alpha power ratio and IAF for depression detection. However, these features' interhemispheric asymmetries show significant differences between healthy and MDD groups in our dataset.

To evaluate the ability of proposed features in depression detection, classification was performed using frontal interhemispheric alpha asymmetry [3, 10, 12], theta absolute power [5, 6], beta absolute power [4], and alpha absolute power [5, 6] features that were used in previous studies. The results of classification using these features are illustrated in Figure 4. This figure shows that the proposed asymmetry-based features show better classification performance than traditional frequency-based features.

In this study, the ability of asymmetry features in depression prediction has been investigated using SVM, LR, and MLP classifiers. According to Figure 3, occipital beta absolute power asymmetry and temporal theta absolute power asymmetry show good classification performance using SVM and MLP classifiers. This research has a limited number of features for training classifiers. It is expected that by increasing the number of data, classification performance increased too.

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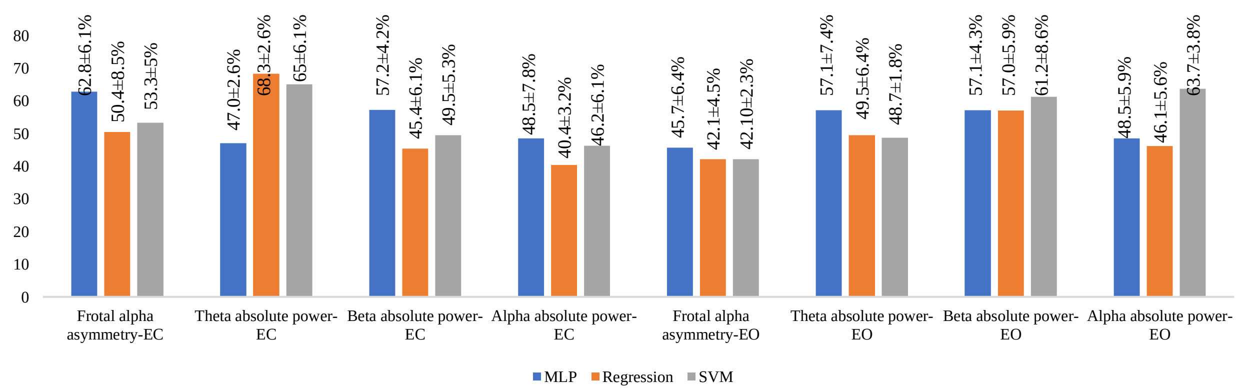

Figure 4. Classification accuracy of healthy and depressed subjects using features proposed in [3-6, 10, 12]. The results were reported based on the mean ± standard deviation of folds

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Appendix

Mann-Whitney U-test takes the value of two groups as a vector. The asymmetry features are as a matrix (i.e. it is a 4×2 matrix in 19-electrode analysis). Therefore, there are 24 4×2 matrixes per group as Figure a. It is impossible to use this matrix as input for statistical analysis in Matlab (it takes two n×1 vectors as input). So, 4×2 asymmetry matrixes are reshaped into 8×1 vectors. Now, based on Figure b, there are 24, 8×1 vectors per group. By accumulating these vectors in one vector the proper input for the statistical test was performed for each group. Since the Mann-Whitney test is a non-parametric test the length of each input vector was reported as the degree of freedom (i.e. when all of the electrodes were used in the analysis, the length of the input vector is 4×2×24 = 192 for each group). Because we do not have 1 feature for each subject, the degree of freedom is not equal to 24.

The rank mean of one group is compared to the overall rank mean to determine a test statistic called a Z-value. Below is the formula to compute Z-value for the Mann-Whitney test:

$$z = (U_1 + 0.5) - \left(\frac{U_1 + U_2}{2}\right) / \sqrt{\frac{n_1 n_2 (n_1 + n_2 + 1)}{12}}$$

Where U_1, U_2, n_1, and n_2 indicate the U-value of group 1, the U-value of group 2, the number of subjects in group 1, and the number of subjects in group 2, respectively. A positive Z-value indicates an upward trend and a negative Z-value indicates a downward trend in data.

4×2 asymmetry matrix	Subject 1
4×2 asymmetry matrix	Subject 2
4×2 asymmetry matrix	Subject 3
. . .	. . .
4×2 asymmetry matrix	Subject 24

Figure a. Schematic of initial inputs

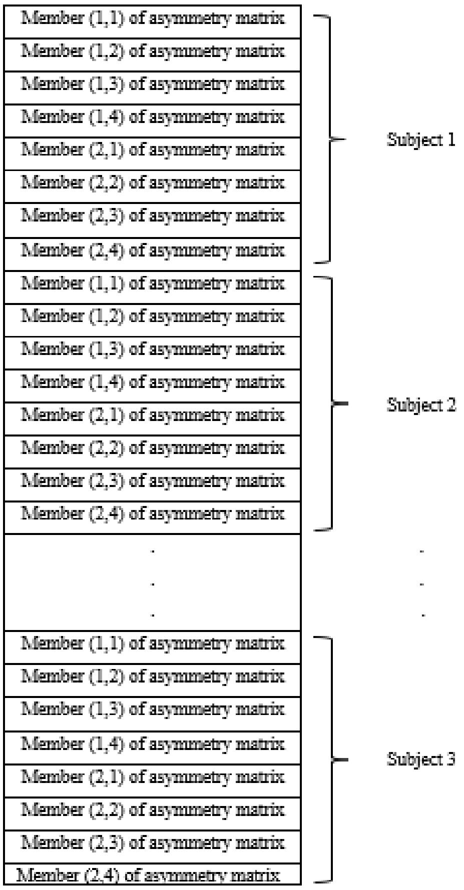

Figure b. Schematic of final inputs