Author(s): Liu, Wenya; Zhang, Chi; Wang, Xiaoyu; Xu, Jing; Chang, Yi; Ristaniemi, Tapani; Cong, Fengyu

Title: Functional connectivity of major depression disorder using ongoing EEG during music perception

Year: 2020

Version: Accepted version (Final draft)

Please cite the original version:

Liu, W., Zhang, C., Wang, X., Xu, J., Chang, Y., Ristaniemi, T., & Cong, F. (2020). Functional connectivity of major depression disorder using ongoing EEG during music perception. Clinical Neurophysiology, 131(10), 2413-2422. https://doi.org/10.1016/j.clinph.2020.06.031

Journal Pre-proofs

Functional connectivity of major depression disorder using ongoing EEG during music perception

Wenya Liu, Chi Zhang, Xiaoyu Wang, Jing Xu, Yi Chang, Tapani Ristaniemi, Fengyu Cong

PII: S1388-2457(20)30416-8
DOI: https://doi.org/10.1016/j.clinph.2020.06.031
Reference: CLINPH 2009314

To appear in: *Clinical Neurophysiology*

Received Date: 25 November 2019
Revised Date: 7 May 2020
Accepted Date: 29 June 2020

Please cite this article as: Liu, W., Zhang, C., Wang, X., Xu, J., Chang, Y., Ristaniemi, T., Cong, F., Functional connectivity of major depression disorder using ongoing EEG during music perception, *Clinical Neurophysiology* (2020), doi: https://doi.org/10.1016/j.clinph.2020.06.031

Functional connectivity of major depression disorder using ongoing EEG during music perception

Wenya Liu[a,b], Chi Zhang[a], Xiaoyu Wang[a], Jing Xu[c], Yi Chang[c], Tapani Ristaniemi[b], Fengyu Cong[a,b,d,e]

[a]School of Biomedical Engineering, Faculty of Electronic and Electrical Engineering, Dalian University of Technology, 116024, Dalian, China

[b]Faculty of Information Technology, University of Jyväskylä, 40014, Jyväskylä, Finland

[c]Department of Neurology and Psychiatry, First Affiliated Hospital, Dalian Medical University, 116011, Dalian, China

[d]School of Artificial Intelligence, Faculty of Electronic Information and Electrical Engineering, Dalian University of Technology, 116024, Dalian, China

[e]Key Laboratory of Integrated Circuit and Biomedical Electronic System, Liaoning Province. Dalian University of Technology, 116024, Dalian, China

Corresponding author:

1. Fengyu Cong, School of Biomedical Engineering, Faculty of Electronic and Electrical Engineering, Dalian University of Technology, 116024, Dalian, China

Email: cong@dlut.edu.cn

2. Jing Xu, Department of Neurology and Psychiatry, First Affiliated Hospital, Dalian Medical University, 116011, Dalian, China

Email: xujing_doc@aliyun.com

3. Yi Chang, Department of Neurology and Psychiatry, First Affiliated Hospital, Dalian Medical University, 116011, Dalian, China

Email: changee99@gmail.com

Highlights:

Major depression causes altered connectivity in delta and beta bands during music perception.

Beta band connectivity is a promising biomarker for the diagnosis of major depression disorder.

Naturalistic music stimuli lead to frequency-specific functional connectivity.

Abstract

Objective: The functional connectivity (FC) of major depression disorder (MDD) has not been well studied under naturalistic and continuous stimuli conditions. In this study, we investigated the frequency-specific FC of MDD patients exposed to conditions of music perception using ongoing electroencephalogram (EEG).

Methods: First, we applied phase lag index (PLI) method to calculate the connectivity matrices and graph theory-based methods to measure the topology of brain networks across different frequency bands. Then, classification methods were adopted to identify the most discriminate frequency band for the diagnosis of MDD.

Results: During music perception, MDD patients exhibited a decreased connectivity pattern in the delta band but an increased connectivity pattern in the beta band. Healthy people showed a left hemisphere-dominant phenomenon, but MDD patients did not show such a lateralized effect. Support vector machine (SVM) achieved the best classification performance in the beta frequency band with an accuracy of 89.7%, sensitivity of 89.4% and specificity of 89.9%.

Conclusions: MDD patients exhibited an altered FC in delta and beta bands, and the beta band showed a superiority in the diagnosis of MDD.

Significance: Our study provided a promising reference for the diagnosis of MDD, and revealed a new perspective for understanding the topology of MDD brain networks during music perception.

Keywords: functional connectivity, ongoing EEG, major depression disorder, music perception, naturalistic stimuli.

1. Introduction

Major depression disorder (MDD) is currently one of the most prevalent psychiatric disorders, and it substantially disrupts patients' lives. MDD patients are usually characterized by deficits of affective and cognitive functions (Kaiser et al. 2015; Li et al. 2018; Xia et al. 2018). Although many researchers have dedicated themselves to the exploration of the pathophysiology of MDD, the neural mechanisms of its etiology and pathogenesis are still not fully understood. Currently, there are no biomarkers for the clinical diagnosis of MDD (Fingelkurts and Fingelkurts 2015; Gao et al. 2018; Nugent et al. 2019). Conventionally, the clinical diagnosis of MDD frequently depends on some public criteria, such as Diagnostic and Statistical Manual of Mental Disorders V (DSM-5), which makes the diagnosis of MDD very subjective due to human factors and causes faulty diagnostic results (Mumtaz et al. 2015; Nugent et al. 2019). For this reason, noninvasive neuroimaging techniques, such as electroencephalogram (EEG), magnetoencephalography (MEG) and functional magnetic resonance imaging (fMRI), are urgently needed as more effective and intelligent diagnostic tools. EEG is an inexpensive technique that benefits from high temporal resolution. EEG is able to record electrical activity at frequencies related to neuronal activity and to capture the dynamic changes at a millisecond scale. These advantages make EEG a very promising technique for commonly use in the diagnosis of MDD (Baskaran et al. 2012; Mumtaz et al. 2015, 2017).

Many fMRI studies have demonstrated that the pathogenesis of MDD is the abnormality of large-scale brain networks, such as default mode network (DMN) (Zhu et al. 2012; Wu et al. 2013) and affective network (AN) (Avery et al. 2014), or the dysconnectivity of some brain regions, such as corticolimbic pathways (Nugent et al. 2019), rather than the dysfunction of an individual brain region. So, functional connectivity (FC) has proven to be effective to investigate network dysfunction in MDD. FC provides a new line of thought for the diagnosis of MDD patients, and many studies, especially fMRI and EEG studies, have focused on the classification of MDD based on FC analysis (Wang et al. 2017; Gao et al. 2018; Sakai and Yamada 2019). However, FC analysis and MDD classification always focus on resting-state or highly controlled and repeated stimuli, but the differences in FC under naturalistic and continuous stimuli between healthy people and MDD patients have not been well studied. Compared with resting state, listening to continuous music is more closely related to real-world experience (Wang et al. 2020), and emotional arousal can be induced for affective processing (Mikutta et al. 2012). Music therapy has become an attractive tool for MDD treatment, so understanding the mechanism of the brain response during listening to music is the basis for the diagnosis and treatment of MDD (Michael et al. 2005; Maratos et al. 2008). An increasing amount of literature has demonstrated that human brain networks are different across frequency bands in both resting-state and task conditions, and networks in specific frequency bands may reveal different brain functions (Brookes et al. 2012, 2016; Hillebrand et al. 2012, 2016). Previous studies have demonstrated altered FC in MDD in different frequency bands, so FC analysis across different frequency bands is important to the diagnosis of MDD (Mumtaz et al. 2015; Knott et al. 2001; Whitton et al. 2018). Some studies have found that frequency-specific and large-scale brain networks will emerge during music perception to sustain ongoing cognitive tasks (Alluri et al. 2012; Cong et al. 2013; Wang et al. 2020). A review by Maratos et al. emphasized that music therapy was associated with improvements in mood to treat depression (Maratos et al. 2008). Some researchers have already focused on frequency-specific brain responses to music in depression patients and other psychiatric disorders and have found that music therapy can alter FC and modulate brain responses (Michael et al. 2005; Ramirez et al. 2015; Dharmadhikari et al. 2018). These previous studies support our assumption that altered FC exists in different frequency bands during music perception in MDD patients. However, few studies have investigated the mechanism of dysconnectivity and brain responses of MDD patients during music perception.

For electrophysiological neuroimaging techniques, like EEG, the collected signals from one scalp sensor are actually from the whole brain due to the volume conduction effect (Van Den Broek et al.

1998; Schoffelen and Gross 2009; Brunner et al. 2016). Brain connectivity in sensor space is usually confounded by volume conduction, and even with the conduction of source reconstruction methods, source leakage still exists due to the ill-posed nature of the inverse problem (O'Neill et al. 2018). An increasing number of studies have demonstrated that the communication of brain regions or neural populations depends on phase interactions (Womelsdorf et al. 2007; Palva and Palva 2012; He et al. 2019). A zero-lag interaction is considered to be the consequence of volume conduction because signal leakage is instantaneous. Among the phase synchronization methods, phase lag index (PLI) discards the interactions resulting from phase differences of zero, so PLI is not sensitive to the volume conduction effect; thus, it is commonly used in the FC analysis of EEG and MEG studies (Stam et al. 2007; Vinck et al. 2011; Wu et al. 2012). Ruiz-Gómez et al have demonstrated that PLI could reduce the bias introduced by the spurious influence of volume conduction and was superior to the other seven FC synchronization measures (Ruiz-Gómez et al. 2019).

Network analysis methods based on graph theory are widely used to reveal the topology of brain networks (Sporns 2018; Ren et al. 2019). In EEG sensor space, the brain networks are constituted by nodes representing electrodes and edges representing FC strength between every pair of nodes. The various network properties are efficient measures used to quantify brain functional integration and functional segregation (Rubinov and Sporns 2010; Liao et al. 2017). Degree, which is a measure of influence, clustering coefficient, which is a measure of functional segregation, and characteristic path length, which is a measure of functional integration, are network properties that are commonly used to quantify the efficiency of information processing (Achard et al. 2006; He et al. 2007; Gong and He 2015). In this study, we applied degree, clustering coefficient and characteristic path length to quantify the differences between healthy people and MDD patients.

In this study, we collected EEG data from healthy people and MDD patients under conditions of music perception, and used the PLI method to calculate FC across five typically analyzed frequency bands: delta, theta, alpha, beta and gamma bands. After statistical analysis using the network-based-statistic (NBS) method, we compared the two groups through connectivity matrices and graph-theory based network properties in delta and beta frequency bands, which exhibited significant differences. Finally, machine learning methods were used to perform the classification.

2. Methods

2.1 Data acquisition

Nineteen healthy adults (fourteen females and five males) aged 24 to 65 years in the control (CON) group and twenty adults (fourteen females and six males) with MDD aged 23 to 58 years in the MDD group were recruited for this experiment. All the patients were from the First Affiliated Hospital of Dalian Medical University in China. This study was approved by the ethics committee of the hospital, and all the participants signed the informed consent before their enrollment. None of the participants reported hearing loss or formal training in music. MDD patients were primarily diagnosed by a clinical expert, and the course of the disease varied from 2 and 36 months. All the participants were tested according to Hamilton Rating Scale for Depression (HRSD), Hamilton Anxiety Rating Scale (HAMA) and Mini-Mental State Examination (MMSE). The means and standard deviations (SD) of age, gender, education and clinical measures for both groups are listed in Table 1. During the experiment, participants were told to sit comfortably in a chair and listen to a piece of music. An 8.5-minute long musical piece of modern tango by Astor Piazzolla was used as the stimulus due to its rich musical structure and high range of variation in musical features, such as dynamics, timbre, tonality and rhythm (Alluri et al. 2012, 2013).

The EEG data were recorded by the Neuroscan Quik-cap device with 64 electrodes arranged according to the international 10-20 system. Electrodes placed at the left and right earlobes were used as the references. The data were down-sampled to 256 Hz for further processing and visually checked to remove obvious artifacts from head movements. Eye movements artifacts were rejected by independent

component analysis (ICA), and 50-Hz artifacts were removed by short time Fourier transform (STFT). STFT was applied to filter the data into five typically analyzed frequency bands, namely, the delta (0.5-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), beta (13-30 Hz) and gamma (30-80 Hz) bands, for further analysis.

2.2 Phase synchronization

In this study, phase synchronization was measured between all the pairs of channels by the PLI method, which is an asymmetry index that measures the distribution of phase differences (Stam et al. 2007; Vinck et al. 2011). Due to the instantaneous spread of current, the same sources collected by two electrodes are considered to cause a zero-lag phase difference, which is rejected by PLI. Therefore, PLI is less sensitive to the volume conduction effect, and it can reveal the true coupling strength between pairs of channels.

For an EEG signal $x(t)$, $t = 1,2,3,\cdots,T$ from one channel, the analytical signal $z(t)$ can be constructed by Hilbert transform,

$$z(t) = x(t) + i\tilde{x}(t) = \frac{1}{\pi} PV \int_{-x}^{\infty} \frac{x(\tau)}{t-\tau} d\tau, \quad \#(1)$$

where $\tilde{x}(t)$ is the imaginary part, and PV refers to the Cauchy principal value. Then, the instantaneous amplitude $A(t)$ and the instantaneous phase $\varphi(t)$ can be computed as follows:

$$\begin{cases} A(t) = \sqrt{[\tilde{x}(t)]^2 + [x(t)]^2} \\ \varphi(t) = arctan\frac{\tilde{X}(t)}{x(t)}. \end{cases} \quad \#\ (2)$$

Therefore, the phase difference $\Delta\varphi(t)$ of two signals $x_a(t)$ and $x_b(t)$ at time t can be formulated as:

$$\Delta\varphi(t) = \varphi_a(t) - \varphi_b(t). \quad \#(3)$$

Then, the PLI index can be defined via

$$PLI = |< sign[\Delta\varphi(t)] >|, t = 1 \ldots T. \quad \#(4)$$

The value of PLI index varies between 0 and 1. A value of 0 indicates no coupling or coupling with a phase difference centered around 0 mod π, and a value of 1 indicates perfect phase synchronization between two signals at a constant lag except 0 or π.

In this study, for the 8.5-minute EEG data with a sampling frequency of 256 Hz, we first removed four unusable electrodes. Then, we removed the first and last 10 seconds of the EEG data to avoid transition effects, and we segmented the EEG data into non-overlapping epochs by a time window of 10 seconds, so there were a total of 49 epochs. Then, an adjacency matrix of 60×60 was calculated by PLI for each epoch and each frequency band.

2.3 Network analysis

Graph theory is normally used after the calculation of the adjacency matrix to quantify the topology of brain networks. In this study, we used three commonly used network measures to quantify influence, functional segregation and functional integration, including degree, clustering coefficient and characteristic path length. All the network measures mentioned above were computed using the Brain Connectivity Toolbox (Rubinov and Sporns 2010) (http://www.brain-connectivity-toolbox.net).

For an adjacency matrix $\boldsymbol{G}$, with N nodes, w_{ij} represents the connection strength between node i and node j, where $0 \leq w_{ij} \leq 1$. The diagonal elements mean self-connections of nodes, so $w_{ii} = 0$, $i = 1, 2,\cdots,N$.

2.3.1 Degree

Degree is considered an important marker of network development and resilience, and for a weighted network, the degree of node i can be defined as follows:

$$k_i = \sum_{j \in N} w_{ij} \quad \#(5)$$

2.3.2 Clustering coefficient

Clustering coefficient is a measure of functional segregation which is a reflection of the local organization of a network by depicting the tendency of a node forming local triangles (Rubinov and Sporns 2010), and its definition for a weighted network of node i is described as follows:

$$C_i = \frac{2t_i}{k_i(k_i - 1)}, \quad \#(6)$$

where $t_i = \frac{1}{2}\sum_{j,h \in N}(w_{ij}w_{ih}w_{jh})^{\frac{1}{3}}$ is the geometric mean of triangles around i. The clustering coefficient for the whole network is defined as the mean of clustering coefficient for all nodes,

$$C = \frac{1}{N}\sum_{i \in N} C_i. \#(7)$$

2.3.3 Characteristic path length

Characteristic path length is the average of shortest path length between all pairs of nodes and is commonly used to measure functional integration. Characteristic path length is a reflection of the efficiency of a network (Bullmore and Sporns 2009). The definition is described as follows:

$$L = \frac{1}{N}\sum_{i \in N} \frac{\sum_{j \in N,\ j \neq i} d_{ij}}{N - 1}, \quad \#(8)$$

where $d_{ij} = \sum_{a_{uv} \in g^{w}_{i \leftrightarrow j}} \frac{1}{w_{uv}}$ is the shortest path length between node i and node j, and $g^{w}_{i \leftrightarrow j}$ is the shortest weighted path between i and j.

2.4 Statistical analysis

To determine in which frequency band a significant difference exists between the CON group and MDD group, Network Based Statistic Toolbox was applied in this study (Zalesky et al. 2010). The NBS method can control the family-wise error when multiple univariate testing is performed at each connection of a network. NBS method is used to identify significant brain network substructures formed by some suprathreshold links but not to identify individual links as being significant. The threshold is used on the test statistic computed for each pairwise connection, and different thresholds can construct different level of sparse graphs. After averaging the adjacency matrices across time windows for each subject, statistical analysis was performed between the CON group and MDD group for each frequency band. A significance level of corrected $P < 0.05$ and a nonparametric permutation test of 5000 permutations were used in this study. T-test was selected for the statistical test, and different test statistic thresholds (t-statistic) were tested to identify the most significant brain network substructures.

2.5 Classification

Considering the limitations of using sliding windows without overlapping, which will lead to the problem that FC topology may not been well described within one fixed time window (Liuzzi et al. 2019), we averaged every six time windows (the connectivity matrices within one minute) to generate

one classification sample to highlight the main connectivity patterns during music perception. To improve classification performances, we constructed sparse networks based on the notion of connected graphs to remove redundant information, which can ensure that every node has a connection to another node for a sparse network. The detailed method for threshold selection can be found in reference (Atay and Biyikoğlu 2005).

In this study, we used the adjacency matrices obtained by PLI to perform classification, and we compared the classification performance using original networks and sparse networks between delta and beta frequency bands and six classifiers, including decision tree (DT), Gaussian mixture model (GMM), k-nearest neighbor (KNN), naïve Bayes (NB), random forest (RF) and support vector machine (SVM). We unfolded the adjacency matrix to a vector as one sample. Because of the symmetry property of the adjacency matrix, we can obtain $N(N-1)/2 = 60(60-1)/2 = 1770$ variables for each sample. Therefore, we can get 152 samples for the CON group and 160 samples for the MDD group. To avoid overfitting, principal component analysis (PCA) was applied for dimension reduction before classification.

To assess the performance of classification, we calculated some statistical evaluation measurements including accuracy, sensitivity, and specificity (Yan et al. 2019), which can be calculated by:

$$\text{accuracy} = \frac{TP + TN}{TP + FP + TN + FN}, \quad \#(9)$$

$$\text{sensitivity} = \frac{TP}{TP + FN}, \quad \#(10)$$

$$\text{specificity} = \frac{TN}{TN + FP}, \quad \#(11)$$

where TP, TN, FP and FN represent true positive, true negative, false positive and false negative, respectively. To obtain a reliable classification result, we shuffled the data order, used 10-fold cross validation, and ran 10 times for each classifier. Then, we averaged the classification results to calculate the final performance for each classifier and each frequency band.

3. Results

3.1 Phase synchronization

After statistical analysis by NBS for each frequency band, a significant difference only existed in two frequency bands: delta and beta bands (delta: $P = 0.0450$, theta: $P = 0.2386$, alpha: $P = 0.3447$, beta: $P = 0.0344$, gamma: $P = 0.0649$). The adjacency matrices for these two frequency bands of the CON group and MDD group are shown in Figure 1. For the delta frequency band, the connectivity strength increased in the MDD group (delta: $\text{mean} = 0.0867$, $\text{SD} = 0.0197$) compared to the CON group (delta: $\text{mean} = 0.0853$, $\text{SD} = 0.0178$;). However, for the beta frequency band, the connectivity strength of the MDD group ($\text{mean} = 0.0408$, $\text{SD} = 0.0133$) decreased compared with that of the CON group ($\text{mean} = 0.0485$, $\text{SD} = 0.0143$). From Figure 1, we can see that short-distance synchronization was stronger than long-distance synchronization, and the whole brain connectivity was formed by many small modules.

The significant brain network connections between the CON group and the MDD group in delta and beta frequency bands are shown in Figure 2. We can see that there were 13 significant connections in the delta band distributed within right central brain areas and between right temporal and left parietal brain regions. While in the beta band, there were 43 significant connections characterized mostly by long-distance edges, which were distributed mostly within frontal brain areas and between frontal and parieta-occipital brain areas. The substructures were considered to be important indicators of the

differences between the two groups, which can be promising biomarkers for MDD under conditions of music perception.

3.2 Network analysis

We calculated the degree of each node in delta and beta frequency bands for both groups, as shown in Figure 3. We obtained the lateralization index (LI) by the formula: $LI = (L - R)/(L + R)$, where L and R represented the degree of left and right hemisphere, respectively (Desmond et al. 1995). Then, we performed t-test for both delta and beta bands, and we obtained $P = 0.0114$ for the delta band and $P < 0.0001$ for the beta band. For the CON group, there was a lateralization effect to the left hemisphere, but for the MDD group, there was no such lateralization effect. From Figure 3, we can conclude that the degree increased in the delta frequency band for the MDD group (delta: $\text{mean} = 0.0867$, $\text{SD} = 0.0040$;) compared with the CON group (delta: $\text{mean} = 0.0854$, $\text{SD} = 0.0022$), but it decreased in the beta frequency band for the MDD group ($\text{mean} = 0.0402$, $\text{SD} = 0.0032$) compared with the CON group ($\text{mean} = 0.0480$, $\text{SD} = 0.0031$); this finding was consistent with the results from the adjacency matrices as shown in Figure 1. Figure 4 shows a boxplot of clustering coefficient and characteristic path length in delta and beta frequency bands of both the CON group and the MDD group. From this finding, we can see that the beta frequency band was the most discriminate for classifying the CON group and the MDD group; therefore, next, we will test the classification performance of each frequency band.

3.3 Classification results

We tested six classifiers on delta and beta frequency bands, and the classification results are listed in Table 2. The top three classification accuracy results are marked in bold font. From Table 2, we can see that SVM demonstrated the best classification performance, with a classification accuracy of 89.7% among the six classifiers in the beta frequency band using sparse adjacency matrices. Therefore, we can conclude that the beta frequency band was the most discriminate for distinguishing the CON group and MDD group, which was in agreement with the results in Figure 4. For the best classification performance, we obtained $\text{accuracy} = 89.7\%$, $\text{sensitivity} = 89.4\%$, and $\text{specificity} = 89.9\%$.

The classification performance of sparse networks was better than that of original networks for all the six classifiers and both delta and beta bands. The top three classification performances were all from sparse networks, which meant that adding a threshold to remove some redundant information can efficiently improve the classification performance. In network analysis, it is reasonable to remove weak connections, which are considered to result from the effect of noise and not to represent the true connections between brain regions.

4. Discussion

To the best of our knowledge, this study is the first attempt to investigate the differences in connectivity between healthy people and MDD patients using frequency-specific ongoing EEG FC analysis under conditions of music perception and then to apply classification methods for diagnosis. First, we calculated FC by PLI, which can efficiently decrease the volume conduction effect for each time window and each frequency band. Then, NBS analysis was applied to identify the significant brain network substructures for each frequency band, and we found that significant substructures only existed in delta and beta frequency bands. Then, network properties, including degree, clustering coefficient and characteristic path length, were calculated for delta and beta bands to explore the differences of in the topology between CON and MDD groups. Based on the network analysis, we found that the beta frequency band was the most discriminate for MDD diagnosis. Therefore, we compared the classification performance with six classifiers between those two frequency bands, and the beta band reached the highest classification accuracy through the SVM classifier after constructing sparse networks.

Some previous EEG studies have demonstrated that the perception of music was associated with the synchronization of different frequency bands (Bhattacharya et al. 2001; Ruiz et al. 2009; Wu et al. 2012; Cong et al. 2013). After statistical analysis of connectivity matrices for each frequency band, we found significant brain network connections in delta and beta bands. From the perspective of music, both the delta and beta bands are associated with music perception. An MEG study has demonstrated that beta rhythms coupled with entrained delta-theta oscillations underpin accuracy in musical processing (Doelling and Poeppel 2015). Arnal et al. also found that delta-beta coupled oscillations were associated with temporal processing (Arnal et al. 2015). Regarding the importance of delta and beta bands during music perception, an altered FC in those two frequency bands may provide an efficient tool for the diagnosis of MDD.

The delta band exhibited increased connectivity in the MDD group with 13 significant connections, and the beta band exhibited decreased connectivity in the MDD group with 43 significant connections, which were mostly constructed by long-distance edges. This contrast between delta and beta bands was also reported in Leuchter's research, which reported that in a resting-state EEG study, the delta band exhibited increased connectivity in the MDD group in fewer highly significant and shorter-distance edges, and the beta band exhibited more significant connections with longer-distance edges (Leuchter et al. 2012). We found that the increased significant connections in the delta band mainly distributed within right central brain areas and between right temporal and left parietal brain regions. The delta band was demonstrated to have a substantial influence on the identification of natural speech fragments in an MEG study (Koskinen et al. 2013). The delta band was already found to be more prominent in the right hemisphere than in the left hemisphere of depressed patients (Kwon et al. 1996), and the delta inter-hemispheric coherence contributed to the classification of MDD patients and healthy controls (Knott et al. 2001). Those findings were consistent with our results that the significant connections in the delta band distributed mostly in the right hemisphere. We also found decreased connectivity distributed mostly within frontal brain areas and between frontal and parietal-occipital brain areas in the beta band in MDD patients. The beta band has been demonstrated to be the predominant frequency band for music perception (Jäncke and Alahmadi 2016), and Alavash et al. found that networks of the listening brain showed higher segregation of frontal control regions relative to those under task-free resting states, which may support that MDD patients were less involved in listening in our study (Alavash et al. 2019). Many fMRI (Veer et al. 2010; Kaiser et al. 2015) and EEG (Fingelkurts et al. 2007; Fingelkurts and Fingelkurts 2015) studies have demonstrated that some brain regions and some specific brain networks indicated decreased FC in the MDD group. Olbrich et al. have demonstrated that MDD was characterized by altered EEG FC within frontal brain areas (Olbrich et al. 2014). With hierarchical brain architectures, global integration indicates higher cognition mediated by long-distance connections. Music perception is a high cognition process in the brain, and global integration is needed. Global integration by modulating long-distance connectivity is crucial for task-dependent functions (Markov et al. 2011; Park and Friston 2013). The decreased long-distance connectivity in the beta band reported in our results, which suggests less communication between remote brain regions, may provide an important biomarker in MDD diagnosis.

The properties based on the graph theory are the quantification of network comparisons. In this study, we compared two network properties, including clustering coefficient and characteristic path length, in delta and beta bands between CON and MDD groups, and those measures have been used in previous studies to identify altered network organizations in MDD patients (Ajilore et al. 2014; Ye et al. 2015). From Figure 4, we can see that more differences appeared in the beta band, which was identical to our results showing that the beta band exhibited more significant connections than the delta band. In the delta band, the MDD group was characterized by higher clustering coefficient and longer characteristic path length, which meant that MDD patients had lower information transfer efficiency and a tendency of regular networks in the delta band. The MDD group showed higher local efficiency in the delta band, and a fMRI study obtained the same findings in MDD patients (Ye et al. 2015). Differently in the beta band, the MDD group presented smaller clustering coefficient and shorter characteristic path length,

indicating that the MDD group had a poor local organization ability and a trend toward random networks. Singh et al. also found that depressed patients displayed smaller clustering coefficient in gray matter networks (Singh et al. 2013). Therefore, the topological changes in brain connectome were significant reflections of patients with MDD (Ye et al. 2015).

Music perception has been demonstrated to have a cortical lateralization effect in the human brain, but based on the literature, different sounds appeared about which hemisphere of the brain does music processing more lateralize to (Ohnishi 2001; Kay et al. 2012). Toiviainen et al. found in a fMRI study that different musical features can cause different hemispheric asymmetry effects (Toiviainen et al. 2014). In the present study, we revealed a left hemispheric lateralization effect in healthy people, and no lateralization effect in MDD patients under naturalistic music listening condition. Alluri et al. demonstrated that left hemispheric primary and supplementary motor areas were more activated than those of the right hemisphere when listening to purely instrumental music (Alluri et al. 2013). The results supported our findings of left hemisphere lateralization in the CON group because we also used a piece of music without lyrics. Furthermore, the left inferior frontal area was reported to be related to the memory of music (Watanabe et al. 2008), which also supported to the reliability of our results. Many studies have reported a lateralized hemispheric dysfunction in major depression (Uytdenhoef et al. 1983; Bench et al. 1993), and this dysfunction was well demonstrated by our results that no hemispheric lateralization effect exists in MDD patients during music perception. Music is capable of inducing emotional arousal (Mikutta et al. 2012), and the left hemisphere predominates during states of low arousal and positive affect (Craig 2005). EEG studies have found that depressed participants showed a hypoactivation in the left frontal lobe, which was related to the elicitation and recognition of emotions and caused diminished positive affect (Wheeler et al. 1993; Punkanen et al. 2011). This may cause the deficiency of affective processing in depressed patients during music processing.

We tested the classification accuracy of delta and beta bands by six classifiers, and the most commonly used SVM classifier exhibited the best performance in the beta band, which was consistent with the results in Figure 4. After eliminating weak connections, the classification performance improved for all the classifiers according to Table 2 because applying feature selection to remove redundant information was necessary for classification. An EEG study on male depression by Knott et al., also showed that the beta frequency band was the most discriminate for classification (Knott et al. 2001). Gao et al. conducted a comprehensive review of studies related to the classification of MDD based on magnetic resonance imaging data and compared the methods and classification accuracies of 66 representative studies (Gao et al. 2018). The classification performance in our study was better than that of 76% of the studies mentioned in Gao's work. EEG was more suitable for clinical applications in MDD diagnosis due to its higher temporal resolution and lower cost than fMRI and MEG (Mumtaz et al. 2017). Furthermore, compared with that recorded under resting state conditions, EEG data recorded under naturalistic and continuous stimuli, such as listening to music, is more close to simulate real-world conditions (Wang et al. 2020), and music can induce emotional arousal, which is related to affective processing in MDD patients (Mikutta et al. 2012; Toiviainen et al. 2014). Therefore, music perception tasks may be superior for use in MDD diagnosis. However, it is still a long way to go for the clinical usability, because current studies are mostly based on small datasets (22 to 90 recordings) acquired under non-naturalistic conditions and highly controlled research settings, and the non-replicability of the research with different methods and experimental conditions also make it challenging for the generalization to clinical diagnosis.

Taken together, when exposed to music listening conditions, both healthy controls and MDD patients exhibited different FC patterns across different frequency bands, and MDD patients were characterized by altered FC in delta and beta bands. Our results, shown above, were well supported by previous studies and can provide a promising perspective for the clinical diagnosis of MDD in the future.

Some important limitations of this study should be declared. First, the analysis was based on the sensor-space level, and the lack of a source reconstruction procedure limited further explanation of the results. Second, the neural correlates and dynamic neural processing of musical emotions are still not well understood (Toiviainen et al. 2014), and the selection of control stimuli, such as music type and duration, still needs further investigation. Furthermore, in the music processing task, how to extract the music-induced activity from ongoing EEG data is quite challenging and still remains an open question (Wang et al. 2020), which is directly related to the reliability of the explanation of the results.

Conflict of interest statement

None of the authors have potential conflicts of interest to be disclosed.

Acknowledgements

This work was supported by National Natural Science Foundation of China (Grant No.91748105 & Grant No.81471742); the Fundamental Research Funds for the Central Universities [DUT2019] in Dalian University of Technology in China; and the scholarships from China scholarship Council (No. 201706060263).

References

Achard S, Salvador R, Whitcher B, Suckling J, Bullmore E. A resilient, low-frequency, small-world human brain functional network with highly connected association cortical hubs. J Neurosci. 2006;26:63–72.

Ajilore O, Lamar M, Leow A, Zhang A, Yang S, Kumar A. Graph theory analysis of cortical-subcortical networks in late-life depression. Am J Geriatr Psychiatry. 2014;22:195–206.

Alavash M, Tune S, Obleser J. Modular reconfiguration of an auditory control brain network supports adaptive listening behavior. Proc Natl Acad Sci U S A. 2019;116:660–669.

Alluri V, Toiviainen P, Jääskeläinen IP, Glerean E, Sams M, Brattico E. Large-scale brain networks emerge from dynamic processing of musical timbre, key and rhythm. Neuroimage. 2012;59:3677–3689.

Alluri V, Toiviainen P, Lund TE, Wallentin M, Vuust P, Nandi AK, et al. From vivaldi to beatles and back: Predicting lateralized brain responses to music. Neuroimage. 2013;83:627–636.

Arnal LH, Doelling KB, Poeppel D. Delta-beta coupled oscillations underlie temporal prediction accuracy. Cereb Cortex. 2015;25:3077–3085.

Atay FM, Biyikoğlu T. Graph operations and synchronization of complex networks. Phys Rev E - Stat Nonlinear, Soft Matter Phys. 2005;72:016217.

Avery JA, Drevets WC, Moseman SE, Bodurka J, Barcalow JC, Simmons WK. Major depressive disorder is associated with abnormal interoceptive activity and functional connectivity in the insula. Biol Psychiatry. 2014;76:258–266.

Baskaran A, Milev R, McIntyre RS. The neurobiology of the EEG biomarker as a predictor of treatment response in depression. Neuropharmacology. 2012; 63:507–513.

Bench CJ, Friston KJ, Brown RG, Frackowiak RS, Dolan RJ. Regional cerebral blood flow in depression measured by positron emission tomography: The relationship with clinical dimensions. Psychol Med. 1993;23:579–590.

Bhattacharya J, Petsche H, Pereda E. Long-range synchrony in the γ band: Role in music perception. J Neurosci. 2001;21:6329–6337.

Brookes MJ, Liddle EB, Hale JR, Woolrich MW, Luckhoo H, Liddle PF, et al. Task induced modulation of neural oscillations in electrophysiological brain networks. Neuroimage. 2012;63:1918–1930.

Brookes MJ, Tewarie PK, Hunt BAE, Robson SE, Gascoyne LE, Liddle EB, et al. A multi-layer network approach to MEG connectivity analysis. Neuroimage. 2016;132:425–438.

Brunner C, Billinger M, Seeber M, Mullen TR, Makeig S. Volume Conduction Influences Scalp-Based Connectivity Estimates. Front Comput Neurosci. 2016;10:1–4.

Bullmore E, Sporns O. Complex brain networks: Graph theoretical analysis of structural and functional systems. Nat Rev Neurosci. 2009;10:186–198.

Cong F, Alluri V, Nandi AK, Toiviainen P, Fa R, Abu-Jamous B, et al. Linking brain responses to naturalistic music through analysis of ongoing EEG and stimulus features. IEEE Trans Multimed. 2013;15:1060–1069.

Craig AD. Forebrain emotional asymmetry: A neuroanatomical basis? Trends Cogn Sci. 2005;9:566–571.

Desmond JE, Sum JM, Wagner AD, Demb JB, Shear PK, Glover GH, et al. Functional MRI measurement of language lateralization in wada-tested patients. Brain. 1995;118:1411–1419.

Dharmadhikari AS, Tandle AL, Jaiswal S V., Sawant VA, Vahia VN, Jog N. Frontal theta asymmetry as a biomarker of depression. East Asian Arch Psychiatry. 2018;28:17–22.

Doelling KB, Poeppel D. Cortical entrainment to music and its modulation by expertise. Proc Natl Acad Sci U S A. 2015;112:E6233–42.

Fingelkurts AA, Fingelkurts AA. Altered structure of dynamic electroencephalogram oscillatory pattern in major depression. Biol Psychiatry. 2015;77:1050-1060.

Fingelkurts AA, Fingelkurts AA, Rytsälä H, Suominen K, Isometsä E, Kähkönen S. Impaired functional

connectivity at EEG alpha and theta frequency bands in major depression. Hum Brain Mapp. 2007;28:247–261.

Gao S, Calhoun VD, Sui J. Machine learning in major depression: From classification to treatment outcome prediction. CNS Neurosci Ther. 2018;24:1037–1052.

Gong Q, He Y. Depression, neuroimaging and connectomics: A selective overview. Biological Psychiatry. 2015; 77:223–235.

He B, Astolfi L, Valdes-Sosa PA, Marinazzo D, Palva SO, Benar CG, et al. Electrophysiological Brain Connectivity: Theory and Implementation. IEEE Trans Biomed Eng. 2019;66:2115–2137.

He Y, Chen ZJ, Evans AC. Small-world anatomical networks in the human brain revealed by cortical thickness from MRI. Cereb Cortex. 2007;17:2407–2419.

Hillebrand A, Barnes GR, Bosboom JL, Berendse HW, Stam CJ. Frequency-dependent functional connectivity within resting-state networks: An atlas-based MEG beamformer solution. Neuroimage. 2012;59:3909–3921.

Hillebrand A, Tewarie P, Van Dellen E, Yu M, Carbo EWS, Douw L, et al. Direction of information flow in large-scale resting-state networks is frequency-dependent. Proc Natl Acad Sci U S A. 2016;113:3867–3872.

Jäncke L, Alahmadi N. Detection of independent functional networks during music listening using electroencephalogram and sLORETA-ICA. Neuroreport. 2016;27:455–461.

Kaiser RH, Andrews-Hanna JR, Wager TD, Pizzagalli DA. Large-Scale Network Dysfunction in Major Depressive Disorder. JAMA Psychiatry. 2015;72:603-611.

Kay BP, Meng X, DiFrancesco MW, Holland SK, Szaflarski JP. Moderating effects of music on resting state networks. Brain Res. 2012;1447:53–64.

Knott V, Mahoney C, Kennedy S, Evans K. EEG power, frequency, asymmetry and coherence in male depression. Psychiatry Res - Neuroimaging. 2001;106:123–140.

Koskinen M, Viinikanoja J, Kurimo M, Klami A, Kaski S, Hari R. Identifying fragments of natural speech from the listener's MEG signals. Hum Brain Mapp. 2013;34:1477–1489.

Kwon JS, Youn T, Jung HY. Right hemisphere abnormalities in major depression: Quantitative electroencephalographic findings before and after treatment. J Affect Disord. 1996;40:169–173.

Leuchter AF, Cook IA, Hunter AM, Cai C, Horvath S. Resting-state quantitative electroencephalography reveals increased neurophysiologic connectivity in depression. PLoS One. 2012;7: e32508.

Li BJ, Friston K, Mody M, Wang HN, Lu HB, Hu DW. A brain network model for depression: From symptom understanding to disease intervention. CNS Neurosci Ther. 2018; 24:1004–1019.

Liao X, Vasilakos A V, He Y. Small-world human brain networks : Perspectives and challenges. Neurosci Biobehav Rev. 2017;77:286–300.

Liuzzi L, Quinn AJ, O'Neill GC, Woolrich MW, Brookes MJ, Hillebrand A, et al. How sensitive are conventional MEG functional connectivity metrics with sliding windows to detect genuine fluctuations in dynamic functional connectivity? Front Neurosci. 2019;13:797.

Maratos AS, Gold C, Wang X, Crawford MJ. Music therapy for depression. Cochrane Database Syst. Rev. 2008;1:CD004517.

Markov NT, Misery P, Falchier A, Lamy C, Vezoli J, Quilodran R, et al. Weight consistency specifies regularities of macaque cortical networks. Cereb Cortex. 2011;21:1254–1272.

Michael AJ, Krishnaswamy S, Mohamed J. An open label study of the use of EEG biofeedback using beta training to reduce anxiety for patients with cardiac events. Neuropsychiatr Dis Treat. 2005;1:357–363.

Mikutta C, Altorfer A, Strik W, Koenig T. Emotions, arousal, and frontal alpha rhythm asymmetry during beethoven's 5th symphony. Brain Topogr. 2012;25:423–430.

Mumtaz W, Malik AS, Yasin MAM, Xia L. Review on EEG and ERP predictive biomarkers for major depressive disorder. Biomed Signal Process Control. 2015;22: 85–98.

Mumtaz W, Xia L, Ali SSA, Yasin MAM, Hussain M, Malik AS. Electroencephalogram (EEG)-based computer-aided technique to diagnose major depressive disorder (MDD). Biomed Signal Process Control. 2017;31:108–115.

Nugent AC, Farmer C, Evans JW, Snider SL, Banerjee D, Zarate CA. Multimodal imaging reveals a complex pattern of dysfunction in corticolimbic pathways in major depressive disorder. Hum Brain Mapp. 2019;40:3940–3950.

O'Neill GC, Tewarie P, Vidaurre D, Liuzzi L, Woolrich MW, Brookes MJ. Dynamics of large-scale electrophysiological networks: A technical review. Neuroimage. 2018;180:559–576.

Ohnishi T. Functional Anatomy of Musical Perception in Musicians. Cereb Cortex. 2001;11:754–760.

Olbrich S, Tränkner A, Chittka T, Hegerl U, Schönknecht P. Functional connectivity in major depression: Increased phase synchronization between frontal cortical EEG-source estimates. Psychiatry Res - Neuroimaging. 2014;222:91–99.

Palva S, Palva JM. Discovering oscillatory interaction networks with M/EEG: Challenges and breakthroughs. Trends Cogn. Sci. 2012;16:219–230.

Park H-J, Friston K. Structural and functional brain networks: from connections to cognition. Science. 2013;342:1238411.

Punkanen M, Eerola T, Erkkilä J. Biased emotional recognition in depression: Perception of emotions in music by depressed patients. J Affect Disord. 2011;130:118–126.

Ramirez R, Palencia-Lefler M, Giraldo S, Vamvakousis Z. Musical neurofeedback for treating depression in elderly people. Front Neurosci. 2015;9:354.

Ren Y, Cong F, Ristaniemi T, Wang Y, Li X, Zhang R. Transient seizure onset network for localization of epileptogenic zone: effective connectivity and graph theory-based analyses of ECoG data in temporal lobe epilepsy. J Neurol. 2019;266:844–859.

Rubinov M, Sporns O. Complex network measures of brain connectivity: Uses and interpretations. Neuroimage. 2010;52:1059–1069.

Ruiz-Gómez SJ, Hornero R, Poza J, Maturana-Candelas A, Pinto N, Gómez C. Computational modeling of the effects of EEG volume conduction on functional connectivity metrics. Application to Alzheimer's disease continuum. J Neural Eng. 2019;16: 066019.

Ruiz MH, Koelsch S, Bhattacharya J. Decrease in early right alpha band phase synchronization and late gamma band oscillations in processing syntax in music. Hum Brain Mapp. 2009;30:1207–1225.

Sakai K, Yamada K. Machine learning studies on major brain diseases: 5-year trends of 2014–2018. Jpn J Radiol. 2019;37:34–72.

Schoffelen JM, Gross J. Source connectivity analysis with MEG and EEG. Hum Brain Mapp. 2009;30:1857–1865.

Singh MK, Kesler SR, Hadi Hosseini SM, Kelley RG, Amatya D, Hamilton JP, et al. Anomalous gray matter structural networks in major depressive disorder. Biol Psychiatry. 2013;74:777–785.

Sporns O. Graph theory methods: applications in brain networks. Dialogues Clin Neurosci. 2018;20:111–121.

Stam CJ, Nolte G, Daffertshofer A. Phase lag index: Assessment of functional connectivity from multi channel EEG and MEG with diminished bias from common sources. Hum Brain Mapp. 2007;28:1178–1193.

Toiviainen P, Alluri V, Brattico E, Wallentin M, Vuust P. Capturing the musical brain with Lasso: Dynamic decoding of musical features from fMRI data. Neuroimage. 2014;88:170–180.

Uytdenhoef P, Portelange P, Jacquy J, Charles G, Linkowski P, Mendlewicz J. Regional cerebral blood flow and lateralized hemispheric dysfunction in depression. Br J Psychiatry. 1983;143:128–132.

Van Den Broek SP, Reinders F, Donderwinkel M, Peters MJ. Volume conduction effects in EEG and MEG. Electroencephalogr Clin Neurophysiol. 1998;106:522–534.

Veer IM, Beckmann C, Van Tol M-J, Ferrarini L, Milles J, Veltman D, et al. Whole brain resting-state analysis reveals decreased functional connectivity in major depression. Front Syst Neurosci. 2010;4:41.

Vinck M, Oostenveld R, Van Wingerden M, Battaglia F, Pennartz CMA. An improved index of phase-synchronization for electrophysiological data in the presence of volume-conduction, noise and sample-size bias. Neuroimage. 2011;55:1548–1565.

Wang X, Liu W, Toiviainen P, Ristaniemi T, Cong F. Group analysis of ongoing EEG data based on fast double-coupled nonnegative tensor decomposition. J Neurosci Methods. 2020;330: 108502.

Wang X, Ren Y, Zhang W. Depression Disorder Classification of fMRI Data Using Sparse Low-Rank Functional Brain Network and Graph-Based Features. Comput Math Methods Med. 2017;2017:1–11.

Watanabe T, Yagishita S, Kikyo H. Memory of music: Roles of right hippocampus and left inferior frontal gyrus. Neuroimage. 2008;39:483–491.

Wheeler RE, Davidson RJ, Tomarken AJ. Frontal brain asymmetry and emotional reactivity: A biological substrate of affective style. Psychophysiology. 1993;30:82–89.

Whitton AE, Deccy S, Ironside ML, Kumar P, Beltzer M, Pizzagalli DA. Electroencephalography Source Functional Connectivity Reveals Abnormal High-Frequency Communication Among Large-Scale Functional Networks in Depression. Biol Psychiatry Cogn Neurosci Neuroimaging. 2018;3:50–58.

Womelsdorf T, Schoffelen JM, Oostenveld R, Singer W, Desimone R, Engel AK, et al. Modulation of neuronal interactions through neuronal synchronization. Science. 2007;316:1609–1612.

Wu D, Yuan Y, Bai F, You J, Li L, Zhang Z. Abnormal functional connectivity of the default mode network in remitted late-onset depression. J Affect Disord. 2013;147:277–287.

Wu J, Zhang J, Liu C, Liu D, Ding X, Zhou C. Graph theoretical analysis of EEG functional connectivity during music perception. Brain Res. 2012;1483:71–81.

Xia MR, Si TM, He Y. Imaging connectomics in depression. CNS Neurosci Ther. 2018;24:991.

Yan R, Zhang C, Spruyt K, Wei L, Wang Z, Tian L, et al. Multi-modality of polysomnography signals' fusion for automatic sleep scoring. Biomed Signal Process Control. 2019;49:14–23.

Ye M, Yang T, Qing P, Lei X, Qiu J, Liu G. Changes of functional brain networks in major depressive disorder: A graph theoretical analysis of resting-state fMRI. PLoS One. 2015;10:e0133775.

Zalesky A, Fornito A, Bullmore ET. Network-based statistic: Identifying differences in brain networks. Neuroimage. 2010;53:1197–1207.

Zhu X, Wang X, Xiao J, Liao J, Zhong M, Wang W, et al. Evidence of a dissociation pattern in resting-state default mode network connectivity in first-episode, treatment-naive major depression patients. Biol Psychiatry. 2012;71:611–617.

Figure legends

Figure 1. Averaged adjacency matrices of the CON group and MDD group across time windows for delta and beta frequency bands. Each adjacency matrix is formed by a 60×60 matrix with zero values in the diagonal. CON, control; MDD, major depression disorder.

Figure 2. The significant brain network connections in delta and beta frequency bands of the CON group and MDD group. The results were conducted by the NBS method using 5000 permutations, corrected p value of $p < 0.05$, and maximum component threshold $t > 3.1$ for the delta band and $t > 2.3$ for the beta band. There are 13 significant connections in the delta band and 43 significant connections in the beta band. CON, control; MDD, major depression disorder; NBS, network based statistic.

Figure 3. The degree of each node in delta and beta frequency bands for the CON group and MDD group. CON, control; MDD, major depression disorder.

Figure 4. Boxplot of clustering coefficient and characteristic path length for the CON group and MDD group in delta and beta frequency bands. The upper and lower black lines represent the maximum value and the minimum value, respectively, and the red cross indicates outliers. The bottom and top edges of the blue box indicate the 25th and 75th percentiles, and the red line and rhombus in the box indicate the median value and the mean value, respectively. CON, control; MDD, major depression disorder.

Table 1. Means and standard deviations of age, gender, education and clinical measures of the CON group and MDD group.

	CON group	MDD group	Analysis

	Mean	SD(Range)	Mean	SD(Range)	*p*-value
Age	38.4	11.8(24-65)	42.9	11.0(23-58)	>0.05
Education	13.6	3.8(6-20)	12.8	3.4(6-16)	>0.05
HRSD	2.4	1.3(0-4)	23.3	3.6(16-28)	<0.01
HAMA	2.4	1.3(0-5)	19.2	3.0(15-25)	<0.01
MMSE	28.2	0.9(27-30)	28.1	1.1(26-30)	>0.05
Duration	0	0	12.8	8.5(2-36)	-
Gender	14 females, 5 males		14 females, 6 males		-

Abbreviations: CON, control; MDD, major depression disorder; SD, standard deviations; HRSD, Hamilton Rating Scale for Depression; HAMA, Hamilton Anxiety Rating Scale; MMSE, Mini-Mental State Examination.

Table 2. The classification accuracy of six classifiers in delta and beta frequency bands.

	Network	DT	GMM	KNN	NB	RF	SVM
Delta	Original	54.7%	49.7%	65.7%	61.2%	62.0%	66.9%
	Sparse	60.9%	53.2%	68.7%	62.5%	69.7%	72.9%
Beta	Original	61.4%	49.5%	77.4%	55.2%	70.9%	78.2%
	Sparse	68.5%	54.8%	**85.6%**	56.7%	**82.3%**	**89.7%**

Abbreviations: DT, decision tree; GMM, Gaussian mixture model; KNN, k-nearest neighbor; NB, naïve Bayes; RF, random forest; SVM, support vector machine.