Classification of MDD patients with using network measures

Andrey Andreev

Baltic Center for Neurotechnology and Artificial Intelligence Immanuel Kant Baltic Federal University Kaliningrad, Russia andreevandrei1993@gmail.com

Abstract—Major depressive disorder (MDD) is a common and debilitating psychiatric illness that affects millions of people worldwide. Despite advancements in the understanding of its underlying mechanisms, the diagnosis and treatment of MDD remain a significant challenge. In this paper, we present an approach for classification patients with MDD based on their functional network measures. Our results demonstrate that a simple Linear Discriminant Analysis achieves high accuracy (83%) for two cases: when we use all network's couplings or when we use only the strongest ones.

Index Terms—Major depressive disorder, Linear discriminant analysis, network measures, graph approach

I. Introduction

Major depressive disorder (MDD) is one of the most common psychiatric disorders in the world. It affects approximately 300 million people globally and is associated with significant disability, morbidity, and mortality. The diagnosis of MDD relies on clinical assessments and subjective reports, which can be time-consuming and subject to interrater variability. Therefore, developing reliable and objective methods for diagnosing MDD is an ongoing challenge that has significant clinical implications.

Machine learning is a rapidly growing field of artificial intelligence that has revolutionized the world of medicine by providing innovative solutions for diagnosing and treating complex medical conditions [1]–[6]. In the field of neuroimaging, machine learning algorithms have been used to predict diagnostic categories based on imaging data, including MDD [7], [8]. One such method is the functional network approach, which involves analyzing the functional connectome of the brain to identify specific patterns of functional connectivity that are associated with MDD. Functional connectivity refers to the temporal correlation between different brain regions, which reflects the strength of neural interactions between them. Many studies have shown that individuals with MDD exhibit altered functional connectivity patterns compared to healthy controls [9]–[14].

In this study, we use machine learning algorithms to classify patients with MDD based on their functional network features. We use functional brain networks constructed by using resting-state functional magnetic resonance imaging data from 85

This work was funded by the Russian Science Foundation (Grant No. 23-71-30010).

participants, including 35 MDD patients and 50 matched healthy controls. Then, we use linear-discriminant analysis (LDA) to classify MDD patients. Our results showed that LDA achieves high accuracy (83 %) in classifying MDD patients when we use all coupling or only the strongest ones.

II. METHODS

A. Experimental data

As experimental data we use the functional connectivity matrices calculated on 166 normalized resting-state functional MRI volumes by using the Pearson correlation coefficient [15]. Each matrix contains 166 rows and 166 columns, the values are in the range [0,1]. The dataset contains 85 subjects: 50 healthy ones as a control group and 35 subjects with a Major depressive disorder.

B. Network measures

To analyze the network's structure we calculate the following measures: mean node strength $\langle k \rangle$, number of edges N_e , and clustering coefficient C.

Mean node strength is calculated as [16]

$$\langle k \rangle = \frac{1}{N} \sum_{i=1}^{N} k_i, \tag{1}$$

where k_i is the strength of i-th node (the sum of weights attached to ties belonging to the node), N is the number of nodes in the graph.

Clustering coefficient is the Watts-Strogatz clustering coefficient calculated as [17]

$$C = \frac{1}{N} \sum_{i=1}^{N} 2n_i / k_i (k_i - 1), \tag{2}$$

where n_i is the number of direct edges interconnecting the k_i nearest neighbors of node i.

C. Classification

To classify patients with Major depressive disorder we use Linear Discriminant Analysis (LDA), a supervised machine learning method that allows to perform dimensionality reduction by projecting the input data to a linear subspace consisting of the directions which maximize the separation between classes [18].

First, we separate each group of subjects (Control and MDD) into train and test ones as 60% and 40% respectively. Then, we fit the LDA model by the train set and test it on the test one by calculating the accuracy of the model:

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN},$$
 (3)

where TP is True positive, FP is False positive, TN is True negative, FN is False negative. As a result, we get 100 values of accuracy for one pair of groups.

III. RESULTS

We investigate the capability of machine learning methods to classify Major depressive disorder using functional network's features. The dataset contains 85 166x166 functional connectivity matrices. For each matrix we calculate 3 network measures: mean node strength $\langle k \rangle$ (Eq. (1)), number of edges N_e , and clustering coefficient C (Eq. (2)).

The coupling strengths in the originally obtained functional networks are uniformly distributed in a range from 0 to 1. In this work we investigate the role of weak couplings on the classification accuracy. We introduce a threshold value Thr and remove the couplings with coupling strength w < Thr [12]. So, increasing Thr leads to leaving only strong couplings in the network. In the process some nodes can become disconnected (it's strength is equal to 0), and we remove those nodes from the network.

Fig. 1 illustrates the dependencies of the network measures on the threshold value Thr for both groups (MDD and Control). $\langle k \rangle$ (Fig. 1(a)) and N_e (Fig. 1(b)) monotonously decrease with increasing Thr, mean values of the measures are very close to each other for both groups, but standard deviation for group with MDD is smaller then for the healthy one. The clustering coefficients (Fig. 1(c)) for both groups are linearly increase for $Thr \in [0,0.65]$, but then decrease for $Thr \in [0.65,0.8]$. One can see, that for small threshold C for control group is higher then for MDD, but for Thr = 0.6 it becomes equal for both groups, and for high threshold they change places.

Then, we use all 3 features together for classification. The accuracy of classification with using such approach is shown in Fig. 2. As one can see, maximal accuracy is achieved for Thr=0 (Accuracy = 0.83) and for Thr=0.7 (Accuracy = 0.81) while minimal accuracy = 0.56 is achieved for Thr=0.4.

IV. CONCLUSIONS

We have applied Linear Discriminant Analysis for classification of patients with Major Depressive Disorder by using functional connectivity matrices. But unlike it was done in paper [12], we have used not the networks itself but their characteristics (measures): mean node strength, number of edges, and clustering coefficient. The dataset contains 85 participants, including 35 MDD patients and 50 matched healthy controls.

We have investigated, how coupling strength influences on the accuracy of classification. Our results showed that LDA

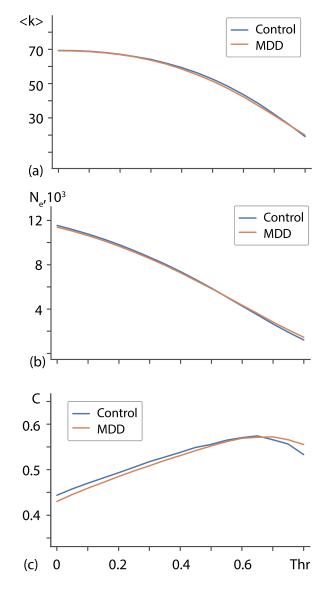


Fig. 1. The dependencies of the network measures on the threshold value Thr for Control (blue) and MDD (red) groups: (a) mean node strength $\langle k \rangle$, (b) number of edges N_e , and (c) clustering coefficient C.

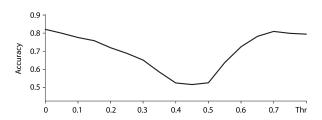


Fig. 2. Accuracy of classification versus the threshold value Thr using all 3 features together.

achieves high accuracy (83 %) in classifying MDD patients when we use all coupling or only the strongest ones. Wherein when we use only the couplings with strength more then 0.4 LDA cannot separate the healthy and MDD groups, the

accuracy is only 56 %.

ACKNOWLEDGMENT

The author thanks Prof. Alexander Hramov for usefull discussion. This work was funded by the Russian Science Foundation (Grant No. 23-71-30010).

REFERENCES

- [1] O. E. Karpov, E. N. Pitsik, S. A. Kurkin, V. A. Maksimenko, A. V. Gusev, N. N. Shusharina, and A. E. Hramov, "Analysis of publication activity and research trends in the field of ai medical applications: Network approach," *International Journal of Environmental Research and Public Health*, vol. 20, no. 7, p. 5335, 2023.
- [2] A. Jha, J. K Aicher, M. R Gazzara, D. Singh, and Y. Barash, "Enhanced integrated gradients: improving interpretability of deep learning models using splicing codes as a case study," *Genome biology*, vol. 21, no. 1, pp. 1–22, 2020.
- [3] R. Islam, A. V. Andreev, N. N. Shusharina, and A. E. Hramov, "Explainable machine learning methods for classification of brain states during visual perception," *Mathematics*, vol. 10, no. 15, p. 2819, 2022.
- [4] H. A. Elmarakeby, J. Hwang, R. Arafeh, J. Crowdis, S. Gang, D. Liu, S. H. AlDubayan, K. Salari, S. Kregel, C. Richter *et al.*, "Biologically informed deep neural network for prostate cancer discovery," *Nature*, vol. 598, no. 7880, pp. 348–352, 2021.
- [5] A. Badarin, V. Antipov, V. Grubov, N. Grigorev, A. Savosenkov, A. Udoratina, S. Gordleeva, S. Kurkin, V. Kazantsev, and A. Hramov, "Psychophysiological parameters predict the performance of naive subjects in sport shooting training," *Sensors*, vol. 23, no. 6, p. 3160, 2023.
- [6] O. E. Karpov, M. S. Khoymov, V. A. Maksimenko, V. V. Grubov, N. Utyashev, D. A. Andrikov, S. A. Kurkin, and A. E. Hramov, "Evaluation of unsupervised anomaly detection techniques in labelling epileptic seizures on human eeg," *Applied Sciences*, vol. 13, no. 9, p. 5655, 2023.
- [7] A. Kuc, S. Korchagin, V. A. Maksimenko, N. Shusharina, and A. E. Hramov, "Combining statistical analysis and machine learning for eeg scalp topograms classification," *Frontiers in Systems Neuroscience*, vol. 15, p. 716897, 2021.
- [8] N. Frolov, M. S. Kabir, V. Maksimenko, and A. Hramov, "Machine learning evaluates changes in functional connectivity under a prolonged cognitive load," *Chaos: An Interdisciplinary Journal of Nonlinear Sci*ence, vol. 31, no. 10, p. 101106, 2021.
- [9] A. V. Andreev, S. A. Kurkin, D. Stoyanov, A. A. Badarin, R. Paunova, and A. E. Hramov, "Toward interpretability of machine learning methods for the classification of patients with major depressive disorder based on functional network measures," *Chaos: An Interdisciplinary Journal of Nonlinear Science*, vol. 33, no. 6, 2023.
- [10] L.-L. Zeng, H. Shen, L. Liu, and D. Hu, "Unsupervised classification of major depression using functional connectivity mri," *Human brain mapping*, vol. 35, no. 4, pp. 1630–1641, 2014.
- [11] A. N. Pisarchik, A. V. Andreev, S. A. Kurkin, D. Stoyanov, A. A. Badarin, R. Paunova, and A. E. Hramov, "Topology switching during window thresholding fmri-based functional networks of patients with major depressive disorder: Consensus network approach," *Chaos: An Interdisciplinary Journal of Nonlinear Science*, vol. 33, no. 9, 2023.
- [12] D. Stoyanov, V. Khorev, R. Paunova, S. Kandilarova, D. Simeonova, A. Badarin, A. Hramov, and S. Kurkin, "Resting-state functional connectivity impairment in patients with major depressive episode," *International Journal of Environmental Research and Public Health*, vol. 19, no. 21, p. 14045, 2022.
- [13] Y. Li, X. Dai, H. Wu, and L. Wang, "Establishment of effective biomarkers for depression diagnosis with fusion of multiple resting-state connectivity measures," *Frontiers in Neuroscience*, vol. 15, p. 729958, 2021.
- [14] E. N. Pitsik, V. A. Maximenko, S. A. Kurkin, A. P. Sergeev, D. Stoyanov, R. Paunova, S. Kandilarova, D. Simeonova, and A. E. Hramov, "The topology of fmri-based networks defines the performance of a graph neural network for the classification of patients with major depressive disorder," *Chaos, Solitons & Fractals*, vol. 167, p. 113041, 2023.
- [15] A. M. Bastos and J.-M. Schoffelen, "A tutorial review of functional connectivity analysis methods and their interpretational pitfalls," *Frontiers in systems neuroscience*, vol. 9, p. 175, 2016.

- [16] M. Rubinov and O. Sporns, "Weight-conserving characterization of complex functional brain networks," *Neuroimage*, vol. 56, no. 4, pp. 2068–2079, 2011.
- [17] D. J. Watts and S. H. Strogatz, "Collective dynamics of 'small-world'networks," *nature*, vol. 393, no. 6684, pp. 440–442, 1998.
- [18] R. O. Duda, P. E. Hart et al., Pattern classification. John Wiley & Sons, 2006.