

A novel deep learning framework on brain functional networks for diagnosis of psychiatric diseases

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Synopsis:

We developed a predicting algorithm based on brain connectivity to quantify the altered brain regions in schizophrenia, bipolar, and attention deficit hyperactivity disorders, to help diagnose them using neuroimaging biomarkers. Functional connectivity was utilized to construct brain graphs, on which the node2vec framework was applied to produce the node embeddings. The concatenation of embeddings was used to derive the region feature vectors to feed support vector machine (SVM) classifiers. Also, we build a model to assist the diagnosis of disorders using a weighted voting ensemble. The achieved accuracy proved to outperform to the state-of-the-art models.

Introduction:

Schizophrenia (SZ) is a severe psychiatric illness characterized by aberrant sensory perception cognition¹. Bipolar Disorder (BP) is a serious mental disorder characterized by severe fluctuations in mood ranging from manic to depression². Attention deficit hyperactivity disorder (ADHD) is, on the other hand, a mental disorder mainly characterized by attention deficits, excessive activity and behavioral impulses, most prevalent in young children³. Despite significant research focusing on mental disorders, the mechanisms underlying these disorders are still not completely understood, consequently, the diagnostic approaches may not be completely specific and reliable. With the recent advance in clinical neuroimaging and availability of medical imaging devices, promising results are obtained in reinforcement of specific diagnosis for SZ, BP, and ADHD patients, for which both medical and behavioral presentations may be confusing^{4,6}.

The diagnosis of these disease and also monitoring their progression or regression can be facilitated by the means of neuroimaging modalities, such as functional magnetic resonance imaging (fMRI), by which, functional connectivity (FC) pattern of the brain can be reconstructed. FC has successfully identified fundamental differences between patients and healthy control subjects.

Methods and Materials:

Rs-fMRI datasets are accessed from the UCLA Consortium for Neuropsychiatric Phenomics (CNP) dataset⁷, which is publicly available in the OpenfMRI database. Data from fifty healthy subjects, as well as fifty SZ and BP each, and forty ADHD patients were inspected during a quality control process. The fMRI data were preprocessed in MATLAB using SPM8⁸ and the package of data processing & analysis for brain imaging (DPARFSF)⁹.

Automated anatomical labeling (AAL) atlas was used to identify the brain regions of interest (ROI). As a result of Pearson's correlation (PC) between time series of brain region, a 116×116 correlation matrix was generated to define the relation amongst different regions of brain and match to the FC network. The FC can be modeled as a weighted graph using the graph theory, where the weak weights are eliminated by setting the values below a specified threshold to zero and retaining the rest.

Recent developments in deep learning, especially in natural language processing, have led several studies to extend language models to graph representation learning. The node2vec algorithm¹⁰ aims to learn a vectorial representation of nodes in a graph by optimizing a neighborhood preserving objective. It has been inspired from the word embedding algorithm word2vec, expanding the prior node embedding algorithm "Deep Walk"¹¹. The node2vec employs a second-order random walk algorithm to calculate the node' neighborhood network. It generally consists of three steps: sampling, training skip gram, and computing embedding

This random walk results in a bag of nodes of neighborhood from sampling by use of flexible biased random walks on the network. The bag of nodes is generated from the random walks and is fed into the skip-gram network. Each node is represented by a one-hot vector and maximizes the probability for predicting the neighbor nodes. The hidden layer output of the network is taken as the graph embedding. By concatenation of these embeddings, a feature vector of nodes for every group is generated.

By applying a grid search approach and obtaining the best parameters of SVM for classification of the groups of patients vs. HC in total regions, we achieved a unique accuracy in each region by calculating the feature discrimination rates. Consequently, features with an accuracy higher than 0.7 was chosen as experts of an ensemble learning model with utilizing majority voting for classification.

Conclusion:

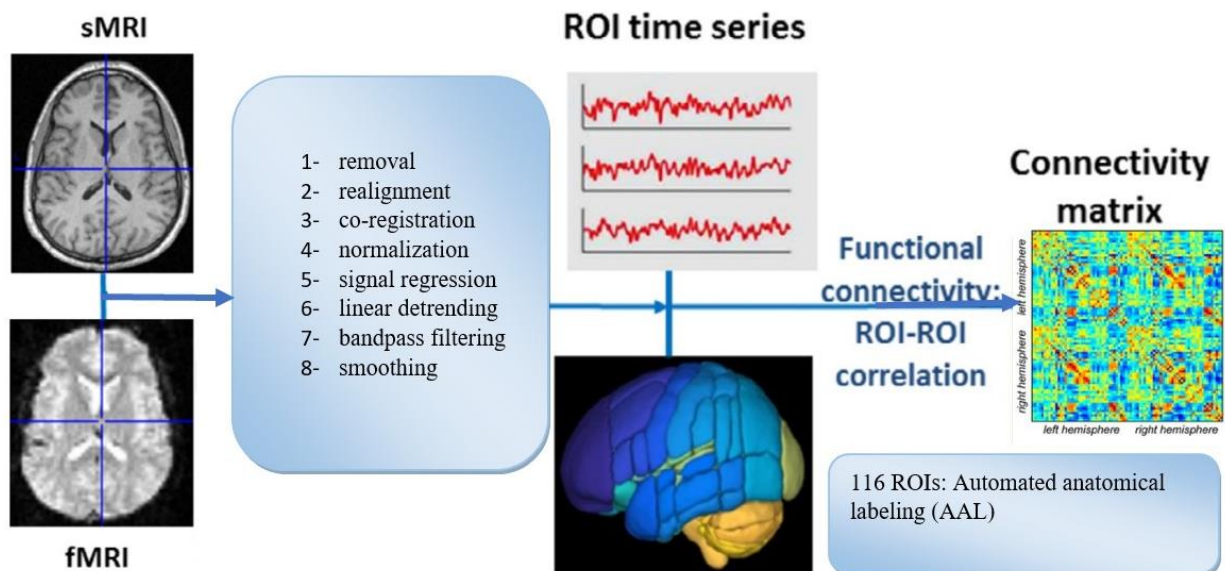
We introduced a decision-making and classification framework takes deep learning-based feature extraction into account with connectivity graphs as the input and altered regions due to dysfunction as the output. Moreover, by utilizing an ensemble learning, we achieved the highest accuracy among the approached proposed in the previous literature. The promising results indicates that proposed method can be used for real-world systems.

Summary of main findings:

We introduce an algorithm to detect altered brain regions in schizophrenia, bipolar, and attention deficit hyperactivity disorders. The classifier achieved an accuracy of 88.33%, specificity of 93.33%, and sensitivity of 84.33% in distinguishing patient groups versus healthy controls.

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A



B

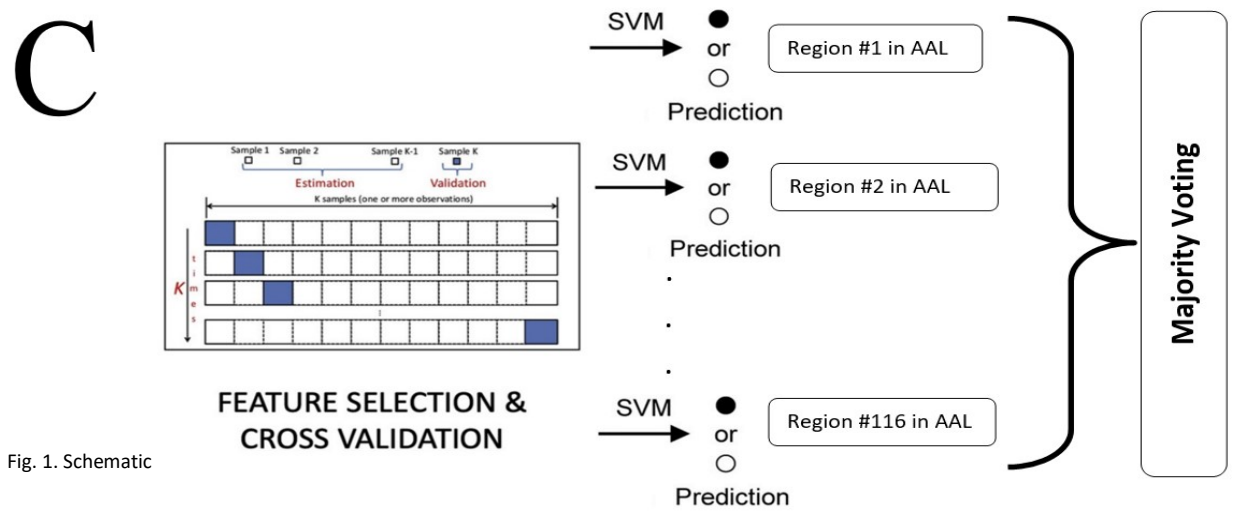
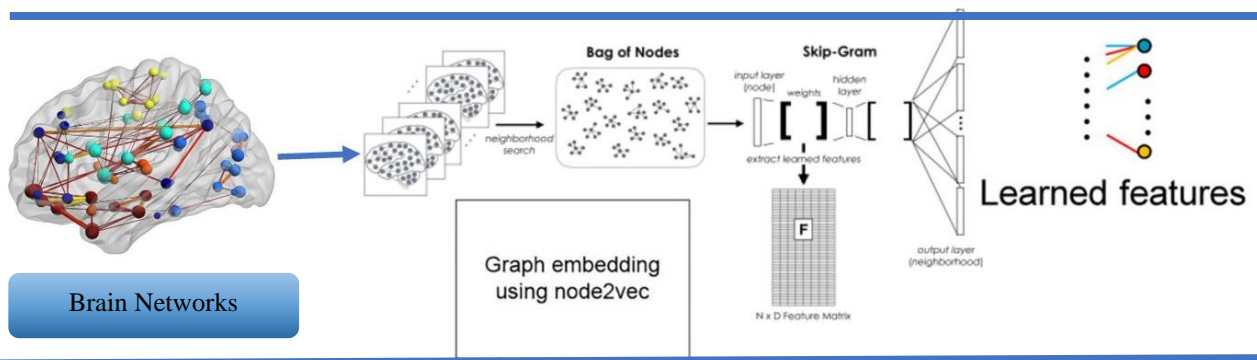


Fig. 1. Schematic

References:

- .1 Chyzyk, D. & Graña, M. Classification of schizophrenia patients on lattice computing resting-state fMRI features. *Neurocomputing* **151**, 151-160.(2019)
- .2 Lish, J.D., Dime-Meenan, S., Whybrow, P.C., Price, R.A. & Hirschfeld, R.M.A. The National Depressive and Manic-depressive Association (DMDA) survey of bipolar members. *Journal of Affective Disorders* **31**, 281-294.(1994)
- .3 Dey, S., Rao, A.R. & Shah, M. Attributed graph distance measure for automatic detection of attention deficit hyperactive disordered subjects. *Frontiers in Neural Circuits* **8**.(2014)
- .4 Liang, M.-J., et al. Identify changes of brain regional homogeneity in bipolar disorder and unipolar depression using resting-state fMRI. *PLoS one* **8**, e79999.(2013)
- .5 Schulz, K.P., et al. Response inhibition in adolescents diagnosed with attention deficit hyperactivity disorder during childhood: an event-related fMRI study. *American Journal of Psychiatry* **161**, 1650-1657.(2004)
- .6 Turner, J.A., et al. A multi-site resting state fMRI study on the amplitude of low frequency fluctuations in schizophrenia. *Frontiers in neuroscience* **7**, 137.(2013)
- .7 Poldrack, R.A., et al. A phenome-wide examination of neural and cognitive function. *Scientific Data* **3**, 160110.(2016)
- .8 Penny, W.D., Friston, K.J., Ashburner, J.T., Kiebel, S.J. & Nichols, T.E. *Statistical parametric mapping: the analysis of functional brain images*, (Elsevier, 2011).
- .9 Yan, C. & Zang, Y. DPARSF: a MATLAB toolbox for "pipeline" data analysis of resting-state fMRI. *Frontiers in Systems Neuroscience* **4**.(2010)
- .10 Grover, A. & Leskovec, J. node2vec: Scalable Feature Learning for Networks. in *Proceedings of the 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining* 855–864 (Association for Computing Machinery, San Francisco, California, USA, 2016.)
- .11 Mikolov, T., Chen, K., Corrado, G. & Dean, J. Efficient estimation of word representations in vector space. *arXiv preprint arXiv:1301.3781*.(2013)
- .12 Pläschke, R.A.-O., et al. On the integrity of functional brain networks in schizophrenia, Parkinson's disease, and advanced age: Evidence from connectivity-based single-subject classification.
- .13 Ramkiran, S., Sharma, A. & Rao, N.P. Resting-state anticorrelated networks in Schizophrenia. *Psychiatry Research: Neuroimaging* **284**, 1.(2019)
- .14 Zhuang, H., et al. Multimodal classification of drug-naïve first-episode schizophrenia combining anatomical, diffusion and resting state functional resonance imaging. *Neuroscience Letters* **705**, 87-93.(2019)
- .15 Jing, R., et al. Machine learning identifies unaffected first-degree relatives with functional network patterns and cognitive impairment similar to those of schizophrenia patients. *Hum Brain Mapp* **40**, 3930-3939.(2019)
- .16 Zou, H. & Yang, J. Multiple functional connectivity networks fusion for schizophrenia diagnosis. *Medical & Biological Engineering & Computing* **58**, 1779-1790.(2020)
- .17 Wismüller, A. & Vosoughi, M.A. Classification of schizophrenia from functional MRI using large-scale extended Granger causality. in *Medical Imaging 2020: Computer-Aided Diagnosis*, Vol. 11597 115971G (International Society for Optics and Photonics, 2021).
- .18 Achalia, R., et al. A proof of concept machine learning analysis using multimodal neuroimaging and neurocognitive measures as predictive biomarker in bipolar disorder. *Asian Journal of Psychiatry* **50**, 101984.(2020)
- .19 Wang, Y., et al. Classification of Unmedicated Bipolar Disorder Using Whole-Brain Functional Activity and Connectivity: A Radiomics Analysis. *Cerebral Cortex* **30**, 1117-1128.(2020)
- .20 Shan, X., et al. Disrupted Regional Homogeneity in Drug-Naive Patients With Bipolar Disorder. *Frontiers in Psychiatry* **11**.(2020)
- .21 Xi, C., et al. Abnormal functional connectivity within the reward network: a potential neuroimaging endophenotype of bipolar disorder. *Journal of Affective Disorders* **280**, 49-56.(2021)
- .22 Pan, P., et al. Increased Global-Brain Functional Connectivity Is Associated with Dyslipidemia and Cognitive Impairment in First-Episode, Drug-Naive Patients with Bipolar Disorder. *Neural Plasticity* **2021**, 5560453.(2021)
- .23 Riaz, A., Asad, M., Alonso, E. & Slabaugh, G. Fusion of fMRI and non-imaging data for ADHD classification. *Computerized Medical Imaging and Graphics* **65**, 115-128.(2018)
- .24 Sen, B., Borle, N.C., Greiner, R. & Brown, M.R. A general prediction model for the detection of ADHD and Autism using structural and functional MRI. *PLoS one* **13**, e0194856.(2018)
- .25 Miao, B., Zhang, L.L., Guan, J.L., Meng, Q.F. & Zhang, Y.L. Classification of ADHD Individuals and Neurotypicals Using Reliable RELIEF: A Resting-State Study. *IEEE Access* **7**, 62163-62171.(2019)
- .26 Shao, L., You, Y., Du, H. & Fu, D. Classification of ADHD with fMRI data and multi-objective optimization. *Computer Methods and Programs in Biomedicine* **196**, 105676.(2020)