Deep Learning Classification Study of First-Episode Treatment-Naïve Schizophrenia Using Brain Cortical Area and Cognitive Features

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Abstract:

Deep learning neural network was for the first time used to discriminate schizophrenia patients from healthy controls. Neuroimaging and coginitive data were accquired as featres. Re-sampling was repeated 100 times and emsemble models were applied. The result show that the classification accuracy is satisfactorily high and robust. And the classification weights show that brain surface area and multiple domains of coginition were of high discriminate value in the disease.

Keywords: schizophrenia; surface area; cognitive performance; deep neural networks

Introduction

Schizophrenia is among the most severe and debilitating of psychiatric disorders. Diagnosis is currently by criterion-based systems. Accumulating evidence have shown that neuroimaging and cognitive changes exist in the course of the disease. Machine-learning algorithms have been successfully deployed in the automated classification of diagnosis. However, the permance of the classification still demand improvement. Meanwhile, a deep neural network (DNN) with multiple hidden layers has shown its ability to systematically extract lower-to-higher level information of image and cognitive data, markedly enhancing classification accuracy.

In this study, we aimed to discriminate first-episode treatment-naïve schizophrenia (SZ) patients from healthy controls (HC) using neuroimaging features along with cognitive performance features by advanced machine learning algorithm, deep neural networks, and investigate the underlying brain cortical area and cognitive abnormalities.

Methods

We recruited 127 SZ patients and 96 age and gender-matched HC. T1 MR images were collected in all participants. Surface-based analyses were performed using FREESURFER to investigate brain surface area. Brain regions of significant difference were extracted as Region of Interests（ROIs）as neuroimaging features. Trail Making Test (TMT), Wechsler Adult Intelligence Scale (WAIS) and the Cambridge Neuropsychological Test Automated Battery (CANTAB) were performed to acquire cognitive features. In the deep learning process, we created five-layered feed-forward neural networks (Schmidhuber, 2015).

Deep learning classification process

All participants (n=223) were randomly assigned to a training set (n=111), a validation set (n=56) and a test set (n=56) where the validation and test sets were unseen during training. This sampling was repeated 100 times. After each re-sampling, all features and diagnose labels of the training set were inputted into the model, z-scores were calculated to yield a zero mean and unit variance for each feature input. We randomly silenced 20% of feature data to avoid data leakage. L1 and max-norm regularizations were used to reduce overfitting. Then, we created five networks and trained each of them to classify SZ and HC for 200 epochs with small mini-batch size of 8 (Masters & Luschi et al., 2018). For each training process, the weight set that had the lowest loss function value in the validation set was chosen, and we created an average ensemble model from the five networks of the best weight set. Four performance indices (accuracy, sensitivity, specificity and the area under receiver operating characteristic curves (AUCs)) were calculated in the expansion test data. (Fig. 1)

Outcome Measures

For 100 data separations, 100 ensemble models were made, the mean and standard deviation of the four performance indices were calculated. We then calculated the mean and the standard deviation of the absolute value of the weights of the first layer and viewed the proportion of weights ($\overline{w}$ + 0.5σ).

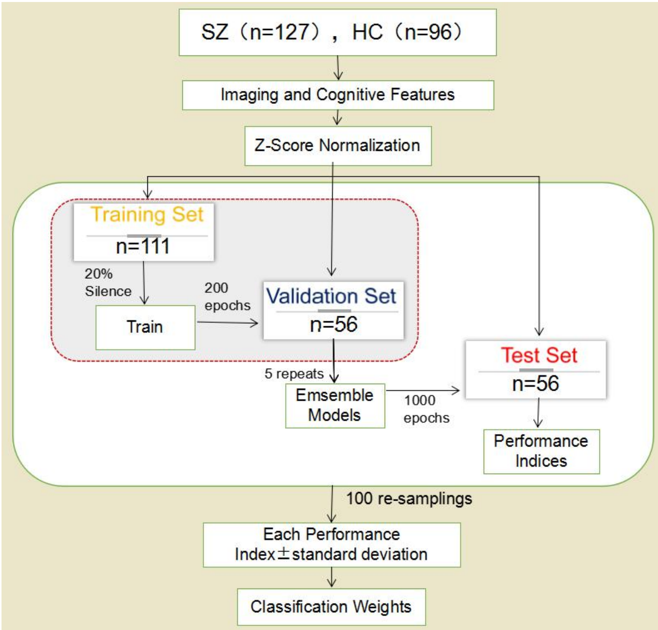

Figure 1: Deep Learning Process.

Results

1. Surface areas of SZ decreased significantly in the frontal lobe (① the rostral middle frontal and the superior frontal gyrus, ② the pars triangularis and pars opercularis cortex) and ③ the right occipital lobe compared with controls (Fig. 2). 2. For 100 data re-samplings, 100 ensemble models were made, the mean and the standard deviation of the four performance indices are calculated for all models. We got the following results: accuracy 81.95 ± 5.58%, sensitivity 79.65±7.51%, specificity 85.67±9.76%, AUC 89.08% ± 5.00%. 3.TMT test sub-scores showed highest classification weights. Operation IQ score also showed high weight. Surface area ROIs and some CANTAB sub-scores had less but substantial discriminative power (Fig. 3 and Fig. 4).

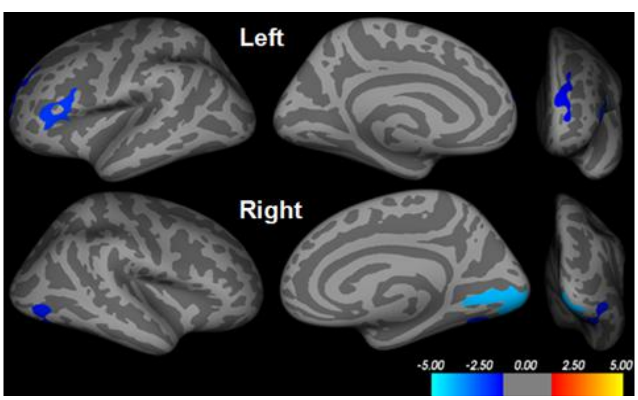

Figure 2: Surface areas comparison between SZ and HC.

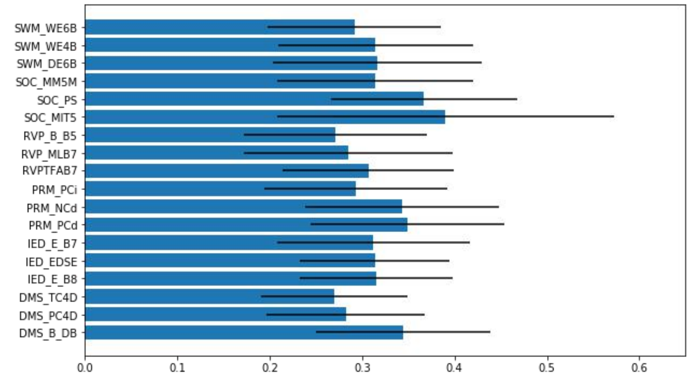

Figure 3: Top 3 Classification weights of sub-tests in each battery of CANTAB.

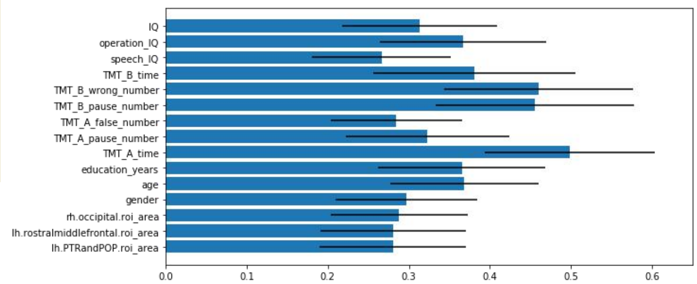

Figure 4: Classification weights of surface areas, IQ, TMT tests, education years, age and gender.

Conlusion

In this work, we used deep learning neural networks to classifiy SZ and HC. We get high and quite robust accuracy, sensitivity, specificity and AUC. And we find brain structure and cognition features that have important value in the disease course. Together, we propose an advanced model for SZ diagnosis and further understanding of disease phenotypes.

Acknowledgments

Funding: National Nature Science Foundation of China Key Project 81630030 and 81130024 (to T.L.); National Key Research and Development Program of the Ministry of Science and Technology of China 2016YFC0904300 (to T.L.);13.5 Project for disciplines of excellence, West China Hospital of Sichuan University (to T.L. and X.H. M.); Natural Science Foundation of China (8157051859 to W.D.). Special thanks to Yusheng Pan.

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