IDENTIFYING SCHIZOPHRENIA USING WHOLE-BRAIN DIFFERENT IMAGING MODALITIES VIA A MULTIVARIATE PATTERN ANALYSIS

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TARGET AUDIENCE: Psychiatrists, neurologists and radiologists will benefit in having another approach in diagnosing schizophrenia.

PURPOSE: Despite many efforts have been spared on studying the pathogenesis of schizophrenia, there are still no objective biological markers that can be reliably used to identify individuals with schizophrenia. Studies focused on chronic or treated schizophrenia had shown the potential clinical value of support vector machine (SVM)[1] in separating schizophrenia patients from healthy controls individually, though the results was inconsistent[2, 3]. However, few efforts has been done to evaluate this in antipsychotic-naïve first episode schizophrenia (FES), which is important for clinical diagnosis and elucidating the core pathogenesis of the illness[4]. We therefore used SVM to characterize structural and functional pattern implicated in antipsychotic-naïve patients with schizophrenia and also to examined the diagnostic potential of structural neuroanatomy and functional activity，which were presented by gray matter volume (GMV) and amplitudes of low-frequency (0.01–0.08 Hz) fluctuations (ALFF) of the blood oxygen level-dependent (BOLD) resting-state functional magnetic resonance imaging (fMRI) signal[5] separately.

METHORDS: The study was approved by the local research ethics committee, and written informed consent was obtained from all participants. Diagnoses of schizophrenia were determined by the consensus of two experienced clinical psychiatrists using the Structured Interview for the DSM-IV Axis I Disorder, Patient Edition (SCID). Psychopathology ratings were obtained using the Positive and Negative Syndrome Scale (PANSS). A total number of 216 subjects, including 108 antipsychotic-naïve first-episode schizophrenia patients and 108 healthy controls with age, gender and years of education matched, were recruited and scanned structural and rest-state functional MRI at baseline. The MRI examinations were performed on a 3-Telsa GE MRI system with an 8 channel phase array head coil. High resolution T1-weighted images were acquired with a volumetric three-dimensional spoiled gradient recall sequence (TR=8.5msec, echo time=3.4msec, flip angle=12°, slice thickness=1 mm) while the resting-state fMRI sensitized to changes in BOLD signal levels were obtained via a GE-EPI sequence (TR/TE=2000/30msec, flip angle=90°, slice thickness=5mm with no gap, 30 axial slices, 200 volumes in each run). During MR examination, subjects were instructed to relax with their eyes closed without falling asleep. VBM analyses of T1 images were performed using SPM8 (http://www.fil.ion.ucl.ac.uk/spm) and the VBM8 toolbox (http://dbm.neuro.uni-jena.de/vbm). Whilst the ALFF maps were calculated using DPARSFA Version2.2 (http://www.restfmri.net). Subsequently, SVM implemented in the PROBID software package (http://www.brainmap.co.uk/probid.htm) was used to investigate the diagnostic accuracy of whole brain structural and functional parameters in predicting diagnosis of schizophrenia. The combined classification accuracy was obtained by integrating the above two kernels into one model. Statistical significance of classification accuracy for each modality was set at p < 0.001 after permutation testing (1000 times).

RESULT: Demographics like age, gender and years of education were not significantly different between the two groups (p>0.05). All the subjects are right-handed. SVM allowed the classification of the two groups with diagnostic accuracy of grey matter volume was 68.5% (P<0.001, sensitivity=68.5% specificity=68.5%), while the diagnostic accuracy of ALFF was 76.4% (P<0.001, sensitivity=77.8% specificity=75.0%). The set of regions showed different value between the two groups mainly are right insula, right thalamus, left occipital middle gyrus and right occipital superior gyrus for GMV (Figure 1) and left frontal superior medial gyrus, right occipital inferior gyrus, right temporal superior gyrus and right precuneus for ALFF (Figure 2). The combination of the two kernel yielded an accuracy of 81.5% (P<0.001) with sensitivity and specificity up to 82.4% and 80.6% respectively. Receiver Operating Characteristic (ROC) curves of these modalities were also obtained as showed in Figure 3.

DISCUSSION: To our knowledge, this is the first study involved the largest sample of antipsychotic-naïve FES to investigate the feasibility of multivariate pattern analysis. Consistent with our hypothesis, both structural and functional MRI show potential value in differentiating schizophrenia from healthy controls individually, while the combination of the both may lead to better discrimination than the use of either modality on its own. Such findings also provide evidences to support the anatomical and functional deficits mainly involving fronto-striato-parietal networks could be used as a biomarker for schizophrenia, though the accuracy is not high enough.

CONCLUSION: This study demonstrates that multivariate pattern analysis methods can be used to identify antipsychotic-naïve FES from healthy controls based on different imaging modalities. Further probing with the integration of different imaging modalities as well as cognitive, neuropathological and genetic information may give a better insight into biomarkers of the condition.

Figure 1. The discrimination maps for GMV. These regions were identified by set the threshold to ≥30% of the weight vector scores. Warm color (positive value) indicated regions contributing to identifying the patients with schizophrenia. While cool color (negative weights) indicates higher parameter values for healthy controls than schizophrenia.
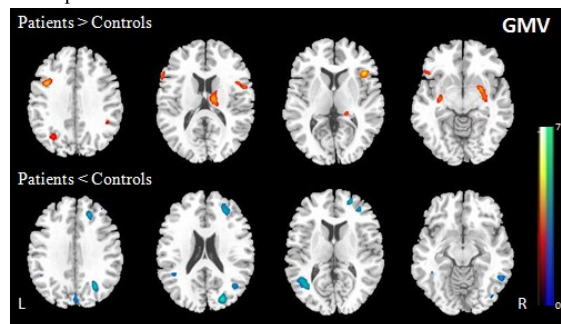
Figure 2. The discrimination maps for ALFF. These regions were identified by set the threshold to ≥30% of the weight vector scores. Warm color (positive value) indicated regions contributing to identifying the patients with schizophrenia. While cool color (negative weights) indicates higher parameter values for healthy controls than schizophrenia.
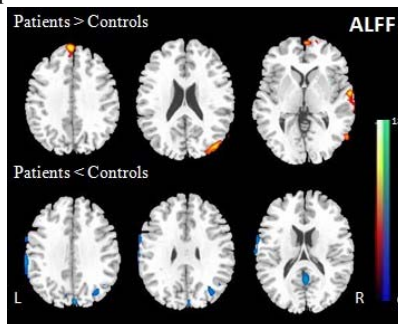
Figure 3. ROC curves for the comparisons between patients and healthy controls using the three kernels, which yielded an accuracy of 68.5% for the GMV (68.5% sensitivity, 68.5% specificity), 76.4% for the ALFF (77.8% sensitivity, 75.0% specificity) and 81.5% for the combination (82.4% sensitivity, 80.6% specificity) , statistically significant at P＜0.001.
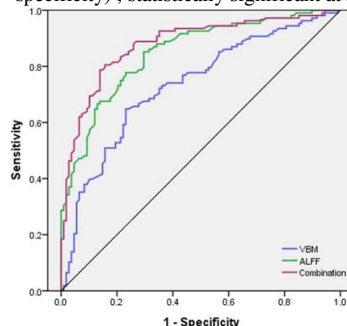
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