

Combining Anatomical and Functional MRI in Diagnosis of Drug-naïve First Episode Schizophrenia

Wenting Ren¹, Peilin Lv², Wei Deng³, Qizhu Wu¹, Xiaoqi Huang¹, Tao Li³, Qiyong Gong¹, and Su Lui¹

¹Huaxi MR Research Center (HMRRRC), Department of Radiology, West China Hospital of Sichuan University, Chengdu, Sichuan, China, People's Republic of

²Department of Anesthesiology, West China Hospital of Sichuan University, Chengdu, Sichuan, China, People's Republic of, ³Department of Psychiatry, West China Hospital of Sichuan University, Chengdu, Sichuan, China, People's Republic of

Introduction

Although numerous morphometric and functional MRI studies have revealed anatomical and functional deficits mainly involving fronto-striato-parietal networks in patients with schizophrenia [1], it is still unclear whether the findings of MRI could be used for the diagnosis of this severe psychological disease, especially for drug-naïve first episode schizophrenia (FES). Furthermore, increased evidences have been found to support the neural-network deficits in the core pathogenesis of schizophrenia [2]. Thus, a method taking account of multiple regional information and inter-regional correlations should be used for the distinction of FES patients from healthy controls. The present work aims to combine anatomic and functional MRI indiscriminate 100 drug-naïve FES from 100 healthy controls by utilizing a support vector machine (SVM) classification approach.

Method

The study was approved by the local ethical committee and written informed consent was obtained from all subjects. A total of 100 right-handed drug-naïve FES patients and 100 age, sex, height, weight, handedness and years of education matched normal controls were recruited in this study. The diagnoses of schizophrenia patients were determined using the structured clinical interview for DSM-IV patient edition. All patients were evaluated using the Global Assessment of Functioning Scale and clinical severity was evaluated using the PANSS which provides a total score, positive and negative symptom scores, and six indices of thought disturbance, activation, paranoia, depression, anergia and complementary. All subjects were scanned on a 3T Magnetic resonance scanner (EXCITE, General Electric, Milwaukee, USA) with a spoiled gradient recall sequence generating high-resolution T1-weighted volumetric 3D images and a gradient-echo echo-planar imaging sequence for resting-state fMRI. VBM8 in SPM8 was used to calculate the alterations of gray matter volume (GMV) in FES. The amplitude of low frequency (0.01–0.8 Hz) fluctuations (ALFF) of BOLD signals, which is thought to reflect spontaneous neural activity [3], were calculated by DPARSF software package (<http://www.restfmri.net>) to characterize regional cerebral function. SVM classification approach was used to calculate the sensitivity, specificity and accuracy for distinction of FES patients from healthy controls by fusing information from GMV and ALFF. This included three steps, i.e., firstly, a SVM based classifier ensemble is constructed using GMV; Secondly, ALFF were analyzed in SVM. Finally, the results obtained from the above two stages are combined into a single module using majority voting (Combined GMV-ALFF). The significant were set at $P < 0.001$ after permutation testing.

Results

The SVM classification between schizophrenia and controls using combined VBM and ALFF maps were show in the left of Figure 1. The classification yielded an accuracy of 83.5% (82% sensitivity, 85% specificity) with $P < 0.001$ after permutation testing. The most discriminating regions of GMV and ALFF were identified by setting the threshold to the top 30% of the weight vector scores (Figure 1) and these regions were listed as below (Table 1).

Discussion

To our knowledge, current study provides the first evidence for evaluating the MR diagnostic value in a large sample of antipsychotic-naïve first-episode schizophrenia. Combining anatomical and functional MRI, a relative high accuracy was identified, supporting the anatomical and functional deficits mainly involving fronto-striato-parietal networks could be used as a biomarker for the diagnosis of schizophrenia. The findings also offer us a promising objective method for the translation of MR findings in individual psychiatric patients.

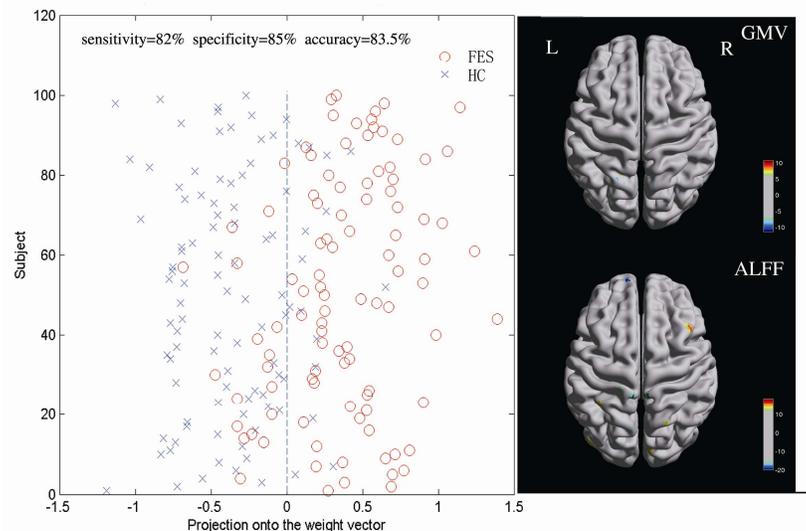


Figure 1. The left figure demonstrates the results of SVM approach to discriminate FES from HC using combined GMV and ALFF. The right figure shows the most discriminating regions identified by setting the threshold to the top 30% of the GMV and ALFF weight vector scores separately. Red indicates higher values in the FES than the HC group, while blue indicates higher values for the HC than the FES group.

Table 1. Most important discriminating regions of GMV and ALFF results between FES and HC.

Modality	Region	Coordinates(x y z)	w _i
GMV	<i>FES>HC</i>		
	Left Thalamus	-4 -21 9	9.712
	Right superior frontal	20 59 11	8.108
	<i>HC>FES</i>		
	Left superior parietal	-19 -57 68	8.565
ALFF	Left inferior parietal	-21 -58 65	8.743
	Right middle occipital	33 -87 1	9.725
	<i>FES>HC</i>		
	Right middle frontal	47 23 47	16.29
	Right superior parietal	25 -65 68	15.74
	<i>HC>FES</i>		
	Left superior middle	1 66 15	20.01
Left inferior parietal	-42 -51 57	19.82	
Left cuneus	1 94 23	22.89	
Left calcarine	1 -98 -4	19.04	

w_i: weight of each cluster centroid *i*; FES: drug-naïve first episode schizophrenia; HC: healthy controls.

References

- Nivedita Agarwal, et al., *Radiology* 2010, vol. 255, p. 23-41
- Su lui, et al., *Am J Psychiatry* 2009, vol. 166, p. 196-205
- Cordes D, et al., *Am J Neuroradiol* 2001, vol. 22, p. 1326-33