

SUPPLEMENTARY MATERIAL

MATERIALS AND METHODS

Ethics Statement

This study was approved by the Ethics Committee of the Second Xiangya Hospital of Central South University and all participants gave written informed consent.

Participants

Twenty late-onset schizophrenic patients (15 females, 5 males) with an average age of 46.9 years and average education of 8.4 years were recruited *via* the Institute of Mental Health of the Second Xiangya Hospital, Central South University. Schizophrenia was diagnosed by psychiatrists using the Structured Clinical Interview in DSM-IV-TR-Patient Version. Psychotic symptoms were evaluated using the Positive and Negative Syndrome Scale (PANSS) by two trained psychiatrists^[1]. Seventeen healthy controls (13 females, 4 males) with an average age of 47.4 years and average education of 8.2 years) were recruited from the local area *via* poster advertisement and screened using the DSM-IV-TR-Non-Patient Version. The inclusion and exclusion criteria were consistent with previous work^[2].

MRI Acquisition and Data Analysis

High-resolution whole brain volume T1-weighted sagittal images were acquired using a 1.5T GE MRI scanner (Twin-speed, Milwaukee, WI) with a 3D spoiled gradient echo pulse sequence (orientation: sagittal; repetition time = 12.1 ms; echo time = 4.2 ms; flip angle = 15°; field of view = 240 × 240 mm²; matrix size = 256 × 256; slice thickness = 1.8 mm; gap = 0 mm; 172 slices).

The VBM8 Toolbox (<http://dbm.neuro.uni-jena.de/vbm.html>) for Statistical Parametric Mapping (SPM8; <http://www.fil.ion.ucl.ac.uk/spm>)^[3] with MATLAB 2010a (MathWorks, Boston, MA)^[4] was used to preprocess and analyze the MRI data. The data preprocessing was performed as previously described^[5].

Voxel-wise comparisons of gray matter volume between groups were performed in SPM8 with the two-sample *t*-test controlling for confounding factors including age, gender, and years of education. A gray matter mask was used to restrict the search volume for analysis. This gray matter mask was defined by binarizing the SPM8 priori gray matter template to a binary mask by thresholding each voxel with a probability >0.4 to define gray matter regions for analysis.

Statistical differences in gray matter volume between groups were set as $P < 0.05$ (combined threshold of $P < 0.001$ and critical cluster size of 1075) using topological false discovery rate (FDR) correction^[6, 7].

Statistical Analysis

Demographic data comparisons between groups were performed using the independent-sample *t*-test and χ^2 test with SPSS version 15.0 (SPSS, Chicago, IL). The mean volumes of clusters with group differences shown by VBM analysis were extracted using MarsBar 0.41 (<http://marsbar.sourceforge.net/>) and log_roi_batch v2.0 (<http://www.aimfeld.ch>). Partial correlation analysis was performed between the mean volumes of the clusters and clinical factors including PANSS scores, duration of psychosis, and chlorpromazine equivalent value controlling for age, gender, and years of education (two tailed, $P < 0.05$).

REFERENCES

- [1] Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull* 1987, 13: 261-276.
- [2] Chen L, Chen X, Liu W, Wang Q, Jiang T, Wang J, *et al.* White matter microstructural abnormalities in patients with late-onset schizophrenia identified by a voxel-based diffusion tensor imaging. *Psychiatry Res* 2013, 212: 201-207.
- [3] Ashburner J, Friston KJ. Voxel-based morphometry--the methods. *Neuroimage* 2000, 11: 805-821.

- [4] MATLAB 2010a (2010). Natick: The MathWorks, Inc.
- [5] Lu F, Huo Y, Li M, Chen H, Liu F, Wang Y, *et al.* Relationship between personality and gray matter volume in healthy young adults: a voxel-based morphometric study. PLoS ONE 2014, 9: e88763.
- [6] Vieta E, Suppes T, Ekholm B, Udd M, Gustafsson U. Long-term efficacy of quetiapine in combination with lithium or divalproex on mixed symptoms in bipolar I disorder. J Affect Disord 2012, 142: 36-44.
- [7] Geller B, Luby JL, Joshi P, Wagner KD, Emslie G, Walkup JT, *et al.* A randomized controlled trial of risperidone, lithium, or divalproex sodium for initial treatment of bipolar I disorder, manic or mixed phase, in children and adolescents. Arch Gen Psychiatry 2012, 69: 515-528.

Table S1. Regions with reduced gray matter volume in patients with late-onset schizophrenia compared with healthy controls

Brodmann area	Anatomical region	Cluster size (no. voxels)	P value	MNI (mm)			Peak intensity
			topological FDR corrected	X	Y	Z	
24	Middle cingulate gyrus	1075	0.011	-7	-25	39	5.21

Topological FDR corrected $P < 0.05$. Late-onset schizophrenia patients, $n = 20$; healthy controls, $n = 17$.