Magnetization Transfer Imaging in distinguishing Early and Adult Onset Schizophrenia in drug-naive first-episode patients

X. Huang[1,2], Y. Wang[3], S. Lui[1], W. Deng[2], L. Ouyang[3], H. Tang[1], T. Li[2], B. Song[1], X. Zhou[1], S. Maclean[4], V. Sluming[5], Q. Gong[1]

[1]Huaxi MR Research Center (HMRRC),Department of Radiology, West China Hospital of Sichuan University, Chengdu, Sichuan, China, People's Republic of, [2]Department of Psychiatry, West China Hospital of Sichuan University, Chengdu, Sichuan, China, People's Republic of, [3]School of Life Science and Technology, University of Electronic Science and Technology of China, Chengdu, Sichuan, China, People's Republic of, [4]Neurologische, Universitatsklinikum, Goettingen, Germany, [5]Division of Medical Imaging, Faculty of Medicine, University of Liverpool, Liverpool, United Kingdom

Introduction

Early-onset schizophrenia (EOS) is thought to be a unique subtype of schizophrenia which represents a more severe form of the disorder compared with its adult-onset schizophrenia (AOS) counterpart (1). It is less affected by environmental factors. Study of the brain abnormalities involved may provide insight into the etiology of schizophrenia. Various methods including voxel-based-morphology (2) and diffused tensor imaging (2) have been employed to reveal the structural alterations in the brain of the EOS patients. Magnetization transfer (MT) imaging, however, proves to be sensitive to detect the alteration of tissue integrity (4), and reduction of the MT ratio (MTR) has been reported in widespread cortical areas in both chronic and the first episode schizophrenia, independent of the structural abnormalities (5). We therefore aimed to explore the MTR changes of the cerebral tissue in first-episode drug-naive patients with EOS versus AOS using voxel-wised analysis.

Methods

The study was approved by the local ethical committee and written informed consent was obtained from all subjects. Six subjects with EOS (mean age of 16.17 ± 0.983, one male and five females) and eight AOS patients (mean age of 27.63 ± 6.545, four males and four females) were recruited prior to any kind of antipsychotic treatment. Psychiatric diagnosis was based on structured clinical interview for DSM-IV (SCID) in accordance with the criteria of DSM-IV. There was no significant difference in disease duration between EOS and AOS ($p > 0.05$). All MR images were acquired using a 3T MR imaging system (EXCITE, General Electric, Milwaukee, USA) with an 8 channel phase array head coil. High-resolution T1-weighted images were acquired coronally using a 3D SPGR pulse sequence generating 160 contiguous slices (TR/TE =8.5/3.4 msec; field of view 24 cm^2; slice thickness, 1 mm; slice gap 0; matrix 256 x 256; flip angle 12°). Axial MT images were acquired using a dual spin-echo MT sequence generating 50 contiguous 3 mm axial slices (TR /TE =37/5 msec; Field of View 24 cm^2, matrix 320 x 192; flip angle 40°) with and without a saturation pulse respectively. To facilitate the analysis, T1-weighted images of both with and without MT effect were co-registered by applying the mutual information registration algorithm using SPM2 (http://www.fil.ion.ucl.ac.uk/spm/software/). MTR for each voxel was calculated using the following formula: $MTR=\frac{(m_0 - m_s)}{m_0} * 100$ where m_0 is the signal intensity without saturation pulse (T1 signal) and m_s is signal intensity with saturation pulse (T1 plus MT). Whole brain voxel-wised analysis was performed to compare EOS with AOS by taking age as a covariate.

Results

In comparison with AOS, EOS presented with significantly higher MTR in white matter of the left hemisphere including the centrum ovale majus, hippocampus and insular (Fig 1, t=4.02, p<0.001, cluster size=58, 62, 52 respectively), whereas significantly lower MTR of the cerebral regions were found in patient with EOS including the white matter of left inferior and middle frontal gyrus, and the grey matter of right inferior frontal gyrus and right cerebellum (Fig 2, t=4.02, p<0.001, cluster size=144,65,67 and 52 respectively).

Conclusion and discussion

The present study is the first to compare EOS and AOS using voxel-wised MTR analysis which outweighs the conventional ROI method in not requiring a prior hypothesis. To avoid compounding factors arising from the medication we only recruited treatment-naive patients, and our study sample size is small. However, we found regional differences of higher or lower MTR in both white and grey matter between EOS and AOS. This suggests that the changes of MTR in the brain of patients with schizophrenia are heterogenous, rather than uniformly decreasing as reported in previous study (5), further indicating EOS is a unique subtype of schizophrenia which distinguishes itself from AOS in MT imaging. Our findings of lower MTR in the frontal region agree with the report of white matter abnormalities in the frontal area in patients with EOS, and it has been suggested that these frontal abnormalities, in part, explain the onset of schizophrenia symptoms in early adulthood (6). Nevertheless, further study on a large cohort of patients is warranted to verify current results, and to improve our understanding of the schizophrenia.

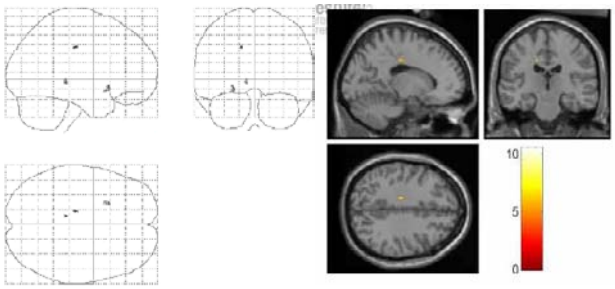

Fig 1. Statistical parametric maps on the left show the cerebral regions of EOS that has a higher MTR than those of AOS after correction for age. The results are shown superimposed on T1-weighted orthogonal images on the right (template was created as image averaged across subjects). The colored bar to the right indicates the Z score level.

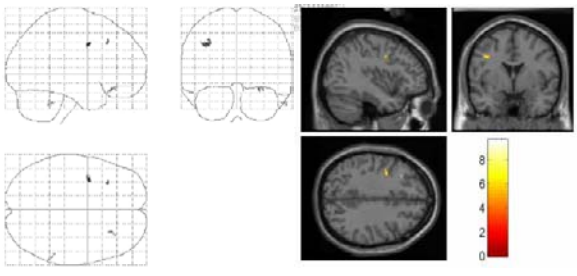

Fig 2. Statistical parametric maps on the left show that the cerebral regions of AOS has a higher MTR than those of EOS after correction for age. The results are shown superimposed on T1-weighted orthogonal images on the right (template was created as image averaged across subjects). The colored bar to the right indicates the Z score level.

Reference

1. Gordon CT et al, Schizophr Bull 1994; 20: 968–976
2. Elizabeth RS et al, Am J Psychiatry 2000; 157: 1475–1484
3. Kumra S et al, Am Acad Child Adolesc Psychiatry 2005; 44: 934-941
4. Gong QY et al, Br J Radiol 2004; 77: 405-413
5. Manny S et al, Arch Gen Psychiatry 2003; 60: 779-788
6. Kumra S et al, Biol Psychiatry 2004; 55: 1138-1145