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Altered grey matter volume and cortical thickness in patients with schizo-obsessive comorbidity

Yong-ming Wang[a,b,c,d], Lai-quan Zou[a,e], Wen-lan Xie[a,d], Zhuo-ya Yang[a,d], Xiong-zhao Zhu[f,g], Eric F.C. Cheung[h], Thomas Alrik Sørensen[c,i], Arne Møller[c,j,k], Raymond C.K. Chan[a,b,c,d,*]

[a] Neuropsychology and Applied Cognitive Neuroscience Laboratory, CAS Key Laboratory of Mental Health, Institute of Psychology, Beijing 100101, PR China
[b] Sino-Danish College, University of Chinese Academy of Sciences, Beijing 100190, PR China
[c] Sino-Danish Center for Education and Research, Beijing 100190, PR China
[d] Department of Psychology, University of Chinese Academy of Sciences, Beijing, PR China
[e] Department of Psychology, School of Public Health, Southern Medical University (Guangdong Provincial Key Laboratory of Tropical Disease Research), Guangzhou, Guangdong, PR China
[f] Medical Psychological Center, The Second Xiangya Hospital, Central South University, Changsha, Hunan 410011, PR China
[g] Medical Psychological Institute of Central South University, Changsha, Hunan 410011, PR China
[h] Castle Peak Hospital, Hong Kong Special Administrative Region, PR China
[i] Centre for Cognitive Neuroscience, Institute of Communication and Psychology, Aalborg University, Denmark
[j] Department of Nuclear Medicine and PET Centre, Aarhus University Hospital, Denmark
[k] Centre of Functionally Integrative Neuroscience, Aarhus University, Denmark

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ABSTRACT

Recent findings suggest that schizo-obsessive comorbidity (SOC) may be a unique diagnostic entity. We examined grey matter (GM) volume and cortical thickness in 22 patients with SOC, and compared them with 21 schizophrenia (SCZ) patients, 22 obsessive-compulsive disorder (OCD) patients and 22 healthy controls (HCs). We found that patients with SOC exhibited reduced GM volume in the left thalamus, the left inferior semi-lunar lobule of the cerebellum, the bilateral medial orbitofrontal cortex (medial oFC), the medial superior frontal gyrus (medial sFG), the rectus gyrus and the anterior cingulate cortex (aCC) compared with HCs. Patients with SOC also exhibited reduced cortical thickness in the right superior temporal gyrus (sTG), the right angular gyrus, the right supplementary motor area (SMA), the right middle cingulate cortex (mCC) and the right middle occipital gyrus (mOG) compared with HCs. Together with the differences in GM volume and cortical thickness between patients with SOC and patients with only SCZ or only OCD, these findings highlight the GM changes specific to patients with SOC.

1. Introduction

Schizo-obsessive comorbidity (SOC) has been proposed to delineate the subgroup of schizophrenia (SCZ) patients who also have significant obsessive-compulsive (OC) symptoms (Attademo et al., 2016; Cunill and Castells, 2011; Swets et al., 2014). In previous studies, the incidence of OC symptoms in SCZ patients has been found to be 10 times higher than the general population (Esslinger et al., 2015; Peng et al., 2014; Tonna et al., 2015). Patients with SOC are characterized by earlier onset, higher hospitalization rate (Owashi et al., 2010), more severe cognitive deficits (Cunill et al., 2013; Schirmbeck et al., 2013) and more severe psychotic symptoms (Faragian et al., 2012; Frías et al., 2014) compared with patients with SCZ alone. However, whether SOC represents a distinct diagnostic entity is not clear (Attademo et al., 2016; Poyurovsky et al., 2012). The brain structural abnormality of patients with SOC has not been clearly established and may exhibit both similarities and differences compared with patients with only SCZ or only obsessive-compulsive disorder (OCD).

Previous meta-analytic studies have reported that SCZ patients have a significantly greater loss of total grey matter (GM) volume compared with healthy controls (HCs) (Fusar-Poli et al., 2013; Vita et al., 2015), mainly in the medial frontal cortex (Gupta et al., 2014), the rectus gyrus, the superior temporal gyrus, the insula (Shah et al., 2017) and the thalamus (Cooper et al., 2014). Studies investigating cortical thickness have reported decreased cortical thickness in the superior frontal gyrus, the medial parietal lobe, the lateral occipital lobe (Sprooten et al., 2013) and the limbic system in SCZ patients (Oertel-Knöchel et al., 2013). Brain functional studies have reported that SCZ

* Correspondence to: Institute of Psychology, Chinese Academy of Sciences, 16 Lincui Road, Beijing 100101, PR China.
E-mail address: rckchan@psych.ac.cn (R.C.K. Chan).

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patients have abnormalities mainly in the cortico-striato-thalamo-cerebellar circuitry (Andreasen and Pierson, 2008; Attademo et al., 2016; Sheffield and Barch, 2016).

Previous meta-analytic studies in OCD have reported inconsistent findings in GM volume changes in the frontal lobe (Carlisi et al., 2016), the cingulate cortex, (Eng et al., 2015), the parietal lobe, the occipital lobe, the temporal lobe, the hippocampus (Boedhoe et al., 2016) and increased GM volume in the striatum and the thalamus (Piras et al., 2015). One cortical thickness meta-analysis reported reduced cortical thickness in the superior and inferior frontal gyrus, the middle temporal gyrus, the inferior parietal lobule and the precuneus in OCD patients (Fouche et al., 2016), but another study reported significant surface expansion of the thalamus and the orbitofrontal cortex (oFC) (Shaw et al., 2015). Brain functional studies have reported that OCD patients have abnormalities mainly in the orbito-striato-thalamic circuitry (Abramovitch et al., 2013; Milad and Rauch, 2012).

Previous studies did not investigate the brain morphological changes in patients with SOC comprehensively. Whether the overlapping regions in SCZ and OCD patients such as the frontal lobe, the striatum and the thalamus, are characterized by GM changes similar to patients with SOC has not been established. One imaging study has demonstrated that patients with SOC have smaller whole brain GM volume compared with HCs (Lee et al., 2006). Another study only investigated GM volume of the frontal lobe, the putamen and the hippocampus in SCZ patients with OC symptoms. Results from this study showed that these patients only have smaller GM volume in the left hippocampus compared with SCZ patients without OC symptoms (Aoyama et al., 2000).

In this study, we aimed to investigate changes in GM volume and cortical thickness in patients with SOC by comparing them with SCZ patients, OCD patients and HCs by applying whole brain analysis using magnetic resonance imaging (MRI). We investigated both GM volume and cortical thickness, because the former is a voxel-based quantitative method to measure the intensity within each voxel in whole brain GM structure (Hutton et al., 2009; Lemaitre et al., 2012), while the latter is a surface-based measure that estimates the distance between the GM boundary and the outer cortical surface (Oertel-Knöchel et al., 2013; Salat et al., 2004; Winkler et al., 2010; Xiao et al., 2015). Cortical thickness measurement takes the geometry of cortical convolutions into consideration and takes into account cortical folding patterns (Anticevic et al., 2008) and cytoarchitectural abnormalities (Narr et al., 2005). However, this method cannot survey the subcortical regions, which require voxel-based GM volumetric methods. Previous studies have also demonstrated that GM volume and cortical thickness each has its own specific developmental trajectories (Rimol et al., 2012) and may be determined by different genes (Grieve et al., 2013). The pathophysiology of psychiatric disorders may be better investigated when both VBM and cortical thickness analyses are performed concurrently (Palaniyappan and Liddle, 2012). In addition, investigating the correlation between GM structure and different subscale scores in patients with SOC could clarify the relationship between symptom dimensions and brain structural abnormality.

Studies investigating the GM changes in the overlapping brain regions such as the frontal lobe, the striatum and the thalamus in SCZ and OCD patients have reported inconsistent results (Gaser et al., 2004; Piras et al., 2015). Moreover, the size of the striatum is known to be affected by antipsychotic medications (Smieskova et al., 2009). Given the above, we could only hypothesize that patients with SOC would exhibit more severe GM changes mainly in the frontal gyrus than patients with only SCZ or only OCD.

2. Materials and methods

2.1. Participants

Participants in this study were 22 patients with SOC, 21 SCZ patients, 22 OCD patients and 22 HCs. All patients were treated at the Department of Psychiatry, Second Xiangya Hospital of the Central South University in Changsha, Hunan, China. Consensus diagnoses of the patients were determined by two experienced psychiatrists using the Structured Clinical Interview for DSM-IV Axis I Disorder, Patient Edition (SCID-IV) (First, 1994). Patients with SOC met the diagnostic criteria of SCZ and OCD concurrently, while SCZ and OCD patients met the diagnostic criteria of SCZ and OCD separately. HCs were selected using the non-patient edition of the SCID to confirm the absence of any mental disorders.

The exclusion criteria of all participants were serious physical illness or neurological disorders; a history of nicotine, alcohol or substance dependence; an intelligence quotient (IQ) of less than 70; and contraindications for MRI scanning such as pregnancy, claustrophobia and having metallic implants in the body. For HCs, participants with any personal and/or family history of psychiatric disorder were also excluded.

The study protocol was designed in keeping with the Declaration of Helsinki and was approved by the Ethics Committee of the Second Xiangya Hospital of the Central South University. All participants gave written informed consent.

2.2. Instruments

The Positive and Negative Syndrome Scale (PANSS) was used to assess SCZ symptoms by trained psychiatrists (Kay et al., 1987). The Yale–Brown Obsessive-Compulsive Scale (Y-BOCS) was used to assess OC symptoms (Goodman et al., 1989). The subtests ‘common sense’, ‘arithmetic’, ‘similarity’ and ‘digital span’ of the Chinese version of the Wechsler Adult Intelligence Scale - Revised were used to estimate the IQ of the participants using a well-established prorating method (Gong, 1992).

2.3. Image acquisition

Imaging data were obtained using a Siemens SKYRA 3T MR scanner (Siemens Medical, Erlangen, Germany) at the Second Xiangya Hospital of the Central South University, Changsha, China. T1-weighted anatomical images were acquired with a sagittal oriented magnetization prepared rapid gradient echo (MPRAGE) sequence. The parameters were as follow: repetition time (TR) = 1900 ms, echo time (TE) = 2.01 ms, inversion time = 900 ms, field of view (FOV) = 256 mm, flip angle = 9°, in-plane matrix resolution = 256 × 256, slice thickness = 1 mm, slices = 176, voxel size = 1 × 1 × 1 mm^3.

2.4. Structural imaging data analysis

Structural abnormalities of brain images were first screened by a radiologist. GM volume and cortical thickness of each participant were analyzed using the Computational Anatomy Toolbox (CAT12; Jena University Hospital, Departments of Psychiatry and Neurology; http://www.neuro.uni-jena.de/cat) in Statistical Parametric Mapping software (SPM12; the Functional Imaging Laboratory of the Institute of Neurology at University College London, UK; http://www.fil.ion.ucl.ac.uk/spm) based on MATLAB R2014b (MathWorks Inc.; https://www.mathworks.com).

For GM volume, voxel-based morphometry method was used. Firstly, the spatial-adaptive Non-Local Means (SANLM) denoising filter was used to remove noise. Secondly, T1 images were affine-registered to a European brains template and spatially normalized to a MNI152 template space and segmented into GM, white matter (WM) and cerebrospinal fluid (CSF). Tissue probability maps were TPM.nii in SPM12, strength of skull-stripping was 0.5, affine preprocessing was light, and voxel size for normalized images was 1. Thirdly, a homogeneity check was carried out and data with artefacts or of poor quality were