Schizophrenia Research 150 (2013) 476–483

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Morphometry of superior temporal gyrus and planum temporale in schizophrenia and psychotic bipolar disorder

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ARTICLE INFO

Article history:
Received 16 April 2013
Received in revised form 7 August 2013
Accepted 12 August 2013
Available online 6 September 2013

Keywords:
Laminar thickness
Superior temporal gyrus
Planum temporale
Schizophrenia
Bipolar disorder
Laterality

ABSTRACT

Structural abnormalities in temporal lobe, including the superior temporal gyrus (STG) and planum temporale (PT), have been reported in schizophrenia (SCZ) and bipolar disorder (BPD) patients. While most MRI studies have suggested gray matter volume and surface area reduction in temporal lobe regions, few have explored changes in laminar thickness in PT and STG in SCZ and BPD. ROI subvolumes of the STG from 94 subjects were used to yield gray matter volume, gray/white surface area and laminar thickness for STG and PT cortical regions. Morphometric analysis suggests that there may be gender and laterality effects on the size and shape of the PT in BPD ($n = 36$) and SCZ ($n = 31$) with reduced laterality in PT in subjects with SCZ but not in BPD. In addition, PT surface area was seen to be larger in males, and asymmetry in PT surface area was larger in BPD. Subjects with SCZ had reduced thickness and smaller asymmetry in PT volume. Thus, the PT probably plays a more sensitive role than the STG in structural abnormalities seen in SCZ.

1. Introduction

Previous neuroimaging studies of schizophrenia have focused on morphometric properties of the superior temporal gyrus (STG). Abnormalities in the posterior or caudal STG which includes the planum temporale (PT) have been associated with auditory hallucinations. Specifically, reduced laterality of the STG and PT (Barta et al., 1997; McCarley et al., 2002) has been replicated by several recent studies (Takahashi et al., 2009; Oertel et al., 2010; Hasan et al., 2011). However, the diagnosis of schizophrenia is often confused with that of psychotic bipolar disorder because of the presence of psychotic symptoms in the latter (Yu et al., 2010; Brown et al., 2011; Hulshoff Pol et al., 2012). While both disorders may have psychotic symptoms at onset (Ellison-Wright and Bullmore, 2010; Rimol et al., 2010; Takahashi et al., 2010; Vita et al., 2011; Yuksel et al., 2012), subsequent assessment of the symptom course usually results in a more clear-cut diagnosis with different treatments. Also the two illnesses exhibit different functional behaviour such as neural responses in auditory oddball tasks (Ethridge et al., 2012). Comparing schizophrenia and psychotic bipolar disorder in neuroimaging studies may shed light on any disparate or common aspects of their etiologies.

Schizophrenia is believed to be a neurodevelopmental disorder with embryonic origins resulting in subtle aberration in cortical properties such as area, thickness and volume in temporal and frontal regions (Palaniyappan and Liddle, 2012). In adulthood, these changes can be detected by magnetic resonance imaging (MRI) technology at the spatial resolution of 1 cubic millimeters (Hartberg et al., 2011; van Haren et al., 2011). The region of interest (ROI) approach focusing on temporal and frontal regions in large clinical populations has proved to be valuable (Giuliani et al., 2005; Palaniyappan et al., 2012), but female gender continues to be underrepresented (Sun et al., 2009). The ROI approach requires precise definitions of anatomical boundaries, which can be compounded by abnormalities in psychotic disorders (Perlini et al., 2012). This can be overcome by viewing the ROI as a laminar mantle composed of gray matter voxels and a gray/white cortical surface (Miller et al., 2000). This approach has been applied in clinical neuroimaging studies of the cingulate in subjects with Alzheimer's Disease (Miller et al., 2003) and schizophrenia (Wang et al., 2007; Calabrese et al., 2008) and of the prefrontal cortex in subjects with major depressive disorder (Ceyhan et al., 2011) and schizophrenia (Harms et al., 2010).

In addition, we recently observed variable cortical thickness in the left PT in three groups of age-matched and gender-matched controls

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http://dx.doi.org/10.1016/j.schres.2013.08.014

and patients with schizophrenia and bipolar disorder (Qiu et al., 2008). That study was focused on the use of a novel surface mapping method rather than on the gross morphometric properties of the PT (volume, thickness and surface area). In the current study, we used an expanded sample with an increased female representation. We sought to analyze differences between schizophrenia and psychotic bipolar disorder at the gross level with respect to accurate anatomical delineation of the STG and PT gray/white cortical surface, and further demonstrate that the effect of psychotic disorders on the PT is more pronounced than on the STG. We hypothesized that the PT and STG would be different in the schizophrenia, bipolar disorder and control groups, and that the differences would be more pronounced in males than in females.

2. Methods

2.1. Subjects

A total of 124 subjects were enrolled from schizophrenia and bipolar disorder studies at the Division of Psychiatric Neuroimaging at Johns Hopkins University School of Medicine. The data was previously collected as part of NIH grant (R01 MH43775-09A1). The Johns Hopkins Medicine Institutional Review Board approved the study, and each person gave written informed consent to participate in the study. The diagnosis of bipolar disorder or schizophrenia patients was based on DSM-IV-R and was determined using a semi-structured interview and two instruments, either the MINI (Sheehan et al., 1998) and DIGS (Nurnberger et al., 1994) or the SCAN (Wing et al., 1990) and the CIDI-SF (Kessler et al., 1998). All diagnoses were made by consensus between a research psychiatrist and a research assistant. Bipolar disorder patients were considered to have psychotic symptoms if they had at least one such episode, including hallucinations or delusions in the context of an affective episode (manic or depression) in clear consciousness. All affected subjects were medicated; however none of the subjects with schizophrenia were on mood stabilizers. Exclusion criteria included a lifetime history of substance dependence, current substance abuse and non-right-handedness (Annett, 1970). The Hollingshead Scale was used to assess socioeconomic status (Hollingshead, 1975).

2.2. MRI

All subjects gave informed consent prior to MRI scanning. T1 weighted 3D volumes were acquired using a 1.5 T Philip MR system and MPRAGE sequence (repetition time = 13.40 ms, echo time = 4.6 ms, flip angle = 20, number of acquisition = 1, matrix 256 × 256), with 1 cubic millimeter isotropic resolution across the entire cranium. Using ANALYZE (Robb et al., 1989), the raw MR data were reformatted from signed 16-bit to unsigned 8-bit and then skull stripped via the watershed module. Intracranial volume (ICV) was calculated from Freesurfer 3.0.5 (Segonne et al., 2004). The large sample size of 94 subjects should outweigh the concerns about how FreeSurfer calculates ICV (Pengas et al., 2009).

2.3. Segmentation

As detailed in Ratnanather et al. (2003) and Qiu et al. (2008), a 3D ROI subvolume encompassing the STG was masked in each hemisphere in each subject. Bayesian segmentation was used to label voxels in the subvolume as gray matter (GM), white matter (WM), or cerebrospinal fluid (CSF); a modification was that in some cases WM and GM tissues were fitted by two Gaussians as it was found that segmentation was improved by increasing the complexity of the mixtures (Lee et al., 2008).

2.4. Cortical surface reconstruction

Using the GM/WM threshold from the segmentation as the isointensity value, triangulated isosurfaces were generated at the GM/WM interface (Han et al., 2001, 2002). Following Ratnanather et al. (2003), gyral and sulcal boundaries were defined by dynamic programming (DP) as curves with maximal and minimal mean curvature between initial and terminal landmarks on the surface.

2.4.1. STG

DP delineation of the STG was initiated with several landmarks. The posterior landmark of the STG boundary began at the intersection of the angular gyrus (AG) and the STG at the most posterior extent of the lateral fissure (LF). The anterior landmark of the STG boundary was located at the superior portion of the temporal pole at the ascending ramus of the LF. The inferior extent of the STG boundary followed from the posterior landmark along the superior temporal sulcus (STS) all the way to the anterior landmark. In the case that a connection between the medial temporal gyrus (MTG) and the STG interrupted the STS, none of this connection was included. The superior extent of the STG boundary followed from the anterior landmark along the LF to the posterior landmark. Identification and placement of these landmarks are illustrated in Supplementary Fig. 1.

2.4.2. PT

The PT was extracted from the dorsal surface of the delineated STG surface. Using the rules first developed (Ratnanather et al., 2003), the surface was delineated along the lateral boundary of the STG and the anterior boundary from the STG to the retroinsular end of the Heschl's Sulcus (HS).

2.5. Validation

Sixty were used for validating the delineation of the STG surfaces. Specifically, the GM in the STG was manually segmented by applying the protocol initially developed for the PT (Honeycutt et al., 2000) and extended it for the STG (see table 1 in Ratnanather et al., 2003). Histograms of set distances from the delineated surface and the corresponding isosurface of the GM volume, i.e. shortest distance of vertices in one surface to one vertex in the other, were computed (Miller et al., 2000; Ratnanather et al., 2003).

2.6. Thickness, surface area and volume

Surface area was calculated as the sum of the area of the triangulated faces of the delineated surface. The volume was calculated as the number of voxels from the 95th percentile of the Labeled Cortical Depth Map (LCDM), which is a histogram of distances of segmented gray matter voxels to the surface (Miller et al., 2000); the 95th percentile was chosen to reflect the uncertainty of the GM segmentation in the GM/CSF region. The corresponding laminar thickness was calculated as the ratio of the volume to the area.

2.7. Statistical analysis

Following Mahon et al. (2012), data from a total of 94 subjects were included in the analysis. We examined the effect of diagnostic group on our three measures of interest, thickness, surface area and volume, for each region of interest (STG and PT). Thus, we tested a total of six responses using MANOVA models, one for each region and measure. MANOVA allows for testing the effect of a categorical predictor variable on multiple continuous dependent variables in a single model and does not hold sphericity as an assumption. In each of our models, we tested for the effect of diagnostic group on total region (left plus right) and laterality (left minus right) measures, and determined significance using Pillai's trace, which is considered to be the most robust of the common MANOVA test statistics (Olson, 1974). Using MANCOVA models including terms to adjust for the potential covariates of age, sex, ICV, education and socioeconomic status did not qualitatively change the results (not shown). We did not adjust for testing the