**Background**

The left inferior frontal gyrus (IFG) is a prefrontal region that includes Broca's area, which is involved specifically in syntactic language expression and verbal memory. The left IFG has been shown to be structurally (Suzuki 2005) and functionally (Kubicki 2003, Ragland 2004) abnormal in schizophrenia.

The IFG is composed of three subregions separable by sulcal landmarks: pars orbitalis, pars triangularis, and pars opercularis. Though the functional differences of the subregions are not entirely clear, they are cytoarchitectonically distinct.

- Voxel-Based Morphometry is a whole-brain comparison of brain tissue composition between groups. A VBM comparison of healthy controls (HC) and chronic schizophrenia (SZ) patients showed volume reduction of the right thalamus and left inferior frontal gyrus, specifically the pars opercularis subregion, in the SZ group.

- To confirm the volume reduction in the left inferior frontal gyrus, the ROI was manually traced on a subset of the same sample. The left and right inferior frontal gyri were divided into three subregions, the pars orbitalis, pars triangularis, and pars opercularis, based on sulcal boundaries.

**Voxel-Based Morphometry**

Voxel-Based Morphometry (VBM) provides a whole-brain, voxel by voxel comparison of brain tissue composition that is rapid and unbiased. After MR images of subject brains are warped to a standard template to correct for global anatomical differences, a voxel-wise comparison is created in the form of a statistical parametric map (SPM) to assess group differences in grey matter density.

In Optimized VBM, the method is improved by the use of: 1) a study-specific template brain for more accurate spatial normalization, 2) study-specific tissue class priors and skull removal for better tissue segmentation, and 3) modulation of voxel intensity by the spatial warping parameters, allowing for a comparison of volume change between groups.

An implementation of Optimized VBM was run using MR images of a group of 30 healthy controls and a group of 30 chronic, medicated schizophrenics. Scans were acquired using an SPGR sequence on a 1.5-T General Electric scanner. All subjects were males between the ages of 20 and 54 and matched for IQ and parental socioeconomic status. Gray matter VBM and analysis was conducted using SPM2 (Statistical Parametric Mapping, Wellcome Institute, London). The SPM software was adapted from scripts written by Christian Gaser and John Ashburner (2004). Regions of the brain were localized using PickAtlas in SPM2 (Maldjian et al. 2003).

**VBM Results**

**Region** | MNI Coordinates of Cluster Maximum | Voxel-level p-value (FDR-corrected) | Cluster-level p-value (FDR-corrected)
---|---|---|---
Left inferior frontal gyrus | -50, 4, 16 | 0.051 | < 0.05
Right thalamus | -22, 4 | 0.066 | < 0.05

**Conclusions**

- Using two different methods, we found convergent evidence of a volumetric difference in the left pars opercularis of the left inferior frontal gyrus in schizophrenia.
- Previous manual tracing studies of schizophrenia have found a volume reduction of the whole left IFG, but did not measure the three subregions separately. Unlike those reports, in this sample there was no overall difference in whole IFG volume between groups, but a regional reduction confined to the left pars opercularis.
- Previous studies of schizophrenia have shown widespread dysfunction in the language network, including structural and functional differences in the superior temporal, dorsolateral prefrontal, and inferior frontal cortices. In addition, there is growing evidence of impaired connection of these regions via frontotemporal white matter tracts. Measurement of the subregions of the IFG can help to define more precisely the structural differences in schizophrenia and their relation to the disorganized thought and other cognitive impairments found in the disorder.
- Future work will include 1) further comparison of VBM and manual tracing results, 2) assessment of sulcal variability in the inferior frontal gyrus, and 3) correlation of the volume reduction with clinical and cognitive measures.

**References**


**Manual Tracing Results**

To confirm the volumetric difference in the left inferior frontal gyrus found using VBM, the IFG was manually traced in 52 subjects from the same sample (27 NC and 25 HC) in both hemispheres. The IFG was then subdivided into three subregions: pars orbitalis, pars triangularis, and pars opercularis. The ROIs were traced on an automated tissue segmentation to improve the reliability of the volume measurement. Tracing was done using 3D Slicer (www.slicer.org) using boundary definitions adapted from previous volumetric studies of the IFG (Suzuki 2005, Tomaiuolo 1999).

**ROI Definition**

The inferior frontal sulcus was the superior boundary for the entire IFG. The inferior boundary was the circular insular sulcus in all slices where the insula was visible, and the lateral orbital sulcus in all other slices.

**Anterior and posterior boundaries:**

The anterior IFG was traced on coronal slices from the most anterior coronal slice where the inferior frontal sulcus was visible to the plane of the vertical ramus. The posterior IFG was drawn on axial slices from the plane of the vertical ramus to the precentral sulcus.

**Subregions:**

The pars orbitalis was bounded superiorly by the horizontal ramus of the sylvian fissure. The pars triangularis was framed by the horizontal and vertical ramus. The pars opercularis was bounded by the vertical ramus and the precentral sulcus.

The volumes of the pars orbitalis (pink in figure), pars triangularis (orange), and pars opercularis (green) were recorded and corrected for total intracranial volume. A one-way analysis of variance (ANOVA) was used to evaluate differences in volume of the subregions of the IFG for both left and right sides.

**References**


**Manual Tracing Results**

- The left pars opercularis was significantly smaller in SZ than in HC (p = 0.027). The right side was not significantly different (p = 0.37).
- There were no significant volume differences between diagnostic groups in the pars triangularis (left: p = 0.416; right: p = 0.816) or pars orbitalis (left: p = 0.161; right: p = 0.897).
- There was no significant volume difference in whole IFG volume (left: p = 0.252; right: p = 0.341).

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