Prefrontal cortex volume deficit in schizophrenia

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Introduction

• A number of characteristics observed in patients with schizophrenia are suggestive of abnormalities in the frontal lobe. Functional MRI studies have reported abnormal prefrontal cortex (PFC) activation during cognitive tasks in schizophrenia (Wible et al., 1995), and postmortem studies reported reduced neuropil and increased neuronal density in the PFC of patients with schizophrenia (Sellem and Goldman-Rakic, 1999).
• There has been considerable interest in structural MRI studies of the prefrontal area in schizophrenia. However, results of volume measurements in this area have not been consistent.
• The purpose of the present study was to determine whether PFC volume is decreased in patients with chronic schizophrenia, and the volume changes affect clinical or psychological features in patients with schizophrenia using 3T MRI instrumentation.

Methods

Subjects: Twenty-seven male patients with chronic schizophrenia and 27 normal control subjects, group matched for age, right-handedness, parental socioeconomic status

Clinical and Psychological measurements:
• Scale for the Assessment of Positive Symptoms (SAPS)
• Scale for the Assessment of Negative Symptoms (SANS)
• Alternating Semantic Category Test: Subjects completed word fluency task using alternating semantic categories (Downes et al., 1993).

Data Acquisition: MR images were acquired with a 3-Tesla General Electric scanner (GE Medical Systems, Milwaukee, WI).

Definition of Region of Interest: The PFC was manually parcellated into eight subregions, and measured each of the subregions and clinical or neuropsychological measurements were also examined by Pearson’s (R) and Spearman’s (rho) correlation analysis.

Results

Figure 1. Defined regions of interest. a) 3D model of PFC subregions. b) Coronal slice of PFC subregions.

Figure 2. Scatter plots illustrating the relative volumes of PFC subregions. Relative Volume = [Absolute Volume (cm3)/Intra Cranial Contents Volume (cm3)] x 100(%) Bars indicate means. Probabilities are from independent-samples t-tests. *** p < 0.005, # p < 0.001

Table 1. Relative Volume of Prefrontal cortex Gray Matter in the SZ and NC Groups

<table>
<thead>
<tr>
<th>Region *</th>
<th>Laterality</th>
<th>SZ (n = 27)</th>
<th>NC (n = 27)</th>
<th>1-Factor ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>Superior Frontal Gyrus</td>
<td></td>
<td>0.514</td>
<td>0.091</td>
<td>0.506</td>
</tr>
<tr>
<td>Middle Frontal Gyrus</td>
<td></td>
<td>0.642</td>
<td>0.098</td>
<td>0.719</td>
</tr>
<tr>
<td>Inferior Frontal Gyrus</td>
<td></td>
<td>0.677</td>
<td>0.113</td>
<td>0.710</td>
</tr>
<tr>
<td>Total PFC Volume</td>
<td></td>
<td>2.087</td>
<td>0.231</td>
<td>2.322</td>
</tr>
</tbody>
</table>

Abbreviations: ANOVA, analysis of variance; SZ, schizophrenia; NC, normal control subjects; ICC, intracranial contents.

Conclusions

• We manually parcellated the PFC into eight subregions, and measured each of the volumes by 3T MRI instrument that enabled us to acquire highly precise morphometric measurements.
• Significant volume reductions were observed in the left SFG, bilateral MFG, and bilateral IFG in the schizophrenia group compared to the normal control group.
• Smaller left MFG volumes were associated with more severe negative symptom subscale scores in SANS. This result was consistent with our previous study which reported an association between PFC gray matter volume and the severity of negative symptoms (Wible et al., 2001).
• Larger left IFG volumes were associated with better performance on the alternating semantic category test in the schizophrenia group. This result suggested that abnormalities in specific regions of the PFC might be associated with performance of semantic fluency and executive functions such as switching cognitive set in schizophrenia.
• Smaller FP volumes were associated with more severe subscale scores in SANS and SANS; although volume reduction in FP did not reach statistical significance. Further study focusing on the structure and the role of FP in the clinical features of schizophrenia is planned.

References: