Decreased fronto-limbic volumes in treatment-resistant major depressive disorder


Background

* A predominant pathophysiological model of Major Depressive Disorder (MDD) is based on the occurrence of neurotoxic and neurotrophic processes before and during the illness.

* Changes of grey matter volume have been observed in some brain structures of MDD patients.

* Specific areas involved remain unclear given:
  - Heterogeneity of samples used in previous studies
  - Applying less restrictive statistical thresholds
  - Different pre-processing procedures

Aim: To investigate the effect of illness characteristics on grey matter volumes in different stages of MDD by using recommended MRI parameters to perform a voxel-based morphometry (VBM) analysis.

Methods

**Acquisition parameters**

- 3-Tesla: 3D M-PRAGE images; whole-brain sequence. TR= 6.7 ms., TE= 3.1 ms., 170 slices.

**Image processing**

- **SPM** to perform a VBM of grey matter volume among the 4 groups and its post-hoc comparison.

- to segment the cortical volume in brain areas in order to correlate them with clinical variables.

**Sample**

<table>
<thead>
<tr>
<th>Sample</th>
<th>Healthy controls (32)</th>
<th>First episode (22)</th>
<th>Remitted-Recurrences (22)</th>
<th>Chronic (22)</th>
<th>F/X2</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>46 (8.3)</td>
<td>44 (6.5)</td>
<td>48 (8.7)</td>
<td>49 (8)</td>
<td>1.81</td>
<td>0.15</td>
</tr>
<tr>
<td>Gender: Male/Female</td>
<td>9/23</td>
<td>7/15</td>
<td>2/20</td>
<td>4/18</td>
<td>4.19</td>
<td>0.24</td>
</tr>
</tbody>
</table>

**A) First analysis:** VBM of gray matter volume among 4 groups:

- **ANOVA**
- **T-TEST**
- **Post-hoc analyses**

**B) Second analysis:** Correlation of brain volume structures with clinical variables:

- Medication load
- Duration of illness
- Age at illness onset
- Number of previous episodes
- Hamilton Depression Rating Scale

Results

**A) ANOVA** F=11.10; df=3, 94; p<0.05 (FWE)

VBM Post-hoc comparisons: Treatment-resistant chronic patients had fewer grey matter volume than healthy controls (T=4.75; df=1.94; p<0.05, FWE)

- Left transverse temporal gyrus BA 41, K=114
- Left insula BA 13, K=767
- Left parahippocampal gyrus BA 35, K=180
- Left cingulate gyrus BA 24, K=641
- Left medial frontal gyrus BA 6/8, K=192
- Right superior frontal gyrus BA 8, K=877

K= number of voxels of the cluster

**B) Correlations of brain volumes with duration of illness (months)**

- The rest of clinical variables did not reach p value threshold (<.05)

Y axis = Normalized volumes in mm
X axis = Duration of illness (months)

- Right orbitomedial frontal gyrus
  - r = -.29; p = .023
- Left superior frontal gyrus
  - r = -.34; p = .007

**Conclusions**

The findings show less gray matter volume of frontal, temporal and limbic areas in the most severe group of MDD patients compared to healthy controls.

The duration of illness was the only associated variable with grey matter volume, showing a negative correlation.

Treatment-resistant chronic patients appeared to have a remarkable brain damage, indicating a possible neurotoxic effect of depression.

A longitudinal study would be more appropriate to ascertain whether volume reductions in chronic patients are a result of enduring effects of the disease or having less grey matter causes a more severe disorder.

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