Evidence for Medial Temporal Lobe Pathology in Children with Autism

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Introduction

Autism is a neurodevelopmental disorder characterised by impairments in social communication and interaction; an unusually intense, circumscribed interest or restricted, repetitive and stereotyped patterns of behaviour, interests and activities (ICD-10). However the underlying neuropathology of Autism remains controversial. Here we present evidence of bilateral medial temporal lobe abnormalities in a group of children with Autism.

There is now increasing evidence for medial temporal lobe pathology in Autism. Bachevalier's animal model of Autism has shown that bilateral excision of the hippocampus and amygdala in newborn monkeys leads to a constellation of behavioural impairments akin to those seen in individuals with Autism (1). The role of the medial temporal lobes in Autism is further highlighted by the pattern of behaviour observed in patients with amygdalectomy and post mortem studies of Autistic individuals.

Further, given the profound cognitive impairment associated with Autism and that unilateral brain damage in children is unlikely to result in severe cognitive sequelae, it is reasonable to suspect that the critical neuropathology in Autism affects the medial temporal lobe system bilaterally.

Voxel-based morphometry was developed to characterise cerebral grey and white matter differences in structural MRI scans. It compares segmented images using statistical parametric mapping (SPM) to identify and make inferences about regionally specific differences. Recent theoretical developments enable voxel-based morphometry to be constrained to search exclusively for bilateral structural abnormalities.

Methods

Five children (aged between 9 and 15) diagnosed with Autism were compared to eight aged-matched controls. We have shown that these Autistic children have impaired event memory and intact factual memory (2), consistent with the profile found in patients with medial temporal lobe pathology (3).

All subjects were scanned on a 1.5T Siemens Vision system, using a T1-weighted FLASH sequence. The 3D data sets were analysed in SPM99. (Wellcome Department of Cognitive Neurology, London, UK). Each scan was symmetrically normalised to a symmetric template. The images were segmented using a symmetric probability template as described in Ashburner et al. (1997) (4).

These grey matter images were then duplicated and flipped in the transverse plane. The images were smoothed with an isotropic Gaussian kernel. This renders the voxel values equal to the amount of grey matter per unit volume under the smoothing kernel. Two different smoothing levels were used to sensitise the analysis to differences at the spatial scale of the hippocampus (4mm) and the amygdala (12mm).

The data were then examined for symmetric abnormalities using conjunction analysis. The two component SPMs were obtained by analysing flipped and unflipped data as described in Salmond et al. (5).

Results

The children with Autism showed significant bilateral increases in grey matter density in the amygdala and significant bilateral decreases in the hippocampus and parahippocampal cortex (paraHC cortex). The positions of these abnormalities are shown in the following figures. Additionally there were significant increases in grey matter density in the superior temporal gyrus (STG). These neuropathological findings support the behavioural profile previously found in this group of patients (2).

Table for significant changes in grey matter density and uncorrected p values

<table>
<thead>
<tr>
<th>Structure</th>
<th>Uncorrect. p value</th>
<th>x</th>
<th>y</th>
<th>z</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amygdala</td>
<td>&lt;0.001</td>
<td>±20</td>
<td>-2</td>
<td>-15</td>
</tr>
<tr>
<td>Hippocampus</td>
<td>&lt;0.001</td>
<td>±21</td>
<td>-18</td>
<td>-16</td>
</tr>
<tr>
<td>ParaHC Cortex</td>
<td>&lt;0.001</td>
<td>±28</td>
<td>-4</td>
<td>-33</td>
</tr>
<tr>
<td>STG</td>
<td>&lt;0.001</td>
<td>±58</td>
<td>10</td>
<td>-6</td>
</tr>
</tbody>
</table>

* Intersection of cross hairs indicate position of abnormalities as detected by SPM

Discussion

The evidence gives preliminary support to the hypothesis that the Autistic syndrome is associated with bilateral medial temporal lobe abnormality. We are currently seeking to replicate this finding in a larger cohort of children with Autism.

References

1 Bachevalier, Neuropsychologia, 32, 627-648, 1994
3 Vargha-Khadem et al., Science, 277, 376-380, 1997
4 Ashburner et al., NeuroImage, 6, 209, 1997