Volumetric MRI study of the caudate nucleus in patients with dementia with Lewy bodies, Alzheimer’s disease, and vascular dementia

R Barber, I McKeith, C Ballard, J O’Brien

METHODS

Subjects

Brain MRI was acquired in patients with DLB (n=26; 19 men, mean age 75.8 years, mean duration of illness 36.7 months, mini mental state examination (MMSE)=14), AD (n=21, eight men, mean age 76.9 years, mean duration 41.3 months, MMSE=16), vascular dementia (VaD) (n=18, 10 men, mean age 77.5 years, mean duration 39.7 months, MMSE=18), and healthy controls (n=25, 14 men, mean age 77.5 years, MMSE=28). Subjects were community dwelling and clinical diagnosis was made blind to MRI using standardised criteria: NINCDS/ADRDA1 for AD, consensus criteria2 for DLB and NINDS-AIREN3 for VaD. Pathological confirmation of diagnosis has since been acquired for six patients. Normal controls were recruited from among the spouses and friends of patients with dementia. After complete description of the study to the subjects and their families, written informed consent was obtained.

Clinical assessments

Cognitive function was measured using the Cambridge cognitive examination (CAMCOG),4 which incorporates the MMSE.5 Parkinsonian symptoms were rated using the Hoehn and Yahr staging.6

MRI acquisition

Whole brain T1 weighted three dimensional magnetisation prepared rapid acquisition gradient echo MPRAGE turbo flash sagittal sequence was acquired (slice thickness=1 mm) using a 1.0 Tesla Siemens Magnetom Impact MRI scanner.

Volume estimation of caudate nucleus

Images were transferred to a workstation and analyzed using ANALYZE (Version 7.5.5) software. Data was reformatted into coronal slices (slice thickness=1 mm) and aligned perpendicular to the long axis of the hippocampus. All measurements were conducted blind to diagnosis (by RB). Intrarater reliability was assessed by measuring seven subjects on three occasions. The mean coefficient of variation was 2.6%.

Standardised measurements of the area of the left and right caudate nucleus (in mm²) was obtained on every fourth slice for a length of 20 mm, starting from the first slice showing the head of the caudate nucleus. Volume estimation (in mm³) was calculated by summing the areas outlined and multiplying by 4.

Measurements were normalised to the midsagittal intracranial area to control for variation in head size. Final volumes were expressed as a normalised ratio (units mm³/mm³).

Statistical analysis

Continuous variables were assessed using analysis of variance (ANOVA) with post hoc Bonferroni tests. Kruskal-Wallis ANOVA test was used for non-parametric data. All volumetric comparisons were made using the normalised ratio. Correlations were examined using Spearman’s rank order correlation coefficient (r). All statistical tests were regarded as significant at p<0.05.

Abbreviations: DLB, dementia with Lewy bodies; AD, Alzheimer’s disease; VaD, vascular dementia
Table 1 Summary of normalised CN volumes by diagnostic group

<table>
<thead>
<tr>
<th>Diag</th>
<th>Right CN (SD)</th>
<th>Left CN (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLB</td>
<td>11.7 (2.0)</td>
<td>11.4 (1.7)*</td>
</tr>
<tr>
<td>AD</td>
<td>11.8 (2.4)</td>
<td>11.1 (2.6)**</td>
</tr>
<tr>
<td>VaD</td>
<td>11.7 (1.7)</td>
<td>11.8 (1.7)</td>
</tr>
<tr>
<td>Controls</td>
<td>13.0 (2.1)</td>
<td>13.2 (1.8)</td>
</tr>
</tbody>
</table>

*p<0.05; **p<0.01.
Values expressed as normalised volumes (volume of structure in mm³/intracranial area in mm²) (SD).
CN, caudate nucleus; DLB, dementia with Lewy bodies; AD, Alzheimer’s disease; VaD, vascular dementia.

RESULTS
Subjects with dementia were of comparable age, duration of illness, sex (χ²=5.7, df=3, p=0.124) and cognitive impairment as measured by CAMCOG scores (DLB=48, AD=57, VaD=60; p=0.110) or MMSE (p=0.66). As expected, patients with DLB had higher Hoehn and Yahr scores compared with all other groups (median scores: DLB=3, AD=0, VaD=0; χ²=75, df=3, p<0.001).

Volumetric comparison of caudate nucleus in different groups
There were no significant differences in the normalised volume of the caudate nucleus between patients with dementia (DLB=11.6, AD=11.5, VaD=11.8; p=0.887). However, as summarised in table 1, both the left and right caudate nucleus were smaller in patients with dementia compared with normal age matched controls, although this differences was only significant for the left caudate nucleus in patients with DLB (11.4 v 13.2, p=0.01) and AD (11.1 v 13.2, p<0.01).

Correlation between caudate nucleus volumes and parkinsonian symptoms
In all patients with dementia there was no correlation between caudate nucleus volume and parkinsonian symptoms (DLB r=0.183, p=0.380; AD r=−0.074, p=0.750; VaD r=−0.023, p=0.927).

DISCUSSION
There were no detectable structural differences on MRI in the volume of the caudate nucleus between patients with DLB, AD, and VaD, and the volume of the caudate nucleus did not correlate with parkinsonian symptoms.
By contrast with the differences reported using functional imaging, volumetric analysis of the caudate nucleus on MRI did not discriminate between diagnostic groups. As recently shown, compared with controls there was evidence of atrophy in AD although the similar finding in patients with DLB suggests that this is not a specific feature, inferring this measure has little clinical utility in the discrimination of patients with DLB, AD, or VaD.
Overall, this study indicates that parkinsonian symptoms in DLB are unlikely to be specifically associated with atrophy of the caudate nucleus, and that caudate atrophy on MRI itself does not explain differences in parkinsonian symptoms between DLB, AD, and VaD. The findings suggest that parkinsonian symptoms in DLB are possibly more closely coupled to neurochemical rather than structural changes in the caudate nucleus. Therefore, functional neuroimaging techniques may prove to be a more sensitive method of examining differences in striatal pathology than MRI.

Limitations of this study include the use of antemortem diagnoses, that volume estimation was restricted to the anterior portion of the caudate nucleus, and the clinical measure of parkinsonian symptoms may have been too insensitive to correlate with MRI indices. Strengths included the recruitment of a community population of subjects of comparable age, duration of illness, and level of cognitive impairment, and the use of standardised diagnostic criteria and normalised volumetric measurements.

These preliminary findings need replication in a larger cohort, ideally combining both MRI and functional neuroimaging techniques with postmortem follow up.

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REFERENCES
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