attributed to the excitation of a predominantly crossed occipitopretectal tract.1 Cogan stated that "removal of the pupilloconstrictor zone in one occiput of the cat results in anosocoria with the larger pupil on the opposite side".1 This finding presumably explains the unilateral pupillary dilatation reported here as a negative ictal phenomenon.

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Glial cytoplasmic inclusions are not exclusive to multiple system atrophy

In 1989 Papp et al1 reported finding argyrophilic inclusions in the cytoplasm of oligodendrocytes in cases of multiple system atrophy, and their presence in the sporadic form of this condition has since been confirmed. The value of glial cytoplasmic inclusions as a diagnostic hallmark of multiple system atrophy has been emphasised by one of the authors2 as well as by others.3

At the UK Parkinson's Disease Society Brain Bank in London, tissue is donated by patients with principally movement disorders. Glial cytoplasmic inclusions occurred in all brains from patients with multiple system atrophy (total 56); however, in three of seven cases with a pathological diagnosis of corticobasal degeneration and two of 18 cases with Steele-Richardson-Olszewski syndrome similar intracytoplasmic oligodendrocyte inclusions were identified. These were filamentous argyrophilic structures (figure) immunoreactive with tau and ubiquitin antisera. In corticobasal degeneration they were most numerous in white matter underlying the affected cortex, in the corpus callous, internal capsule, and in one case, the basis pedunculi; occasional similar inclusions were also identified in the affected cerebral cortex and in the brain stem as well as in cerebellar hemispheric white matter, in the absence of any neuronal abnormalities. In the cases of Steele-Richardson-Olszewski syndrome inclusions were most prominent in the cerebellum. We have not counted or mapped the distribution of glial inclusions in our cases, but have the impression that they are less numerous than in multiple system atrophy.

These findings have important implications for histological diagnosis and our understanding of disease pathogenesis. There is increasing awareness of overlap between many neurodegenerative conditions, in particular those associated with parkinsonism; thus the Lewy body, Pick body, neurofibrillary tangle, or the glial cytoplasmic inclusion are not exclusive to any of the conditions in which they abound. One explanation may be that neurons and glia have a limited repertoire of responses to a variety of different stimuli, resulting in morphological similarities between very distinct neurodegenerative diseases. Alternatively, shared pathogenetic pathways may underlie the cytoskeletal abnormalities seen in these conditions, the exact pattern of pathology being dictated by host factors such as age of exposure and genotype.

Letters to the Editor

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2 Lantos PL, Papp MI. Cellular pathology of multiple system atrophy: a review. 7 Natl Neurosci Psychiatry 1994;57:129-33.
as badly when the cancellation task had to be performed in the hemisphere right of the body midline. Unilateral visual neglect therefore does not seem to be body-centric.

This conclusion contradicts that of the two previous reports.1,2 There are at least three possible explanations. Firstly, the method employed here—a cancellation task—has never previously been used to assess the co-ordinate frame of neglect. Secondly, there is a possibility that because the sample size is small (n = 8), the conclusion is not representative of all patients with neglect. The same may be said, however, of the other studies cited. A third possible explanation is that the tasks used in the previous studies assessed different brain functions examined by cancellation tasks. It is not possible to say which, if any, of these explanations is correct.

Although the results of this study suggest that neglect is not body-centric, they do not exclude the general proposition that it is a deficit in representing space. It remains a possibility that the disrupted representation is mapped in another coordinate frame. Two studies have examined the pattern of visual inattention when patients are either reclined 1 or tilt their heads 3 to the left or right. Both found that irrespective of head position, inattention was worse to the left of the environmental vertical. But both investigations also showed that neglect “moved with the head”: patients attended less to the left of the head midline, whatever its orientation, as well as attending less to the left of the environmental vertical.

Another study investigated how patients with neglect performed on a somatosensory exploration task and also found evidence of two forms of deficit 4. One seemed to be body-centric, but the effect barely reached statistical significance; the other was mapped with respect to the “line of sight” and was more significant. It was not possible to distinguish whether the line of sight effect was due to a deficit in head-centric, but they do not support the hypothesis that neglect is body-centric.

I thank Professor C Kennard for useful comments and criticisms.

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1 Karnath HO, Schenkel P, Fischer B. Trunk orientation as the determining factor of the ‘contralateral’ deficit in the neglect syndrome and as the physical anchor of the internal representation of body orientation space. Brain 1991;114:1997-2014.


5 Ladavas E. Is the hemispatial deficit produced by right parietal lobe damage associated with retinal or gravitational coordinates? Brain 1987;110:167-80.


Furthermore, it was reported that a novel mutation from Arg166 to Cys166 located at the HhaI site in exon 6 of the CYP1D6 gene might be associated with Parkinson’s disease (the mutated allele frequency was 0.21).3

We have analysed the CYP1D6 gene according to the method of Tsunekoa et al. in 10 Japanese patients with multiple system atrophy (of sporadic cases; diagnostic criteria by Quinn) to investigate the relation between the polymorphism of CYP1D6 and susceptibility to multiple system atrophy. There was no significant difference in the frequency of the poor metaboliser genotype between the cases and controls (p > 0.05). As the table shows, however, the frequency of the HhaI site located at the HhaI site in exon 6 in the patients (0.45) was significantly higher than that in the controls (0.09) (p < 0.05).

These results suggest that the polymorphism of the HhaI site in exon 6 of the CYP1D6 gene may be a useful molecular marker for susceptibility to multiple system atrophy, as in Parkinson’s disease, and that both diseases may have a mutual pathogenesis associated with the protection against neurotoxic environmental factors. Further studies in a larger number of patients are necessary to confirm these preliminary findings.

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A novel cytochrome P-450IID6 (CYP1D6) mutant gene associated with multiple system atrophy

Parkinson’s disease and multiple system atrophy, including olivopontocerebellar atrophy and striatogigant degeneration, are characterised by pathological changes in the brain, including the basal ganglia.1 Several neurotransmitters, such as 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) and 1,2,3,4-tetrahydroisoquinoline (THIQ) can induce parkinsonism in animals.2,3 The poor metaboliser phenotype of debrisoquine hydroxylation was considered to be associated with susceptibility to Parkinson’s disease,4 and one genomic mutation (poor metaboliser genotype) of cytochrome P-450IID6 (CYP1D6), which metabolises debrisoquine and also possibly detoxifies MPTP and THIQ, has been reported to be overexpressed in Parkinson’s disease.5,6

Genotypes of the HhaI site in the CYP1D6 gene from patients with multiple system atrophy and controls

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Patients with MSA</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>HhaI site</td>
<td>Allele frequency (m/m)</td>
<td>Allele frequency (w/w)</td>
</tr>
<tr>
<td></td>
<td>(m/m)</td>
<td>(w/w)</td>
</tr>
<tr>
<td>Wild type homozygote</td>
<td>0.35</td>
<td>0.65</td>
</tr>
<tr>
<td>Heterozygote</td>
<td>0.05</td>
<td>0.95</td>
</tr>
<tr>
<td>Mutant type homozygote</td>
<td>0.15</td>
<td>0.85</td>
</tr>
</tbody>
</table>

*P < 0.05. Values are the numbers of patients and controls. MSA = multiple system atrophy.