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

J W LANCE
Institute of Neurological Sciences, Prince of Wales Hospital, Sydney, Australia.

Correspondence to: Professor J W Lance, Suite 5A, 66 High Street, Randwick, NSW 2031, Australia.

4 Cogan DG. Neurology of the ocular muscul. Springfield. IL: Charles C Thomas, 1940: 115.

Glial cytoplasmic inclusions are not exclusive to multiple system atrophy

In 1989 Papp et al 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 by the value of glial cytoplasmic inclusions as a diagnostic hallmark of multiple system atrophy has been emphasised by one of the authors as well as by others. 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 callosum, 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 cerebellar white matter. 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 distinctly different 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.

S E DANIEL
J F GIEDDE
T REVESZ
Parkinson's Disease Society Brain Bank.
Institute of Neurology, 1 Wakefield St, London WC1N 1PF, UK

Correspondence to: Dr S E Daniel.


Glia are astrocytes modified

Frontal hemispheric white matter; corticobasal degeneration with argyrophilic cytoplasmic inclusions in oligodendrocytes (some arrowed); modified Bielschowsky originally × 400.
Patient characteristics and cancellation scores

<table>
<thead>
<tr>
<th>Patient (age)</th>
<th>Lesion</th>
<th>Days after stroke</th>
<th>Items cancelled in front*</th>
<th>Items cancelled in right space†</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (70)</td>
<td>R parietal</td>
<td>3</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>B (66)</td>
<td>R parietal</td>
<td>8</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>C (86)</td>
<td>R parietofrontal</td>
<td>10</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>D (65)</td>
<td>R parietal</td>
<td>66</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>E (80)</td>
<td>R frontal</td>
<td>10</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>F (67)</td>
<td>R frontal</td>
<td>9</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>G (71)</td>
<td>R frontal</td>
<td>26</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>H (77)</td>
<td>R frontal</td>
<td>1</td>
<td>14</td>
<td>17</td>
</tr>
</tbody>
</table>

*When head midline is aligned with body midline. †When head midline is turned 45 degrees to the right of body midline.


A novel cytochrome P-450IID6 (CYP11D6) mutant gene associated with multiple system atrophy

Parkinson's disease and multiple system atrophy, including olivopontocerebellar atrophy and striatonigral degeneration, are characterised by pathological changes in the brain, including the basal ganglia. Several neurotoxins, such as 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) and 1,2,3,4-tetrahydroisoquinoline (TIQ), can induce parkinsonism in animals. The poor metaboliser phenotype of debrisoquine hydroxylation was considered to be associated with susceptibility to Parkinson's disease, and one genomic mutation (poor metaboliser genotype) of cytochrome P-450IID6 (CYP11D6), which metabolises debrisoquine and also possibly detoxifies MPTP and TIQ, has been reported to be overexpressed in Parkinson's disease.

Furthermore, it was reported that a novel mutation from Arg<sup>26</sup> to Cys located at the HhaI site in exon 6 of the CYP11D6 gene might be associated with Parkinson's disease (the mutated allele frequency was 0.21). We have analysed the CYP11D6 gene according to the method of Tsuoka et al. in 10 Japanese patients with multiple system atrophy (only sporadic cases; diagnostic criteria by Quinn) to investigate the relation between the polymorphism of CYP11D6 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 CYP11D6 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 pathogenetic association, thus contributing to defense against neurotoxic environmental factors. Further studies in a larger number of patients are necessary to confirm these preliminary findings.

KAZUHIKO IWASHASHI
RYOSUKE MIYATAKE
Department of Neurorsurgery,
YUTAKA TSUOEKA
OHSUMI MATUSHIRO
YOSHISUYUKI ICHIKAWA
Department of Biochemistry,
KYOSHI Hosokawa University Hospital,
Kagawa Medical School,
Kagawa 701-01, Japan
KEIKO SATO
TOSHI YUKI
NABARA Clinical Research Institute

Correspondence to: Dr K Iwashashi, Department of Neurorsurgery, Kagawa Medical School, Kida-gun Miki-cho, Kagawa 761-07, Japan.


Wild type homozygote (w/w)  
Heterozygote (w/w)  
Mutant type homozygote (m/m)  
All is frequency (m-th)

<table>
<thead>
<tr>
<th>Wild type homozygote (w/w)</th>
<th>Heterozygote (w/w)</th>
<th>Mutant type homozygote (m/m)</th>
<th>All is frequency (m-th)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with MSA</td>
<td>4</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Controls</td>
<td>77</td>
<td>12</td>
<td>2</td>
</tr>
</tbody>
</table>

*p < 0·05. Values are the numbers of patients and controls. MSA = multiple system atrophy.