sequence of symptoms in this case may give additional support to the notion that the degree of dystonia and paresis may be inversely related.

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Debrisoquine hydroxylase gene polymorphism in Parkinson's disease and amyotrophic lateral sclerosis

The aetiopathogenesis of Parkinson's disease and amyotrophic lateral sclerosis is considered to be multifactorial, including genetic and environmental factors. Toxic neuronal damage by free radicals is thought to be an important factor in the pathogenesis of these neurodegenerative disorders. The cytochrome P-450 monooxygenase enzymes detoxify toxic environmental compounds and we have previously reported that there is a highly significant excess of cytochrome P-450 debrisoquine hydroxylase (CYP2D6) gene mutation in patients with Parkinson's disease compared with controls. The mutation leads to loss of the normal enzyme and the phenotype known as the poor metaboliser status and confers susceptibility to Parkinson's disease. To see whether the association between the poor metaboliser genotype and Parkinson's disease is selective for this type of neurodegeneration, we have now compared the frequency of poor metaboliser mutations in patients with Parkinson's disease, patients with amyotrophic lateral sclerosis, and controls. We have also studied the frequency of polymorphism of another gene, N-acetyl transferase, which is responsible for metabolising dapsone, a diphenylsulphone via CYP3A4, an isoenzyme of the cytochrome P-450 enzymes.

Blood samples were obtained from 272 cases with idiopathic Parkinson's disease (diagnosed by a neurologist and fulfilling the UPDRS criteria) and 96 cases of clinically definite or probable cases of amyotrophic lateral sclerosis. Samples from 720 healthy controls were also studied. Identification of mutant CYP2D6 were carried out on genomic DNA amplified by the polymerase chain reaction (PCR) followed by restriction fragment analysis as described previously. N-Acetyl transferase polymorphism was studied using PCR for identification of slow acetylators in the patients with Parkinson's disease, patients with amyotrophic lateral sclerosis, and 96 controls.

The table summarises the results. Of 272 cases of Parkinson's disease, 11.8% were poor metabolisers by CYP2D6 genotype (mutant allele frequency = 0.250) whereas only 5.1% and 5% of patients with amyotrophic lateral sclerosis and controls (each p < 0.05) respectively were poor metabolisers.

Changes in N-acetyl transferase polymorphism were, however, not significant between patients with amyotrophic lateral sclerosis and those with Parkinson's disease.

We conclude that CYP2D6 polymorphism leading to poor metaboliser status is significantly more common in Parkinson's disease compared with amyotrophic lateral sclerosis. This finding further strengthens the initial observation that CYP2D6 polymorphism confers increased susceptibility to Parkinson's disease. Further studies on the functions of CYP2D6 are required to identify those at risk for developing Parkinson's disease as well as the various factors leading to development of Parkinson's disease.

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Debrisoquine hydroxylase (CYP2D6) and N-acetyl transferase (NAT) polymorphism in Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS), and controls (390)

<table>
<thead>
<tr>
<th>Genotype</th>
<th>PD</th>
<th>PMs</th>
<th>MAF</th>
<th>NAT</th>
<th>Slow Ac</th>
<th>MAF</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP2D6</td>
<td>No</td>
<td>PMs</td>
<td>MAF</td>
<td>No</td>
<td>PMs</td>
<td>MAF</td>
</tr>
<tr>
<td>PD</td>
<td>272</td>
<td></td>
<td>0.250</td>
<td>272</td>
<td>0.500</td>
<td>0.7</td>
</tr>
<tr>
<td>PMs</td>
<td>96</td>
<td></td>
<td>0.050</td>
<td>96</td>
<td>0.63</td>
<td>0.75</td>
</tr>
<tr>
<td>MAF</td>
<td>720</td>
<td></td>
<td>0.500</td>
<td>96</td>
<td>0.63</td>
<td>0.75</td>
</tr>
</tbody>
</table>

PMs = poor metabolisers; MAF = mutant allele frequency; Slow Ac = slow acetylators; ALS = amyotrophic lateral sclerosis.

Glioneuropomal cyst of the cerebellopontine angle

Intracranial cysts may be intracerebral or extracerebral. Arachnoid and subarachnoid cysts are the most common extracerebral types. These can be of developmental, traumatic, or inflammatory origin. Extracerebral cysts lined by epithelial ependymal cells are reported under a variety of names—ependymal, gloiopendymal, neuroepithelial, choroidal epithelial, and epithelial cysts—and at a variety of sites with the location at the cerebellopontine angle being exceptional. We report the case of a huge cyst located near the right bulbopontine junction, A 21 year old woman complained of a nasal tone to her voice—rhinolalia—for one year. There was no head trauma, infection, or other CNS disorder. Neurological examination showed a palsy of the right ninth cranial nerve. Routine laboratory profiles were normal. Brain MRI found a cystic lesion in the posterior cranial fossa that filled the right cerebellopontine angle cistern and compressed the brainstem (figure, left). The fourth ventricle, medulla oblongata, and pons were shifted to the left. There was no

MRI showing a gloiopendymal cyst of the right cerebellopontine angle. Left, preoperative view; showing a severe brainstem compression, right, one year after operation, with disappearance of the lesion.
Debrisoquine hydroxylase gene polymorphism in Parkinson's disease and amyotrophic lateral sclerosis.

K Ray-Chaudhuri, C Smith, A C Gough, N Novak, V Chamoun, C R Wolf and P N Leigh

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