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>3</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>2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>G (71)</td>
<td>R frontal</td>
<td>1</td>
<td>1</td>
<td>1</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.

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 reclined1 or tilt their heads2 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:5 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.1 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 or retinotopic coordinates. The results of the present study would also be consistent with either a head-centric, retinotopic, or object centred deficit, but they do not support the hypothesis that neglect is body-centric.

I thank Professor C Kennard for useful comments and criticisms.

MASUD HUSAIN
Mead Ward, Innere Stadt, St Thomas’ Hospital, Lambeth Palace Road, London SE1 7EH, UK

A novel cytochrome P-450IID6 (CYP1D6) 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.1 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.2 The poor metaboliser phenotype of debrisoquine hydroxylation was considered to be associated with susceptibility to Parkinson’s disease,1 and one genenic mutation (poor metaboliser genotype) of cytochrome P-450IID6 (CYP1D6), which metabolises debrisoquine and also possibly detoxifies MPTP and TIQ, has been reported to be overexpressed in Parkinson’s disease.3,4 Furthermore, it was reported that a novel mutation from Arg216 to Cys217 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).5

We have analysed the CYP1D6 gene according to the method of Tsunekoa et al10 in Japanese patients with multiple system atrophy (only 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 mutation 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 genetic defence 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 Neurosurgery, YUTAKA TSUNEOKA
YOSHIKI MATSUO
YOSHIYUKI ICHIKAWA
Department of Biochemistry, KIYOSHI HOSOKAWA
University Hospital, Kagawa Medical School, KAGASA
YOSHIHIKO TOSHIYUKI
WAKARA
Clinical Research Institute of National Sanatorium, Minamikyogawa
Hospital, Okayama, 701-03, Japan

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


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

<table>
<thead>
<tr>
<th>Wild type homozygote (cts/cm³)</th>
<th>Heterozygote (cts/cm³)</th>
<th>Mutant type homozygote (cts/cm³)</th>
<th>Allele frequency (m³ : m⁷)</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.

Complete remission of narcolepsy after surgical treatment of an arachnoid cyst in the cerebellopontine angle

Narcolepsy (excessive daytime sleepiness with cataplexy) has rarely been associated with intracranial or extra-axial brain lesions. Such lesions have predominantly been in the brainstem or diencephalon but their functional relation with the mechanism of narcolepsy remains unclear. Recent evidence confirming a strong linkage between narcolepsy and some phenotypes of HLA in the Japanese population has not yet been related to a detailed account of the brainstem disorder responsible.

Intracranial extrinsic or extra-axial lesions with symptomatic narcolepsy are extremely rare. The present case is unique in describing reversible narcolepsy in a patient with a left cerebellopontine angle arachnoid cyst in whom surgical decompressive treatment of the cyst has induced complete remission of all symptoms.

A 24 year old woman rapidly developed excessive daytime sleepiness when 14 years of age, with repeated attacks several times a day without any other narcoleptic symptoms. At that time, she was disturbed by frequent quarrels between the parents. Her parents divorced when she was 18 years old. While she was a high school student (16–18 years old), other narcoleptic symptoms became apparent. She had frequent oppressive presleep dreams, such as the fall of an aeroplane on to her head (hypnagogic hallucination). She often felt paralysed during the presleep stage (sleep paralysis). She never complained of disturbed nocturnal sleep, even during periods when excessive sleepiness occurred, often during the daytime. A sudden change of emotion—for example, when startled by a loud sound or in a rage against her brother—caused transient motor paralysis, and sometimes she dropped down on to her knees (cataplexy). She finished high school and was employed by a city bank where her job was often interrupted by excessive daytime sleepiness. In August 1992 she consulted our department and CT showed a large cyst in the cerebellopontine angle. Magnetic resonance imaging (T1; figure) confirmed a cerebellopontine angle arachnoid cyst with shift of the brainstem, which prompted her immediate admission. General physical examination was normal except that she was obese (75 kg for 157 cm height). Neurological examination was normal. A multiple sleep latency test was not performed and an EEG examination during the daytime showed bilateral alpha rhythm, alpha blocking by eye opening, and paradoxical alpha blocking during stages 1 and 2 of sleep; REM sleep was not seen, nor any presleep symptoms. Auditory brainstem response showed normal latency on both sides. Cisternography with contrast medium given by lumbar puncture showed non-filling of the cyst after three hours. The cyst was vaguely stained in 24 hours and the contrast medium was completely washed out from the cyst in 48 hours. Blood analysis was normal. She was HLA-DR2 positive. Cerebral angiography showed no anomaly in the verteobasilar system other than an avascular mass lesion in the left cerebellopontine angle.

An operation performed in September 1992 at the age of 22 years was to marsupialise the arachnoid cyst as widely as possible into the surrounding cisterns. The arachnoid membrane was hypertrophied, and the cisterns were adherent.

Within four weeks of the operation, the narcoleptic symptoms completely disappeared. After two months, she returned to her job and has been asymptomatic since.

A few cases of reversible symptomatic narcolepsy have been reported. Matsuda et al described a patient with ischaemic infarction in the upper ventral brainstem who developed hypersomnia and cataplexy after treatment with sodium valproate and phenytoin. These two symptoms disappeared after discontinuation of the antiepileptic drugs. Onofri et al reported hypersomnia and cataplexy in a case of left midtemporal primary B cell lymphoma. The radiotherapy and immunosuppressive treatment induced complete disappearance of the symptoms and regression of the tumour. Presumably, lymphoma cells might have infiltrated the brainstem. Rubinstein et al reported a case of CNS sarcoidosis presenting with hypersomnia. Computed tomography showed an 8 mm round area of contrast enhancement located in the hypothalamus. Whole brain irradiation resulted in dramatic clinical improvement with disappearance of the hypothalamic lesion on CT. These three cases relate the narcoleptic symptoms to destructive lesions in the brainstem or diencephalon. The complete narcoleptic tetrad has not been mentioned in any of these reports.

Symptomatic narcolepsy secondary to cerebellopontine angle extra-axial mass lesions such as acoustic neurinoma, meningioma, etc, has not been reported to our knowledge. This arachnoid cyst in the cerebellopontine angle region was a benign mass that distorted the brainstem. Brainstem dysfunction of ischaemic origin might have caused the symptomatology in the present case. This could explain the reversible narcolepsy except that there were no other brainstem symptoms or signs.

Several functional networks in the brainstem have been postulated to play a part in the genetics of REM sleep. More than one region may be responsible for the genesis of narcolepsy. Possibly individual variations of the brainstem vascular system might be involved in ischaemic processes for the incidental initiation and development of the narcoleptic tetrad in this unique subject. Hence, distortion of the brainstem seems to be able to cause the same narcoleptic tetrad as the idiopathic type (which is believed to be irreversible), and the genetically predisposed group, suggesting that there is a pathological process in the brainstem in common to them all.

HIROTAKE NAKANO
MOTOHIDE OGASHIWA
Department of Neurosurgery,
National Center of Neurology and Psychiatry,
Kodaira-shi, Tokyo, 187, Japan

Correspondence to: Dr Hirotake Nakano.