Brain MRI showing clearly defined hyperintense signal alteration in globus pallidus bilaterally (arrows).

which led to her admission to our department two months after the acute event. As well as these anterograde memory problems and a retrograde amnesia for about a week she showed normal behaviour and the neurological examination disclosed normal results. In neuropsychological testing she showed an IQ of 109 (WAIS) that was supposed to be somewhat lower than her pre-morbid level, although it was in the normal range. Results of tests of language function and semantic memory (token test: 0 errors, Boston naming test: 82 out of 85), visuospatial abilities (copy of the Rey figure: 36/36), and "frontal" functions (phonetic fluency: 19 words beginning with "s" in two minutes, semantic fluency: 26 animals in two minutes) were all within the normal range. Memory function as assessed by a German version of the Warrington recognition memory test yielded results below the 5th percentile for words (37/50) and faces (36/50). Recall of the Rey figure (7.5/36) and the results of a list learning task (10/15 after five learning trials) were also highly impaired. The patient therefore had a rather pure non-material specific disorder of episodic memory. After nine months formal testing showed only a slight improvement in her memory performance. She is still not able to return to night school or her part time job, but she has learned to make extensive use of a diary and a timetable. She had occupational therapy in an outpatient clinic for several months.

Brain MRI (figure) performed three weeks after onset showed bilateral hyperintense lesions in the globus pallidus. Additional involvement of basal temporal structures was suspected, but could not be shown clearly because of movement artefacts. In a second MRI examination about two months later these hyperintense lesions in the globus pallidus had partly disappeared and the basal temporal structures were normal.

The symmetric lesions in the globus pallidus resemble the findings of Squier and colleagues⁴ in their neuropathological study, who pointed out that the pallidum is rich in serotonin releasing neurons. They suspected that a local release of serotonin might have led to prolonged vasospasm and necrosis. The hippocampi, essential for episodic

memory function, are also rich in serotonin releasing neurons and are known to be targets of MDMA neurotoxicity in animals.³ Therefore we propose that in the present case MDMA ingestion led to alterations in the globus pallidus (seen in MRI but clinically silent) and in the hippocampi (causing persistent memory problems). In post-mortem studies of patients who died after MDMA ingestion, other mechanisms of damage were suspected.⁵ In the present case there was no hyperthermia and a water intoxication could be ruled out by normal serum sodium concentration. The sudden onset with a suspected generalised seizure could point to cerebral anoxia due to asphyxia as another possible reason for the patient's memory disorder, but the fit was observed and no apnoea or even cyanosis was reported.

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Rotated drawing: a mini mental state examination performance with strong lateralising significance

Neuropsychological evidence clearly has a strong bearing on our understanding of the process of object recognition.¹ Of particular relevance are recent reports of a few patients who have drawn dramatically misoriented, although otherwise quite accurately reproduced, drawings when attempting to copy a line drawing.² The copies are almost invariably rotated relative to the model by 90°,³⁻⁶ or in one case by either 90° or 180°.⁷ It has been difficult to draw conclusions about the localising significance of this unusual neuropsychological sign. However, it is notable that, with the exception of one report of two instances of transient global amnesia,⁴ all of the cases have involved right sided³⁻⁶ or bilateral⁷ pathology. These data suggest that the sign has some lateralising significance. However, previous investigations have involved only single case data.

The records of a consecutive series of 63 patients were reviewed. All had been admitted for the purposes of rehabilitation, and all had had a cerebrovascular accident with subsequent hemiparesis. Forty one of the patients were male and 22 were female. All had been administered the mini mental state examination (MMSE),⁸ which includes a geometric figure to be copied. The figure is oblong, and the standard administration position involves the placement of the figure with the principal axis of the figure aligned

"horizontally". In the present study the figure was presented on a sheet of paper, placed in the patient's midline, with the main axis of the page aligned "horizontally" on the desk. A separate blank sheet of paper was positioned closer to the patient (also in the patient's midline, and also with the main axis of the page aligned "horizontally") on which the patient attempted their copy.

Seven of the 63 patients grossly rotated their copies of the MMSE figure relative to the original. As measured by the alignment of the principal axis, these misorientations were invariably by 90°, so that the principal axis was "vertically" oriented. The major component parts of the drawings were positioned in appropriate (albeit rotated) relative positions, although there were occasional omissions of minor components. Some patients also rotated drawings on other tests.⁶ The seven patients who rotated items on copy were not significantly different from those who did not rotate in terms of sex (six male, one female *v* 35 male, 21 female), age (63.1 *v* 62.4 years, SD 12.9), or years of education (6.57 *v* 6.24 years, SD 3.57). However, all of the patients who rotated the figures on copying had right sided lesions. Interestingly, all seven of these patients also showed some evidence of left sided visuospatial neglect.

The data from the present study show some strikingly consistent features, which are similar to those reported previously. Firstly, all of the patients in the study who rotated their drawing of the MMSE did so by 90°, so that the principal axis of elongation of the figure was vertically positioned. With one exception,⁷ previous studies of rotated drawing have always involved the rotation of the Rey complex figure (the principal axis of which is horizontal) to an orientation in which the principal axis was vertical.³⁻⁶ We have recently been able to investigate this phenomenon in more detail using two of the patients reported in the present study.⁶ When the orientation of the principal axis was systematically presented in all of the cardinal orientations, drawings were generally rotated only from a horizontal orientation, and were invariably rotated to a vertical orientation. Thus it is not surprising that the copying task from the MMSE, where the original drawing is horizontally oriented, is a sensitive indicator of such rotations.

Secondly, in the present study all of the patients who rotated the MMSE on copy had lesions in the territory of the right middle cerebral artery. This finding of a strong rightward lateralisation of lesion is also consistent with the literature, which has involved right sided³⁻⁶ or bilateral lesions⁷ in all patients who were suitable for the purposes of localisation.⁴ However, the lesion location within the right hemisphere has varied greatly, often exclusively involving the frontal lobes,^{3,7} by contrast with the present study. These data suggest that rotated drawing might well have lateralising relevance as a clinical sign—although its localising relevance within one hemisphere is less clear.

One interesting clinical feature of the present investigation is the co-occurrence of rotated drawing and left visuospatial neglect. None of the previous case reports of rotated drawing have involved features of neglect; nor have the actual reproductions of patient performance depicted in these papers shown the classic signs of left neglect.^{3-5,7} However, it is possible that the co-occurrence of rotated drawing and neglect in the present

study is a result of a sampling bias. The patients in this study represent a series of admissions to a rehabilitation unit—where the referral of patients with right hemispheric lesions is most common when it involves the obvious and remediable signs of left hemiparesis and hemispatial neglect. It is likely that those such as the patient of Solms *et al.*,⁷ whose bilateral frontal pathology was largely asymptomatic in the standard neurological and neuropsychological examination, would never have been admitted to the unit.

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A novel point mutation in the GTP cyclohydrolase I gene in a Spanish family with hereditary progressive and dopa responsive dystonia

The GTP cyclohydrolase I (GTP-CH I) gene is the causative gene of hereditary progressive and dopa responsive dystonia (HPD/DRD) in both Japanese and non-Japanese patients.^{1,2} We report a novel missense mutation in the GTP-CH I gene in a Spanish family with HPD/DRD.

We studied eight members of a Spanish family with HPD/DRD (figure, A), and 30 unrelated normal controls. The four affected members met the clinical criteria for HPD/DRD.³ Fragments of DNA containing the entire coding region of the GTP-CH I gene were obtained from genomic DNA by polymerase chain reaction (PCR) according to the method of Ichinose.¹ Direct nucleotide sequencing of PCR products was performed with an automated DNA sequencer (ALFexpress, Pharmacia Biotech) using the same primers as for amplification.

We found a single base pair change at position 25 of exon 4 in the GTP-CH I gene, which consists of a C → A substitution (figure, B), leading to an amino acid change (Arg178Ser). As the C → A mutation abolishes a restriction site for Mbo II, to show linkage between this novel mutation and the four

affected members of this HPD/DRD family. The restriction fragment length polymorphism (RFLP) generated by Mbo II consisted of two fragments in healthy subjects (113 and 187 bp) and one additional fragment in patients (300 bp) (figure, A). The restriction pattern in all four affected members was consistent with the heterozygous status. No asymptomatic members of the HPD/DRD family or unrelated normal controls showed such a restriction pattern.

This is the first reported mutation in the GTP-CH I gene in a Spanish family with HPD/DRD. It supports the idea that the GTP-CH I gene is the causative gene of HPD/DRD worldwide. However, it is necessary to take into account that in some 14q-linked cases of HPD/DRD no mutations

have been identified yet.^{1,2} Mutations in some regulatory regions of the GTP-CH I gene may explain these negative findings.

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A

B

(A) Pedigree of the Spanish HPD/DRD family (solid symbols represent affected members), and agarose gel electrophoresis of MboII digested polymerase chain reaction products. (B) Direct sequence analysis of amplified genomic DNA containing exon 4 of the GTP-CH I gene.