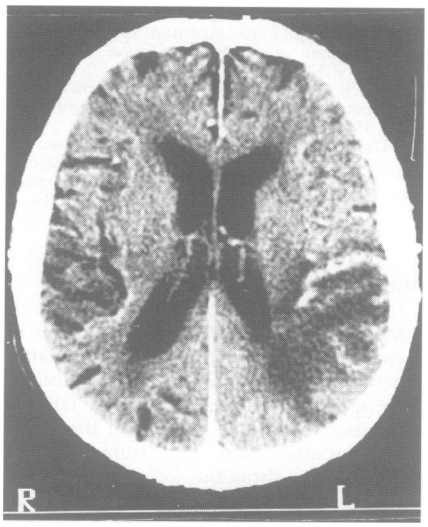

Axial CT with injection of contrast, showing two recent areas of hypodensity in the right frontal and left frontoparietal regions corresponding to pial vessel infarcts in the territory of the right and left middle cerebral artery.

artery,[4] the proximal carotid "stump"[3] or, in the iatrogenic circumstances of this patient, the aorta. Periorbital directional Doppler, however, demonstrated normal flow in the ophthalmic artery. Secondly, embolisation through extracraniomeningeal anastomosis could be responsible but it is unlikely as these are considered too narrow to allow an embolus responsible for such a large left hemispheric infarction to pass. A third possibility is embolisation of thrombotic material breaking off from the distal soft "white tail" of the thrombus located in the left internal carotid artery.[2] This hypothesis is lacking support: there was arteriographic evidence of internal carotid artery occlusion for at least six years and a "soft white tail" has little chance of persisting for six years after occlusion of the internal carotid artery. Fourthly, infarctions might result from haemodynamic alterations in blood flow, but at onset there was no evidence of haemodynamic attacks with a low flow state during the transluminal angioplasty. Furthermore, the two ischaemic areas were not similar to those described in watershed infarcts.[6] Therefore evidence for cortical low flow infarcts in this patient is lacking.

We believe that the most likely cause of the left hemispheric infarction is an embolism across the circle of Willis, in this case embolisation through the anterior communicating artery caused by thrombotic material broken away from thrombi located either in the aorta or the contralateral, stenosed right internal carotid artery where thrombotic material was floating in the lumen. This hypothesis is strongly supported by the presence of left and right hemispheric infarcts of the same age. Embolism across the circle of Willis seems the only plausible mechanism for left hemispheric infarction in our patient.

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MATTERS ARISING

Elementary visual hallucinations in migraine and epilepsy

We would like to add a cautionary note to the highly interesting study by Panayiotopoulos[1] on the different elementary visual hallucinations in migraine and epilepsy. The paper concludes that visual hallucinations in occipital epileptic seizures are predominantly multicoloured as opposed to predominantly black and white patterns in migraine.

To be able to reach this conclusion, there needs to be certainty that the diagnosis was correct. This is most likely the case for the patients with epilepsy as in all there was either evidence of spike and slow wave activity or a structural occipital lobe lesion. The group of patients assigned to the migraine group are, however, not clearly defined. The appreciable difficulty in being able to differentiate between migraine and epilepsy is stated but too little is said about the possibility of false diagnosis in the migraine group. So it is possible that some of the patients diagnosed as having migraine actually have occipital epilepsy. This would in turn falsify the conclusion of the study.

To illustrate the difficulty of ascribing a diagnosis of migraine to patients without evidence of spike and slow wave activity or a structural occipital lobe lesion we refer to a patient we described earlier[2] who experienced visual hallucinations (distorted vision and false colours). She was repeatedly diagnosed as having migraine. Doppler sonography of the posterior cerebral arteries during symptoms showed increased blood flow velocity typical of local autoregulatory hyperperfusion due to increased neuronal activity. This enabled the diagnosis of migraine to be excluded and a diagnosis of occipital epilepsy to be established. Ictal EEG was non-specifically slowed.

As we do not know how many of the migraine group in Panayiotopoulos's study really had migraine, we urge caution in the interpretation and application of the proposed conclusion.

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Panayiotopoulos replies:
In my report on elementary visual hallucinations in migraine and epilepsy I thought that I was unduly overemphasising that visual partial epileptic seizures may be misdiagnosed as migraine and the need for a precise description of the visual hallucinations in these two conditions. If anything, I was biased stressing the possibility of falsely diagnosing migraine instead of epilepsy rather than the other way round. Two out of the four illustrative cases were selected to demonstrate this diagnostic error.

Therefore, I thank Wilder-Smith for his letter, which reassured me that my above fears were unfounded as he stresses the same point—namely, that visual partial seizures may be misdiagnosed as migraine. He goes one step further however, arguing that some of my patients diagnosed with migraine may have had occipital epilepsy. I do not think that this mistake was made because in all 50 patients the diagnosis of migraine was based on strict clinical criteria, a long follow up, response to treatment, and not only on a normal or equivocally abnormal EEG. In particular, all 47 patients with classic migraine had the characteristic migrainous visual prodrome lasting 5–20 minutes before the onset of mainly unilateral headache characteristic of migraine. Not a single patient in the migraine group had any suggestion of epileptic seizures, which, given my special interest in these conditions,[1 2] I would be able to recognise.

The author also wishes to discuss his published case which, like my cases, was misdiagnosed as migraine. I did not cite his report because although the "coloured" visual hallucinations of this patient were consistent with my findings, misdiagnosis was not indicated and previous attacks were monolectically described as "migraine". More clinical details along the lines of my report and previous reports[1] from Wilder-Smith would be more enlightening. The patient had clusters of "15-30 second attacks of distorted vision and false colours" associated with simultaneous and equally brief ictal EEG changes. The diagnosis of visual partial seizures should be clear and if these were of acute onset in adult life, MRI instead of Doppler would be more appropriate. More confidence in the clinical symptoms, which is the main point of my report, may have avoided the need for further investigations and delaying treatment.

Certainly, none of my patients with migraine had any clinical similarity with such a patient. I hope that Wilder-Smith is not suggesting that these patients with migraine should have transcranial Doppler sonography to verify the diagnosis.

Further experience and more confidence in clinical diagnosis, obtained through meticulous evaluation of symptoms in classic migraine and occipital lobe epilepsy, may be needed. This is the main message of my report.

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1 Panayiotopoulos CP. Difficulties in differentiating migraine and epilepsy based on clinical and EEG findings. In: Andermann F, Lugaresi E, eds. *Migraine and epilepsy*. London: Butterworth Publishers Inc, 1987: 31–46.
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Antiganglioside antibodies in the CSF of patients with motor neuron diseases and Guillain-Barré syndrome

In a recent report in this *Journal* Stevens *et al* described increased titres of antiganglioside antibodies (AGAs) in the CSF of patients with amyotrophic lateral sclerosis.[1] They concluded that patients with amyotrophic lateral sclerosis have raised CSF IgM antibodies to all gangliosides except asialo-GM1 (A-GM1), due to a chronic intrathecal immune response. The authors did not, however, evaluate other motor neuron disorders related to amyotrophic lateral sclerosis and with sometimes borderline diagnosis.[2] We have studied AGA reactivity in the CSF of 23 patients whose diagnosis included (*a*) four strictly defined patients with amyotrophic lateral sclerosis; (*b*) 13 patients with lower motor neuron signs, from which six had a syndrome of multifocal motor neuropathy with conduction block and two had overactive tendon reflexes in limbs, with weak, wasted, twitching muscles, but no Babinski sign or ankle clonus; and (*c*) three patients with Guillain-Barré syndrome and three patients with chronic inflammatory demyelinating neuropathy. Thirty three subjects were tested as controls, including 28 patients with other neurological disease and 10 people whose CSF was normal and in whom irrelevant diseases, such as migraine or tensional headache, were found after later studies (normal controls).

Serum and CSF were assayed for antibodies to gangliosides GM1, GD1b, GD1a, and A-GM1 by enzyme linked immunosorbent assay (ELISA) according to the method described by Nobile-Oracio *et al*.[3] Results were expressed as the mean absorbance obtained from the well coated with ganglioside minus the absorbance obtained from a bovine serum albumin coated well. Results were considered positive when this difference exceeded 0·1. Concentrations of AGA were considered to be increased if this titre was higher than 3 SD from the mean of the results obtained in the 10 normal controls. In patients with high antibody titres by ELISA, reactivity to gangliosides was confirmed by high performance thin layer chromatography according to the method described by Ilyas *et al*.[4] Total CSF IgM concentration was measured by ELISA.[5] Intrathecal production of IgM AGAs was determined by measuring the optical density values per unit weight of IgM in serum and CSF, and expressing results as the ratio CSF values:serum values.[5]

Mean (SD) blood and CSF variables measured in patients and control groups

	Normal control group	*Other neurological diseases group*	*Patient group*	*P value**
Albumin index	1·80 (0·50)	2·40 (3·40)	1·50 (0·90)	NS
IgG index	0·35 (0·18)	0·34 (0·18)	0·68 (0·65)	NS
IgM index	0·05 (0·02)	0·05 (0·021)	0·33 (0·61)	NS
CSF: serum ratio (GM1)	0·49 (0·08)	0·44 (0·26)	5·40 (13·03)	0·0005
CSF: serum ratio (GD1b)	0·58 (0·33)	0·36 (0·19)	1·80 (3·20)	0·05
CSF: serum ratio (A-GM1)	0·58 (0·33)	0·46 (0·28)	3·60 (7·20)	0·004

*Analysis of variance.

Increased CSF anti-GM1 IgM antibody concentrations, with intrathecal synthesis, were found in six of the 23 patients (two patients with amyotrophic lateral sclerosis, two patients with lower motor neuron signs and hyperreflexia and two patients with Guillain-Barré syndrome), and in one of 28 patients of the group of patients with other neurological diseases (Fisher's test; P = 0·037). Intrathecal synthesis of anti-A-GM1 and anti-GD1b IgM antibodies was also detected in four of these six cases. Two of these patients, one with amyotrophic lateral sclerosis and one with Guillain-Barré syndrome, also had low positive titres of anti-GM1 IgM antibodies in serum. The ratio of CSF values:serum values for the AGAs was significantly higher in the patient group than in the group with other neurological diseases and the control group (table). No intrathecal synthesis of anti-GM1 IgM antibodies was found in CSF of the patients with other neurological diseases and normal controls, even in the cases when such antibodies were present in serum. In patients with Guillain-Barré syndrome there was no correlation between CSF anti-GM1 antibody titres and the degree of blood-brain barrier disruption expressed as the CSF:serum albumin ratio. In the patients with intrathecal synthesis of anti-GM1 antibodies, no abnormalities in cell count, albumin, IgG, IgM, albumin index, IgG index, or IgM index were detected. Intrathecal synthesis of AGA was not associated with a lower functional status or clinical evolution.

According to these results CSF antiganglioside reactivity is present in some patients with specific motor neuron disorders—namely, amyotrophic lateral sclerosis and lower motor neuron signs with hyperreflexia—but not in other forms of lower motor neuron signs. It seems highly specific for these neurological disorders, excluding the acute demyelinating inflammatory polyneuropathies, the clinical pattern of which is easy to differentiate from motor neuron disorders. The reactivity against GM1, GD1b, and A-GM1 suggest that Galβ(1,3)NAcGal is the common reactive epitope. It is still necessary to clarify if cases of amyotrophic lateral sclerosis and other motor neuron disorders where CSF antiganglioside reactivity is negative, represent a different pathogenetic mechanism, a failure of detection of intrathecal AGA reactivity due to a change in antibody profile during the evolution of the disease, or an imprecise detection method.

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Stevens *et al* reply:

The authors report significantly increased antibody titres and evidence of intrathecal synthesis of antibodies to asialo-GM1 (AGM1), GD1b, and GM1 in the CSF of patients with amyotrophic lateral sclerosis and lower motor neuron disease, as well as from Guillain-Barré syndrome. They conclude that CSF immunoreactivity to AGM1, GD1b, and GM1 is specific for these disorders. Although they interpret their data as affirmative for an intrathecal immunological process in motor neuron disease,[1] they report antibody spectra differing from those in our sample of patients with amyotrophic lateral sclerosis. On closer scrutiny, this seems not to be the case, as anti-AGM1 IgM antibodies do appear in CSF of nine of 35 patients of our previously reported sample. Anti-AGM1 antibodies are not, however, part of the panel of antibodies that are typically raised in this disease.

Although the comparative approach of Iniguez *et al* is up to date, due to the small sample size the results are difficult to interpret in terms of specificity and sensitivity—for example, the CSF-IGM and the IGG index of their patients are raised (which was not the case in our study) but are not reported as significant due to large within-group variation. The results within the three