LETTERS TO THE EDITOR

Exacerbation of epilepsy by obstructive sleep apnoea

Identification and avoidance of factors that trigger or exacerbate seizures is important in patients with epilepsy. The most common factors are sleep disturbance, alcohol ingestion, drugs, stress, and photosensitivity. The present case is the first report of seizures exacerbated by obstructive sleep apnoea. Treatment with continuous positive airway pressure (CPAP) given through a nasal mask abolished nocturnal seizures and greatly reduced the frequency of daytime attacks.

The patient, now aged 30 years, was born three weeks prematurely. Moderate mental retardation was noted at the age of five years and subsequent chromosomal analysis disclosed trisomy 4p. Dysmorphic features associated with trisomy 4p[1] included dysplasia of the nasal bones, hypertelorism, and a short neck. Radiology of the cervical spine showed incomplete fusion of the neural arch of C5 with a small spinous process of C6. He was not obese. Epilepsy began at 12 years of age with atypical absence and tonic-clonic seizures. Treatment with valproate, ethosuximide, nitrazepam, carbamazepine, clobazam, and vigabatrin in various combinations had failed to control his attacks. He was referred to the National Hospital for Neurology and Neurology-National Society for Epilepsy at Chalfont with the following pattern of seizures: tonic seizures causing a sudden fall to the ground between three times a day to three times a week; tonic seizures characterised by elevation and stiffening of both arms occurring four to five times a day; and episodes three to four times a night in which he would have serial tonic seizures over one hour periods, interspersed with rocking movements and rolling from side to side. His medication on admission comprised slow release carbamazepine (400 mg twice daily), vigabatrin (1.5 g twice daily), and temazepam (10 mg at night). The vigabatrin was replaced with lamotrigine (150 mg twice daily) and temazepam was stopped, with only a modest improvement in seizure frequency.

Because of a history of loud nocturnal snoring and daytime hypersomnolence, the patient underwent a sleep study. Overnight observation and continuous monitoring of oxygen saturation (SpO_2) disclosed a baseline SpO_2 of 95%, with frequent cyclical dips to 80%. During the study, which lasted seven hours 47 minutes, there were 106 episodes of desaturation to below 90%, each episode lasting 20 seconds. The cyclical dips were associated with upper airway obstruction, consistent with the syndrome of obstructive sleep apnoea. Rhinolaryngological assessment disclosed a deviated nasal septum, but it was considered that the level of obstruction was at the level of the palate and secondary to his dysmorphic features. It was decided to try nasal CPAP before proceeding to sleep nasendoscopy and uvulopalatopharyugoplasty.

The patient tolerated the CPAP mask well and his snoring was abolished. A repeat sleep study showed that nocturnal oxygen saturation averaged 97% with no significant dips. An immediate improvement in daytime alertness was noted. On follow up three months later, all the nocturnal attacks had been abolished and his daytime tonic seizures were reduced to two per week, without falling. His daytime alertness remained much improved and he no longer had morning headaches. The improvement has now been maintained for more than two years.

Obstructive sleep apnoea typically presents with daytime sleepiness and unrefreshing and restless nocturnal sleep.[2 3] It is usually associated with obesity but may also occur in patients with nasopharangeal abnormalities and in patients taking sedatives or alcohol. The diagnosis depends on awareness of the condition and can be confirmed by sleep studies. Treatment with nasal CPAP is often successful but surgery to correct significant narrowing of the nose or pharynx is sometimes required.[3] In the present patient, the obstruction was related to his dysmorphism, but the sedative effect of his antiepileptic medication may also have contributed.

Obstructive sleep apnoea may have exacerbated this patient's epilepsy simply by producing interrupted and unrefreshing sleep. Sleep deprivation is a potent trigger for seizures.[4] Alternatively, the hypoxaemia associated with the obstructive sleep apnoea may have triggered the seizures. Hypoxaemia is known to precipitate seizures in patients with epilepsy.[5]

Obstructive sleep apnoea should be considered as a cause of poor seizure control in any patient with disturbed sleep, as the correct diagnosis can lead to highly effective non-pharmacological treatment. Failure to make the correct diagnosis may result in the patient being treated with more antiepileptic medication that could exacerbate obstructive sleep apnoea and thereby worsen seizure control.

Since submitting this communication, Tirosh and colleagues[6] reported four boys with neurodevelopmental deficits and obstructive sleep apnoea. Treatment with CPAP produced several clinical benefits including a significant decrease in seizure frequency in one boy.

We thank Dr CI Roberts who referred the patient.

T C BRITTON
M O'DONOGHUE
J S DUNCAN
National Hospital for Neurology and Neurosurgery, National Society for Epilepsy, Chalfont St Peter, Buckinghamshire SL9 0LR, UK

N P HIRSCH
The National Hospital for Neurology and Neurosurgery, Queen Square, London WC1N 3BG, UK

Correspondence to: Dr T C Britton, The Neuroscience Unit, Mapother House, King's College Hospital, Denmark Hill, London SE5 9RS, UK.

1 de Grouchy J, Turleau C. *Clinical atlas of human chromosomes*, 2nd ed. New York: John Wiley, 1984:57–61.
2 Douglas NJ. The sleep apnoea/hypopnoea syndrome and snoring. *BMJ* 1993;**306**:1055–1060.
3 Kimoff RJ, Cosio MG, McGregor M. Clinical features and treatment of obstructive sleep apnoea. *Can Med Assoc J* 1991;**144**:689–95.
4 Raina P, Veres J. Correlations between night sleep duration and seizure frequency in temporal lobe epilepsy. *Epilepsia* 1993;**34**:574–9.
5 McNamara JO. Human hypoxia and seizures: effects and interactions. *Adv Neurol* 1979;**26**: 137–43.
6 Tirosh E, Tal Y, Jaffe M. CPAP treatment of obstructive sleep apnoea and neurodevelopment deficits. *Acta Paediatr* 1995;**84**:791–4.

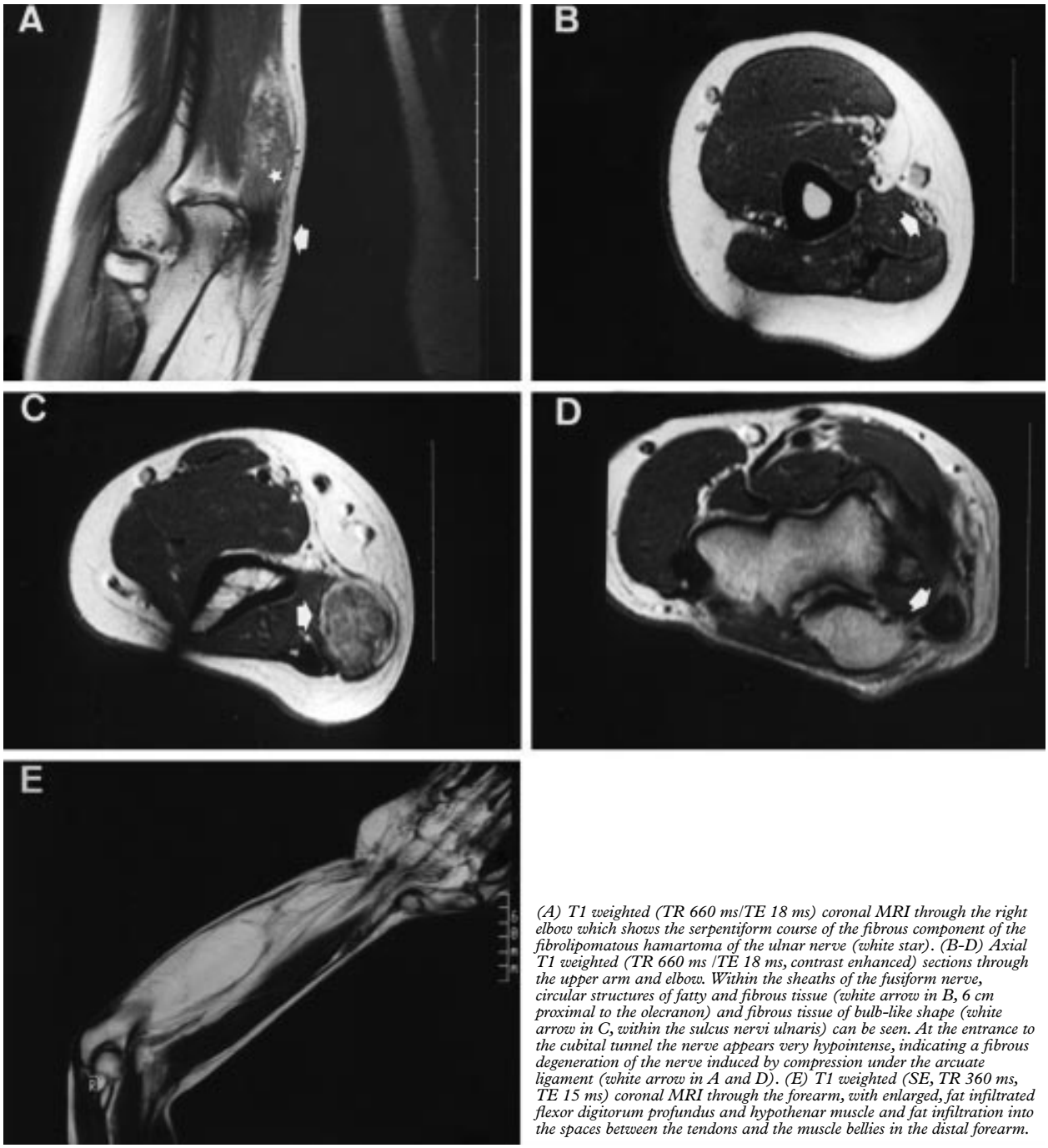
Fibrolipomatous hamartoma of the proximal ulnar nerve associated with macrodactyly and macrodystrophia lipomatosa as an unusual cause of cubital tunnel syndrome

Fibrolipomatous nerve tumours are rare benign tumours that are usually slowly progressive and that predominantly affect the median nerve at the level of the wrist and hand, usually causing carpal tunnel syndrome.[1] The tumour is sometimes associated with macrodactyly and lipomatous macrodystrophy of muscles and subcutaneous fat in the region supplied by the affected nerve.[1 2] In this report we focus attention on fibrolipomatous hamartoma at a previously undescribed location as an unusual cause of cubital tunnel syndrome. Furthermore, we point out that on the basis of the characteristic features of fibrolipomatous hamartoma on MRI, a non-invasive diagnosis can be made.

The 35 year old female patient was born with a giant fourth finger (about twice as thick as the neighbouring fingers) of the right hand which grew proportionally with the other fingers during early childhood. The family history was unremarkable. For cosmetic reasons, the finger was amputated at the age of three. When the patient was 27 years old, she experienced hypaesthesiae and paraesthesiae in the cutaneous area of the right ulnar nerve and a stabbing pain in the ulnar arm. She also noticed a slight weakness in the flexion of the fourth and fifth fingers, of wrist flexion, and flexion of the hand muscles innervated by the ulnar nerve. At the same time she noticed a thickening of the ulnar nerve at and above the elbow, with electrical sensations elicited by nerve percussion. During the next eight years, the symptoms were progressive. Recently, a clinical examination disclosed the sensory deficits mentioned above and weakness of muscles supplied by the ulnar nerve (MRC grade 3). The ulnar side of the forearm and the hypothenar and the fifth finger showed hyperplasia. The flexion of the elbow was restricted by a palpable sausage-like elastic tumour in the sulcus nervi ulnaris and the distal upper arm. There were no naevi, angioma, or neurofibroma.

In nerve conduction studies, the maximal motor conduction velocity over the elbow nerve segment was 44 m/s on the affected and 57 m/s on the non-affected side and the amplitudes of the elicited muscle compound potentials in the abductor digiti minimi muscle were reduced to 0.6 mV. Antidromic sensory nerve action potentials could not be elicited in the right ulnar nerve with stimulation at the wrist or proximal to the elbow. Electromyography disclosed signs of chronic neurogenic changes in all muscles supplied by the right ulnar nerve. Clinically and electrophysiologically the diagnosis of cubital tunnel syndrome was made.

T1 weighted MRI of the right upper arm and elbow (figure A-D) showed a fusiform enlargement of the ulnar nerve, with an extension from 6.5 cm proximal to 2 cm distal of the olecranon. The largest axial diameter of the nerve tumour was 2.3 cm. The coronal section showed serpentiform fibrous components within the nerve (figure A). On the axial section through the upper arm 6 cm proximal to the olecranon, circular structures of fatty and fibrous tissue could be seen within the nerve (figure B). The nerve had its largest diameter within the sulcus nervi ulnaris and mainly consisted of fibrous tissue, with a bulb-like configuration on the



(A) T1 weighted (TR 660 ms/TE 18 ms) coronal MRI through the right elbow which shows the serpentiform course of the fibrous component of the fibrolipomatous hamartoma of the ulnar nerve (white star). (B-D) Axial T1 weighted (TR 660 ms /TE 18 ms, contrast enhanced) sections through the upper arm and elbow. Within the sheaths of the fusiform nerve, circular structures of fatty and fibrous tissue (white arrow in B, 6 cm proximal to the olecranon) and fibrous tissue of bulb-like shape (white arrow in C, within the sulcus nervi ulnaris) can be seen. At the entrance to the cubital tunnel the nerve appears very hypointense, indicating a fibrous degeneration of the nerve induced by compression under the arcuate ligament (white arrow in A and D). (E) T1 weighted (SE, TR 360 ms, TE 15 ms) coronal MRI through the forearm, with enlarged, fat infiltrated flexor digitorum profundus and hypothenar muscle and fat infiltration into the spaces between the tendons and the muscle bellies in the distal forearm.

axial slice (figure C). At the entrance to the cubital tunnel, the nerve was compressed by the transverse fibres of the arcuate ligament (figure A and D). Here, the nerve seemed pathologically hypointense, indicating a fibrous degeneration of the nerve induced by compression. In T1 weighted MRI of the forearm, the ulnar nerve was surrounded by fatty tissue and had a normal diameter in its course along the forearm. The flexor digitorum profundus and flexor carpi ulnaris were found to be increased in volume and had a high content of intramuscular fat (figure E). In the distal forearm, fatty tissue infiltrated the spaces between the tendons and the muscle bellies. The blood vessels were of normal diameter.

The patient has a non-hereditary congenital malformation, with a combination of a slowly progressive fibrolipomatous hamartomatous tumour of the ulnar nerve at an unusal location in the elbow region, unusual macrodactyly of a single finger, and lipomatous dystrophy with enlargement of ulnar forearm flexors and hypothenar. The causal relation between fibrolipomatous hamartoma, macrodactyly, and lipomatous macrodystrophy of soft tissues remains obscure. Besides others, a neurogenic cause has been discussed on the basis of findings in neurofibromatosis.[3]

Fibrolipomatous hamartoma is usually located in the distal median nerve and causes carpal tunnel syndrome.[1 2 4] Only one case of fibrolipomatous hamartoma proximal to the elbow, in the brachial plexus, has been described before.[5] In our patient, MRI detected an enlarged flexor carpi ulnaris muscle and a thick ulnar nerve as a previously unmentioned combined cause of a clinically relevant ulnar nerve entrapment in the proximal and distal part of the cubital tunnel. The proximal fibro-osseous tunnel is formed by the medial collateral ligament and the distal sulcus nervi ulnaris; the distal part of the tunnel is formed by the humeral and ulnar insertions of the flexor carpi ulnaris muscle and the arcuate ligament. Furthermore, the massively thickened nerve can also be mechanically lesioned within the sulcus nervi ulnaris by flexion-extension movements in the elbow.

The differential diagnosis of a palpable, unilocal fusiform nerve enlargement comprises fibrolipomatous hamartoma, lipomas within the nerve sheath, and segmental or plexiform neurofibromatosis. In our patient,

MRI disclosed serpentiform nerve fascicles surrounded and separated by fibrous and fatty tissue within the expanded nerve sheath as typical features of fibrolipomatous hamartoma.[2 4] Fibrolipomatous hamartoma can clearly be distinguished from lipomas within the nerve sheath, which are characteristic focal masses that dislocate and compress the normal nerve bundles,[6] and from segmental and plexiform neurofibromatosis, in which the neurofibroma has MRI signal characteristics of soft tissue and not of fat. Furthermore, in plexiform neurofibromatosis, the tortuous nerve is studded by small tumours.[6 7] The unique features of fibrolipomatous hamartoma as identified by MRI , allow the identification of this benign nerve tumour preoperatively. This facilitates the decision to decompress affected nerves at the preferential sites of nerve entrapment and helps to avoid diagnostic nerve biopsy or even resection of an ambiguous nerve tumour.

B-U MEYER
S RÖRICHT
Department of Neurology, Charité, Virchow Klinikum, Humboldt-Universität zu Berlin, Berlin, Germany

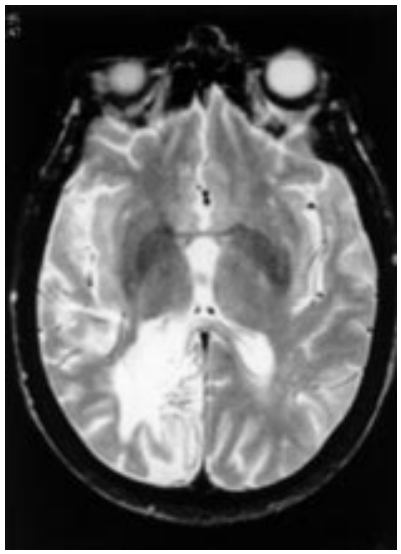
Correspondence to: Dr Bernd-Ulrich Meyer, Department of Neurology, Charité, Virchow Klinikum, Augustenburger Platz 1, 13353 Berlin, Germany. Telephone 030-450-60012; fax 030-450-60901.

1 Silverman TA, Enzinger FM. Fibrolipomatous hamartoma of nerve. A clinicopathological analysis of 26 cases. *Am J Surg Pathol* 1985;**9**:7-14.
2 Boren WL, Henry REC, Wintch K. MR-diagnosis of fibrolipomatous hamartoma of nerve: association with nerve territory-oriented macrodactyly (macrodystrophia lipomatosa). *Skeletal Radiol* 1995;**24**:296-7.
3 Yaghmai I, McKowne F, Alizadeh A. Macrodactylia fibrolipomatosis. *South Med J* 1976;**69**: 1565-8.
4 Walker CW, Adams BD, Barnes CL, Roloson GJ, FitzRandolph RL. Case report 667. *Skeletal Radiol* 1991;**20**:237-9.
5 Price AJ, Compson JP, Calonje E. Fibrolipomatous hamartoma of nerve arising in the brachial plexus. *J Hand Surg [Br]* 1995;**20**:16-8.
6 Suh J-S, Abenoza P, Galloway HR, Everson LI, Griffiths HJ. Peripheral (extracranial) nerve tumours: correlation of MR imaging and histologic findings. *Radiology* 1992;**183**:341-6.
7 Friedman DP. Segmental neurofibromatosis (NF5): a rare form of neurofibromatosis. *AJNR Am J Neuroradiol* 1991;**12**:971-2.

Ipsilateral mydriasis in focal occipitotemporal seizures

Occipital epilepsy is characterised by seizures which usually begin with oculomotor or elementary visual symptoms and often spread to other cortical and subcortical regions. We think that the present case report is of particular interest because of the nature of partial status comprising positive (clonic jerks of eyes and left face) and negative motor components (left hemiplegia) with dilatation of the right pupil; these clinical features were shown to be related to a lesion in the right occipital lobe by MRI and EEG. To our knowledge, the association of these data has not been previously reported.

A 37 year old man had a history of chronic renal failure due to an idiopathic mesangiocapillary glomerulonephritis since he was 20 years old. He underwent a renal transplantation which was unsuccessful because of an arterial thrombosis. Two years later, a second kidney was transplanted to the patient. Shortly afterwards, while he was immunosuppressed with steroids and azathioprine, he had a *Listeria monocitogenes* meningoencephalitis. Treated promptly with ampicilline, he had an excellent outcome, except for recurrent generalised seizures due to a residual lesion in the right occipital lobe, shown by CT. The patient was treated with oral 100 mg phenytoin thrice daily and required haemodialysis because of the progressive worsening of his renal function owing to chronic organ rejection. One year later, he was admitted to our hospital because of fever of unknown origin. A few days after admission, he developed a focal status epilepticus characterised by stupor, tonic deviation of the head and clonic jerks of the eyes to the left, full dilatation of the right pupil with sluggish reaction to light, clonic movements of the left face, and left hemiplegia with hyperreflexia and extensor plantar response. No previous clonic movements were seen on plegic limbs. Meanwhile, left pupil responses remained normal. Laboratory studies showed evidence of chronic renal failure and the serum concentrations of phenytoin were 5 μg/ml (reference range 8-20 μg/ml). After intravenous administration of 1000 mg diphenylhydantoin, the seizures stopped and simultaneously the pupillary dilatation disappeared. Thereafter, pupillary assessment showed no abnormalities. A left hemiparesis and extensor plantar response were transient postictal findings. A long TR/long TE (2000/80) MRI showed a fairly well defined area of hyperintensity on the right occipital lobe, without any sign of a mass effect (figure). Lumbar puncture disclosed a clear CSF under normal opening pressure, with no pleocytosis and containing normal amounts of glucose and proteins; microbiological studies were negative. Several hours after the status had finished, an EEG disclosed sharp spikes and slow waves over the right temporo-occipital region. Fever responded to empirical antibiotic therapy. The clinical course was uncomplicated and the patient continued on phenytoin, being free from seizures after one year of follow up.



A long TR/long TE (2000/80) MRI showing a fairly well defined area of hyperintensity on the right occipital lobe.

Our patient showed a focal status epilepticus with right pupillary dilatation and tonic deviation of the eyes and head to the left; other associated clinical features were clonic movements of the left face and left hemiplegia. All these phenomena disappeared dramatically on phenytoin treatment, thus indicating their epileptic pathogenesis. Although an ictal EEG was not recorded, major although indirect arguments in favour of a right occipitotemporal onset are the interictal EEG spikes as well as the MRI lesion located on that area.

Hemiplegia may be a well known negative ictal phenomenon.[1] Its association with clonic movements at other levels, as seen in our patient, suggests its ictal mechanism. The absence of previous convulsions on plegic areas further supports that idea. The concomitance of clonic and atonic seizures has only been previously described in a few series and is a very uncommon clinical pattern. However, it is difficult to ascertain that such paresis in this case is directly due to neuronal discharges. Postictal (Todd's) paralysis may appear in the context of partial status epilepticus, probably due to local fluid changes and this could be another explanation for the hemiplegia in our patient.

Unilateral mydriasis during fits should arouse the suspiction of brain herniation and proper imaging studies should be performed to rule out such a possibility, and that was the case in our patient. Only eight cases with ictal mydriasis have been reported as far as we know. Five patients showed the pupil abnormality contralateral to the epileptic scalp EEG focus and three had ipsilateral mydriasis.[2]

The exact pathophysiology of pupil changes during seizures remains unclear; it has been stated that miosis would represent an excitatory component[3] whereas dilatation would be interpreted as a negative ictal phenomenon.[1] Descending inhibition of the Edinger-Westphal nucleus would result in pupillary dilatation and impairment of the pupillary light reflex; this could be mediated by leu-enkephalin fibres which may produce pronounced inhibition of this nucleus in experimental studies.[4] Animal experiments performed in macaques showed that electrical stimulation of the anterior occipital lobe produced contralateral ocular deviation with asymmetric dilatation of both pupils that was greater in the homolateral eye[5]; these features were found in our patient, although we did not see changes in the diameter of the left pupil and the reason for this disparity is unknown. This finding was by contrast with the contralateral mydriasis obtained when the frontal eye field was stimulated[5] and in patients with frontal epilepsy. The exact anatomical basis for the changes in pupil diameter during fits remains to be elucidated although the reports and experiments commented on herein, including our case, indicate that an ictal pupil dilatation found in a patient with contralateral epileptic movements suggest occipitotemporal pathology on the same side as the mydriasis; if all these changes are ipsilateral, a frontal lesion should be suspected on the opposite side.

J MASJUAN
J GARCÍA-SEGOVIA
M BARÓN
J C ALVAREZ-CERMEÑO
Department of Neurology, Hospital Ramón y Cajal, Madrid, Spain

Correspondence to: Dr Jaime Masjuan, Servicio de Neurología, Hospital Ramón y Cajal, Crta de Colmenar Viejo km 9.1, 28034 Madrid, Spain. Telephone 34-1-3368399; fax:34-1-3369016.

1 Lance JW. Pupillary dilatation and arm weakness as negative ictal phenomena [[letter]]. *J Neurol Neurosurg Psychiatry* 1995;**8**:261–2.
2 Gadoth N, Margalith D, Bechar M. Unilateral pupillary dilatation during focal seizures. *J Neurol* 1981;**225**:227–30.