



Figure Seizure frequency, drug doses and plasma concentrations of lamotrigine in the patient studied.
LTG = lamotrigine; PB = phenobarbitone; CBZ = carbamazepine.

nasogastric tube was inserted and intravenous fluids (0.9% NaCl) were started. An iv bolus injection of 10 mg of diazepam given over five minutes did not affect seizure activity (fig). Further 10 and 20 mg iv boluses of diazepam were injected after one and four hours respectively with a decrease in the number of seizures (up to 1/hour).

On the second day, an iv infusion of diazepam was started at a dose of 40 mg/24 hours and the same infusion rate was maintained for the third day. As seizures were continuing (1–2/hour) and with increasing frequency, on the fourth day the diazepam infusion rate was doubled (that is, 80 mg/24 hours). No effect was observed and the rate of infusion of diazepam was kept at 80 mg/24 hours for the fifth day.

During the first hours of the fifth day fits were occurring at a frequency of 6–7/hour. Since an intravenous preparation of phenytoin (a very effective drug in status epilepticus) is not available in Italy, lamotrigine was started at 7 am on the fifth day (30 hours after doubling the infusion rate of diazepam). Consent was obtained from the Protocol Review Committee and from the patient's parents. A 600 mg loading dose of lamotrigine (100 mg capsules, Wellcome Research Laboratories, Beckenham, UK) was given over four hours (200 mg × three administrations at two-hour intervals), followed by two additional 200 mg doses over the next 20 hours. Five hours after starting lamotrigine the fits became less frequent (five fits during the subsequent six hours and three during the following 13 hours). As the seizures remained well controlled (two to three per day), after three days the patient was discharged on phenobarbitone (100 mg twice a day), carbamazepine (400 mg three times a day) and lamotrigine (200 mg twice a day). The range of plasma drug concentrations (µg/ml) over the observation period were: phenobarbitone 30.7–35.6, carbamazepine 6.9–10.3, diazepam 0.5–1.8 and lamotrigine 0.4–4.9.

Our patient had a generalised convulsive status epilepticus, a condition which is known to be particularly resistant to treatment and to present frequent spontaneous remissions. However, both the inefficacy of diazepam at the increased rate infusion (that is, 80 mg) and the marked fall in frequency of fits five hours after lamotrigine administration suggest that the termination of status epilepticus in our patient may reasonably be attributed to lamotrigine. Single oral doses of drug (120–240 mg) had been found to be rapidly effective

within one to two hours in reducing interictal spike activity and the photosensitive range in epileptic patients.^{2,3} In addition, lamotrigine has been recently reported to dramatically reduce very frequent generalised tonic-clonic seizures⁴ and atypical absences⁵ and to stop the occurrence of non-convulsive status episodes.⁵

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First description of myasthenia gravis in Spain

Non medical classical literature occasionally yields detailed observations on some neurological disease which was unrecognised at the time. In the eighteenth century old literary traditions such as idealistic descriptions of protagonists, were replaced by a more realistic approach; heroes were portrayed as normal human beings, and this resulted in the description of real people complete with their medical conditions.

Sir Thomas Willis is usually credited with the first description of myasthenia gravis in western medical literature.¹ His report in 1672 of a woman who was able to "speak freely" on occasions but at other times became "mute as a fish" has been ascribed by some authors to hysteria rather than myasthenia. Masteller² recently suggested the existence of a still earlier historical description of myasthenia in an American Indian, in 1644. The first well documented case of myasthenia published in English medical literature was reported by Samuel Wilks of Guy's Hospital, London in 1877.³ The term myasthenia gravis was coined in 1895 by Jolly.⁴

In the Spanish literature, the first report of myasthenia appeared in a book written by Benito Pérez Galdós, a famous Spanish writer living in the second half of the nineteenth century. In *Tristana*,⁵ published in 1892, Galdós wrote:

"From her life full of work she was left with a nervous weakness and weakness of the eyelid muscles. She opened her eyes only halfway, and this with difficulty on certain days, or at times when certain winds ruled, sometimes reaching the point where she had to lift up her upper eyelid with her fingers when she wanted to see well any person. In addition, she was ill from her chest, and when the winter came along she was very ill."

Myasthenia gravis seems the most likely explanation for this clear description of an old woman with intermittent ptosis.

Galdós was an excellent observer of Span-

ish society during his lifetime. In addition to his well-recognised literary merits, he deserves the credit for the first description of myasthenia in the Spanish literature.

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MATTERS ARISING

Neuropsychological deficits in patients with minor head injury after concussion and mild concussion

I read with interest the report by Drs Leininger, et al,¹ further documenting "organic" mental deficits in patients with "minor head injury." Unfortunately, Dr Leininger and colleagues have failed to describe the basis for characterising their patients as having sustained "minor head injuries," other than implying that these patients suffered only brief periods of loss of consciousness. The emphasis on "organic" neurological deficits in patients with "minor head injury" is extremely appropriate and long overdue.

In my view, however, the major problem in this area is in the definition of "minor head injury." In most series the patients are considered to have suffered only "minor head injury" if they have suffered short duration loss of consciousness and no major disturbance of language or motor or visual functions. Most neurologists would affirm that only a relatively limited portion of the brain is actually involved in these specific four areas of brain function, and patients can easily sustain damage to large areas of brain tissue focally or diffusely without disruption of these particular and relatively limited areas of brain. Thus patients classified in this simplistic fashion as having suffered "minor head injury" may in reality have suffered loss of considerable portions of their brain and the discovery of "organic" neurological deficits should come as no surprise.

It would be much more helpful to the medical community and to those with this epidemic disease if the term "mild head injury" were confined to patients documented not to have lost brain tissue either focally or diffusely. However, diffuse loss of brain tissue

is difficult to document until loss of brain bulk can be documented on delayed CT or MRI scans.

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The paper by Leininger, *et al*¹ reported that the pursuit of litigation had no effect on neuropsychological status after cerebral concussion, and that the cognitive deficits were attributable to cerebral dysfunction. These conclusions, drawn from a clinical series of symptomatic patients, warrant scrutiny.

The authors provide no information as to how they classified their patients into groups "pursuing claims for compensation" or "pursuing litigation". Merely asking patients if they have filed a lawsuit does not provide the information necessary to classify their claim status. Some of the patients may have been injured in work-related accidents, and in the United States, been unable to sue their employers, regardless of fault. In nonwork-related motor vehicle accidents, claims for damages may have been made against insurers without any litigation. Furthermore, the patients studied could have filed lawsuits after their neuropsychological evaluations; all of them were seen within 22 months of their injury. These results are contrary to our own.

In a recent paper Binder and Willis² reported a very strong relationship between the pursuit of a claim and performance on a measure specifically designed to assess motivation to remember, the Portland Digit Recognition Test. Our study compared minor head trauma patients to patients with well-documented cerebral dysfunction who were not seeking financial compensation. Our minor head trauma patients were much more chronic, seen an average of two years after their trauma, than the patients studied by Leininger *et al*, a factor which may have affected the results.

Leininger *et al* equated the cognitive deficits of the concussed patients with cerebral dysfunction. The possible existence of comorbidities in the minor head injured patients make this relationship tenuous, however. The majority of the minor head injury patients were injured in motor vehicle accidents. Consequently, they may have had orthopaedic injuries and been treated with analgesic medications. Some of them may have developed anxiety disorders or depression as a result of their accidents and may have been treated with psychotropic medications. The authors provided no information on chronic pain, psychiatric status, or medication use. These variables are also associated with cognitive abilities^{3,4} and may have accounted for the differences between the concussed and control subjects. Controlled studies of consecutive acutely injured patients followed prospectively⁵ have shown normalisation of cognition within a few weeks of minor head trauma, using measures no less sensitive than those employed in the study of symptomatic patients by Leininger *et al*.

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Low plasma iron status and akathisia

Barton *et al*¹ reported a significant inverse correlation between plasma iron levels and akathisia rating. Their findings are important. However, three of their akathisia group had low plasma iron levels (about 50 µg/100 ml). Since the association between restless legs syndrome and low plasma iron is generally accepted,² their three patients might not have akathisia but the restless legs syndrome.

Although akathisia and restless legs syndrome are clinically similar (floor pacing, marching on the spot, and body rocking occur in both conditions),³ the symptoms of akathisia are prominent throughout the waking hours. Conversely, the symptoms of restless legs are more prominent at night.⁴ It suggests that the circadian rise of possibly some hormone could be related to the symptoms of restless legs syndrome, but not to those of akathisia. Sandyk *et al*,⁵ pointed out that one of the possibilities may be melanocyte stimulating hormone (MSH).

Further research is required to differentiate between akathisia and restless legs syndrome, and measuring MSH may be helpful.

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Bowie and Ebmeier reply:

We are pleased to answer Terao's and Yoshimura's comments relating to the differential diagnosis of our akathisia patients, particularly the patients with plasma iron

levels about 50 µg/100 ml. Using Walters' summary of the clinical characteristics of restless leg syndrome, the three patients in question: 1) did not suffer parasthesias; 2) motor restlessness was in evidence during the day, but not during the night; 3) periodic movements in sleep had not been observed, although no systematic observation during sleep had taken place; 4) there was some dyskinesia lying still, or sitting quietly, as evidenced by patients' akathisia scores; 5) none of the patients was suffering from sleep disturbance; 6) there was no family history of restless leg syndrome, and finally, 7) symptoms and signs occurred during waking hours and not at night.

We would therefore maintain that these patients had neuroleptic induced akathisia rather than restless leg syndrome. This, of course, leaves open the possibility of a "common pathway" of both syndromes evidenced by the association with lower iron levels. Terao and Yoshimura state that "the association between restless leg syndrome and low plasma iron is generally accepted" referring to Ekbom's seminal paper.² In fact, Ekbom found iron deficiency in only 19 of 77 unselected patients. On the other hand, he states that in patients with iron deficiency of less than 60 µg/100 ml, the incidence of restless legs was 24%. This suggests to us that iron deficiency is neither a necessary nor a sufficient cause of restless leg syndrome, or indeed (drug-induced) akathisia.

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Pupillary disturbances in migraine: what is the relation to autonomic dysfunction?

The proposal that decreased cervical sympathetic outflow (and an increase in facial blood flow) follows trigeminal nerve activity during migraine¹ is not consistent with greater eyelid separation and meiosis on the side of the headache and the poor correlation between meiosis and ptosis during and between migraine attacks. Although the pupillary reflex to darkness is regarded primarily as a sympathetic reflex, pupillary dilatation in darkness occurs in the human sympathectomised eye but is less complete. In the analysis of pupillary light reflexes it is important to remember that a well-defined degree of central sympathetic tone is necessary for the full development of the constrictor action.

Electrical stimulation of the infratrochlear nerve causes unilateral meiosis in normal volunteers² thus raising the possibility of a contribution of iris trigeminal fibres towards the development of meiosis during migraine headache through antidromic discharge. In contrast to electrical stimulation of the ophthalmic division of the trigeminal nerve (which was found to be relatively ineffective), mechanical stimulation of the nerve, both with and without stellate ganglionectomy,