LETTERS TO THE EDITOR

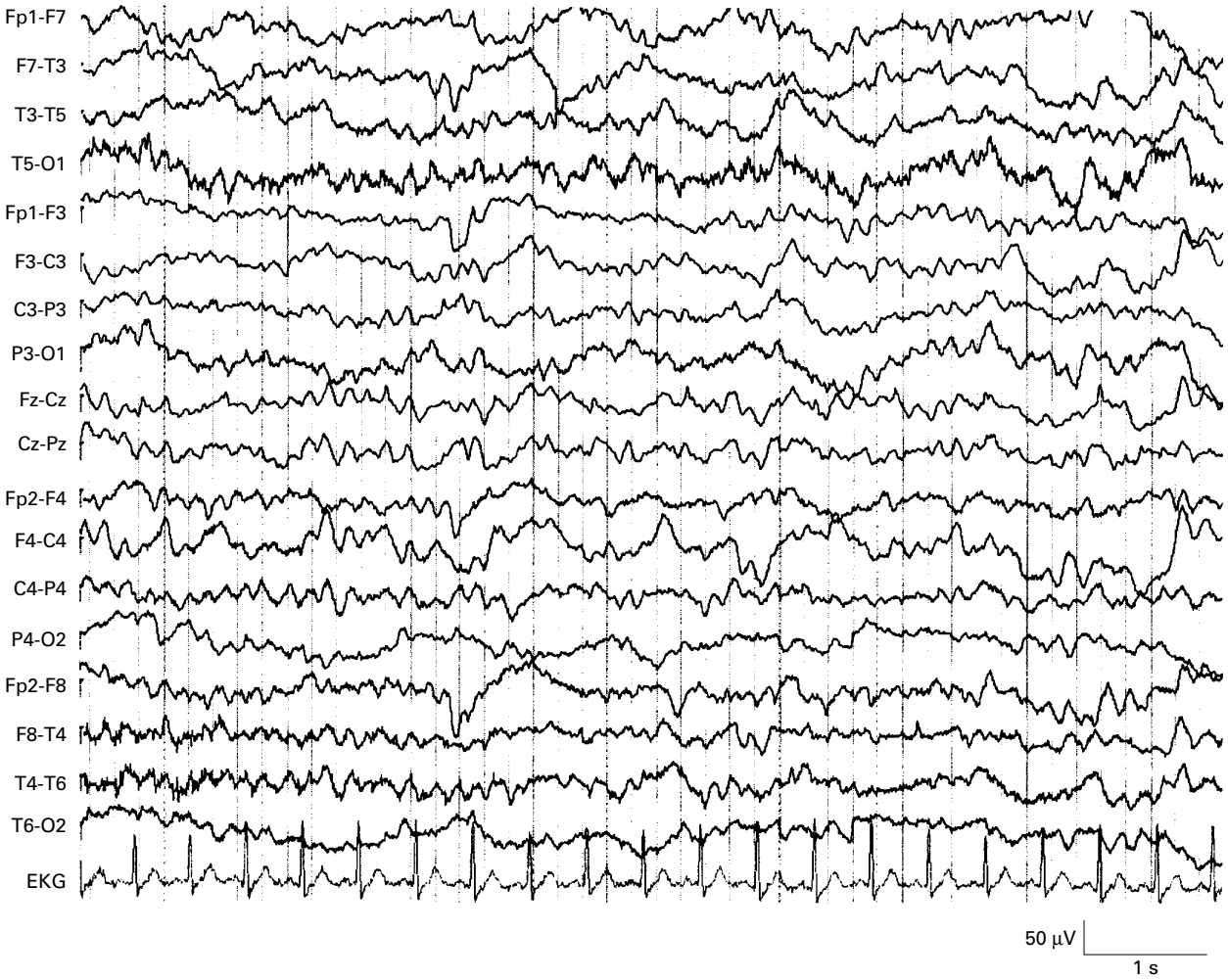
Treatment of paroxysmal sympathetic storm with labetalol

First described by Penfield in 1929, paroxysmal sympathetic storm is characterised by episodic hyperhidrosis, hypertension, hyperthermia, tachypnoea, tachycardia, and posturing. It has commonly been associated with closed head traumatic brain injury, agenesis of the corpus callosum, hydrocephalus, and suprasellar or diencephalic tumours.[1 2] Penfield hypothesised that these sympathetic spells were caused by epileptiform discharges in thalamic nuclei irritated by increased intracranial pressure, thereby leading him to name this entity "diencephalic autonomic seizures".[2] Electroencephalograms obtained on patients during these autonomic attacks, however, have not shown epileptic activity, and anticonvulsant therapies have not proved useful in their treatment.[2 3] Bromocriptine and morphine have been the standard treatments for paroxysmal sympathetic storm, and propranolol has been shown to reduce the hyperpyrexia seen during autonomic spells.[3 4] In this case report, we describe a patient treated successfully with labetalol, but not metoprolol, suggesting that β1 antagonism alone is not sufficient to suppress paroxysmal sympathetic storm.

A 21 year old white man was an unrestrained passenger in a motor vehicle accident and developed a closed head shear injury. He was admitted to a hospital where a head CT showed hydrocephalus necessitating a ventriculoperitoneal shunt placement. A head MRI showed abnormal T2 signal in the corpus callosum and the dorsal midbrain consistent with shear injury. Although initially comatose, he improved to near baseline over the next few months. He was admitted to our hospital 15 months later with a shunt infection, necessitating treatment with vancomycin, shunt externalisation, and, eventually, replacement. During and after resolution of the shunt complications, he developed episodes of sympathetic hyperactivity while under continuous monitoring in an intensive care unit. These attacks were characterised by (1) diaphoresis throughout the entire body, (2) tachycardia (heart rate 140–160 bpm) measured by automated pulse oximetry or by ECG, (3) hypertension (blood pressure 170–180/100 mm Hg) measured by arterial line pressure transducers or by sphygmomanometer, (4) fevers to 39.1 °C orally, and (5) flexor posturing. He was alert during these episodes, and responded to questions appropriately with denial of any acute onset of discomfort or pain. Furthermore, these attacks were not correlated with periods of bladder distension (Foley catheter in place) or impaction (radiograph not suggestive of retained stool). Individual episodes lasted 5–10 minutes and recurred at 5–10 minute intervals. Clusters of these spells would last 1 to 2 hours with more than three clusters a day.

Multiple CSF and blood cultures were negative. Serial head CT showed marked reduction of hydrocephalus and no brain stem abnormalities after shunt correction. No other intracranial pathology was noted. Plain films and MRI of the spine showed no myelopathic findings suggesting autonomic dysreflexia. Abdominal and pelvic CT did not show any hidden masses or lesions. Toxicology screen at onset of symptoms was negative. Electroencephalograms obtained during these episodes of dysautonomia disclosed theta and delta slowing with some sharply contoured waves, but no definite ictal or interictal epileptiform activity (figure).

Although initially treated successfully with bromocriptine (5 mg twice daily) and morphine (15 mg every 6 hours), he was withdrawn from morphine with a methadone taper at the request of his parents secondary to concerns over addiction. He was then started on metoprolol (25 mg thrice daily) with little effect on the frequency or severity



EEG obtained during episodes of paroxysmal sympathetic storm (tachycardia with heart rate of 120 bpm) shows predominant delta and theta waves (greater on the right than on the left) with no clear epileptiform activity, indicating that these attacks are not of seizure origin.

of the hyperautonomic episodes. Replacement with 100 mg labetalol twice daily led to reduction in the frequency of events to about one a day. Subsequent increase of the medication to 200 mg twice daily resulted in a marked decrease to less than one paroxysmal sympathetic storm over several days. At the time of discharge, the patient had returned to his preadmission baseline.

The current observations lend support to the prevailing view that paroxysmal sympathetic storm may represent disruption of autonomic function in the diencephalon and brainstem. Bullard has proposed that the clinical syndrome may be the result of a release phenomenon within the brainstem and/or diencephalon from loss of overriding cortical or subcortical inhibition.[3] More recent case studies suggest localisation to the central sympathoexcitatory regions including the paraventricular hypothalamic nucleus, lateral periaqueductal grey matter, lateral parabrachial nucleus, or rostral ventrolateral medulla.[3] Compromised autonomic neuronal integrity centrally is not surprising in the setting of infection after traumatic brain injury.

Various medications can potentially be used in managing central sympathetic storm. Imidazoline agonists and specific α2 adrenoceptor antagonists, such as clonidine and methyldopa,[5] have recently been shown to have sympathoinhibitory actions centrally within the rostral ventrolateral medulla. These agents have so far been used in the treatment of essential hypertension, tetanus, or autonomic dysreflexia. β Blockers such as propranolol however, have long been the mainstay of treatment of the hypertension, tachycardia, and hyperpyrexia associated with paroxysmal sympathetic storm.[6 7] This non-selective β adrenergic antagonist acts through inhibition of peripheral catecholamine activity, and being highly lipophilic, may also exert central effects through membrane stabilisation or receptor blockade. Moreover, propranolol may reduce sustained muscle contraction.[7] Taken together, these findings suggest that non-selective β receptor antagonism is sufficient to inhibit the clinical manifestations of diencephalic seizures.

The present case suggests that β1 receptor antagonism alone is not sufficient to treat hyperautonomia during paroxysmal sympathetic storm. This patient was initially placed on starting doses of metoprolol, a selective β1 antagonist, with little clinical effect in controlling the frequency of the autonomic attacks; however, labetalol, an α1 and β1-β2 adrenergic receptor antagonist did lead to an observable decline in symptoms. Both sympatholytic agents were given at doses typically used in initiating treatment of systemic hypertension, suggesting that the observed response seen with labetalol could not be explained solely by a dosage phenomenon. Prior studies also demonstrate that small amounts of propranolol (20 mg four times a day) can achieve similar responses to those seen with labetalol,[6 7] further arguing against a dose dependent effect. Thus, at a minimum, either α1 or β2 receptor blockade, likely in addition to β1 blockade, is necessary in the treatment of paroxysmal sympathetic storm.

The discrepancy in response between metoprolol and labetalol could result from their different effects on the cardiovascular system or CNS. The β1-β2 adrenergic receptor blockade by labetalol decreases blood pressure and heart rate through negative inotropic and chronotropic effects, and by inhibiting renin release. In addition, labetalol has vasodilator properties resulting from α1 blockade and partial β2 agonism. These reduce peripheral vascular resistance, blood pressure, and coronary vascular resistance, a potential advantage over other β blockers. Alternatively, differences in central activity may explain the increased efficacy of labetalol over metoprolol. As both agents are lipophilic, their central access should not differ significantly; rather, differences in receptor antagonism (β1 versus α1, β1, β2) would more likely explain the therapeutic discrepancy. As proposed with propranolol,[4] inhibition of β2 receptors by labetalol may exert a stabilising effect within the CNS through indirect inhibition of sympathetic nerve activity.

In the present case, we report the use of labetalol as an alternative agent in the treatment of paroxysmal sympathetic storm. It likely exerts both a central and peripheral blockade of α1 and β adrenergic receptors to produce inhibition of autonomic dysregulation. The clinical ineffectiveness of metoprolol further suggests a necessary role for β2 and/or α1 receptors in the clinical presentation of paroxysmal sympathetic storm. Labetalol may prove an alternative equal to or better than morphine in the treatment of these spells, especially when addiction and dependency are of concern.

D DO
V L SHEEN
E BROMFIELD
Departments of Neurology, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115, USA and Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Correspondence to: Dr E Bromfield
ebromfield@partners.org

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Moyamoya disease presenting with singing induced chorea

Moyamoya disease is a relatively uncommon, chronic cerebral vasculopathy of unknown aetiology that is characterised by unilateral or bilateral stenosis or occlusion of the proximal portion of the carotid arteries, together with an abnormal vascular network at the base of the brain. Most childhood cases manifest with the signs and symptoms of cerebral ischaemia or infarction, whereas intracerebral haemorrhage prevails in adults.[1 2] We describe here a case of moyamoya disease in a 29 year old multiparous woman, who presented with involuntary limb movements induced by singing.

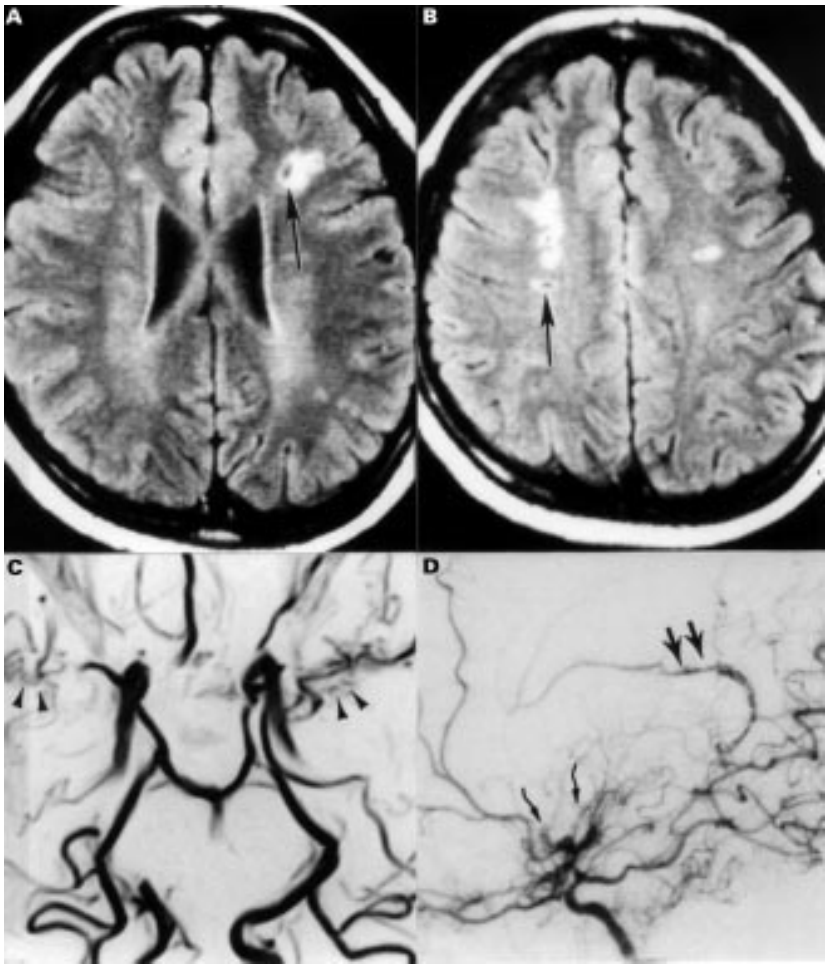
A 29 year old woman, gravida two, para two, presented to the neurological outpatient clinic at Chungbuk National University Hospital with recurrent episodes of brief involuntary movements affecting her left hand and arm. The movements were characterised as unilateral, brief, coarse, irregular, and wavering. There was no history of neuroleptic drug therapy, or family history of involuntary movement.

General physical, neurological, and neuropsychological examinations were unremarkable. Baseline blood tests, ECG, and chest radiography all yielded normal results. The episodes of the patient's involuntary movements were unique, in that they usually appeared while she was opera type singing in a choir at church. They were also occasionally provoked by some conditions of hyperventilation such as blowing to cool hot soup, or blowing the dust off a table. This suggested an underlying ischaemic pathophysiology and prompted us to investigate changes in brain vasculature and parenchyma. The short lived choreiform movements were usually preceded by a tingling sensation in her left hand, which occasionally extended to the left leg.

An EEG between ischaemic episodes disclosed diffuse slow waves bilaterally over the hemispheres; these slow waves increased as "build up" with the appearance of delta waves during hyperventilation. Magnetic resonance imaging showed areas of high signal intensity in both frontal subcortical regions, suggestive of focal ischaemic lesions (fig A and B). We determined the patient's cerebral vascular reserve using technetium-99m-HMPAO brain SPECT with acetazolamide challenge. This demonstrated a decreased vascular reserve in both frontal and temporal lobes, as well as in the basal ganglia. Magnetic resonance angiography and subsequent four vessel angiography showed nearly complete obstruction of the terminal portion of each internal carotid artery and the outline of a moyamoya network (fig C and D). Staged encephaloduroarteriosynangiosis was performed on the left and right sides, 1 week apart, resulting in an eventual amelioration of the patient's involuntary movements.

Chorea is one of the rarer, although acknowledged, presenting features of moyamoya disease; chorea is usually observed in children.[3 4] It is suggested that about 6% of patients with moyamoya disease have chorea.[5] Other types of involuntary movements have been described in patients with moyamoya disease: Valsalva related seizures,[6] recurrent episodes of carpopedal spasm,[7] recurrent torticollis,[8] and limb shaking transient ischaemic attack.[9] Hemichorea is characterised by unilateral, brief, coarse, irregular, wavering, involuntary movements, and is usually caused by some asymmetric, focal brain lesion. The clinical presentation of our patient was associated with opera type singing.

Singing requires both hyperventilation and the breath holding Valsalva's manoeuvre. Hyperventilation causes an increase in arterial oxygen tension, which subsequently causes vasoconstriction, which, in turn, reduces blood flow. In addition, Valsalva's manoeuvre increases cerebral venous pressure, which then increases intracranial blood volume and intracranial pressure, thereby reducing the arterial perfusion pressure. Thus, in those regions of the basal ganglia and cortex that are already critically perfused, hyperventilation and Valsalva's manoeuvre can easily lead to transient ischaemic insult, which may be clinically manifested by involuntary movements. It seems likely that hyperventilation and breath holding act synergistically to reduce brain perfusion. In this patient, the hemichoreic episodes were attributed to hypoperfusion of the contralateral cerebral hemisphere, and not to epilep-



(A and B) FLAIR axial images, showing bilateral focal ischaemic lesions in the frontal white matter. Low signal intensities surrounded by hyperintense rims are chronic lacunae (arrows) (C) Time of flight MR angiography, indicating that both middle cerebral arteries were unidentifiable. Note multiple tortuous flow signals, suggestive of moyamoya vessels (arrowheads). (D) Right internal carotid angiogram, demonstrating middle cerebral artery occlusion, moyamoya vessels (curved arrows), and the leptomeningeal collateral blood flow from the posterior circulation (straight arrows).

togenic activity. Staged left and right encephaloduroarteriosynangiosis, using a frontal branch of the superficial temporal artery, was carried out, 1 week apart. This procedure eventually ameliorated the patient's choreic movements.

Chorea is not unusual in moyamoya disease. However, the causes of chorea are manifold and careful neuroradiological and clinical evaluation is required to distinguish them.[10] Our findings emphasise that moyamoya disease should be included in the differential diagnosis of adult onset chorea. Recognition of this uncommon form of occlusive carotid disease is important in the early diagnosis and proper management of neurological deficits.

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S-H HAN
Department of Neurology, Chungbuk National University Hospital, Chungbuk 361–711, Korea

Y-G KIM
Department of Neurosurgery

S-H CHA
Department of Radiology

S-Y CHUNG
Department of Pediatrics, Our Lady of Mercy Hospital, Catholic University Medical College, Inchon, Korea

Correspondence to: Professor Seol-Heui Han
shhan@med.chungbuk.ac.kr

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Late recurrence of glossopharyngeal neuralgia after IXth and partial Xth nerve rhizotomy: treatment by microvascular decompression

Glossopharyngeal neuralgia, or vagoglossopharyngeal neuralgia as some would prefer,[1] is a rare condition, occurring with a frequency of about 1% of that of trigeminal neuralgia. Medical treatment, particularly with carbamazepine, is usually effective. A significant number of patients do, however, become refractory and go on to surgical treatment. The best established surgical treatment is rhizotomy of the glossopharyngeal and upper vagal nerve roots, which seems to be invariably effective if the diagnosis is correct although it is not without morbidity and even mortality.[2] Late recurrence after such treatment, as described below, has not previously been reported and raises interesting issues of mechanism and method of treatment which are considered in this brief report.

The patient initially presented in 1988 as a 23 year old woman with typical glossopharyngeal neuralgia, experiencing severe intermittent pain in the left side of the throat, the back of the tongue, and the ear. The pain was aggravated by talking and swallowing and relieved, to some degree, by pressure on the left side of the neck. At first there was a good response to carbamazepine. When medication was stopped after several months the pain returned and was less well controlled with a further course of the drug. Neurological examination, CT, and MRI were normal. In 1989 she underwent posterior fossa craniectomy and exploration of the IXth and Xth cranial nerve roots. No lesion, in particular no vascular compression, was identified. The left IXth nerve root and the two uppermost Xth nerve rootlets were divided adjacent to the brain stem. Her postoperative course was uncomplicated and she remained entirely symptom free for over 9 years.

In 1998, now aged 33 years, she developed recurrence of her original pain which she described as essentially identical to that at the initial presentation. Again the pain responded to carbamazepine but required a high dose (1200 mg daily) which was accompanied by troubling side effects (drowsiness and dizziness). In addition she was not completely pain free. Neurological examination and further MRI were normal. In October 1998 a further posterior fossa exploration was carried out. The previously divided nerve roots were identified and the completeness of the initial section confirmed. There was now, however, a large, ectatic vertebral artery to which the proximal ends of the previously sectioned roots were adherent and which was distorting the remaining Xth nerve rootlets and the XIth nerve. A microvascular decompression was carried out with a Teflon patch being placed between the ectatic artery and the normal and previously sectioned nerve roots. The procedure was without complication and the patient has remained well and entirely pain free since that time (18 months).

The first description of glossopharyngeal neuralgia is credited to Weisenberg in 1910, in a patient in whom the pain was secondary to a cerebellopontine angle tumour. The pain is characteristic although two variants have been described; an otitic form with pain predominantly deep in the ear, in the external acoustic meatus, and the mastoid region and an oropharyngeal form in which the pain is experienced in the pharynx, the tonsillar area,

the soft palate, and the posterior third of the tongue. For patients refractory to medical treatment several surgical options are available including extracranial avulsion, intracranial preganglionic root section, trigeminal tractotomy, either open[3] or percutaneous CT guided, and microvascular decompression. As mentioned at the outset, intracranial root section has been the most often employed and is generally regarded as curative. It was, however, realised early that section of the upper vagal rootlets is important in that some cases without the additional section were either not relieved or experienced early recurrence.[2] More recently microvascular decompression has been employed, particularly by Jannetta *et al*, with complete relief of pain in 76% and substantial improvement in a further 16% in the largest series, with a mean follow up of 48 months.[4] As with trigeminal neuralgia, the actual incidence of presumed causative "neurovascular conflict" and, indeed, the exact mechanism of causation are as yet unresolved questions.

The particular dilemma posed by the present case had both a diagnostic and a therapeutic arm, referable in each case ultimately to mechanism. The only reported cases of recurrence after preganglionic section are the small group, referred to above, in whom only the IXth nerve root had been cut and who subsequently responded to section of the upper vagal rootlets and one patient who had had both a IXth and partial Xth rhizotomy and who later responded to a trigeminal nerve procedure. In these cases failure was typically either immediate or not long delayed. In the largest series reporting the results of treatment[2] and in a smaller series with long follow up[5] there were no recurrences after preganglionic section of the IXth and upper Xth roots. Likewise, after total sensory root section via the posterior fossa (Dandy procedure) trigeminal neuralgia does not recur.

In our case, assuming completeness of the initial section, there seemed to be, essentially, three possible explanations for the recurrent pain. Firstly, that the pain was due to involvement of the remaining non-trigeminal somatic afferent components of the spinal trigeminal nucleus (in the VIIth and the remainder of the Xth cranial nerves); secondly, that it was some form of postdenervation pain akin to the anaesthesia dolorosa described after Vth nerve section[1] and in one instance after IXth nerve section; and, thirdly, it was a form of trigeminal neuralgia, there being a reported coincidence of the two forms of neuralgia in a few cases.[2] The close similarity of the recurrent to the initial pain, both in nature and site, the long period since the initial pain, and the response to carbamazepine all favoured the first possibility. On the basis of this diagnosis, coupled with the patient's relative youth and, it must be said, her strong insistence, re-exploration was undertaken as described above. Whatever one's position on the vascular compression theory of the cause of cranial nerve neuralgias the findings were impressive and, in conjunction with the undesirability of further nerve section, encouraged treatment by microvascular decompression alone. The immediacy of pain relief, sustained now for 18 months, supports this decision. It might be argued that the presumed vascular compression was overlooked at the first procedure but there are several points against this. Firstly, both procedures were performed by the same surgeon, experienced in posterior fossa surgery, and the area of compression was in the same place as the initial section;. Secondly, the young age at first presentation is against a vascular pathology, particularly where the vertebral artery is causative; and thirdly, there is a reported incidence of new vascular compression in re-exploration for recurrent trigeminal neuralgia.

In conclusion, the salient points to emerge from this brief report are that vagoglossopharyngeal neuralgia can recur after IXth and partial Xth nerve section and that this patient provides evidence for a pure vagal neuralgia. This supposition is supported by the finding that even the most caudal vagal rootlets may carry general somatic afferent fibres to the spinal trigeminal tract.[1] In addition, the two separate episodes with differing pathologies raise the interesting question of whether there is a particular propensity for neuralgia which may or may not require a vascular trigger. This bears on the point raised by Adams *et al* as to why there are so many possibly causative vessels and so few neuralgias.[6]

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B K OWLER
Department of Neurosurgery, Royal Prince Alfred Hospital Camperdown, NSW, 2050, Australia

I JOHNSTON
Department of Surgery, University of Sydney, Sydney, NSW, 2006, Australia

M KENNEDY
Department of Medicine, Manly Hospital, Manly, NSW 2095, Australia

Correspondence to: Dr I Johnston, GPO Box 811, Hobart, Tasmania 7001, Australia
hdtd@bigpond.com

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Immunohistochemistry distinguishes between Pick's disease and corticobasal degeneration

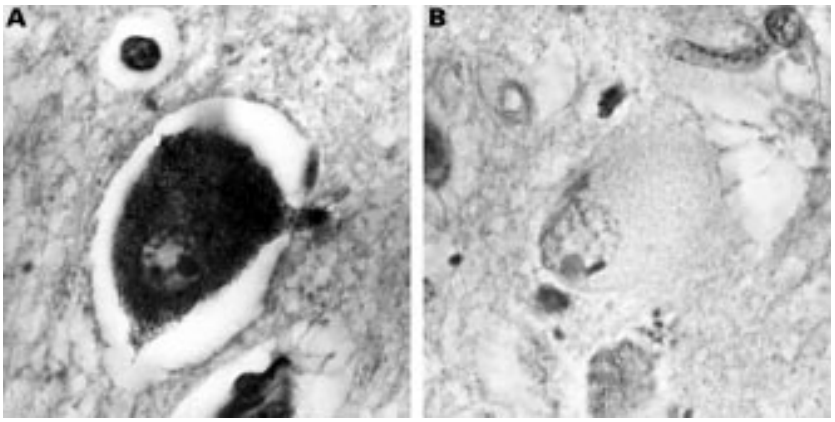
The clinical syndrome of frontotemporal dementia is associated with several neurodegenerative disorders: Pick's disease, corticobasal degeneration, motor neuron disease-associated dementia (MND-dementia), frontotemporal dementia and parkinsonism linked to chromosome 17 (FTDP-17), and frontal lobe degeneration (FLD). These disorders, although they do not match the frequency of Alzheimer's disease, are far from uncommon, and present clinicians and neuropathologists with formidable, if not insurmountable diagnostic difficulties. However, recent advances in cellular and molecular pathology, biochemistry, and molecular genetics have been instrumental in their nosological definition. The discovery of a mutation in the tau protein gene on chromosome 17 in 1998 has established that several phenotypically heterogeneous familial dementias with a confusing variety of names all belong to FTDP-17.[1 2] Most but not all frontotemporal dementias are characterised by intracellular inclusions formed by abnormal cytoskeletal components, both in neurons and in glial cells. Pick's disease, corticobasal degeneration, and FTDP-17 belong to the larger group of tauopathies, as their hallmark lesions contain tau protein, distinguishing them from MND-dementia and FLD, two disorders without tau pathology. Of the three tauopathies, FTDP-17 can be defined by its genetic abnormality, whereas the differential diagnosis of Pick's disease and corticobasal degeneration remains difficult and controversial.

Clinically Pick's disease is characterised by frontal and anterior temporal lobe dysfunction and progressive dementia, whereas neuropathologically the underlying frontotemporal atrophy is complemented histologically by the presence of large, swollen, achromatic neurons, the Pick cells, and by tau positive intraneuronal inclusions, the Pick bodies. The clinical features of corticobasal degeneration include asymmetric extrapyramidal signs, parkinsonism, and the "alien limb" phenomenon (apparent purposeful movements which are not under voluntary control) followed by cognitive impairment. Histologically there is neuronal loss, astrocytosis, and tau positive neuronal and glial inclusions, but the most prominent feature is the presence of large, swollen neurons, morphologically indistinguishable from Pick cells. It is the occurrence of these cells in both disorders which causes most of the differential diagnostic problems.

In the human central CNS six tau isoforms are generated by alternative splicing and these are then postranslationally phosphorylated. At molecular level the electrophoretic profiles of aggregated tau proteins in these neurodegenerative disorders are disease specific. For example, although both Pick's disease and corticobasal degeneration are tauopathies, characterised by tau positive cellular inclusions, their tau profile is apparently different: the tau doublet is 64 and 69 kDa in corticobasal degeneration, but 55 and 64 kDa in Pick's disease.[3] Here we report the use of tau antibodies which, exploiting the different phosphorylation patterns of these two disorders, has made a more accurate neuropathological diagnosis possible.

Sections from the frontal lobe and the temporal lobe (including the hippocampus) from 10 cases of corticobasal degeneration and 10 cases of Pick's disease were examined by immunohistochemistry, using phosphorylation independent (SMI51, TP007, TP70, 304, 189) and phosphorylation dependent (AT180, AT270, AT8, 12E8) anti-tau antibodies. All sections were immunostained according to a standardised protocol using the avidin-biotin complex (DAKO) with appropriate positive and negative controls. All the swollen neurons and neuronal and glial inclusions were positively immunostained with all the anti-tau antibodies in corticobasal degeneration. However, in Pick's disease all the antibodies but one immunostained the Pick bodies and the large swollen Pick cells: antibody 12E8 gave negative results (figure A and B).

Phosphorylation at the site of Ser262/Ser356 is thought to be one of the most prominent factors affecting the biological activity of tau.[3] In corticobasal degeneration antibody 12E8 detected the phosphorylated epitopes Ser262 and/or Ser356, whereas in



Positive and negative immunostaining in large, swollen neurons by anti-tau antibody 12E8 in corticobasal degeneration (A) and in Pick's disease (B), respectively. ABC method (DAKO).

Pick's disease these sites remain unphosphorylated and consequently this antibody did not label any of the Pick bodies or Pick cells.[4] These findings are important both from a practical and from a theoretical point of view. The immediate practical implication is a more accurate neuropathological diagnosis, enabling Pick's disease to be distinguished from corticobasal degeneration; this, in turn, is essential for improving clinical investigations. In addition, new insights into the molecular pathology of these disorders contribute to the nosological definition and better understanding of a complex group of neurodegenerative diseases.

K BELL
N J CAIRNS
P L LANTOS
Institute of Psychiatry, King's College London, Department of Neuropathology, Denmark Hill, London SE5 8AF, UK

M N ROSSOR
Institute of Neurology, University College London, Department of Clinical Neurology, Queen Square, London WC1N 3BG, UK

Correspondence to: Dr PL Lantos
npath@iop.kcl.ac.uk

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CORRESPONDENCE

Neurological emergencies: acute stroke

We greatly enjoyed reading the recently published review on acute stroke by Davenport and Dennis.[1] Their didactic approach and strict compromise to distinguishing between evidence based approaches and their personal beliefs deserve compliment. We would like to contribute by clarifying some information on two topics.

Firstly, the authors make a brief comment on the use of anticoagulants in the treatment of cerebral venous thrombosis (CVT) indicating that a recent randomised trial showed a non-significant favourable effect.[2] This may lead to a misinterpretation. Most experts currently agree that anticoagulation should be used in the acute treatment of CVT based on the available evidence. In 1991, Einhaulp *et al*[2] published the results of their randomised double blind prospective study comparing heparin and placebo. This study was prematurely interrupted after enrolling 20 patients because of the dramatic differences noted in outcome in favour of the heparin group (basically eight patients recovered fully and no deaths occurred in the heparin arm whereas only one patient recovered completely and three others died in the placebo group). Concerns about possible methodological flaws in this German trial fueled some controversy about its results. This led to a new trial by the Cerebral Venous Sinus Study Group[3] which randomised 60 patients with CVT to receive nadroparin or placebo for 3 weeks. Poor outcome was defined as death, Barthel index of less than 15 at 3 weeks or Oxford handicap score equal or greater than 3 at 12 weeks. The results showed poor outcome in six of 30 patients (20%) in the nadroparin arm and seven of 29 (24%) in the placebo group at 3 weeks and four of 30 (13%) in the nadroparin treated patients versus six of 29 (21%) in the placebo group (absolute risk reduction of 7% and relative risk reduction of 38% for a non-statistically significant difference). But also very remarkably, there were no new symptomatic cerebral haemorrhages even among the 15 patients treated with anticoagulation who had haemorrhagic lesions on the initial CT. Finally, the same authors performed a meta-analysis combining the results of the two available trials[2 3] which showed a "modest but clinically important" (although not statistically significant) benefit in the use of anticoagulation (absolute risk reduction of 14% in mortality and 15% in death or dependency, with relative risk reductions of 70% and 56% respectively). When combined with the proved safety of anticoagulation even in the setting of pre-existent haemorrhagic infarct and the highly unpredictable course of patients with CVT, these results should encourage the use of anticoagulation in the treatment of CVT.

Secondly, Davenport and Dennis mentioned the use of decompressive craniectomy as one of the interventions that may be used in patients with stroke who are rapidly deteriorating from raised intracranial pressure. However, they questioned whether this aggressive approach was associated with "improved survival with acceptable quality of life".[1] Growing experience with our patients as well as the available literature seems to indicate that it does, especially when decompressive surgery is performed early. Schwab *et al*[4] studied 63 patients with complete middle cerebral artery (MCA) infarctions and evidence of increased intracranial pressure treated with either early (within 24 hours of symptom onset) or late craniectomy. Mortality was 27% (compared with 78% in historical controls) and all suvivors were reported to be able to walk short distances without assistance and none were left with global aphasia. Mean Barthel index scores were 68.8 in the early hemicraniectomy group, 62.6 in the late hemicraniectomy group, and 60 in historical controls (but the very high mortality in this last group may account for a less dramatic difference in functional outcome). Similar favourable results were reported by Carter *et al*[5] in their a retrospective analysis of 14 patients treated with decompressive surgery after massive non-dominant hemispheric infarctions. Eight of their 11 surviving patients were able to function with minimal to moderate assistance (Barthel index >60) 1 year after the surgery. Depression and failure to reintegrate socially were often found in this group of patients[5] as opposed to the experience reported by Schwab *et al*.[4]

In conclusion, decompressive craniectomy seems a valuable treatment option in cases of malignant MCA infarction, especially when involving the non-dominant hemisphere. This surgery is potentially lifesaving and reported functional outcomes are encouraging. Therefore, it needs to be considered early in every patient with complete MCA strokes showing incipient signs of increased intracranial pressure.

A RABINSTEIN
Department of Neurology, University of Miami School of Medicine, 1501 NW 9 Avenue, Miami, FL 33136, USA

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Davenport and Dennis reply:

We are grateful for Rabinstein's interest and comments. Although our interpretation of the available data may be more conservative, we do indeed consider anticoagulation for CVT, but do not think that it is appropriate in all cases. Similarly, we have considered craniectomy for "malignant" MCA occlusion, but so far we have not thought it appropriate to proceed. We note the good outcomes from the published case series and await the results of randomised trials with interest. However, many of the case series have involved rather younger than average

patients, who have a greater capacity for functional recovery than older people (who make up the bulk of our case load), in whom we doubt whether such good functional outcomes are achievable.

R J DAVENPORT
M S DENNIS
Department of Clinical Neurosciences, Western General Hospital, Crewe Road, Edinburgh EH4 2XU, Scotland, UK

Correspondence to: Dr R J Davenport
rjd@skull.dcn.ed.ac.uk

Illusory movements of the paralysed upper limb in stroke

Feinberg *et al* have recently reported the association between anosognosia for hemiplegia and the illusion of movement of the paralysed upper limb.[1] They considered the illusion a form of confabulation that is distinct from other phantom phenomena. This explanation is not supported by my findings in a patient with a stroke who experienced transient purposeful movements of his paretic hand.

The patient was a 66 year old right handed man who presented with acute onset weakness of his right arm and leg and slurring of his speech. He was known to be hypertensive and a non-insulin dependent diabetic patient. Neurological examination confirmed the presence of right hemiplegia with facial involvement and mild to moderately severe dysphasia. Muscle power, as measured by the Medical Research Council (MRC) scale, was 1/5 and 2/5 in the upper and lower limbs respectively. Spinothalamic and posterior column sensations were intact. No visual field defects were found on examination using the confrontation method. There was no astereognosis or sensory extinction of tactile or visual stimuli. The patient was alert and cooperative. His comprehension of spoken and written language was good but there was evidence of moderately severe nominal dysphasia. The rest of the physical examination was normal. Brain CT confirmed the presence of a non-haemorrhagic infarct in the left corona radiata. The patient scored 19 on the mini mental state examination. There was no evidence of hemineglect as assessed clinically and with the line bisection test. The patient was correct in 8/10 items of the anosognosia for hemiplegia questionnaire.[1]

Six weeks after his stroke the patient developed an itchy skin condition, probably a drug hypersensitivity reaction. When he scratched his skin with his left (good) hand to relieve the itching he thought that his right hand was also simultaneously scratching the same skin area. The right hand "stopped working" when he ceased scratching his skin but the perception of movement recurred each time he scratched the same or a different skin area until his symptoms resolved 2 weeks later. The use of the left hand for other activities did not result in a similar phenomenon. The patient had good insight into his motor functional disability and described his perceived hand movements as a "silly situation".

The case reported here demonstrates that illusory movements in stroke are independent of anosognosia for hemiplegia. This finding is in agreement with those of a previous study.[2] It also suggests that illusory movements are unlikely to be the product of confabulations. Confabulation is primarily a memory disorder and results from lesions in the forebrain and medial temporal lobe that disrupt connections of the limbic system.[3] The patient reported here did not have an amnestic syndrome; neither was his brain lesion (as demonstrated with CT) in the limbic system area. It seems likely that the illusory movements described by Feinberg *et al* were phantom phenomena associated with reorganisation of cortical maps and neural plasticity.[4]

A M O BAKHEIT
University of Plymouth, Mount Gould Hospital, Plymouth PL4 7QD, UK

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Feinberg and Roane reply:

The patient described by Bakheit is of interest but is not relevant to our investigation.[1] To be included in our investigation, patients were required to have *right* hemispheric strokes and *left* hemiplegia. Furthermore, 10/11 patients in our study had left hemispatial neglect and left hemisensory defect. The patient described by Bakheit had a right hemiplegia, and had *no* neglect or sensory defects. Therefore, Bakheit's patient would not have qualified for our study and cannot be fairly compared with our study population. Additionally, the factitious movements described in Bakheit's patient differed from those experienced by our patients in two significant respects. Firstly, Bakheit's patient experienced a "mirroring" phantom movement of the plegic right limb only when the normal hand was active. In our study, to minimise the potentially confounding role of completion, we specifically excluded from the main analysis those patients who only experienced illusory limb movements when the nonplegic limb was active. Secondly, the phantom movements experienced by Bakheit's patient were restricted to a particular idiosyncratic action—namely, scratching—as opposed to our patients who experienced illusory limb movements when simply asked to raise the left arm, an action which apparently failed to elicit factitious movement in Bakheit's patient. Therefore, according to the criteria set out in our investigation, the movements experienced by the patient of Bakheit would not be catagorised as illusory limb movements in our study. Finally, it should be further noted that our patients were examined within a week of onset (some within a day) of acute hemiplegia, before significant "reorganisation of cortical maps and neural plasticity" is likely to have occurred. The patient of Bakheit is reported to have had phantom movements at 6 weeks after onset of hemiplegia when cortical reorganisation and neural plastic effects are more likely to have occurred.

In our opinion, Bakheit has committed the same error that we have previously cautioned against.[2 3] He has failed to distinguish "phantom limb movements" in his patient from illusory limb movements that occur in association with right hemispheric damage and hemineglect. Patients with true phantom limbs, as in Bakheit's case, do not deny the identity of the actual arm and recognise the phantom movements as illusory. By contrast, the patients with illusory limb movements in our study all denied ownership of the plegic arm and believed in the reality of the factitious movements. It is in this group in which we found illusory limb movements and which bears a relation to anosognosia and represents a variety of confabulation. Finally, we point out that confabulation is not confined to amnestic patients, and occurs in other conditions such as Anton's syndrome.

TODD E FEINBERG
Yarmon Neurobehavior and Alzheimer's Disease Center, Beth Israel Medical Center, 317 East 17th Street, New York, New York 10003,USA

DAVID M ROANE
Department of Psychiatry, Beth Israel Medical Center, 16th Street and 1st Avenue, New York, New York 10003,USA

Correspondence to: Dr Todd E Feinberg

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Social deprivation and prevalence of epilepsy and associated health usage

I read the study of Morgan *et al* on social deprivation and prevalence of epilepsy and associated health usage[1] with great interest and would like to add some remarks from my experience in the most impoverished region of the United States, near the Mississippi Delta. I would caution that it is especially in a poor and traumatised population, extremely difficult to differentiate between true electrical events and non-epileptic (or pseudo) seizures.[2] We have known since Charcot about the correlation between psychological traumatic states, to which poverty is intimately related and conducive, and "hysterical" seizures.[3–5] There is a substantial comorbidity of epileptic and non-epileptic seizures.[2] In fact, what I see here in Mississippi is more often than not a mixture of both and without proper, expensive testing, such as video EEG, it is sometimes impossible to make the difference. Because of the way the data were collected, it is difficult to know from the paper of Morgan *et al*[1] whether pseudoseizures were properly taken into account when assessing the prevalence of epilepsy. The same caveat applies to the ascertainment of psychiatric comorbidity. A thorough neuropsychiatric screening of the clientele of an epilepsy clinic would disclose a much higher psychiatric comorbidity than the record linkage used here. Because of the way neurologists are trained, at least in the United States, most psychiatric comorbidity in neurology patients in general probably goes undiagnosed.

What the usage data of Morgan *et al* do show is how vain the treatment of neurological illness remains without addressing its social ecology. This certainly is true in Wales as well as in Mississippi.

M PRETER
Departments of Psychiatry and Neurology, University of Mississippi Medical Center, 713 Northwest Avenue, Durant, MS 39063–3007, USA

Correspondence to:
mpreter@psychiatry.umsmed.edu

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The authors reply:

We thank Preter for his interest in our paper and for his comments identifying the problems associated with correctly diagnosing epilepsy. As we have indicated in the paper, these problems are intensified by record linkage techniques with the possibility of both false positive and false negative results. We discussed in some detail the issue of false negatives as we think this to be the greater problem within our study and so Preter's comments about false positives, particularly pseudoseizures, are most useful. Patients with pseudoseizures, however, will still place a demand on epilepsy services and therefore remain an issue in the allocation of resources within areas of high social deprivation.

We also accept that our ascertainment of psychiatric morbidity will be skewed towards the more severe forms of psychiatric comorbidity as, by our methodology, they will have to have come into contact with secondary care services. It is, however, these patients, excluded from our second analysis, who will have the greatest influence upon social and material deprivation.

We think, however, that despite these caveats, the findings of the study remain valid. As is often the case, a record linkage study raises as many questions as it answers and more detailed research is required in this area.

C L MORGAN
Z AHMED
M P KERR
Department of Psychological Medicine, University of Wales, College of Medicine, Heath Park, Cardiff CF4 4XW, UK

Correspondence to: Dr M P Kerr.
KerrMP@cf.ac.uk

Neuropsychological abnormalities in first degree relatives of patients with familial Parkinson's disease

We enjoyed reading the paper by Dujardin *et al*[1] who investigated possible preclinical features of asymptomatic relatives in families with Parkinson's disease. A battery of neuropsychological tests disclosed impaired frontal executive function in 15 of 41 first degree relatives of patients with familial Parkinson's disease. Nine showed general frontal executive impairment. The other six only had lower scores in parts of motor dynamic sequences and word fluency. The authors concluded that this dysexecutive syndrome could be a premorbid expression of Parkinson's disease. It could represent an early nigrostriatal dysfunction in first degree relatives of probands with familial Parkinson's disease who may thus carry a higher genetic risk of developing the disease.

Dujardin *et al* describe modifications of the cognitive status which we reported in unaffected co-twins of patients with Parkinson's disease[2] After this, 3 years ago our group published a similar study[3] to the one by Dujardin *et al.* As they do not mention our findings, we briefly discuss our data in relation to their results. We compared 35 motor asymptomatic first degree relatives (mean age 52.6 (SD 10.6) years) of families with at least two members affected by Parkinson's disease to 29 relatives (mean age 52.1 (SD 4.1) years) of patients with sporadic Parkinson's disease and to 32 healthy controls (mean age 51.9 (SD 4.6) years). To account for a possible "low dopamine syndrome", we studied memory, frontal lobe function, mood, personality traits, somatic complaints, and fine motor abilities. Tests used were the short form of the Wechsler adult intelligence scale, the auditory verbal learning test, the controlled oral word association test, the Wisconsin card sorting test (Nelson version), the paranoid depression scale, the revised version of the Freiburg personality inventory, a list of complaints, and a standardised finger tapping test. We found that first degree relatives of both patients with familial Parkinson's disease and those with sporadic Parkinson's disease differed significantly from controls in several tests. They had lower scores in total fluency and fewer categories in the Wisconsin card sorting test. Relatives of both patients with familial Parkinson's disease and with sporadic disease expressed more impulsiveness, more strain, and less extraversion on personality assessment. In addition, relatives of patients with familial Parkinson's disease had more errors than controls in the Wisconsin card sorting test. Relatives of patients with sporadic Parkinson's disease showed more depression, more somatic complaints, and inhibitedness than controls and also less extraversion, less emotionality, and a lower tapping rate of the right hand. Our results, both motor and nonmotor, were comparable with those of patients with early stage Parkinson's disease and are in keeping with some of the findings of Dujardin *et al*.

On average, our proband sample was 14 years older than that of Dujardin *et al*, and by contrast with these authors, we included assessment of depression as a possible confounder of the neuropsychological test results. Depression may have a substantial impact on cognitive function,[4] and a history of depression is thought to be a risk factor for developing Parkinson's disease.[5] In our study, there were no correlations between cognitive impairment and depression. We therefore considered frontal lobe dysfunction and depression as independent signs of the "low dopamine syndrome" in our samples. Another important result of our investigation was that, apart from one personality trait ("aggressiveness"), we could not establish differences between relatives of patients with familial Parkinson's disease and those of patients with sporadic Parkinson's disease in any test item, nor were there item clusters in subsets of probands. Thus, according to our data, frontal lobe dysfunction and depression can be found to a variable degree in some relatives of patients with both the familial and the sporadic form of Parkinson's disease. It should be kept in mind that the finding of such neuropsychological abnormalities does not prove that their origin is genetic.

B KIS
I HEBERLEIN
J HAGENAH
H JACOBS
C KLEIN
P VIEREGGE
Department of Neurology, Medical University of Lübeck, Ratzeburger Allee 160, 23538 Lübeck, Germany

Correspondence to: Professor P Vieregge
vieregge_p@neuro.mu-luebeck.de

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BOOK REVIEW

Juvenile Myoclonic Epilepsy: the Janz Syndrome. Edited by B SCHMITZ and T SANDER. (Pp 207, £42.50). Petersfield: Wrightson Biomedical, 2000. ISBN 1 871816 42 4.

Have you ever had that feeling that something is just on the tip of your tongue but you can't quite get at it or that if only you had one more piece of the jigsaw, you would be able to see the whole picture? Welcome to juvenile myoclonic epilepsy. It is one of the most rewarding conditions in epilepsy to diagnose and treat. Indeed juvenile myoclonic epilepsy has the unusual, dual virtues of being both common and treatable. But what is it? This book introduces the condition—prevalence 3%-11% of all epilepsy, easily diagnosed if you think to ask for early morning twitchiness or clumsiness, characteristic EEG appearance etc. But then come all the tantalising clues that leave one on the brink of understanding. It is obviously genetic and a linkage to chromosome 6 has been suggested for years, now honed down to near the HLA gene. But a recent analysis has tried to subdivide juvenile myoclonic epilepsy according to electroclinical criteria to obtain more homogeneous groups for genetic analysis and this has suggested genetic heterogeneity. Why are there so many focal elements in this generalised epilepsy syndrome? These include focal clinical seizure manifestations, focal EEG changes, focal imaging changes such as thickening of the grey matter detectable by mathematical techniques. What is the overlap with other syndromes such as childhood absence epilepsy and why are seizures triggered by reading or praxis in some cases?

At least all can agree that it usually gets better with valproate but comes back if you stop the drug. Unfortunately this text does not discuss other newer medications. Experience with them is largely anecdotal except the treatment of the myoclonus with benzodiazepines and piracetam.

This book summarises our knowledge of juvenile myoclonic epilepsy in a readable and concise but comprehensive text. The trouble is that we are on a threshold between descriptive knowledge and understanding so juvenile myoclonic epilepsy remains one jigsaw piece short of a picture. It will be of interest primarily to those in the epilepsy and genetics fields.

MARK MANFORD