Facial diplegia with paraesthesias: facial nerve enhancement in three-dimensional MRI

Facial diplegia (bilateral facial paralysis) is a rare clinical finding that can be the presenting symptom in a wide range of diseases. It occurs in about 50% of patients with Guillain-Barré syndrome (GBS). Guillain-Barré syndrome causes regional and functional variants with unusual features. Ropper described four patients with facial diplegia and distal limb paraesthesias, and he defined them as having a rare variant form of GBS because of shared clinical, electrophysiologi- cal, and CSF features. The aetiology and nosological position of facial diplegia presenting in this variant form is still controversial. We experienced a patient who had bilateral facial paralysis, distal limb paraesthesias, and diminished reflexes whose contrast enhanced three-dimensional MRI (3-D MRI) showed enhancing lesions in the bilateral facial nerves. A 27-year-old woman had nasal discharge and coughing. One week later she noticed paraesthesias in her fingers and toes. Nine days after the onset of her neurological symptom, she developed bilateral facial weakness. On admission (day 12) she showed moderate, bilateral facial paralysis that caused her difficulty in moving her forehead, in approximating her eyelids, and in lifting the corners of her mouth. Taste, smell, and taste were preserved. The other cranial nerves were normal. A motor examination showed normal strength in her limbs. Superficial and deep senses were normal even though she had distal limb paraesthesias. Deep tendon reflexes were absent in all her limbs and her plantar responses were flexor type. Cerebellar ataxia and autonomic nervous dysfunction were excluded. Chest radiography was normal. Laboratory studies of the identifiable causes of facial diplegia (sarcoidosis, Lyme disease, syphilis, infectious mononucleosis, herpes simplex virus, diabetes mellitus, and connective tissue disease) were all negative. On day 12, the CSF examination detected mild increase in protein concentration (57 mg/dl) without pleocytosis. The blink reflex was elicited and both the R1 and R2 components were reduced, but their latencies were not prolonged on day 15. Motor and sensory nerve conduction velocities, and median and tibial nerve frespences were all normal on day 18. Auditory brainstem responses were normal. On day 19, when her facial diplegia was moderate, conventional brain MRI detected no abnormality. A contrast enhanced 3-D MRI, which was obtained by spoiled gradient recalled acquisition in the steady state sequence using a 1.5 tesla system after injection of gadolinium-diethylenetriamine penta-acetic acid (Gd-DTPA), was performed. The intracranial segments of the bilateral facial nerves were remarkably enhanced by Gd-DTPA (figure). On day 45, when her symptoms were no longer present, there were no abnormal enhancements of her facial nerves. After showing symptoms of upper respiratory infection, the patient experienced the acute onset of facial diplegia, distal limb paraesthesias, and areflexia but no other neurological deficits. The CSF examination showed albuminocytological dissociation, and clinical and laboratory examinations excluded the possibility of viral or bacterial infection, Lyme disease, tumour, sarcoidosis, cerebrovascular disease, diabetes mellitus, bilateral Bell’s palsy, and congenital and familial disorders. The patient’s illness followed a monophasic course. We therefore diagnosed this case as having “facial diplegia with paraesthesias”, which should be included for the differential diagnosis whenever sudden bilateral facial paresis occurs. Routine brain MRI showed no abnormalities, whereas contrast enhanced 3-D MRI showed Gd enhancement of the bilateral facial nerves. The MRI findings indicate the involvement of the peripheral facial nerves in our patient. Fullbright et al reported an additional case of GBS with multiple cranial nerve enhancements seen on Gd enhanced MRI. The mechanism of abnormal enhancement of the cranial nerves in the patients with GBS is not entirely understood; however, it is widely regarded as disruption of the blood nerve barrier by the inflammatory infiltrate. Ramsey et al evaluated the MRI findings obtained with Gd contrast enhancement in five patients who had facial paralysis: GBS (n=1), herpes simplex polyneuritis (n=1), meningeval lymphoma (n=1), and bilateral Bell’s palsy (n=2). Gd enhanced MRI has been shown to be the procedure of choice for demonstrating inflammatory lesions of the facial nerves. Nagaoka et al showed oculomotor nerve enhancement on 3-D MRI in Fisher’s syndrome, the best known variant of GBS. Ours is the first report of facial nerve enhancement in “facial diplegia with paraesthesias” and “facial diplegia with paraesthesias”. These findings suggest that 3-D MRI with Gd-DTPA can be used to identify inflammatory conditions that produce peripheral lesion of the cranial nerves in GBS variants.

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References:

Restless legs syndrome associated with spinal cord lesions

Restless legs syndrome may be either a primary or a secondary disorder. The primary form of the syndrome is often familial whereas the secondary form is mainly associated with iron deficiency or pregnancy. Almost all patients with restless legs syndrome show periodic leg movements during sleep. The pathogenesis of both restless legs syndrome and periodic leg movements is still speculative. Yokota et al hypothesized an association of periodic leg movements with spinal cord lesions. However, none of these patients had the typical clinical features of restless legs syndrome. Restless legs syndrome associated with myelopathy is documented in one patient with a Borrelia induced myelitis. We report three patients who developed a restless legs syndrome in close temporal association with spinal cord lesions.

Case 1 was a 35 year old woman who presented with a 3 week history of painless restlessness of her left lower leg that occurred only at rest, particularly in the evening and at night. The restlessness was partially relieved by walking. With the onset of these symptoms, the patient had noticed a numbness of her left hemibody below the breast. Nine months previously, a numbness of the right leg had subsided spontaneously within 1 week. On examination, the patient had decreased senses for touch, pain, and temperature over the left hemibody below the T6 dermatome. Examination of the spinal cord was normal. No abnormality was documented in MRI studies of the spinal cord. However, a single dose of 100 mg levodopa plus benserazide led to a dramatic improvement of the restless legs syndrome. The levodopa treatment was continued and resulted in complete relief.

Case 2 was a 49 year old man who had a traumatic atlantoaxial dislocation that necessitated operative stabilization of the cervical spine. Preoperative MRI studies showed a compression of the medulla and the cervical cord. When we saw the patient 3 years later, he complained of a sensation of cold, pain, and restlessness in both lower legs that was present only at rest, particularly in the
eversion, and was relieved by walking around and rubbing the legs with cold water. The onset of these symptoms was only a few weeks after the accident. Clinical examination disclosed a mild dysarthropenia and atrophic pareses of the left sternomastoid and the left hand muscle. Tendon reflexes were hyperactive and plantar responses were extensor bilaterally. The patient’s gait was spastic, but he was able to walk unassisted. In both legs, pain and temperature sensation were markedly reduced. The diagnosis of a restless legs syndrome secondary to a traumatic lesion of the medulla and the cervical cord was made. Treatment with 100 mg levodopa plus benserazide and 100 mg tramadol resulted in satisfactory relief of the restless legs syndrome.

Case 3 was a 65 year old man who developed slowly progressive spastic tetraparesis and ascending sensory disturbances in both legs. An MRI study showed a cervical spondylopathy myelopathy at the level C3-C6 and the patient underwent spinal cord decompression. Five years later, he was referred to our hospital because of an intense restless legs syndrome secondary to a traumatic lesion of the medulla and the cervical cord injury, and cervical spondylopathy myelopathy. Similar to idiopathic restless legs syndrome and other secondary forms, restless legs syndrome due to myelopathy may respond well to dopaminergic drugs.

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Coma in thrombotic thrombocytopenic purpura

Patients with thrombotic thrombocytopenic purpura (TTP) can present with devastating neurological abnormalities. Mortality may be as high as 95%, but current treatment has reduced this to about 10% and early treatment improves the rate of recovery. We describe two patients who presented with predominantly neurological symptoms and signs who, because of a delay in making a diagnosis of TTP, were referred for treatment at a late stage. Both patients were reviewed by neurological and haematological experts, who considered that the prognosis was poor.

The first case was a 49 year old woman with a longstanding diagnosis of schizoaffective disorder and a previous left sided cerebrovascular accident. She was admitted to her local hospital with a 3 day history of drowsiness, confusion, epistaxes, and spontaneous bruising, having been noted to be increasingly agitated and disoriented over the preceding 6 weeks. Her only medication was trifluperazine and paroxetine. The second case was a 58 year old man, previously fit and well, who presented to his local hospital with a 3 week history of confusion, drowsiness, jaundice, and right upper quadrant pain. He was taking no medication. The initial findings in both patients are summarised in the table. In both a diagnosis of TTP was made, although this was not confirmed until 5 days after admission in the first case, and both patients were transferred to the intensive care unit for plasma exchange and further management.

Treatment was started in both cases with five cycles of plasma exchange over the course of 3 days, using 31 cryoprepared fresh frozen plasma, and in the first patient this was followed by a course of oral prednisolone and azathioprine. Both made an excellent recovery, with an improvement in consciousness level, a rise in platelet count, disappearance of red cell fragments, a fall in LDH and bilirubin concentrations, and normalisation of renal function. The first patient was self ventilating with no neurological deficit at time of transfer back to the referring hospital. The second patient had a Glasgow coma score of 15 by the fifth day of treatment, the only focal neurological being a bilateral internuclear ophthalmoplegia (INO). Three months later the ophthalmoplegia had resolved and the patient was self caring with minimal disability. Both patients were extensively investigated to look for an underlying cause for TTP, but none was found.

Thrombotic thrombocytopenic purpura is a syndrome comprising a pentad of features—fever, thrombocytopenia, microangiopathic haemolytic anaemia, neurological abnormalities, and renal dysfunction. Not all five features are required to make the diagnosis.
diagnosis—often fewer are present—and there is no pathognomonic test, so diagnosis may be difficult. It is often considered along with haemolytic uraemic syndrome (HUS) to form part of a range of diseases called the thrombotic microangiopathies. In these disorders, intravascular platelet aggregation (there is minimal fibrin deposition) leads to obstruction of arterioles and capillaries, causing local ischaemia. Thus TTP is seen when the renal microcirculation is affected, and HUS when the renal microcirculation is affected. An episode of TTP may present as a one off illness, may be recurring, or may arise in association with drugs, neoplasia, pregnancy, or HIV infection.

Thrombotic thrombocytopenic purpura presents with neurological manifestations in over 50% of episodes, with headache, confusion, and somnolence being most common, leading to focal neurological deficit, convulsions, and eventually coma and death. These clinical features are often fleeting and fluctuating and several important points regarding interferon-β1b should be made. Firstly, brain CT may be normal or may show multiple hypodense areas indicative of generalised cerebral oedema. Secondly, brain MRI may also be normal, although it is likely to show marked hypointensity on T2 weighted images. Coma has been shown to be a bad prognostic indicator. Of importance is the finding that despite the presence of substantial neurological function, normalising on brain CT strongly suggest the potential for full clinical recovery.

Plasmapheresis is now the treatment of choice: plasma infusion alone should not be regarded as an acceptable alternative but as a short term measure only. Fresh frozen plasma is the usual replacement fluid, although it is likely to show marked hypointensity on T2 weighted images. Coma has been shown to be a bad prognostic indicator. Of importance is the finding that despite the presence of substantial neurological function, normalising on brain CT strongly suggest the potential for full clinical recovery.

Anaphylactoid reaction to methyl prednisolone developing after starting treatment with interferon β-1b

Courses of intravenous methyl prednisolone are routine and are used, for disabled relapses in relapsing-remitting multiple sclerosis. The Interferon β-1b Multiple Sclerosis Study Group’s research published in 1993 showed that interferon β-1b reduces the frequency of relapses in patients with multiple sclerosis. We present the case of a 35 year old man with multiple sclerosis who became allergic to intravenous methyl prednisolone after the initiation of treatment with interferon β-1b and discuss what part the drug could have played in this.

A 35 year old man with asthma presented early in 1994 with “dizziness”, double vision, and paraesthesia in the right leg extending into the trunk. He had been shown to have bilateral pyramidal signs in the legs with extensor plantar responses and gait ataxia. His CSF contained oligoclonal bands. Visual evoked potentials were normal and brain MRI showed multiple periventricular high density lesions with a similar lesion identified on imaging of the cervical cord, all consistent with demyelination. A 3 day course of intravenous methyl prednisolone in May 1994 was associated with improvement in his initial symptoms. Four months later he presented with a Vth nerve palsy which again responded to a 3 day course of intravenous methyl prednisolone.

Between September 1995 and February 1996 he had a further four unforeseen 3 day courses of intravenous methyl prednisolone for various symptoms related to his multiple sclerosis. In March 1996 he was started on interferon β-1b (8 MIU subcutaneously on alternate days).

In June 1996 he was admitted with pyramidal weakness of the left limbs, altered sensation in the left leg and urgency of micturition. Soon after starting his first dose of intravenous methyl prednisolone he felt a “jump” in his throat, developed an urticarial rash on his limbs and trunk and began wheezing audibly. Inhalation of salbutamol was ineffective. Treatment was stopped and his peak expiratory flow rate (PEFR) measured as 485 l/min. Chlorpheniramine (10 mg) was given intravenously and after 5 minutes his PEFR had returned to normal and his normal PEFR at 550 l/min. Further methyl prednisolone was not given on this occasion.

In August 1996 he was admitted with symptoms similar to those at his admission in June 1996. Ten minutes after starting his first dose of intravenous methyl prednisolone his chest felt tight and he started developing a similar urticarial rash. Again treatment was stopped. Fifteen minutes later the rash had worsened and he felt swelling in his mouth.

His symptoms settled after 10 mg intravenous chlorpheniramine. Further methyl prednisolone was not given. After this episode he chose to stop interferon β-1b.

In September 1996 he developed wheeze and a rash after the first dose in a course of intravenous methyl prednisolone. Subsequent doses in that course were preceded by chlorpheniramine. In November 1996 he developed nasal congestion and a rash after 500 mg methyl prednisolone. Again subsequent doses were preceded by a dose of chlorpheniramine. Since then he has been given chlorpheniramine before each dose of intravenous methyl prednisolone, which he has tolerated well.

Allergic reaction to steroids is rare and anaphylactoid reaction to methyl prednisolone is rarer still with only three reports in the literature. One of these reactions occurred in the course of treatment for multiple sclerosis. The allergic reactions are more likely to be the carrier to the steroid itself. Pathology in multiple sclerosis is thought to be due to a delayed type hypersensitivity reaction. The mechanism of action of interferon β-1b is more complex and is unknown, although several mechanisms are postulated. There is evidence that, among its many effects on the immune system, interferon β can increase interferon-β2, and that interferon-β2 can stimulate a Th2 response (found in allergic type responses). These effects would explain the sequence of events in this man. However, evidence suggests that interferon β can increase suppressor cells which may allow Th1’s (found in delayed type hypersensitivity reactions) and Th2 responses. It remains uncertain whether the sequence of events here is due to an effect of interferon β-1b or to co-infec-

tion. However, clinicians should be aware that the complexity of the effects of interferon β-1b on the immune system may lead to unexpected clinical outcomes.

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A 17 year old girl was referred by her general practitioner due to the sudden onset of numbness on the dorsum of her right foot associated with snapping her foot on walking. She had been well until 6 weeks previously when she developed tinnitus for which she received a 1 week course of oral penicillin V. She was also taking minocycline for mild acne. As her throat recovered she developed symmetric peripheral polyarthritis and upper respiratory tract infections. 6 weeks later she developed a mononeuropathy of the right common peroneal nerve at the neck of the fibula. On examination she had a right foot drop with weakness of ankle dorsiflexion (Medical Research Council grade 3/5). There was sensory loss in the distribution of the common peroneal nerve. She was otherwise neurologically intact with normal reflexes. There were no skin lesions and her joints were quiescent.

She had an erythrocyte sedimentation rate of 87 mm/h, a C reactive protein concentration of 112 mg/l and an antistreptolysin-O titre (ASOT) of 1600 units/ml. Autoimmune screen, antineuronal antibodies, and cryoglobulins were all negative apart from an atypical perinuclear antineutrophil cytoplasmic autoantibody (p-ANCA) IgG titre of 160. Renal function was normal in the right tibialis posterior muscle nerves, but delayed and inconstant in the right peroneal nerve with mild slowing of nerve conduction velocity. A sural nerve biopsy showed an inflammatory axonal neuropathy. Vasculitis after streptococcal infection has been well described.

We read with interest the short report on sensory loss in lateral medullary infarction by van Audens and Bogousslavsky.1 Unusual sensory variants include contralateral leg and lower trunk with ipsilateral lower face hypesthesia; or contralateral upper trunk, arm, and face hypesthesia; or contralateral hypesthesia with facial sparing; or hemibody sensory loss.2,3 We recently encountered a patient with sensory loss of the spinothalamic type involving only the contralateral leg and lower trunk from vertebral artery dissection. The sensory level in our patient with facial sparing differs from those in the literature; it suggests a thoracic hemispheric lesion and is false localization.

A 44 year old, right handed man with no relevant history presented with sudden onset of vertigo and left eye pain. There was no history of trauma or neck manipulation. However, the patient had had a dental abscess involving the lower incisors requiring draining 4 weeks previously. He had a 30 pack-year history of smoking. Vertigo developed while he was changing his car tyre. He noted that the vertigo was worse when he sat down and put his head between his knees. The vertigo lasted 15 minutes and was associated with profuse sweating in the upper half of his body. There was no nausea or vomiting. This recurred twice that day each time lasting 15 minutes.

Examination disclosed normal visual acuity and fundoscopy. There was scleral injection in the left eye. The left pupil was 4 mm compared with 5 mm on the right. Both reacted briskly to light. There was counterclockwise rotary nystagmus in the primary position. The eye movements were normal. Corneal reflex was intact, as was sensation to the upper and lower face. The other cranial nerves were normal. The gag reflex was brisk. There was no cranial bruit, Töne, power, and reflexes were normal. The sensory examination was normal in all modalities. There was no upper limb ataxia. He tilted to the left on sitting and on standing he fell to the left. The next day he noted loss of pinprick and appreciation of temperature on the right leg and trunk with a sensory level at T9 with preservation of touch, vibration, and joint position sense in all limbs (figure).

Brain MRI showed a small infarct in the lateral medulla and left cerebellum in the


A sensory level on the trunk and sparing the face from vertebral artery dissection: how much more subtle can we get?

Letters, Correspondence, Book reviews

Table Nerve conduction study results confirming a mainly axonal neuropathy of the right common peroneal nerve

<table>
<thead>
<tr>
<th>Nerve/site</th>
<th>CMAP Amplitude</th>
<th>Terminal latency</th>
<th>Velocity</th>
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<td>4.9 ms</td>
<td>51.9 m/s</td>
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<tr>
<td>Right peroneal</td>
<td>3.7 mV</td>
<td>5.3 ms</td>
<td>44.8 m/s</td>
</tr>
<tr>
<td>Ankle</td>
<td>3.2 mV</td>
<td>114.0 m/s</td>
<td></td>
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<tr>
<td>Neck of fibula</td>
<td>3.4 mV</td>
<td>3.2 mV</td>
<td></td>
</tr>
<tr>
<td>Behind knee</td>
<td>3.9 mV</td>
<td>5.0 m/s</td>
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<tr>
<td>Behind knee</td>
<td>9.1 mV</td>
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<tr>
<td>Neck of fibula</td>
<td>6.7 mV</td>
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<td>Left supra</td>
<td>Absent</td>
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<tr>
<td>Left peroneal</td>
<td>3.0 µV</td>
<td>3.3 ms</td>
<td>39.4 m/s</td>
</tr>
</tbody>
</table>

CMAP = Compound muscle action potential.

Sudden unexpected death: a rare event in a large community based prospective cohort with newly diagnosed epilepsy and high remission rates

It is now accepted that mortality in epilepsy is significantly increased, with standard mortality ratios raised twofold. Early deaths are usually attributable to the underlying cause of epilepsy and mortality in chronic cases is commonly due to the epilepsy itself.1 Of the deaths that are directly related to epilepsy, the commonest category is sudden unexpected death in epilepsy (SUDEP). This is widely defined as a sudden unexpected, non-traumatic and non-drowning death in a person with epilepsy with or without evidence of a seizure and excluding documented status epilepticus in which postmortem examination does not disclose a cause of death. Less common causes are status epilepticus, accidents due to seizures, drowning, and aspiration.2

The National General Practice Study of Epilepsy (NGPSE) is a prospective, population based, observational study of 792 patients with newly diagnosed epilepsy (564 definite cases and 228 probable cases) followed up for 8000 patient-years and has provided valuable insights into the prognosis and mortality of epilepsy. Fifty per cent of the definite cases were between the ages of 15 and 59 years—encompassing the age band in which the phenomenon of SUDEP is most commonly found. The overall standardised mortality ratio among patients with definite epilepsy in this cohort was 3.0 (95% confidence interval 2.5–3.7).3

The true incidence of SUDEP is not precisely known. Studies have varied in their methodology and study populations have ranged from those in death certificates and coroners’ registers (more community based) to epilepsy surgery cohorts and institutionalised patients (patients with chronic epilepsy).4 Figures derived from community based prospective studies indicate numbers of up to 1:1100.5 Patients with chronic epilepsy seem to have a much higher incidence of SUDEP and a tertiary clinic based population with chronic epilepsy in the United Kingdom had an estimated incidence of 1.200 patients. This is in some contrast with the two SUDEP deaths in 5000 patient years reported by the MRC Anti-epileptic Withdrawal Study Group for patients in remission from epilepsy.6

We report the first sudden unexpected death in epilepsy in the NGPSE. A 42 year old man known to have poorly controlled idiopathic generalised epilepsy treated with phenytoin and sodium valproate, was found dead in bed, having been well in the hours and days preceding death. He was known to misuse alcohol and was questionably compliant with medication, both factors thought to increase the risk of sudden death. A necropsy did not disclose any relevant pathology—consistent with the definition of SUDEP.

Mortality has been studied in detail in this large cohort and it was only in the 13th year of follow up (8000 patient-years) that the first SUDEP was reported. This could falsely give the impression that SUDEP is a rare occurrence and it must be borne in mind that in large community based cohorts such as the NGPSE, most patients enter remission from seizures and it is the patients who continue to have epilepsy that are most at risk from sudden death. Indeed in this cohort, the number of patients who still have active epilepsy, using International League Against Epilepsy


(A) Drawing of sensory deficit; (B) MRI showing clot in the left vertebral artery and infarcts in the lateral medulla and cerebellum (arrows), (C) arrowhead pointing at the occlusion of the left vertebral artery.
criteria for remission (no seizures for 5 years or more with or without medication) and on follow up are 111 from an original 792 who had definite or probable epilepsy. On its own, therefore, it does not provide a true indication of the incidence of SUDEP but it is nevertheless interesting finding the incidence of SUDEP in a large, community based cohort.

Financial support and sources of funding for the NGPSE were the National Hospital for Neurology and Neurosurgery, Brain Research Trust, and the National Society for Epilepsy.

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Opportunities for improving the quality of care in malignant cerebral glioma

There is scope for improving the services offered to patients with malignant glioma. Clinical audit has highlighted several important issues including some variation in the management of patients aged over 60, delays in beginning treatment, and problems with communication between different departments involved in patient care. A multidisciplinary Working Group, funded by the NHS Executive, recently developed evidence based guidelines for the management of these patients by surgery, radiotherapy, and chemotherapy. The group also considered the views of patients and their relatives about follow up and psychosocial aspects of care.

We have derived a package of audit measures from these guidelines that allow treatment centres to assess the care that they provide.1 Proformas within the package cover various topics—for example, technical aspects of treatment, breaking the news of the diagnosis, the support of patients and relatives, and palliative care while in the community. Information is drawn from case records, feedback from patients, relatives and general practitioners. A review of the policy a centre has already developed.

We piloted the proforma by reviewing the case records of 60 patients diagnosed at two treatment centres in London between 1992 and 1994. The table shows some results using one proforma which could highlight the breaking of the news of the diagnosis. We found, for example, that overall most case records (67%, 40/60) did not record what the patient and their relative had initially been told about the prognosis. However, there did seem to be a difference between centres. At one, clinicians rarely recorded what they had said to patients and relatives whereas at the other this was recorded in just over 50% of cases. Patients at one centre were also more likely to be seen subsequently by counselling or palliative care services. Neither centre had the benefit of a dedicated specialist nurse in neuro-oncology.

The lack of a record does not, of course, mean that the diagnosis and prognosis were not actually discussed in some depth with the patient and relative. However, clearly it is likely to be helpful for others involved in the care of the patient to have sight of such a record. It is also possibly relevant that an earlier study found that only a quarter of a sample of 75 patients drawn from different centres seemed to be fully aware of the likely prognosis for their disease as they began treatment.2

The aim of the guidelines developed by the Working Group has been to suggest methods which will help decision making in general terms rather than provide firm guidance on how particular patients should be treated. For example, an initial assessment of patient disability is recommended. Ten of the 60 case records we audited included some assessment of disability, but none formally recorded the patient’s performance status, an important prognostic factor, using either the WHO clinical performance status or the Karnofsky score.

The current review of cancer services after the Calman-Hine report1 represents an opportunity for the development of neuro-oncology services in Great Britain. A few centres have made progress towards the ideal of neuro-oncology clinics with specialist nurse support and well developed links with rehabilitation and palliative care. The guidelines and audit measures developed by the Working Group will need to be adapted for other circumstances, but treatment centres and purchasers may find them a useful tool in assessing and developing their services.

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CORRESPONDENCE

MRI in vertebral artery dissection

In a recent report, Auer et al described the clinical and imaging findings in 19 cases of extracranial vertebral artery dissection retrospectively.1 We make the following comments.

Firstly, the authors described the “sensitivity” and “specificity” of digital subtraction angiography (DSA), magnetic resonance imaging/angiography (MRI/A), and duplex sonography for diagnosing extracranial vertebral artery dissection.1 These figures were based on the percentage of probable and definite features among the 19 patients. Nevertheless, sensitivity of a test is the number of cases with true positive results divided by the total number of positive results (including both true and false positives), and specificity is the number of cases with true negative results over the sum of true and false negatives. The authors misquoted the terms “sensitivity” and “specificity” in their report, as the diagnostic criteria of the various tests have not been applied to a control group to disclose the false positive cases and true negative cases. Secondly, the criteria for case inclusion were not defined. Apparently, extracranial vertebral artery dissection was diagnosed by either radiological features on MRI/A (which may be “pathognomonic” or “suggestive”) in the appropriate clinical context or confirmatory radiological features on DSA (which may be “specific” or “indirect”). The accuracy and usefulness of DSA, MRI/A, and duplex sonography cannot be compared directly, as none is a “gold standard” diagnostic method used and because results of the present study simply reflected the proportion of cases diagnosed by the authors.

Dissection of neck arteries was thought to be an uncommon cause of ischaemic stroke. The true incidence of this condition remains unknown as angiography is not performed in every patient during the acute or subacute phase. Younger patients are more likely to undergo early angiography when there is a history of recent neck trauma2 or pain, or when no other causes of stroke are apparent. This selection bias may underestimate the
incidence of stroke due to arterial dissection in older patients and those without neck trauma or pain.

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Auer and Felker reply:
Cheung et al state in their comment, that dissections of neck arteries are an underestimated cause of stroke, because angiography is not performed in every patient during the acute and subacute phase. This bias is even more important in the case of vertebral artery dissection if the initial symptoms are nonspecific. Non-invasive diagnostic methods are likely to be performed earlier in these patients and this was our motivation to report on the magnetic resonance angiography of vertebral artery dissection.

The diagnosis of vertebral artery dissection is often based on the consensus of clinical and neuroradiological features. We agree with Cheung et al, that no single “gold standard” test for a dissection exists. Imaging procedures more often show indirect signs which have to be interpreted in the appropriate clinical context. Therefore, the “inclusion criterion” we used for this retrospective analysis was the clinical and neuroradiological consensus on the diagnosis of vertebral artery dissection. The sensitivity of DSA, ultrasound, and MRI/angiography was assessed from the findings of the affected and the contralateral normal vertebral arteries, there were no false positive results. The term specificity could have been misleading, because it did not refer to the overall specificity of a test but to the frequency of findings that reached a level of specificity sufficient to establish the diagnosis of vertebral artery dissection.

Further prospective studies on the sensitivity and specificity of magnetic resonance for the diagnosis of vertebral artery dissections are certainly necessary, but our retrospective evaluation already showed that MRI and MR angiography will have a major contribution in future. As a non-invasive means, magnetic resonance can be employed without risk in patients with non-specific symptoms and may provide specific findings that are not accessible with other methods. This will lead to a better estimation of the true incidence of dissections and will improve the early diagnosis and management of dissections in individual patients.

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Clinical usefulness of MRI in multisystem atrophy.

Schrag et al suggest that certain putaminal and infarctual changes on MRI are useful in distinguishing between patients with multisystem atrophy (MSA) and patients with idiopathic Parkinson’s disease.1 The specificity and positive predictive value of these changes were both about 90%. However, whether these changes will be useful in clinical practice or epidemiological research is unclear for several reasons.

The number of patients included was small and so the confidence intervals were wide. For example, the specificity of the MRI changes for MSA could be as low as 80%. Moreover, only patients with clinically probable MSA were included. In this group of patients the clinical diagnosis alone had positive predictive value as high as that of MRI and so there would seem to be little added value of MRI (14/15 (93%) patients with probable MSA had the diagnosis confirmed on MRI). A more relevant question is whether the MRI changes are equally specific in those with possible MSA in whom the clinical diagnosis is much less certain. Indeed it is also unclear from this study whether the MRI changes are specific to MSA as patients with other conditions that enter into the differential diagnosis were not included. It may therefore be more correct to state that the MRI changes are helpful in excluding Parkinson’s disease rather than in confirming MSA.

Finally, the positive predictive value of MRI quoted in this study is likely to be an overestimate compared with its routine use in other movement disorders. Schrag et al included a very high proportion of patients with MSA (nearly 50%) compared with Parkinson’s disease. As the positive predictive value is directly related to the prevalence of the disease in a given population, this resulted in a high positive predictive value. In a typical movement disorder clinic, fewer than 10% of patients will have MSA, in which case, even if the specificity of MRI is 90%, the positive predictive value would only be about 50%—that is, only half of those with the MRI changes would turn out to have the disease.

It is, therefore, too early to include specific MRI changes as part of the diagnostic criteria for MSA.

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A dubious therapy for patients with multiple sclerosis

Plohm et al investigated the effects of computer training of attentional deficits in patients included was small (about 45 in each group); secondly, that the 1:1 proportion of patients with Parkinson’s disease and those with multiple system atrophy (MSA) atrophy is unrepresentative of the real life situation in which the ratio is >1:1. A more ideal study might include 100 patients with MSA (to help counter the criticism of small numbers) and more than 1000 patients with Parkinson’s disease, but would be impractical, particularly for the Parkinson’s disease group, who, unlike patients with atypical disease, are not usually subjected to MRI. We agree that, as clearly stated in the abstract, our study was restricted to a comparison between multisystem atrophy, Parkinson’s disease, and controls, and are currently conducting a further study additionally including patients with other degenerative syndromes. Since the completion of the report, patients with Machado-Joseph disease have been added with similar infratentorial abnormalities. We also agree that in the diagnosis of clinically probable MSA, there is little added value of MRI; involvement of the cerebellum and its pathways is usually already clinically evident before its demonstration by MRI or CT, and even in cases without cerebellar involvement the diagnosis is still a clinical one. Moreover, as we emphasised, a minority of patients with probable multisystem atrophy may have MSA. Therefore, unlike others, we have never proposed MRI changes as part of the diagnostic criteria for multisystem atrophy. As discussed, the sensitivity of the method may be lower early, and higher late in the disease. However, for the purpose of validation of a proposed diagnostic aid imaging findings need to be related to a clinically probable diagnosis rather than that of any other condition.

The “gold standard” is definite, pathologically confirmed disease, but this was achieved in only one patient in our series. In conclusion, we nevertheless think that our, admittedly imperfect, blinded MRI study (the first conducted in MSA) has helped to determine the prevalence of certain MRI abnormalities in patients with clinically probable MSA in comparison to patients with Parkinson’s disease and controls. It has also, perhaps more importantly, revealed the limitations of MRI in this context. However, expert clinical evaluation remains the cornerstone of the diagnosis in life, and it is also more cost effective than resorting to expensive imaging techniques.

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Letters, Correspondence, Book reviews

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patients with multiple sclerosis. They conclude that “significant improvements of performance could almost exclusively be achieved by the specific training programs”. The validity of this conclusion is called into question by severe methodological shortcomings of their study.

Before training, three baseline measurements of attentional functions were administered with 3 week intervals. For evaluation of training effects the median value of the three baseline measurements was compared with the values obtained after training. This statistical approach manifests a curious misunderstanding of the purpose of repeated baseline measurements. They serve to determine a baseline measurement, the mean is lower than the third measurement after which training began. This difference inflates apparent improvement in the first training period. It may seem specific training effects if the group had a steeper baseline than the control group. A possible reason for different baselines are different severities of initial impairment. We (Motz, Grömminger, Göttert, Goldenberg, unpublished data) have administered the PASAT, another test of attentional capacities, four times with weekly intervals to 30 patients with chronic brain damage from different aetiologies. During intervals these patients did not receive any training of attentional functions. Thus, the repeated measurements determined a baseline without therapy. None the less, performance on PASAT improved from test to test. There was a negative correlation between performance and improvement. Patients with poor initial performance improved more than those with better performance.

The allocation of patients to treatment groups in the study of Plohmann et al was not randomised. Patients were trained in those two functions that were affected most, and group comparisons were made between patients who had been trained in a function and those who were not. Thus the training group tended to start from a lower level of performance than the control group. Figures 2 and 3 of their paper illustrate this effect impressively. If, as suggested by our results with the PASAT, initial level of impairment has a systematic influence on improvement independently of any therapy, the allegedly specific training effect may be accounted for by this factor in initial level.

Whether or not the results of Plohmann’s et al study are reliable has clinical and ethical implications. Multiple sclerosis is one of the most common neurological diseases, and I have the suspicion that no other neurological disease has given rise to a comparable number of scientifically unfounded therapies and advice. The above critique raises the question whether computer assisted retraining of attention is one of them. It may be relatively harmless in that it has no organic side effects. None the less, if its efficacy cannot be proved, it would be a waste of money, time, and patients’ hopes.

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Plohmann and Kappos reply:
We thank Goldenberg for his interest in our paper. After having been actively involved in planning and conducting controlled trials in multiple sclerosis in the past 15 years, we can only agree that it is a risk of drawing wrong conclusions from unreliable data cannot be overstressed in this area. All the same we cannot follow Goldenberg’s reasoning. His critique is probably based on his own unpublished observations but is neither supported by the available literature nor by our own data.

His main critique is that the effect described in our paper may only reflect non-specific practice effects. These effects are dependent on the interval between test presentations and the population studied, and differ from test to test according to their respective stability and reliability. In our study we assessed patients with multiple sclerosis in a stable or eventually slightly progressive phase of their disease. For cognitively impaired patients with multiple sclerosis it has been shown in longitudinal studies that they lack practice effects compared to cognitively intact patients. In our data a possible but in no way significant practice effect was found between the first (T1) and second (T2) baseline measurements and improvement and—this is not the case with two exceptions (“divided attention” and “flexibility”)—not at all between T2 and T3. Clearly significant improvement of performance could only be seen between all three baseline measurements and T4 (Friedman two way analysis of variance, Wilcoxon signed ranks test). Also the assumption that the median might be lower than the third measurement and therefore might not be an adequate starting point for statistical comparisons is not supported by our data. In most of the control tests the median is equivalent to T3 or even larger.

Goldenberg’s second point is that the initial level of performance has a systematic influence on improvement independently of any therapy. Furthermore, on the basis of his results concerning the PASAT, he assumes a negative correlation between initial performance and improvement. As our patients had received specific training in those two functions that were severely impaired and thus started from a lower level of performance, Goldenberg claims that the specific training effects may be accounted for by differences in initial level of impairment. For this reason we reanalysed our data. For each training group we built subgroups of patients according to their initial capability (low, medium, high) and printed the course of performance during the baseline measurement (T1-T3). Our results do not confirm Goldenberg’s assumption that initial level of performance has a systematic or inverse influence on improvement.

Nevertheless, as already stated in our original paper, due to the small sample size of our study the results do not allow a definite assessment of the training and its effects in patients with multiple sclerosis; but they provide enough evidence to encourage further studies in a larger population of patients. Thus, we have started a prospective multicentre study in comparison with three Swiss neurological rehabilitation centres to further assess and possibly improve this kind computer assisted retraining of attentional functions.

The unpublished additional data mentioned in our letter have been submitted with this letter and are available on request (tables 1a-1c, figures 1 and 2).

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Neurology and the gastrointestinal system

Neurology and the gastrointestinal system,1 or an analysis of the “brain-gut” axis would be incomplete without allusion to the neuroendocrine system, and its mediation, via somatostatin, in the regulation of splanchic blood flow and gastric acid secretion.2 3 These actions could account for the established haemostatic action of somatostatin in oesophageal varical bleeding,4 and for the perception, derived from meta-analysis, that similar benefits might occur in non-varical upper gastrointestinal haemorrhage.5 On the basis of the involvement of somatostatin in the regulation of gastric blood flow and acid secretion, it also seems reasonable to attribute gastric erosive bleeding, so-called Cushing’s ulcers, which occur in CNS disorders,6 to derangements in neuroendocrine pathways.

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Combining their unique and authoritative experience, the authors present a comprehensive and up-to-date evaluation of multiple sclerosis and the associated demyelinating diseases, a benchmark account against which current and future efforts must be measured.

How to move on, to provide anything remotely resembling a useful review of the remaining 25 chapters? Several merit particular attention. "Prion diseases" (DeArmond and Prusiner) and "tumours of the nervous system" (Lantos, Vanden Berg, and Kleihard) are both new to Greenfield's book. Both represent topics whose biology and pathology have changed at a breathtaking pace over the past five years, a sure challenge to any textbook harbouring ambitions of definitiveness. Typically, both rise to the call with apparent ease. The chapter on prion disease is only 35 pages long, but this is nevertheless a comprehensive and fine account of an extraordinary area of the human neurology and neuropathology. There are excellent descriptions not only of conventional demyelinating prionopathies, but also of rarer, more recently recognised entities such as fatal familial insulinaemia. The important reversals and molecular dissection of the disease are amply covered, and space is even found for speculation concerning the possible involvement of prions, in yet another evasive and tantalising disease, inclusion body myositis.

The tumour chapter—an all embracing 200 pages with more than 3000 references (I lost count)—is again quite masterly. The bread and butter tumours are capably described, and there are instructive and useful accounts of other important areas—familial tumours, metastatic disease, etc. Again, the narrative is as contemporary as a large text can be, and more up to date than most, with succinct descriptions of the NF1 siblings neurofibromin and merlin, and of their biology, as far as is known. Surprisingly, in this genre chapter, paraneoplasia is perhaps a little brief.

It would be unforgivable also to omit mention of the chapter on peripheral neuropathy (Thomas, Landon, and King). Just 100 pages long, this yet again is a joy to read. The first fifth is devoted exclusively to a description of the normal peripheral nerve, an outstanding account. The whole chapter is (predictably) beautifully illustrated, with authority spread deep and thick and even across the whole landscape of peripheral nerve disease, from new immunological concepts in relation to inflammatory neuropathies, to the molecular genetic advances in inherited nerve disease. So, it is not easy to criticise. I managed to amass a perfectly miserable haul of just one typo (though quite a howler—"BACH for BALO" in a bold, italicised, large font header). The editing is lightly but highly effectively achieving biological coherence are very few outright omissions. I could find no account of Hashimoto's encephalopathy, which is a shame; I suspect many years of further use might fail to add appreciably to this one omission.

This is such a good book. Do buy one. It is well worth the investment, and will stand by you and repay you all the days of your working life.
neurovascular clinic and stroke unit, how to overcome resistance to change, how to participate in or set up large multicentre trials etc. Whether you read this book will largely depend on your point of view.

LIZ WARBURTON


In choosing the title for this book, the editors have wisely avoided the use of the term “neuropsychiatry”, which in Britain, at least, implies a primarily psychiatric audience. I think that this book should be read by a much wider audience, including neurologists interested in behaviour and cognition. There are relatively few books available that bridge this important divide. The editors have assembled an impressive international cast who cover most of the hot topics at the interface of neurology and psychiatry.

The first section is dedicated to the frontal lobes with contributions from neuropsychology and frontal lobe abnormalities on structural scanning in schizophrenia. The second section deals with basal ganglia disorders with excellent overviews of neuropsychological findings and behavioural psychopharmacology. The third section is dedicated to memory and its disorders, with extremely readable overviews of advances and controversies in the neuropsychology of memory and clinical disorders. The fourth section deals with psychiatric manifestations of patients with a known brain pathology and structural imaging in the psychoses. Stricter editorial intervention could have avoided some redundancy and overlap with an earlier chapter. Section five covers for what is for many people the central ground of neuropsychiatry—namely, epilepsy—with excellent accounts of the behavioural and psychiatric changes seen in the context of chronic epilepsy. The sixth section takes a developmental perspective, particularly related to schizophrenia, and the final two chapters of the book deal with advances in brain imaging, namely magnetic resonance spectroscopy and imaging of patients with hallucinations.

The editors have deliberately decided not to write a comprehensive textbook, but rather to choose areas of advance and controversy, and in doing so have produced a very readable text. The book is in many ways a celebration of the immense contributions of Professor Alwyn Lishman to the study of the brain and mind. I can thoroughly recommend it to everyone working in this exciting area.

JOHN HODGES