Facial diplegia with par aesthesias: 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 approximately 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 par aesthesias, and he defined them as having a rare variant form of GBS due to shared clinical, electrophysiological, and CSF features. The anatomy 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 par aesthesias, 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 paraphaesthesia in her fingers and toes. Nine days after the onset of her neurological symptoms, 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, particularly on the left.

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 paraphaesthesia. 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, syphils, infectious mononucleosis, herpes simplex virus, diabetes mellitus, and connective tissue disease) were all negative. On day 12, the CSF examination detected mild increases 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 f reponses were normal on day 18. Auditory brainstem responses were normal. On Day 18, 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 intracanalicular 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 par aesthesias, 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 paraphaesthesias”, 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. Fulbright 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. Rama rsey 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 paraphaesthesias”. 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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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, 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 reported 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 has been 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 lower 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 legs showed normal cell count, normal protein content, increased CNS synthesis of IgG, and positive oligoclonal bands. In MRI studies of the spinal cord, no abnormality was observed and the MRI was not performed. Transcranial magnetic stimulation showed a slightly prolonged central conduction time of motor evoked potentials recorded over the left abductor hallucis muscle. Otherwise, multimodality evoked potentials were normal. A myelitis due to multiple sclerosis accompanied by a symptomatic unilateral restless legs syndrome was diagnosed. The patient was treated with 500 mg prednisolone intravenously over 5 days without any clinical effect. However, a single dose of 100 mg levodopa plus benzerazide 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 had shown 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
evening, 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 dysarthrophonia and atrophic paralyses of the left sternomastoid and the left biceps 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 levedopa 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 sensation of restlessness in both legs located in the feet and calves. The restlessness occurred when sitting and lying for more than 20 minutes. It was pronounced at night and improved when he was walking around. The patient had started simultaneously with the motor and sensory disturbances due to the cervical spondylopathy myelopathy and did not improve postoperatively. On examination, the patient was mildly impaired in carrying out motor tasks and his gait was moderately spastic. He had reduced touch and vibration senses in both upper limbs. A restless legs syndrome due to a cervical spondylopathy myelopathy was diagnosed. Treatment with pergolide resulted in an excellent control of the restless legs syndrome.

Our patients meet the criteria for the diagnosis of restless legs syndrome. Over a follow up period of at least 6 months, restless legs syndrome symptoms were sufficiently relieved by dopaminergic treatment. The association of myelopathy and restless legs syndrome may be merely coincidental. However, the close temporal relation between the onset of myelopathy and restless legs syndrome strongly suggests that restless legs syndrome was secondary to the spinal cord lesion.

The pathogenesis of restless legs syndrome and periodic leg movements is still speculative. In patients with myelopathy and periodic leg movements, it is hypothesised that a spinal cord lesion may permit the expression of spinal periodic leg movements generator by interruptingdescending inhibitory spinal pathways. Our finding of restless legs syndrome in three patients with myelopathy provides evidence that disinhibition of spinal pathways may also be involved in its pathogenesis.

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 neurologists and haematologists, who considered that the prognosis was poor.

The first case was a 49 year old woman with a longstanding diagnosis of schizophrenia 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.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (y)</th>
<th>Sex</th>
<th>Platelet count (x10^7/L)</th>
<th>Peripheral blood film</th>
<th>Clotting screen+fibrogen</th>
<th>Bilirubin (µmol/L)</th>
<th>Lactate dehydrogenase (U/L)</th>
<th>Creatinine (µmol/L)</th>
<th>Glasgow coma score</th>
<th>Neurological findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>49</td>
<td>F</td>
<td>19</td>
<td>Normal</td>
<td>67</td>
<td>931</td>
<td>3/15</td>
<td>121</td>
<td>15</td>
<td>Pupils equal and reactive, corneal reflexes intact</td>
</tr>
<tr>
<td>Patient 2</td>
<td>58</td>
<td>M</td>
<td>17</td>
<td>RBC fragments ++</td>
<td>Normal</td>
<td>49</td>
<td>3/15</td>
<td>131</td>
<td>3/15</td>
<td>RBC fragments ++</td>
</tr>
</tbody>
</table>

In conclusion, our report suggests that restless legs syndrome may occur secondary to spinal cord lesions due to different causative diseases including multiple sclerosis, spinal 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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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 of TTP.
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 cerebral 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,1 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.2 These clinical features are often fleeting and fluctuating and several important points regarding interpretation should be made. Firstly, brain CT may be normal or may show multiple hypodense areas indicative of generalised cerebral oedema.3 Secondly, brain MRI may also be normal, although it is likely to show marked enhancement on T2 weighted images.4 Coma has been shown to be a bad prognostic indicator. Of importance is the finding that despite the presence of substantial neurological function, normal findings on brain CT strongly suggest the potential for full clinical recovery.5 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.6 Fresh frozen plasma is the usual replacement fluid, although it remains to be determined whether cryoprecipitate or solvent/detergent fresh frozen plasma is more effective. These plasmas lack von Willebrand factor, and since ultrafiltration von Willebrand factor multimers have been demonstrated in TTP, it is postulated that additional factor exacerbates the disease. Platelet transfusions should be avoided (unless there is life threatening bleeding) as they may worsen the condition. These two cases illustrate that patients with TTP may present to the intensive care unit with profound coma, such that many clinicians would consider the prognosis so poor that further active management would be inappropriate. In addition, the cases show that patients can survive and even make a full recovery despite a delay in diagnosis and appropriate treatment.

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

Courses of intravenous methyl prednisolone are a routine part of management 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.1 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 was found 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. 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 was given in May 1994 and 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 1994 and February 1996 he had a further four uneventful 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, and began wheezing auditorily. Inhalation of nebulised salbutamol was ineffect- tive. 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.1,2 One of these reactions occurred in the course of treatment for multiple sclerosis. The allergic reactions are more likely to be to the carrier than 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 unknown, although several mechanisms are postulated. There is evidence that, among its many effects on the immune system, interferon β can increase intercellulin-2, and that intercellulin-2 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 is more likely to suppress both Th1 (found in delayed type hypersensitivity reactions) and Th2 responses.3 It remains uncertain whether the sequence of events here is due to an effect of interferon β-1b or to coinci- dence. 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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Poststreptococcal neutropoerythropy

Streptococcal infection can lead to a wide range of sequelae. Peripheral nervous system injury is not well known as one of its possible complications. We report a case with a typical history for a poststreptococcal vasculitis causing an axonal neuropathy of the right common peroneal nerve.
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 stamping 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 had also been developing a low grade fever and night sweats which persisted as the numbness developed. There was no history of trauma or compression of the 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. A nasopharyngeal swab was negative for group A betahemolytic streptococci. Antistreptolysin-O titre (ASOT) of 1600 was followed by azathioprine and prednisolone. The decline in her ASOT and rate of fibrin in the walls of some superficial dermal vessels consistent with a vasculitis. A 3 day course of intravenous methylprednisolone was followed by azathioprine and prednisolone. The decline in her ASOT and rate of fibrin in the walls of some superficial dermal vessels consistent with a vasculitis. It is unlikely that the streptococcal infection has unmasked a connective tissue disorder due to the negative autoimmune screen apart from the atypical perineuritis in the right sural nerve. There were no casts on urine microscopy. There was no evidence of arthritis or pericarditis. The only abnormality apart from the atypical perineuritis in the right sural nerve was a fibrous tissue deposit in the walls of some superficial dermal vessels consistent with a vasculitis.

Sensory examination was normal to all modalities. There was no upper limb ataxia. There was no upper limb ataxia. There was no upper limb ataxia.

We read with interest the short report on sensory loss in lateral medullary infarction by Vuadens and Bougossavskiy.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.1,2 We recently encountered a patient with sensory loss of the spinohalamic 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 hemiscal lesion and is false localisation.

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 drainage 4 weeks previously. He has 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 nausia 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 counter-clockwise rotatory nystagmus in the primary position. The eye movements were normal. Corneal reflex was intact, as was sensation to light touch to the upper and lower face. The other cranial nerves were normal. The gag reflex was brisk. There was no cranial bruit, Töle, power, and reflexes were normal.

Sensory examination was normal for 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 following: Table: Nerve conduction study results confirming a mainly axonal neuropathy of the right common peroneal nerve

<table>
<thead>
<tr>
<th>Nerve</th>
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<th>Terminal latency</th>
<th>Conduction velocity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right tibial</td>
<td>3.2 mV</td>
<td>4.9 ms</td>
<td>41.0 m/s</td>
</tr>
<tr>
<td>Ankle</td>
<td>6.0 mV</td>
<td>5.3 ms</td>
<td>42.0 m/s</td>
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<tr>
<td>Behind knee</td>
<td>3.4 mV</td>
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CMAP = Compound muscle action potential.

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

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<td>4.6 ms</td>
<td>49.3 m/s</td>
</tr>
<tr>
<td>Ankle</td>
<td>6.0 mV</td>
<td>4.9 ms</td>
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<tr>
<td>Behind knee</td>
<td>3.4 mV</td>
<td>5.3 ms</td>
<td>44.0 m/s</td>
</tr>
</tbody>
</table>

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


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 or more. Early deaths are usually attributable to the underlying cause of epilepsy and mortality in chronic cases is commonly due to the epilepsy itself. 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.

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). Figures derived from community based prospective studies indicate numbers of up to 1:1100. 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.

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
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 departments involved in patient care.

In a recent report, Auer et al described the clinical and imaging findings in 19 cases of extracranial vertebral artery dissection retrospectively. 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 report 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 local circumstances, but treatment centres and purchasers may find them a useful tool in assessing and developing their services.

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Record of explanation given to patients and relatives after the diagnosis and referral for counselling or palliative care services. Figures are numbers (percentages of patients)

<table>
<thead>
<tr>
<th>Service</th>
<th>Centre A w=30 (%)</th>
<th>Centre B w=30 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis explained to patient</td>
<td>8 (27)</td>
<td>6 (20)</td>
</tr>
<tr>
<td>Prognosis explained to patient</td>
<td>17 (57)</td>
<td>3 (10)</td>
</tr>
<tr>
<td>Prognosis explained to relative</td>
<td>15 (50)</td>
<td>8 (27)</td>
</tr>
<tr>
<td>Referral to counselling or palliative care service</td>
<td>12 (40)</td>
<td>2 (7)</td>
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</tbody>
</table>


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. The authors described the “sensitivity” and “specificity” of digital subtraction angiography (DSA), magnetic resonance imaging angiography (MRA), and duplex sonography for diagnosing extracranial vertebral artery dissection. 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 MRA (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, MRA, and duplex sonography cannot be compared directly, as neither one is “gold standard” diagnostic method was 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 trauma 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.


Auer and Felber reply:
Cheung et al state in their comment, that dissections of the 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 non-specific. Non-invasive diagnostic methods are likely to be performed earlier in these patients and this was our motivation to report on the neuroradiological features 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 there is 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 compared 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.


Clinical usefulness of MRI in multisystem atrophy

Schrag et al suggest that certain putaminal and infarctional changes on MRI are useful in distinguishing between patients with multisystem atrophy (MSA) and patients with idiopathic Parkinson’s disease. 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. Furthermore, 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 a 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 at postmortem). 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 for 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 most movement disorder clinics. 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 for MSA 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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Schrags and Quinn reply:
Counsell and Hughes raise several potential drawbacks to our study that we willingly acknowledge. Firstly, that the number of 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 >10:1. 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 (a condition with similar infratentorial abnormalities) have been added to this study. 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,1 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 a pathological one.

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 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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A dubious therapy for patients with multiple sclerosis

Plöhmann et al investigated the effects of computer training of attentional deficits in...
patients with multiple sclerosis. They conclude that “significant improvements of performance could almost exclusively be achieved by the specific training programmes”. 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 that is, a rate of change without any therapy. The critical value is therefore the mean (or median) of the baseline measures but the difference between them. If therapy is efficient, the difference between pretraining and post-training measurement should be greater than that between two consecutive baseline measurements. This crucial comparison is not presented.

The selection of the median of the three baseline measurements as starting point for calculation of improvements during the first training period poses further problems. If there was any improvement from the first to the third measurement, the median is lower than the third measurement after which training began. This difference inflects apparent improvement in the first training period. It may signify 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, Göttler, Goldenberg, unpublished data) have administered the PASAT,2 another test of attentional capacities, four times with weekly intervals to 30 patients with chronic brain damage from different aetologies. 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 improvements in initial level.

Whether or not the results of Plohmann 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. The above critique raises the possibility that at least computer assisted rettaining 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 the 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 which 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.2 In our data a possible but in no way significant practice effect was found between the first (T1) and second (T2) baseline measurement and—without 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 measurements (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 letter, 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 retaining 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 activity of somatostatin in oesophageal variceal bleeding,4 and for the perception, derived from meta-analysis, that similar benefits might occur in non-variceal 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 remodelling in neuroendocrine pathways.

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“All we really understand about neurological disease we have learned from pathological studies.”

Self evidently not a perfect truth, but it is a fair approximation, particularly if “understand” is properly weighted. Take multiple sclerosis as a random example. We have been taught a great deal about the course and dynamics of the disease—for example, by new imaging techniques, but MRI has come closest to contributing to our understanding of the disorder when married to pathological studies, or when used as a surrogate marker of pathology. The huge power of the new genetics has now set its sights on multiple sclerosis, and although proceeding apace and well in to the genome screen approach, it too has yet to contribute major insights to our understanding of multiple sclerosis. Animal models, even the aged EAE, can only offer suggestions which live or die according to correlative studies of multiple sclerosis tissue or patients. And my own area of interest, the cell biology of oligodendrocytes studied—by cell culture, is no better or worse than these other tools: it can make suggestions which must be tested by direct examination of tissue—by pathology.

It follows that good neurology must depend on a decent grounding in pathology, and a neurological training which fails to include this emphasis pathology is a poor and incomplete one. Calman’s prescription for postgraduate education presents an opportunity formally to ensure that training schemes do not permit the possibility of such deficiency. So would the sixth edition of Greenfield’s Neuropathology feature on an idealised neurological curricular reading list? It could not fail to.

To continue with the above example, the account of demyelinating disease—and with what better subject to start? Considering Greenfield’s own contributions to the pathology of multiple sclerosis, the most conspicuous at present is his definitive study of axon loss in multiple sclerosis, which surely is one of the finest wheels to be reinvented. This must be as good an account as any available. It is (not withstanding the book’s two volumes and 2200+ pages) not overly long—86 pages, but strikingly well structured, generously (and often beautifully) illustrated with 95 figures, the great majority photomicrographs and many in colour, and closely and carefully argued, with over 500 references. Princes and McDonald have combined and distilled their unique and enormous experience to provide a scholarly, authoritative, and yet wholly readable review 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 dementing prionopathies, but also of rarer, more recently recognised entities such as familial insomnia. The nature of recoveries 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 brain 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 NF siblings neurofibromin and merlin, and of their biology, as far as is known. Surprisingly, in this gene 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 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—BAL for BALO—in a bold, italicised, large font header). The editing is lightly but highly effectively achieved; typographical errors 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.

NEIL J SCOLDING


I was very keen to read this book—mainly because I have heard one of the authors state publicly that stroke patients are being transported by air ambulance to emergency rooms in parts of California and I was wondering whether he would advocate this in print. Sadly the nearest he got was “The message to the public is simple: the goal is to take the patient to the emergency room as fast as possible using emergency medical transportation and transfer the patient to a hospital that has brain imaging tests available on a 24 hour a day 7 day a week basis.” Not quite, but the tenor of the book is described—controversial, not overtly dangerous but rather premature, and, for most parts of the United Kingdom, a work of fiction (at least for the moment).

It is one of those slimline varieties meant for the white coat pocket and is obviously aimed at the emergency room doctor eagerly awaiting an acute stroke patient. “How to move on, to provide anything remotely resembling a useful review of the remaining 25 chapters?” Several merit particular attention. “Prion diseases” (DeArmmond 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 dementing prionopathies, but also of rarer, more recently recognised entities such as familial insomnia. The nature of recoveries 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.

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BOOK REVIEWS
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