LETTERS TO THE EDITOR

Postictal psychosis related regional cerebral hyperperfusion

Postictal psychosis is a known complication of complex partial seizure in particular temporal lobe epilepsy. It usually runs a benign and self-limited course. A postictal phenomenon with focal cerebral hypofunction (similar to Todd’s palsy), rather than ongoing seizure activity, has been postulated. Surface EEG is either normal or showing non-specific slow waves. Antipsychotic medications are prescribed instead of antiepileptic drugs. Until recently, the pathogenic mechanisms have remained unknown. In this communication, we report on two patients with postictal psychosis, during which a cerebral SPECT study showed a hyperperfusion signal over the right temporal lobe and contralateral basal ganglion. As hyperperfusion in ictal cerebral SPECT is closely linked to epileptic activities, our findings support a contrary explanation for postictal psychosis.

Prolonged video-EEG telemetry study was performed in patients who underwent presurgical evaluation for epilepsy surgery. Antiepileptic drugs were withdrawn to facilitate seizure recording. A diagnosis of temporal lobe epilepsy was based on analysis of the electroclinical events and, if applicable, postoperative outcome after anterior temporal lobectomy. Psychosis was diagnosed according to the fourth edition of the diagnostic manual of mental disorders (DSM-IV) criteria of brief psychotic disorders without marked stressor.

Patient 1 was a 34 year old Chinese woman with complex partial seizures since the age of 18. Her seizure control was suboptimal on a combination of antiepileptic drugs. Brain MRI showed a small hippocampus on the right. Interictal EEG showed bilateral temporal sharp waves and ictal recordings confirmed a right temporal epileptogenic focus. A Wada test confirmed right hippocampal memory dysfunction. Six hours after her last secondary generalised tonic-clonic seizure after video-EEG telemetry, she began to develop emotional lability, talking nonsense, motor restlessness, and auditory hallucination. A cerebral SPECT study was performed 4 days after her last seizure. Her psychotic features persisted although she was taking antipsychotic medication (pimozide). Cerebral SPECT showed a clear hyperperfusion signal over the right lateral temporal neocortex and contralateral basal ganglion. An interictal cerebral SPECT study was repeated at 4 weeks after postictal psychosis which showed a complete resolution of hyperperfusion signal in the right temporal lobe and basal ganglia. Anterior temporal lobectomy was performed and she became seizure free after surgery.

Patient 2 was a 44 year old man with intractable complex partial seizures since the age of 30. His seizures were intractable to multiple antiepileptic drugs. Brain MRI showed left hippocampal sclerosis. Interictal cerebral SPECT showed a relative hyperperfusion area over the left hemisphere. Interictal surface EEG was non-lateralising but ictal EEG disclosed a right hemispheric onset. On withdrawal of antiepileptic drugs, seven complex partial seizures with secondary generalised tonic clonic seizures were recorded within a period of 72 hours. His usual antiepileptic drugs were then restarted. Thirty hours after his last secondary generalised tonic-clonic seizure, he began to develop emotional lability, talking nonsense, restlessness, auditory hallucination, persecutory delusion, and delusion of superstition. Cerebral SPECT study, performed 2 days later while his psychotic features persisted, showed two relative hyperperfused areas over the right temporal neocortex and contralateral basal ganglion in addition to the original hyperperfused area over the left hemisphere. An antipsychotic agent (thioridazine) was
started after the cerebral SPECT. His psychotic symptoms resolved 2 weeks later with full recovery.

Cerebral SPECT performed during the interictal period (IP) and during postictal psychosis (PP) were analysed visually and areas of hypoperfusion were identified. Quantitative data at regions of interest (ROIs) were measured on coronal and axial slices containing basal ganglia (BG), mesial (MT), and lateral (LT) temporal lobe structures. Asymmetry index (ASI) was calculated as \((\text{ROI} \text{~focus} - \text{ROI} \text{~contralateral}) / \text{ROI} \text{~focus} \times \text{ROI} \text{~contralateral}\)\times 200%. We set an arbitrary change of ASI >100% to be significant. As there were only two patients, statistical testing was not performed.

Both patients showed postictal psychosis and had a regional increase in rCBF over the right temporal neocortex and the left basal ganglia compared to their interictal study (figure). Quantitative analysis for patient 1 showed changes of ASI during IP and PP over right MT was +75% (-6.4647 to -1.6528); over the right LT was +116.7% (1.07927 to 12.55764); and over the left BG was +206.8% (-2.07373 to 2.21574). Quantitative analysis for patient 2 showed changes of ASI during IP and PP over right MT was +78.6% (13.14217 to 12.64158); and over left BG was +155.9% (-5.85556 to 3.27522).

Postictal psychosis is a distinct clinical event associated with temporal lobe epilepsy. The diagnosis of postictal psychosis requires a close temporal relation between bouts of complex partial seizures and the onset of psychosis. The psychosis usually develops after a cluster of seizures, with or without auras. The clinical course of postictal psychosis is usually benign and unpredictable.1 In our patients, the duration of psychiatric disturbances lasted from 4 to 10 days, which is in keeping with the good prognosis. Antipsychotic drugs, such as haloperidol and fluphenazine are usually prescribed.1

The underlying mechanism of postictal psychosis is unknown. Postictal cerebral hypofunction has been postulated as an analogue to Todd’s paralysis after seizure.1,2 However, the presence of increased rCBF during postictal psychosis, may suggest an alternative explanation as ictal SPECT has been shown to be highly sensitive and specific in demonstrating seizure foci.3

To conclude, our results are contradictory to the hypothesis of a cause of psychosis in postictal psychosis. We think that the hyperperfusion areas are responsible for the postictal psychosis. Further serial studies with cerebral SPECT or PET may enhance our understanding on the mechanism of postictal psychosis.


Oncofetal matrix glycoproteins in cerebral arteriovenous malformations and neighbouring vessels

Cerebral arteriovenous malformations (AVMs) are thought to be congenital lesions exhibiting features of either mature vascular walls or embryonal anastomotic plexes. It is generally assumed that changes in size are dependent on enlargement of the venous compartment, organisation in the setting of microhaemorrhages, and glissosis. However, recent findings are consistent with the hypothesis of ongoing angiogenesis.2

Previous research from this laboratory disclosed that peculiar isoforms of fibronectin (FN) and tenascin (TN) typically occur in fetal and neoplastic tissues.5 These isoforms are a blend of structurally different glycoproteins that result from alternative splicing of the primary transcript and are mainly expressed in the extracellular matrix. Their expression is undetectable in normal adult tissues, with the exception of the vessels in the regenerating endometrium. To gain further insight into the pathobiology of the AVMs the present report sought to ascertain whether these lesions also express oncofetal FN and TN isoforms.

Tissue samples were obtained after neurosurgical excisions of ruptured AVMs. All 10 patients had experienced an intracerebral haemorrhage as the first clinical manifestation of their disease. There was no drug history before bleeding. Control specimens from two right gyrri recti and one cerebellar tonsil were obtained, respectively, from operations for ruptured aneurysms of the anterior communicating artery or for Arnold Chiari disease.

Immunochemical evaluations were performed on 5 μm thick cryostat sections using a protocol reported previously.6 Owing to the limited amount of available material, only in a few cases was some fresh tissue retained to allow western blots. Distribution of FN and TN isoforms was investigated using three monoclonal antibodies (mAbs) or two Ab fragments, obtained by a phage display technology, respectively. These Abs, prepared in our laboratory, were found to work on fresh frozen material. According to the previous characterisations the BC-1 mAb and the TN-11 Ab fragments are specific for isoforms occurring almost exclusively in fetal tissues and in tumours, with the recognised TN isoform being typically associated with anaplastic gliomas (table). The antibodies were blocked using the specific antigens. The antibodies were VII the recombinant protein containing the epitope produced in E Coli. For the mAb BC-1 we used the recombinant protein containing the type-III repeat 7B–8–9. For the Ab IST-4 we used the recombinant protein containing the type-III repeat 2–8.

For the recombinant antibodies TN-11 and TN-12 the recombinant type-III repeat C and the recombinant fragment containing the BG-III repeat were used in the control specimens.4 All 10 AVMs were found to contain large amounts of FN and TN, as shown by intense immunostaining with the use of the IST-9 / IST-4 mAbs and the TN-12 Ab fragment. The staining was localised either in the endothelium or the subendothelial layer. A positive response was found in several artery-like vessels and in a few vessels with thinner walls. Using the mAb BC-1, staining was present in the TN-11 Ab fragment showed occurrence of type III repeat C TN isoform in the inner layers of the vascular components of the nidus, irrespective of their morphology.

Six out of the 10 examined specimens were found to contain portions of cerebral tissue surrounding the angiomatous nidi. In all these cases the wall of several vessels exhibited intense staining with the use of the TN-11 Ab fragment. Using the BC-1 mAb we used the recombinant protein containing the ED-B sequence (ED-B-FN), and the type III repeat C TN isoform were absent.

The TN-11 Ab fragment showed occurrence of type III repeat C TN isoform in the inner layers of the vascular components of the nidus, irrespective of their morphology.
angiogenesis in and around these lesions. Further support to the hypothesis of ongoing angiogenesis in normal brain. This evidence provides possible requirement of angiogenesis in AVMs and in vessels of adjacent cerebral tissue. Similarly, the type III repeat C TN isoform, recognised by the Ab fragment TN-11, was found to occur in the vascular walls of anaplastic gliomas. Northern blot analysis showed that the mRNA isoform was undetectable in normal tissues and some malignancies, but was present in large amounts in fetal tissues, including brain, and in glioblastomas.

Recent advances in the pathology of cerebral AVMs suggest that these lesions might not be static. Tyrosine kinase, an endothelial cell-specific receptor tyrosine kinase, is present in the wall of vessels of the cerebral tissue adjacent to the angiomatous nidus. Bar=10 µm. The present findings indicate that a specific response to haemodynamic stress in AVMs might result from maintenance of pro-angiogenic features in AVMs without specific relation to individual vessels. The distribution of this isoform was found to be highly restricted in normal adult tissues. By contrast, ED-B+ FN isoform exhibited widespread distribution in the vasculature of fetal tissues, including brain, and of several types of malignancies. It was therefore regarded as a marker of angiogenesis.

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Furthermore, use of the cell proliferation marker MIB-1 showed endothelial proliferation in arterioles, venules, and capillaries of the cerebral tissue neighboring AVMs.

The present findings indicate that a particular FN isoform, mainly expressed by the vasculature of fetal and tumorous tissues, as well as a TN isoform typically detected in the walls of vessels in anaplastic gliomas, also occur in AVMs and in vessels of adjacent cerebral tissue, but that both isoforms are absent in normal brain. This evidence provides further support to the hypothesis of ongoing angiogenesis in and around these lesions.

Hashimoto’s encephalopathy presenting as “myxoedematous madness”

The neuropsychiatric sequelae of hypothyroidism range from lethargy and mental slowing to the florid psychotic illness referred to as “myxoedematous madness”. The last condition is characterised by frank hypothyroidism accompanied by psychosis, and may respond completely to thyroxine. More recently described is a syndrome of subacute encephalopathy, associated with high titres of thyroid autoantibodies, raised CSF protein, EEG abnormalities, and perfusion deficits in the presence of normal structural neuroimaging. In most cases, the encephalopathy occurs without any gross change in circulating concentrations of thyroid hormones, suggesting that an inflammatory process is responsible for the cerebral dysfunction. In the absence of pathological data, the evidence for a specific pathogenetic mechanism is largely circumstantial: a small vessel vasculitis and immune complex deposition have both been suggested. Although none of the published cases of Hashimoto’s encephalopathy has described psychosis as a primary feature, it is possible that “myxoedematous madness”, a condition first described in detail by Asher in 1949, lies in a range of encephalopathic phenomena mediated by autoimmune mechanisms. This suggestion would certainly be consistent with the range of clinical presentations of other autoimmune cerebral vasculitides. As autoimmune thyroiditis is the commonest cause of hypofunction failure in this country, it is likely that cases have been present in at least some of Asher’s original 14 cases. Although most had florid myxoedematous features at psychiatric presentation, this may simply reflect the fact of diagnosing subclinical thyroid disease before rapid laboratory assays became widely available. Many features of the present case, however, favoured an endocrine rather than an inflammatory mechanism, suggesting that the condition of “myxoedematous madness”, though rare, remains a valid diagnostic entity.

A 63 year old market stallholder without medical or psychiatric history was brought to a local psychiatric hospital by police. His business had been in decline for several months, and his family had noticed uncharacteristic emotional liability. In the weeks preceding admission he had experienced delusions and hallucinations, and exhibited uncharacteristic behaviour. He had reported a vision of the crucifixion, and hearing the voice of his dead mother. He claimed that his house was occupied by the devil, drove around aimlessly in his car, and appeared constantly fearful and withdrawn. On the day of admission he had made a bonfire in the garden and burned his wife’s clothes, family photographs, furniture, and business papers. When his wife and son tried to intervene he
became aggressive and threatened them with a saw. The general practitioner was called and suspected an acute psychosis, and a saw was found in the patient's pocket. He denied depression, but displayed no insight into the irregularity of his behaviour. No psychotic features were seen, although during the admission he consistently rationalised all reported psychotic phenomena. He was aggressive towards staff and made repeated attempts to abscond. General physical examination was unremarkable. Neurological examination was normal except for spoken language, which was fluent and grammatical, but contained word finding pauses, circumlocutions, and occasional semantic errors (for example, “I just want to get my feet back on the table”). Formal neuropsychological testing, and a screen of laboratory tests for reversible causes of encephalopathy, were performed on admission, and results are presented below (column A). Attention is drawn to his mild naming deficit, and poor persistence of the follow up SPECT differed minimally, if at all, from the first examination. In summary, therefore, this patient presented in clear consciousness with a first episode of acute psychosis, and evidence of subtle executive and linguistic neurological deterioration in the aetiology of Hashimoto's encephalopathy: a steroid responsive disorder associated with high anti-thyroid antibody titres: report of 5 cases. N Engl J Med 1999;14:228–33.


### Alien hand sign in Creutzfeldt-Jakob disease

The clinical picture of Creutzfeldt-Jakob disease (CJD) includes various movement disorders such as myoclonus, parkinsonism, hemiballism, and dystonia. We report on a patient with CJD who manifested the alien hand sign. We suggest that CJD should be included in the differential diagnosis of diseases which present with an alien hand.

Creutzfeldt-Jakob disease, one of the human prion diseases, is characterised by rapidly progressive memory and motor deterioration.1 Involuntary movements occur in above 90% of the patients in the course of the disease, the most common being myoclonus.1 Other movement disorders range from tremor to hemiballism and dystonia, and hemiballism.1 We report on a patient with CJD who presented with an alien hand.

Alien hand is a rare and striking phenomenon defined as “a patient’s failure to recognise the action of one of his hands as his own”.2,3 One of the patient’s hands acts as a stranger to the body and is unconscious. Thus, there is loss of feeling of ownership but not loss of sensation in the affected hand. Originally described in callosal tumours,4 the aetiology of alien hand also includes surgical callosotomy,5 infarction of the medial frontal cortex, occipitotemporal lobe, and haemorrhage,6 and corticobasal degeneration.6–7

A 70 year old, right handed Jewish man born in Argentina, living in Israel for the past 20 years, was admitted to the Neurology Department. Until a month before admission, he was apparently healthy and helped in the accounting office of the village where he lived. His neurological illness had presented insidiously during the past month with lassitude of gait and fine tiredness. He also manifested behavioural changes, became aggressive, and had visual hallucinations, perceiving insects and mice moving through his visual field. Often, he expressed his fear from seeing that the “ceiling was
The literature seems to describe distinct forms of alien hand. All share the occurrence of involuntary movements contrary to the patient’s stated intent, but the types of movement differ. In the callosal form, there are purposeful movements of the non-dominant hand. In the fronto-occipital form, there is grasping and utilisation behaviour of the dominant hand. In the corticobasal degeneration, there are aimless movements of either hand. When a consequence of parasomnia or vascular pathology, alien hands can perform complex acts such as trying to tear clothes or undoing buttons. The description by MacGowan et al. has characteristics of the callosal form (especially in patient 2). However, our case suggests that the alien hand sign in CJD may appear in a different type, performing less complex movements which resemble those reported by Riley et al. in corticobasal degeneration. These authors described the alien limb as “involuntarily rising and touching the mouth and eyes” (patient 1). The patient thought that she “was powerless to stop this movement” and when directed to stop responded, “I don’t want to”. Another patient’s left arm was at times “elevated in front of him”, while he was “unaware of this situation until his attention was called to it” (patient 10). Another related phenomenon coined as “arm levitation” was reported in progressive supranuclear palsy. In these patients the arm involuntarily raised and performed semi-purposeful movements.

One common denominator between CJD, corticobasal degeneration, and progressive multifocal leukoencephalopathy, in which an alien hand sign has also been described, is multifocality. In corticobasal degeneration, it was proposed that more than one site is affected or that a “release” phenomenon occurs accounting for the aetiologic of alien hand. In CJD, bilateral cortical damage to motor areas might be the origin of their subsequent isolation and disconnection. We suggest that CJD should be added to the differential diagnosis of diseases presenting with an alien hand with or without myoclonus.

We are indebted to Professor Eran Zarei, Department of Physiology, University of California, Los Angeles, USA.

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Recurrent peripheral neuropathy in a girl with celiac disease

The involvement of the peripheral nervous system (PNS) in children with celiac disease is particularly rare. Furthermore, in both children and adults with celiac disease, neurological complications are chronic and progressive.

We report on a 12 year old girl affected by celiac disease, who on two separate occasions presented with an acute peripheral neurological syndrome after accidental reintroduction of gluten in her diet.

This patient was born uneventfully to healthy, non-consanguineous parents with no family history of neurological or metabolic diseases. At the age of 6 months she was diagnosed as having celiac disease according to the European Society of Paediatric Gastroenterology and Nutrition criteria. Since then she was on a strict gluten free diet and was asymptomatic until the age of 10 years when severe diarrhoea, vomiting, and abdominal pain manifested 6 days after the intake of corn flakes. She thought to be gluten free. No previous infections had been noticed. One week after the onset of these symptoms she experienced acute weakness and pins and needles sensation confined to her legs. At that time her parents stopped her intake of corn flakes on the suspicion that these were responsible for the symptoms. Despite this, symptoms worsened during the next 2 days, confining her to bed.

At hospital admission, she was alert and mentally stable. Results of general physical examination were unremarkable. Neurological examination disclosed symmetric, predominantly distal, weakness of the legs; the knee jerks and ankle reflexes were depressed; plantar reflexes were flexor. Distal stocking glove decreased in pin prick and temperature with sparing of proprioception and light touch. Coordination tests were normal.

Laboratory investigations showed a white cell count of 9300/mm³. The results of the following investigations were within the normal limits: haemogram, erythrocyte sedimentation rate, serum urea, nitrogen, electrolytes, creatinine, glucose, transaminases, bilirubin, immunoglobulins (Igs), lead, iron, copper, urinalysis, urinary porphyrin, folate acid, and vitamins A, B₁₂, B₆, and B₉. Antibody to Campylobacter jejuni, antinuclear antibodies, specific and non-specific organ autoantibodies, IgA and IgG antigliadin antibodies (AGAs), IgA antideaminoacids antibodies (EMAs), and IgA antireticulocyte antibodies (ARA), assayed by enzyme linked immunosorbent assay (ELISA) and immunofluorescence (IF) were also negative. Lumbar puncture was not performed. Anti-bodies against gangliosides GM₁ and GQ₁b, myelin associated glycoprotein and myelin

basic protein were not tested. Nerve conduc-
tions were studied with a predomi-
nately motor demyelinating peripheral neu-
ropathy (table). Her symptoms improved spontane-
ously and she was discharged home after 2 weeks. For 2 years she was asympto-
matic on a gluten free diet.

At the age of 12 she presented acutely with severe abdominal pain 8 days after a weekly intake of bread meant to be gluten free. Two weeks later, due to persisting gastrointestinal symptoms, her parents excluded the bread from her diet. After 2 further weeks, while the abdominal pain was gradually improving, she had a new episode of acute weakness in the lower limbs and sensory abnormalities in-
cluding burning paraesthesiae. On neurologi-
cal examination the legs showed marked diminution in power; absent deep tendon reflexes, and a reduction in pain and temperature; light touch, perception of posi-
tion, and vibration were preserved. Walking was impaired and the patient was bedridden. Otherwise the examination was normal.

A haemogram showed white cell counts of 9700/mm$^3$. Laboratory investigations were within normal values as in the past. IgA and IgG, AGA, EMA, and IgA ARA were negative. Nerve conduction studies confirmed the presence of a predominantly motor demyelinating neu-
ropathy (table). The parents refused consent for a lumbar puncture or nerve biopsy.

Over the next 2 weeks her neurological dis-
sabilities spontaneously improved until full recovery was complete. After 4 weeks, AGA, EMA, and ARA were still negative.

On her most recent admission, 1 year after the onset of her first neurological symptoms, she is still on a strict gluten free diet and has no residual symptoms or signs.

The natural history of celiac disease is well known and the typical celiac enteropathy is often associated with several other disorders. However, as celiac disease is a relatively common and lifelong condition, it is likely that some of these associations may occur by chance.

This patient, who was diagnosed as having frank celiac disease at the age of 6 months, experienced two episodes of acute peripheral neuropathy, at the age of 10 and 12 years, respectively. Two major pieces of evidence strongly support the assumption of a gluten derived disease: (1) the episodes occurred on both occasions when gluten was accidentally reintroduced in the diet; and (2) the response to a gluten free diet was reasonably rapid, occurring within weeks.

The present case, however, differs clinically from those with neurological involvement pre-
viously reported. In the paediatric age group, in fact, neurological complications of celiac disease are rarely encountered and are mostly confined to the CNS; to the best of our knowledge, there are only two previously reported cases of PNS involvement in children with celiac disease. In both cases, however, these were chronic axonal polyneuropathies presenting during a gluten free diet.$^1$

In both episodes in the present case neuro-
physiology was strongly supportive of a demyelinating peripheral neuropathy, which is most commonly attributed to a direct immune mediated attack to the myelin. By contrast, wallerian and axonal degeneration may be caused by vasculitis, and nutritional, metabolic, and toxic factors.

An autoimmune pathogenesis in associ-
ation with strong evidence of a genetic suscep-
tibility has been proposed for celiac disease. Although it is well established that AGA, EMA, and ARA are reliable indicators of sensitisation to gluten at least at the time of diagnosis, in the clinical practice at follow up, during a gluten challenge, pathological values of these antibodies may not be detected.$^2$ In the present case the time course of the disease might be suggestive of an antibody mediated response. However, we could not detect pathological concentrations of AGA, EMA, or ARA antibodies either during the course of the disease or at follow up.

It is known that in celiac disease many immunological perturbations can occur out-
side the gastrointestinal tract. Crossing of the antigens through a damaged small intestinal mucosa, deposition of immune complexes in target organs, a reactivation of immune surveil-
ance, mechanism of molecular mimicry, and activated T cell response may contribute to the pathogenesis of the diseases associated with celiac disease. Direct toxic effects of gliadin and vitamin deficiency are other pos-
sible pathogenic mechanisms of damage to the nervous system. Although we ruled out a vitamin deficiency it is still questionable whether a toxic neuropathy can be the case.

In conclusion, this case shows two major issues: an acute polyneuropathy can be a complication of celiac disease in childhood and its benign course could help in the understanding of the underlying pathogenic mechanisms.

We are grateful to Professor Angela Vincent (Oxford) for her helpful suggestions in reviewing the manuscript.

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examined using a rating scale for the examination of frontal release signs (FRSS), with nine operationally defined items, each on a seven point semi-quantitative scale. The nine reflexes were paratonia and palpmomentum, hand grasp, foot grasp, glabellar, rooting, snout, sucking (tactile) and sucking (visual). Neuropsychological measures included the assessment of frontal lobe function (trailmaking tests A and B, behavioural dyscontrol scale, and the controlled word association test) and generalised cognitive impairment (CAMCOG). Depression was assessed using the Hamilton rating scale for depression, 15 item geriatric depression scale, and diagnostic criteria for DSM IV major depressive disorder. Family history of depression, wish to die, and suicidal ideation within the past year were also recorded, as were blood pressure and a checklist for chronic physical illness.

Table 1. Primitive reflexes in patients with peripheral vascular disease (n=25) and controls (n=25)

<table>
<thead>
<tr>
<th>Reflex</th>
<th>Parkinson</th>
<th>Foot grasp</th>
<th>Glabellar</th>
<th>Palpmomentum</th>
<th>Paratonia</th>
<th>Rooting</th>
<th>Snout</th>
<th>Sucking (tactile)</th>
<th>Sucking (visual)</th>
</tr>
</thead>
<tbody>
<tr>
<td>U</td>
<td>274.0</td>
<td>312.5</td>
<td>199.5</td>
<td>287.5</td>
<td>287.0</td>
<td>235.5</td>
<td>287.5</td>
<td>264.0</td>
<td>287.5</td>
</tr>
<tr>
<td>pValue</td>
<td>0.15</td>
<td>1.0</td>
<td>0.001*</td>
<td>0.15</td>
<td>0.29</td>
<td>0.01*</td>
<td>0.44</td>
<td>0.08</td>
<td>0.30</td>
</tr>
</tbody>
</table>

*Higher mean score in people with peripheral vascular disease.

Small numbers of patients, which may also have obscured other significant findings between the two groups, limit the present study. However, there is some evidence that clinically relevant cerebrovascular disease may accompany peripheral vascular disease and that the frequent disruption of frontal/subcortical brain function may not present with hard neurological signs. As it is possible that silent brain infarction was present in patients with peripheral vascular disease, further studies incorporating brain imaging are required before there can be a clearer understanding of the relation between peripheral and central vascular pathology.

I thank Dr Robert Howard for supervision of this study and Professor and Mr Paul Baskerville for allowing me to interview patients under their care. The study was carried out as part of a University of London MA thesis.

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Factitious clock drawing and constructional apraxia

A 45 year old man presented with a 1 day history of headache, possible seizures, and left sided weakness. On the day of presenta-

tion, the patient's wife had twice found him, inexplicably, on the floor. After the second such episode she brought him to hospital for evaluation. Examination disclosed a complete left hemiplegia and hemianesthesia, although muscle tone was documented to be normal and the plantar responses downgoing bilaterally. Brain CT was normal and routine blood examination was unremarkable. There were no further seizure-like episodes and the patient was transferred to this hospital 10 days later, hemiplegia unchanging, for possible angiography and further investigations.

He was an exsmoker with hypercholesterolaemia and peripheral vascular disease which had been treated by a left femoral angioplasty 5 years earlier. The angioplasty was complicated by the occurrence of a small area thought to be related to dye injection, and phenytoin had been prescribed for a short time thereafter. There was a remote history of heavy alcohol use, but he had been abstinent for several years. His father had had a stroke at the age of 65.

Six months earlier the patient had also collapsed at home and been taken to hospital with a left hemiplegia. Brain CT at that time was normal, as were carotid Doppler studies and an echocardiogram. During that admission to hospital, several generalised seizure-like episodes were seen, some with retained consciousness, and he had again been started on phenytoin therapy. A follow up carotid to brain MRI was normal and it was concluded that the hemiplegia was non-organic in origin. He was described to have made a gradual, near complete, recovery from this first hemiplegic episode and was scheduled for an imminent return to work at the time of his relapse.

On transfer to this hospital the patient was alert, oriented, and cooperative. Although up to date on current affairs and able to describe the investigations performed at the transferring hospital, he scored only 23/30 on a mini mental state examination, with absent three word recall, impaired registration, and poor copying of a two-dimensional line drawing. Further bedside neuropsychological testing showed other findings indicative of constructional apraxia and left hemineglect. Specifically, when asked to draw a clock with the time at 10 minutes to 2 o'clock, all the numbers, and the clockhands, were placed on the right hand side of the clock outline (figure A). Copying of three dimensional line drawings was also significantly impaired (figure B). When asked to point to a left hand to right hand landmark sequence, he missed two out of five. There was also an ataxic gait that was not considered due to the patient's age and condition. The plantar response was flexor bilaterally. Sensory examination showed decreased pinprick and absent light touch, joint position sense, and vibration sense on the entire left side. There was also an impaired perception of a tuning fork's vibration on the left side of the forehead, with a distinct demarcation in the midline. The rest of the physical examination was unremarkable.

Brain CT and MRI, CSF examination, and routine EEG were normal. Routine haematological and metabolic analyses plus erythrocyte sedimentation rate, serum lactate, prothrombin time, partial thromboplastin time, fasting serum glucose, HbA1c, serum Ig survey, and thyroid stimulating hormone were all within normal limits. A hypercoagulability profile was negative. A lipid profile showed mild hyperlipidaemia with increased low
A 53 year old, right handed, black man, presented to the emergency room a few hours after developing an intense headache and left hemisphere symptoms, including left hemiparesis with dense sensory deficits. His blood pressure was 240/160. Neurological examination disclosed left lower facial droop, dysphasia/hemianesthesia. His seizure-like episodes at presentation are presumed to have been non-epileptic in origin (as had been suspected during his previous admission to hospital) although this cannot be definitively proved.

The inability to copy line drawings or to draw a clock is, from a neuropsychologist's perspective, typically associated with parietal lobe dysfunction, usually of the non-dominant hemisphere, especially if associated with left hemispatial neglect. To our knowledge, this is the first reported case of factitious clock drawing and constructional apraxia. Bedside mental status testing also demonstrated the more common simulated deficits of impaired attention and absent three word recall. In retrospect, the severe neglect on clock drawing was perhaps "too good to be true", especially in the light of the near normal line bisection demonstrated on the same day. The mirror image distortion of the house was also very unusual and, furthermore, the mirror reversal itself is evidence of lack of clinical neglect. The distortion of the cube, however, could easily be misinterpreted as evidence of organic constructional impairment if seen in the absence of the other relevant clinical and laboratory information.

During follow up, the patient admitted to feeling tremendous occupation related stresses, and described how he had come to feel like. Despite repeated questioning, however, no evidence could be gathered from the patient to support this speculation.

Anosognosia and mania associated with right thalamic haemorrhage

Both anosognosia and secondary mania are associated with right hemispheric lesions. These two non-dominant syndromes, however, are rarely described as occurring together. We present a patient with a right thalamic haemorrhage giving rise to profound denial of hemiplegia and elated mood. This case suggests mechanisms for the common production of mania and anosognosia.

A 53 year old, right handed, black man, with a history of alcohol misuse and dependence and untreated hypertension, was brought to the emergency room a few hours after developing an intense headache and left sided numbness and weakness. On admission he was described as "belligerent," "agitated," and "confused." Blood pressure was 240/160. Neurological examination disclosed left lower facial droop, decreased left corneal and gag reflexes, and left hemiparesis with dense sensory deficits. With increasing obtundation, the patient was transferred to the intensive care unit and intubated. Brain MRI showed a large, left sided, hyperacute thalamic bleed with mass effect and oedema. The patient was extubated 2 days later and 4 days after the stroke he was described as being drowsy and inattentive, but was able to answer questions...
appropriately. Neurological examination showed contralateral gaze preference, supranuclear vertical gaze palsy, difficulty converging, left sided flaccid hemiparesis, and dense, left sided hemianesthesia. Deep tendon reflexes were absent on the left and Babinski's reflex was present on the left. In addition, visual extinction and neglect were present.

At the time of onset of right sided weakness the patient insisted that he was “fine,” and an ambulance was called over his objections. After being extubated, the patient acknowledged that he had had a stroke, but, despite his hemiparesis, insisted that he was ready to go home and go back to work. His belief in his ability to walk led to near falls, and he was more often heard closer to the nurses’ station for closer observation. He told the nurses that someone else’s arm was in his bed. On one occasion, holding up his left arm with his right, he told the nurse to, “take it away; it keeps scratching me.” That the left arm “smelled funny” was another reason he wanted the nurses to take it away.

Four weeks after the stroke he first acknowledged that his left arm belonged to him, though not confusedly recalled being otherwise. By this time he had a moderate hemiplegia and recognised “a little weakness,” but continued to insist that he was well and able to return to work. By the 6th week and 8 weeks after stroke the patient more consistently acknowledged that he was weak on the left side of his body. A request for disabled housing “so that I won’t be a burden to my family” seemed to indicate an appreciation of his impaired ability, but this insight was fleeting; on tests of praxis he demonstrated a tendency to use the hand as object. Memory performance remained intact. His initial recall of two paragraphs scored formally within the low average range and after a 30 minute delay, he was able to recall most of the information initially encoded, scoring formally within the average range.

Structural brain MRI on admission to the emergency room showed a large right thalamic hemorrhage with mass effect and oedema, with oedema extending into the cerebral peduncle, suggesting susceptibility consistent with deoxyhaemoglobin. Also present was increased T2 signal bilaterally in frontal areas consistent with ischaemic changes. Brain CT 30 days after stroke showed, in a stepped fashion, decreased cerebral lesion, moderate cerebellar atrophy and mild to moderate prominence of the frontal cortical sulci compatible with cerebral atrophy.

Structural MRI performed 44 days after the stroke showed a right thalamic haematoma. Functional MRI performed the same day demonstrated a 2 cm area of absent cerebral blood volume at the posterior margin of the right thalamus without any evidence of decreased cerebral blood volume within the right parietal, frontal, or temporal cortex.

This is a case of anosognosia of hemiplegia and mania co-occurring in a patient with a large right thalamic haemorrhage. Although anosognosia and mania are not generally thought of as occurring together, when Babinski’s introduced the term anosognosia he did so in his example of a case in which the patient, thought of as “a little overexcited,” and in a later paper he presented a case in which there was “a certain agitation, which expresses itself by exaggerated logorrhea, a decrease in attention, and a tendency to exotic ideas.”

Epileptic cardiac asystole

A patient is reported on with habitual episodes of collapse and loss of consciousness associated with EEG evidence of focal epileptiform discharges. Simultaneous ECG recordings disclosed 25 seconds of cardiac ventricular asystole occurring 24 seconds after the onset of electrical seizure activity. After changes to antiepileptic medication and the insertion of a permanent cardiac pacemaker he has had no further episodes. In cases of epileptic cardiac dysrhythmia, isolated EEG or ECG recordings may prove insufficient and prolonged simultaneous EEG/ECG monitoring may be required.
less commonly (only 1 of 74 seizures recorded). A review in 1996 of the “ictal bradycardia syndrome” showed only 15 documented cases in the literature of either bradycardia or asystole associated with seizures. Most patients had temporal lobe seizures. The longest duration of asystole previously reported is in a 17 year old man with temporal lobe epilepsy who sustained a 22 second pause in cardiac output. More typically the asystolic periods in documented cases are in the region of 5–10 seconds. Shorter duration asystole may not compromise cerebral function sufficiently to cause loss of consciousness. Implantation of a cardiac pacemaker is advocated but does not ensure that lapses of consciousness are eliminated if these are directly related to the seizure rather than to the secondary asystole. We report on a patient with epileptic cardiac asystole of 25 seconds duration demonstrated by prolonged simultaneous EEG/ECG monitoring which responded well to pacemaker insertion.

A previously well 34 year old right handed builder was referred with a 1 year history of fortnightly episodes of loss of consciousness. There was no associated warning, aura, chest pain, or palpitations and the patient was only aware of the episode once consciousness was lost. 16 Channel ictal EEG (eight channels illustrated with ECG) showing electrographic seizure onset and subsequent bradycardia and asystole.
restored and he found himself lying on the floor. On recovery there was no confusion, drowsiness, dysphasia, or diuresis. Often, however, he sustained soft tissue injuries to his face and scalp.

Witnesses reported that the patient would, without warning, suddenly collapse on the ground where he would remain unresponsive, inaccessible, and motionless for 90 to 120 seconds. On two occasions he appeared confused and disorientated immediately before a collapse. During the period of unconsciousness he would demonstrate no involuntary movements, orofacial automatisms, or cyanosis but he would become pale and “ashen” while staring straight ahead with a glazed look. On one occasion of the episode his right corner would return to normal and within 2 minutes he would have fully recovered. Unusually during one reported episode of unconsciousness he was seen to briefly extend the fingers of both hands.

He was admitted to his local hospital and CT, MRI, interictal EEG, and 24 hour ECG were normal. No episodes were witnessed while he was an inpatient but they were thought to have been caught in the oratory and therefore before he was started on phenytoin, with no benefit. Carbamazepine was added, again with minimal effect.

The patient was then referred to the Epilepsy Assessment Centre of The National Society for Epilepsy and National Hospital for Neurology and Neurosurgery for further investigation and management.

Cardiovascular and neurological examination was normal as were MRI and routine interictal EEG. Sixteen channel ambulatory EEG using an Oxford Instruments digital EEG receiver was performed continuously for 340 hours before an episode was captured. Interictal rare spikes were seen over the right hemisphere he was seen to briefly extend the fingers of both hands.

In a neurological examination, the patient's mental state and cranial nerves were normal. Evidence of muscular atrophy and mild weakness were prominent features. There was no familial history of neurological disorder, including entrapment neuropathies. After a few months, he noted a slowly progressive weakness of the pelvic girdle and lower limbs. The thorax showed poor respiratory movement, and the patient showed paradoxical movement of the abdomen in the supine position. Tendon reflexes were hypotonic in all limbs. The patient's sensations of touch and pain were mildly impaired in the four limbs. The patient's sensations of touch and pain were mildly impaired in the four limbs. The patient's sensations of touch and pain were mildly impaired in the four limbs. The patient's sensations of touch and pain were mildly impaired in the four limbs.

Respiratory insufficiency in a patient with hereditary neuropathy with liability to pressure palsy

Hereditary neuropathy with liability to pressure palsies (HNPP) typically presents recurrent pressure palsies of peripheral nerves, such as the axillary, median, radial, ulnar, or peroneal nerves, at common entrapment sites. Respiratory muscle weakness has not been previously reported in HNPP. We describe a patient with HNPP with marked respiratory failure and proximal muscle weakness were prominent features.

The patient started to have dyspnoea on exertion at the age of 44. At the age of 47, he noted a slowly progressive weakness of the pelvic girdle and lower limbs. The thorax showed poor respiratory movement, and the patient showed paradoxical movement of the abdomen in the supine position. Tendon reflexes were hypotonic in all limbs. The patient's sensations of touch and pain were mildly impaired in the four limbs. The patient's sensations of touch and pain were mildly impaired in the four limbs. The patient's sensations of touch and pain were mildly impaired in the four limbs.

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Respiratory insufficiency in a patient with hereditary neuropathy with liability to pressure palsy

Hereditary neuropathy with liability to pressure palsies (HNPP) is an autosomal dominant disorder, the molecular basis of which is a 1.5 mb deletion in chromosome 17p11.2 including the peripheral myelin protein-22 (PMP-22) gene. HNPP typically presents recurrent pressure palsies of peripheral nerves, such as the axillary, median, radial, ulnar, or peroneal nerves, at common entrapment sites. Respiratory muscle weakness has not been previously reported in HNPP. We describe a patient with HNPP with marked respiratory failure and proximal muscle weakness were prominent features. The patient started to have dyspnoea on exertion at the age of 44. At the age of 47, he noted a slowly progressive weakness of the pelvic girdle and lower limbs. The thorax showed poor respiratory movement, and the patient showed paradoxical movement of the abdomen in the supine position. Tendon reflexes were hypotonic in all limbs. The patient's sensations of touch and pain were mildly impaired in the four limbs. The patient's sensations of touch and pain were mildly impaired in the four limbs. The patient's sensations of touch and pain were mildly impaired in the four limbs.
delayed (8.7 ms (normal<8.0)). Sensory nerve conduction studies showed a reduced amplitude of sensory nerve action potentials and conduction slowing in all the nerves tested. Electromyography carried out in the supraspinatus, deltoid, biceps, flexor carpi ulnaris, brachioradialis, quadriceps femoris, biceps femoris, tibialis anterior, and gastrocnemius muscles showed polyphasic motor unit potentials of long duration, but denervation potentials were rare. A left sural nerve biopsy showed scattered tomacula thickening of the myelin sheath and some abnormal thin axonal myelin sheaths. The density of myelinated fibres was reduced (5726/mm\(^2\)). A gene analysis disclosed a 53% gene dose of \textit{PMP-22} related to normal controls, using Southern blots of DNA digested with EcoRI.

Given the possibility of superimposing demyelinating neuropathy, especially chronic inflammatory demyelinating polyneuropathy, oral prednisolone (60 mg/day) was given for 1 month. However, the patient’s clinical condition did not respond to this treatment. Pulmonary dysfunction and proximal muscle weakness were almost steady during the next 3 years.

We examined the patient’s elder sister (64 years old), elder brother (62 years old), and younger sister (58 years old), although they had no neurological complaints. All of them had experienced generalised hyporeflexia or areflexia but no weakness or sensory loss, and nerve conduction studies showed moderate conduction slowing with accentuation at the common entrapment sites, suggesting demyelinating neuropathy.

Our patient recalled experiencing recurrent episodes of transit entrapment mononeuropathies, and the familial occurrence of asymptomatic entrapment neuropathy was detected by nerve conduction studies. The presence of tomacula, and genetic analysis confirmed a diagnosis of HNPP. However, the patient’s dominant clinical features—respiratory failure and proximal muscle weakness—were atypical for HNPP. Although respiratory muscle weakness has been reported in hereditary motor and sensory neuropathy (HMSN), there has been no report of respiratory insufficiency associated with HNPP to our knowledge.

The weakness of the truncal muscles, including the respiratory accessory muscle, is a possible cause of respiratory failure in our patient. On the other hand, he had experienced hyperventilation in the supine posture and paradoxical movement of the abdomen, which suggested diaphragmatic weakness.1 Also, chest radiography showed poor movement of the diaphragm. Although the prolongation of distal latency in the phrenic nerve was mild considering the severity of respiratory failure, assessment of axonal loss is not possible with phrenic nerve stimulation. In fact, phrenic nerve latency is not necessarily associated with pulmonary dysfunction in HMSN.1

Diffuse proximal weakness in our patient is an uncommon finding as for HNPP. Mancardi et al2 reported on three patients with progressive sensory-motor polyneuropathy associated with 17p11.2 deletion, and the initial symptom of one patient was proximal weakness in one arm. We propose that our patient represents a clinical phenotypic variability among HNPP. It may be necessary to pay attention to respiratory function in HNPP.

We thank Dr T Yamamoto from the University of Occupational and Environmental Health for the gene analysis and Mr T Nagase from Chiba University for his technical help with the sural nerve biopsy.

\[\text{Spinal accessory neuropathy and internal jugular} \text{ thrombosis after carotid endarterectomy}\]

Spinal accessory neuropathy is a rare complication of carotid endarterectomy (CEA).1 Internal jugular venous thrombosis after CEA has also been reported rarely, but is likely more common; as internal jugular
venous thrombosis is often asymptomatic, or presents with non-specific pain, it is probably unrecognised in many cases. Concurrent ipsilateral spinal accessory neuropathy and internal jugular venous thrombosis after CEA is expected to be rare, and this is underscored by the published cases. Despite this apparent rarity, a common pathogenetic mechanism for postoperative spinal accessory neuropathy and internal jugular venous thrombosis may well be present, at least in some cases, which may lead to the consideration of the possibility of both when either is discovered.

We report on a patient who developed right spinal accessory neuropathy and internal jugular venous thrombosis after right CEA. A 59 year old man underwent right CEA for possibly symptomatic stenosis. Angiography had shown 90% stenosis of the right internal carotid. The operation was done under general anaesthesia. The carotid bifurcation was unusually distal, necessitating a long dissection and high retraction. No immediate postoperative complications were evident. The next day, the patient complained of mild pain at the operative site, but this did not notice any weakness. The pain spread into his right shoulder within several days; at that time, he also noted difficulty raising his right arm. His symptoms worsened further a few weeks later. The symptoms persisted and he presented for neurological evaluation 4 months after CEA. At that time, he had some induration along the incision site and a palpable cord within the right supraclavicular fossa. There was moderate atrophy of the right sternocleidomastoid and trapezius, with induration along the incision site and a palpable supraclavicular cord within the right supraclavicular fossa. There was moderate atrophy of the right sternocleidomastoid and trapezius, with induration along the incision site and a palpable supraclavicular cord within the right supraclavicular fossa. There was moderate atrophy of the right sternocleidomastoid and trapezius, with induration along the incision site and a palpable supraclavicular cord within the right supraclavicular fossa.

The presence of induration about the incision site and a palpable supraclavicular cord in our patient led us to suspect venous thrombosis. Although the onset of either spinal accessory neuropathy and internal jugular venous thrombosis may include intraoperative inflammation and scarring, leading to thrombosis from venous stasis or endothelial injury. Other causes of internal jugular venous thrombosis include jugular cannulation, blunt cervical trauma, and a hypercoagulable state. Internal jugular venous thrombosis may occur within a week after neck dissection, often with recanalisation after several months.

Common pathogenetic mechanisms for spinal accessory neuropathy and internal jugular venous thrombosis may include intraoperative traction, haematomata, and postoperative inflammation and scarring. Although the onset of either spinal accessory neuropathy or internal jugular venous thrombosis in our patient cannot be determined precisely, it is likely that both developed at about the same time. The delayed worsening of the spinal accessory neuropathy in this case suggests postoperative scarring or inflammation. The lack of improvement after a year, as in some other cases of spinal accessory neuropathy after CEA, implies considerable axonal injury, but does not clarify the manner of injury.

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Ishæmic stroke in a sportsman who consumed MaHuang extract and creatine monohydrate for body building

We report the first case of extensive cerebral infarct in a young sportsman consuming high doses of MaHuang extract and creatine monohydrate. This should warn the community to possible serious adverse effects of energy supplements. A 33 year old man had a severe aphasia on awakening on the morning of 23 January 1994. He did not complain of any other symptoms. He was referred to our department on 26 January 1999. He had a Wernicke aphasia with a slight right sided face and arm weakness and a right Babinski sign. His blood pressure was 140/60 and his pulse 54 per minute. Brain CT showed signs of extensive left middle cerebral artery infarct. Cervical ultrasound duplex scanning and cervical angiography were normal. Cerebral MR examination and EEG were also normal except for a patent foramen ovale.

The patient had no vascular risk factors, in particular no tobacco use, and he was perfectly fit until his stroke. He was a sportsman with 2 hours daily intensive training for body building. He was working as a baggage handler in an international airline company. During a recent journey to Miami, Florida, he bought tablets of “energy pills” in a shopping store to enhance his athletic performances. The first drug contained MaHuang extract (corresponding to 20 mg ephedra alkaloids), 200 mg caffeine, 100 mg L-carnitine, and 200 µg chromium per two capsules. The second drug contained 6000 mg creatine monohydrate, 1000 mg taurine, 100 mg inosine, and 5 mg coenzyme Q10 per scoop. He consumed 40–60 mg ephedra alkaloids, 400–600 mg creatine monohydrate daily for about 6 weeks before his stroke.

Although a paradoxical embolism through a patent foramen ovale in this patient cannot be excluded as it recently occurred during transatlantic flight, there was no deep venous thrombosis and D-dimers were normal. However, ephedrine has an indirect sympathomimetic action. Ephedrine and its metabolites are natural products that are used in non-prescription medications for multiple uses, e.g. during transcutaneous, which contains ephedrine, is used in combination with sympathomimetic drugs. Both ischaemic and haemorrhagic stroke associated with ephedrine use have been reported. Acute myocardial infarction and acute psychosis have also been reported after taking ephedrine and other sympathomimetic drugs. Ephedrine and its metabolites are natural products that are used in non-prescription medications for multiple uses, e.g. during transcutaneous, which contains ephedrine, is used in combination with sympathomimetic drugs. Both ischaemic and haemorrhagic stroke associated with ephedrine use have been reported. Acute myocardial infarction and acute psychosis have also been reported after taking ephedrine and other sympathomimetic drugs.
it remained in the normal range. Whether the use of high doses of caffeine can enhance the cardiovascular effect of ephedrine remains a possibility as stroke after taking a combination of caffeine and amphetamine has been reported. 

Drug addiction in sportsmen and sportswomen is becoming a major concern in our societies, involving both professionals and amateurs. As energy supplements, thought to enhance performance, are easily available in some countries without the need of medical prescription, everybody should be aware that these so called “benign” drugs may have major adverse effects.

This first case report of an extensive cerebral infarct in a young sportsman consuming high doses of MaHuang extract and creatine monohydrate should alert the sport community to this possible adverse effects of energy supplements, particularly when used in multiple combination.

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Petroclival meningioma as a cause of ipsilateral cervicofacial dyskinesias

Hyperkinetic movement disorders of facial and neck muscles such as blepharospasm, hemifacial spasm, facial myokimia, and cervical dystonia have rarely been associated with unilateral brainstem or posterior fossa pathologies. We report a case of unilateral cervicofacial dyskinesias due to an ipsilateral petroclival meningioma.

A 32 year old left handed woman complained about left sided facial dysesthesia of the upper quadrant of her face for 1 year. In addition she had intermittent ipsilateral headache. A left sided facial palsy and hypogeusia developed. When progressive hearing loss and persistent ipsilateral tinnitus occurred she sought medical advice. She was referred to our department for further treatment after a large tumour in the left cerebellopontine angle had been demonstrated by MRI. On admission, the left corneal reflex was absent. There was marked hypoesthesia of the first two divisions of the left trigeminal nerve and a mild left facial palsy. There was also hypogeusia of the left half of the tongue. Speech was slightly dysarthric. During examination dystonic and choreic movements off the left facial muscles were seen. The dystonic grimacing increased when the patient was being observed. There were also intermittent jerky dystonic head movements with turning of the head to the left, associated with slight elevation of the left shoulder. The facial movement disorder was clearly different from hemifacial spasm. There were no tonic or clonic synchronous contractions of facial muscles and no signs of involuntary coactivation. The patient barely noted the dyskinesias. Audiometry showed a hearing threshold at 30 Db on the left side and lack of stapedius reflex on the left side. Oculovestibular response to caloric stimulation was...
decreased on the left side. Furthermore, there was mild left dysphokokinesia.

Neuropathy of the facial nerve was normal on both sides. Needle myography of the left frontalis and orbiculari oculi did not show signs of denervation.

An MRI study showed a large gadolinium enhancing tumour within the left cerebello-pontine angle extending to the cavum Meckel with marked displacement of the brainstem to the contralateral side (figure A and B). Digital subtraction angiography showed a discrete blush of the tumour as typically seen in meningiomas. The tumour was totally removed by a combined transpetrosal supratentorial and infratentorial presigmoidal approach. The resectional course was uneventful and there were no new deficits. The facial palsy improved slightly as well as the trigeminal hypeaesthesia. Audiometry remained unchanged. Postoperative imaging showed no residual tumour and the displacement of the brain stem within the posterior fossa had resolved (figure C). Marked improvement of the left sided cranial facial dyskinesias occurred during the next weeks.

The postoperative improvement of the dystonic and choreic grimacing and the cervical dystonia indicates a causal association between the petroclival meningioma and the segmental hyperkinetic movement disorders. Such a relation is supported also by the absence of a family history of movement disorders and the absence of previous exposure to neuroleptic medication. Hyperkinetic movement disorders due to tumours of the brainstem or of the posterior fossa have been reported only rarely. Asymmetric blepharospasm was recently found in a patient with an ipsilateral mesencephalic cyst.1 Hemifacial spasm was seen in patients with dystonic neurinomas, meningiomas, and epidermoid tumours of the cerebellopontine angle.2 Acoustic neurinomas and anaplastic pontocerebellar glioma can be associated with facial myokymia and spastic parietic facial contracture.3 Also, cervical dystonia due to tumours of the cerebellopontine angle have been reported recently.4

The pathophysiological mechanisms responsible for dystonic movement disorders caused by structural or functional lesions of the brainstem are not fully understood. The possibility of denervation supersensitivity of cranial nerve nuclei has been proposed previously. Alternatively, enhanced excitability of brainstem interneurons has been suggested. This pathophysiological mechanism is supported by the findings of blink reflex studies in patients with blepharospasm, spasmodic dysphonia, and cervical dystonia. Tolosa et al found significantly less inhibition of the test stimulus polysynaptic late response and marked enhancement of the recovery curve of the late response under such conditions compared with the response in healthy subjects.1

Our case provides further evidence that functional impairment by compression and distortion of the brain stem may cause hyperkinetic cervicofacial movement disorders. It is supported also by the knowledge that such movement disorders are accessible to surgical treatment of the underlying pathology. Therefore, patients with cranial or cervical dystonia or choreic dyskinesia should undergo MR imaging to rule out a surgically treatable cause.

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Acute multifocal cerebral white matter lesions during transfer factor therapy

Transfer factor is an active substance of unknown structure present in dialysable leukocyte extract which is assumed to transfer cell mediated immunity in an antigen specific fashion.1 The mechanisms of action of transfer factor are still far from clear; in vitro dialysable leukocyte extract increases macrophage activation and interleukin (IL) 1 production and enhances leukocyte chemotaxis and natural killer function. Transfer factor has been reported to stimulate the cell mediated antigen specific response in patients with various infections2; therefore, treatment with transfer factor has been suggested in patients with selective deficits in cell mediated immunity such as in some refractory neoplasms and chronic infections. Moreover, it has been used in the treatment of uveitis.3 Administration of dialysable leukocyte extract has seemed to be free of hypersensitivity, long lasting side effects, or complications, except for transitory hyperpyrexia.4

We report on a patient in whom multiple cerebral white matter lesions developed after taking dialysable leukocyte extract orally for uveitis. A 28 year old man was admitted to hospital because of headache, mental confusion, and right hemiparesis. He had had recurrent bilateral uveitis from the age of 12 to 14 with relapse of right eye. In January 1995 retinal vasculitis was diagnosed at fundoscopy and in July 1995 he started oral transfer factor as dialysable leukocyte extract twice a week. He complained of generalised weakness after the second dose and the referring symptoms developed after the third dose.

Neurological examination on admission showed mental confusion and severe right spastic hemiparesis with Babinski’s sign. No fever or meningismus were present.

Laboratory examinations on admission showed a slight increase in total serum protein (8.4 g/l, normal 6.0–8.0 g/l, although the serum protein fraction was normal), antistreptolysin titters (355 UI/ml, normal 0–200 UI/ml), and anticardiolipin IgG (30 UI/ml, normal 0–12 UI/ml). Negative results were obtained for antinuclear, anti-DNA, antismooth muscle, and antineutrophil cytoplasmic antibodies, lupus anticoagulant, cryoglobulins, immune complexes, complement fractions, and neoplastic markers.

Serological investigations showed IgG but not IgM against cytomegalovirus (CMV), Herpes simplex, Varicella zoster, Epstein-Barr virus, and JC virus. The Paul Bunnel reaction, anti-HIV, and the markers of hepatitis virus B and C infection were negative.

Cell, protein, and glucose concentrations in CSF were normal. No oligoclonal bands or antibody against CMV, Herpes simplex, Varicella zoster, Epstein-Barr virus, Cox sackie, Adenovirus, Enterovirus or Borrelia burgdorferi were present. Polymerase chain reaction search for Herpes simplex 1 and 2, Varicella zoster, CMV, Epstein-Barr virus, and JC virus in the CSF was negative.

Brain MRI showed several extensive asymmetric lesions in the subcortical and periventricular cerebral white matter, some of which exerted a mass effect on the nearby CSF spaces. All lesions exhibited thick ring-like enhancement after intravenous contrast administration (figure). The brain stem, cerebellum, and cervical spinal cord were spared.

The patient had a progressive spontaneous remission of symptoms and signs. The neurological examination 20 days after onset showed slightly increased deep tendon reflexes on the right side and was normal 40 days later; all laboratory analyses were normal except for antistreptolysin titters (265 UI/ml). Two MR scans at 1 and 4 months after onset showed progressive reduction of the extension of cerebral white matter lesions, which did not show contrast enhancement. A final MR scan 20 months after onset showed further regression of lesions without contrast enhancement but a new large lesion in the left occipital white matter, which showed moderate contrast enhancement at present, after 5 years, the patient is in a good state of health and neurological examination and laboratory tests are normal.

The close temporal relation between assumption of dialysable leukocyte extract therapy and appearance of cerebral white matter lesions in our patient supports the possibility that the association of the two events might not be causal. Despite the absence of biopsy, we reasonably excluded...
the diagnosis of vasculitis or neuro-Bechet’s disease although in the absence of biopsy. In fact, the clinical, laboratory, and MRI findings were not typical and a low titre of anticitrullinated antibodies is found in 2% of healthy subjects.1

The occurrence at different time of focal cerebral white matter lesions highly supports the diagnosis of multiple sclerosis, but some clinical and laboratory findings in our patient are not typical for this condition. Mental confusion is not common at the onset of multiple sclerosis whereas it is often found in acute disseminated encephalitis.2 In addition, CSF without oligoclonal banding argues against a diagnosis of multiple sclerosis, whereas it is commonly found in acute disseminated encephalitis.2 On the other hand the possibility that acute disseminated encephalitis may recur has been accepted3 and on the basis of the patient’s clinical picture and CSF, we favoured such a diagnosis.

The pathogenic mechanisms underlying the triggering, development, and duration of multiple sclerosis and acute disseminated encephalitis are still far from clear despite the progress made in unravelling them. Some findings suggest that acute disseminated encephalitis and multiple sclerosis lie at the two poles of an autoimmune range, in which autoantigen reactivity is only temporary and direct against a single antigen in acute disseminated encephalitis and multiple antigens in multiple sclerosis.

Although the hypothesis that dialysable leucocyte extract had triggered an autoimmune disorder in our patient cannot be proved, our finding is in line with the report of multiple cerebral lesions after therapy with IL-2 in patients with malignancies or HIV infections.3 On the other hand, the fact that acute disseminated encephalitis is often correlated with the administration of foreign proteins, such as during vaccinations or viral infections4 led us to postulate in this patient a cell mediated immunological mechanism. Therefore, an immunological cross reaction between viral antigens (or other foreign material contained in vaccines) and various parts of the nervous system resulting in acute disseminated encephalitis might have occurred. As already noted, dialysable leucocyte extract contains a multitude of immunostimulating or potentially activating substances so it is impossible to pinpoint which one could have been responsible for the demyelinating effect seen in our patient. This notwithstanding, our finding indicates that neurological surveillance is worthy in patients assuming dialysable leucocyte extract therapy.

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Fahr’s disease and Asperger’s syndrome in a patient with primary hypoparathyroidism

Abnormal calcium phosphate metabolism has not previously been associated with Asperger’s syndrome, a form of pervasive developmental disorder. Nor have symmetric calcifications of the basal ganglia, dentate nuclei and cortex, or Fahr’s disease—whether idiopathic or associated with hypoparathyroidism—previously been associated with this handicap. We present the case of a 24 year old man with Asperger’s syndrome, primary hypoparathyroidism, and multifocal brain calcifications.

According to medical history, the patient’s mother had received weekly injections of Depoprovera during pregnancy. A single child born after a normal term delivery, he underwent surgery for an inguinal hernia at 3 weeks. Developmental milestones were only moderately delayed. At 9 months, he rolled instead of crawling. He walked at 15 months, spoke at 2 years with poor articulation, and still speaks in short, unelaborated sentences. His social and language development lagged in grade school and he occasionally got into fights. In late adolescence, antisocial behaviour took the form of shoplifting and repeated long distance calls to pornographic hot lines. As an adult, his social adaptation remains poor: he currently lives with his mother and works irregularly as a dishwasher in a restaurant. He is indifferent, isolated, and resists novelty. He enjoys repetitive and solitary activities such as slot machine games and playing the piano.

Neurological examination showed bilateral hyperreflexia, mild imprecision of fine finger movements, dysgaesthesia on sensory testing, and a manieristic gripping handshake. There were no extrapyramidal movements, dysgraphaesthesia on sensory testing, and a manieristic gripping handshake. There were no extrapyramidal movements, dysgraphaesthesia on sensory testing, and a manieristic gripping handshake. There were no extrapyramidal movements, dysgraphaesthesia on sensory testing, and a manieristic gripping handshake. There were no extrapyramidal movements, dysgraphaesthesia on sensory testing, and a manieristic gripping handshake. There were no extrapyramidal movements, dysgraphaesthesia on sensory testing, and a manieristic gripping handshake. There were no extrapyramidal movements, dysgraphaesthesia on sensory testing, and a manieristic gripping handshake. There were no extrapyramidal movements, dysgraphaesthesia on sensory testing, and a manieristic gripping handshake. 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symptoms. His IQ score was in the low range (WAIS-C=85 at the age of 13; Barbeau-Pinar=82 at the age of 17). He also presented an impairment on the Tower of London test, which measures executive function, and in a task assessing the understanding of others. These two findings are reliably present in pervasive developmental disorders, in this IQ range. In addition, his performance on the Tower of Toronto test disclosed impaired performance in procedural learning. Psychiatric assessment showed scores above the cut off for autism according to the autism diagnostic interview (ADI), a standardised interview that requires specific training and those administering it to have a 0.90 reliability with other researchers. The subject was positive for the diagnosis of autism, being above cut off values in the three relevant areas of communication, social interactions, restricted interests, and repetitive behaviours. Nevertheless, he did not present delay in language acquisition or morphological atypicalities in language development, which corresponds to DSM-IV criteria for Asperger’s syndrome.

Brain CT showed dense calcium deposits in the basal ganglia, thalamus, cerebellum dentate nucleus, and orbitofrontal cortex, consistent with Fahr’s disease (figure). Serum calcium was increased, with no specific brain region in pervasive developmental disorders being affected. For the parathyroid glands showed an absence (normal 1.0–6.55 µM/l), and a nuclear scan with ⁹⁹m Tc was unremarkable. Magnetic resonance imaging showed a retro-odontoid disease that must be considered within the literature, emphasising that as the cause of spinal cord compression is amenable to surgical removal, symptomatic patients result in behavioural and cognitive abnormalities currently indistinguishable from idiopathic pervasive developmental disorder. This case also suggests that careful biological assessment of this group of patients may disclose focal brain lesions associated with identifiable cognitive deficits. Could these clinical coincidences be instructive for a neurodevelopmental model of autism?

Hypertrophic atlantoaxial ligaments: an unusual cause of compression of the upper spinal cord

The craniovertebral junction can be an unusual cause of compression of the upper spinal cord. The finding that the clinical picture of autism can be found in a wide range of medical conditions giving rise to organic brain dysfunction is not new, but the relation between these conditions and autism are often considered meaningless. By contrast, this case, similarly to some others suggests that dysfunction in key brain circuits may result in behavioural and cognitive abnormalities currently indistinguishable from idiopathic pervasive developmental disorder. This case also suggests that careful biological assessment of this group of patients may disclose focal brain lesions associated with identifiable cognitive deficits. Could these clinical coincidences be instructive for a neurodevelopmental model of autism?

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Hypertrrophic atlantoaxial ligaments: an unusual cause of compression of the upper spinal cord

The craniovertebral junction can be affected by several pseudotumorous masses extradurally located, such as rheumatoid panus, hypertrophic non-union of odontoid fracture, post-traumatic cicatrix, synovial cysts, tumorous calcium pyrophosphate dihydrate crystal deposition, taphaceous gout, calcification of the posterior longitudinal ligament, synovial disease-like pigmented villonodular synovitis, and synovial chondromatosis. Hypertrophy of the atlantoaxial ligaments as a consequence of degenerative disease was recently recognised as an individual entity. Only five previous cases have been published. We add another case to the short series available in the literature, emphasising that as the cause of the spinal cord compression is amenable to surgical removal, symptomatic patients should be diagnosed and treated without delay. A 66 year old woman presented with a rapid development of progressive spastic tetraparesis and an unrelated medical history. There was no osteolysis or instability on plain cervical radiography and CT. A bone scan with "Tc was unremarkable. Magnetic resonance imaging showed a retro-odontoid extradural mass that was homogeneous and iso-intense on T1 weighted signal, demorstrated no enhancement after intravenous gadolinum contrast, and was compressing the upper cervical spinal cord (figure). The laboratory tests were normal, confirming the absence of rheumatoid arthritis, metabolic disease, or gout. Surgical removal via a tranoral approach with a minimal bony resection was direct and provided sufficient space to obtain spinal cord decompression. It was followed by a posterior C1-C2 fusion. Macroscopically, the lesion had no capsule and resembled a hypertrophic ligamentum flavum. Microscopically, it was non-inflammatory, hypocellular, and ligamentary pieces found within the mass appeared fibrous and almost disintegrated. The patient regained normal neurological function. Over a 3 year follow up period there was no recurrence.

We focus attention on hypertrophic atlantoaxial ligamentary disease as a degenerative disease that must be considered within the possible causes of high spinal cord compression.

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Preoperative sagittal T1 weighted MRI of the cervical spine with gadolinium enhancement. A retro-odontoid and extradural mass displacing the spinal cord is seen at the craniovertebral junction.

Selective hemihypaesthesia due to tentorial coup injury against dorsolateral midbrain: potential cause of sensory impairment after closed head injury

A 63 year old woman who fell off her bicycle had a left temporal region head injury with evidence of initial loss of consciousness of 5 minutes and scalp excoriation of that area. On arrival at our hospital 30 minutes later she was alert and oriented. Cranial nerve functions, including extraocular motion and hearing function, were preserved. Pain and temperature sensations of the right side, including her face, showed a 70% decrease compared with the left side; however, position and vibration sensations were normal. Other neurological examinations, including motor function, coordination, and deep tendon reflex, were normal. The patient's only complaints were left temporal headache and right hemihypaesthesia.

Brain CT on admission showed a discrete and linear high density at the left ambient cistern without other intracranial lesions. On the next day CT showed an obscure low density lesion at the dorsolateral midbrain in addition to the previous lesion (figure). Brain MRI, taken 3 days later, demonstrated an intraparenchymal lesion, at the surface of the left dorsolateral midbrain in high intensity on a T2 weighted image. The high intensity lesion corresponding to haematoma on CT was seen in the ambient cistern (figure). Taking both CT scans and MRI into consideration, this case was diagnosed as traumatic midbrain contusion.

The loss of pain and temperature sensation improved gradually and the patient was discharged 2 weeks later.

T2 weighted images 1 month later showed a more localised lesion in the same area. The coronal slices showed a high intensity lesion at the level of lower midbrain coinciding with the tentorium level, disclosed as a low line between the occipital lobe and the cerebellar hemisphere (figure).

The neurological deficits almost disappeared 6 months later.

Somatosensory impairment including pain is one of the most common complaints among patients with cranioceveal injury. Responsible lesions for sensory impairment, detectable by neuroimaging studies, almost always accompany associated neurological deficits. To our knowledge, a selective injury at the spinothalamic or trigeminothalamic tracts due to closed head injury has not been highlighted in the neurological literature.

The MR images in our case showed a discrete lesion at the left dorsolateral midbrain. Topographical study at this lower midbrain level showed that the lateral and ventral spinothalamic and ventral trigeminothalamic tracts pass at the surface of this level by carrying a superficial somatosensory sensory input. The lesion shown in our MR images seemed to be localised to these tracts. The medial lemniscus for the deep sensation and lateral lemniscus and nucleus of inferior colliculus associated with hearing function ran ventral and dorsal to these tracts, respectively, which were seemingly spared in our patient. The topographical anatomy seemed to correspond to the neurological manifestations of our patient.

The mechanism of midbrain injury in our patient was speculated to be due to tentorial coup injury based on MR images. The location of contusion was at the lower dorsolateral midbrain, coinciding with the tentorial edge level. Initiation of injury was the surface of the midbrain; however, due to the proximity of the tentorial edge to the midbrain on the injured side, tentorial contact to the midbrain supposedly occurred more readily. Brain MRI findings support the anatomical features of this tentorial coup injury. This injury is not rare in patients with severe head injury, accompanied by other intracranial lesions, and is often caused by lateral displacement of the brain stem relative to the tentorium. It is influenced by congenital variation in the size and shape of the tentorial incisura. The brain stem of the patient with a narrow incisura is more vulnerable to the direct contusive effects than that of a patient with a wider incisura. Therefore, even in minor head injury, this mechanism may occur in patients preconditioned with narrow tentorial incisura, which may have been the case in our patient.

The concept of tentorial coup injury against the midbrain is not new. It usually accompanies various degrees of conscious disturbance and other long tract signs, sensory deficits as well as cerebellar and cranial nerve palsy due to the midbrain lesion or other associated intracranial lesions. The clinical manifestation of our patient may represent one of the mildest forms of the midbrain contusion. The mechanism when we see a patient with post-traumatic sensory deficit, the possibility of this tentorial injury should be kept in mind even in minor head injury.

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CORRESPONDENCE

Toluene induced postural tremor

We read with interest the article by Miyagi et al1 and comment on the medical treatment of toluene induced tremor. Microdialysis experiments in rats have shown that inhalation of toluene increases extracellular γ-aminobutyric acid (GABA) concentrations within the cerebellar cortex which probably explains why GABA agonists including benzodiazepines (for example, clonazepam) are not very effective in toluene induced tremor and ataxia. Rat experiments also showed a 50% reduction in brain catecholaminergic neurons.2 Degeneration of certain cerebellar pathways is probably responsible for the loss of this dopaminergic innervation.3 Dopamine agonists could therefore be of potential interest in the treatment of toluene induced tremor. This hypothesis was explored in a recently described case,4 which showed remarkable clinical and iconographic similarities with that described by Miyagi et al: (a) long history of chronic toluene inhalation, (b) marked postural tremor, (c) progressive worsening of the symptoms despite abstinence from inhalant misuse, and (d) mild cerebral atrophy and marked low signal intensity in globus pallidi, thalami, red nuclei, and substantia nigra on T2 weighted MRI. As in our patient, amantadine hydrochloride (100 mg twice daily) abolished the tremor. In addition, there is evidence that amantadine dysfunction in chronic toluene abuse results in extrapyramidal response and amantadine hydrochloride.5 J Toxicol Clin Toxicol (in press).

Early diagnosis of subependymal giant cell astrocytoma in children with tuberous sclerosis

Nabbout et al6 have attempted to identify the risk factors for the progression of subependymal nodules into giant cell astrocytomas (SEGAs) in tuberous sclerosis complex. In attempting to develop screening strategies that avoid iatrogenic morbidity, patient inconvenience, and excess cost, it is essential that the natural history of these lesions in the general population of patients with tuberous sclerosis complex be understood well.

We think that there are two problems with this study that should make the physician cautious about using the factors identified by Nabbout et al as a basis for a screening programme. The first is that this study was performed in a population that had been referred to a tertiary medical centre, and then had been further selected by virtue of having had at least 3 years tertiary centre follow up and needing two MR scans of the head. The prevalence of astrocytomas and risk factors, and hence the positive predictive value of any screening tool in a general population of patients with tuberous sclerosis complex is likely to be different from those described in the highly selected group studied in this paper.

The second point is that the authors have made a potentially misleading decision to exclude more than half their study sample because they do not have lesions close to the foramen of Monroe. It is not certain that all SEGAs arise from lesions close to the foramen. They may arise in the fourth ventricle. Furthermore, the late presentation of many lesions in the lateral ventricles has, in the past, precluded accurate determination of their point of origin. Our study selects 24 of 60 patients who had met their entry criteria but does not state how many of the excluded 36 patients had no subependymal nodules or nodules that were not “near the foramen of Monroe”. Inclusion criteria are given for what constitutes proximity to the foramen. The authors were apparently not blinded at the point when they selected which patients had lesions near to the foramen and therefore there is an obvious issue of potential selection bias.

The consequence of excluding these patients may have been that false significance is given to their results. The data they present are fragile. Consider, for example, the consequence of introducing from these 36 non-selected patients a hypothetical single case that had a family history of tuberous sclerosis complex and a subependymal nodule which enhanced with gadolinium. The effect would be to remove the stated statistical significance (using Fisher’s exact test) for the outcome and both of these explanatory variables.

Identifying the risk factors that can tell us which SEGAs will subependymal lesions will become invasive is important. As subependymal nodules and SEGAs seem to be histologically identical it is unlikely that pathologists will provide an answer. The study of Nabbout et al suggests some new hypothesis that avoids others. However, the definitive answer will not be provided by studies of selected samples but by follow up of a population based sample of patients with tuberous sclerosiscomplex. In the absence of such a study we would be cautious about implementing screening programmes based on what may be misleading criteria.

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Atypical form of amyotrophic lateral sclerosis: a new term to define a previously well known form of ALS

We read with interest the article by Sasaki et al,7 concerning the atypical form of amyotrophic lateral sclerosis (ALS). The pattern of muscular atrophy in these patients differed from that of typical ALS in that severe muscle involvement was confined to the upper limbs, predominantly the proximal portion and shoulder girdle, sparing the face and the legs until late in the disease’s course or until the terminal stage.

Over the past few years, we have noticed a growing interest in the renaming of this clinical form of ALS, which has its origins and predomination in the proximal muscles of the upper limbs and little or no effect of either a bulbar nature or in the lower limbs. Thus Hu et al8 coined the term flail arm syndrome, to describe a subgroup of patients affected by ALS that predominantly showed signs of lower motor neuron disease in the upper limbs, without significant functional involvement of other regions on clinical presentation. This subgroup of patients was clinically characterised by the display of progressive atrophy and weakness affecting the proximal muscles in the upper limb muscles in a more or less symmetric manner.

Recently, along these lines, Katz et al9 described a series of patients affected by an adult onset motor neuron disorder restricted to the upper limbs, with severe proximal and varying degrees of distal involvement, calling it amyotrophic brachial diplegia syndrome.

Other terms used in the past refer to this form of ALS have been dangling arm syndrome, suspended form, oranguatan sign, dead arm sign, bibrachial palsy, rizomelic amyatrophy, and the idea of naming it a distinctive phenotype of a neurogenic
"man-in-the-barrel" syndrome has even been suggested.

Probably all these terms used to define this variation of ALS are synonyms for an older, well-known condition, the scapulohumeral form, or the chronic anterior poliomyelitis reported by Vulpian in 1886 and known in Franco-German literature as Vulpian-Bernhardt's form of ALS. At certain stages of the disease's clinical course, it is probably difficult to differentiate it from progressive muscular atrophy (PMA).

Some authors have said that PMA with late onset scapulohumeral distribution (over 45 years of age) generally leads to ALS as a matter of course.4

Be that as it may, the truth is that this atypical form of amyotrophic lateral sclerosis behaves differently from typical ALS. The comparative study with the rest of the ALS group supplied important clinical findings, such as little or no functional impairment of the bulbar muscles or legs. Hu et al also made four important statistical discoveries.5

(1) The prevalence of this form of ALS constituted 10% of the ALS group as a whole (p >0.05). (2) The age of onset of this form was similar to the rest of ALS. (3) There was a clear predominance among men (the male/female ratio was 9:1 in this form, compared with 1:5.1 in the total ALS group). (4) There was a longer median survival (a median survival of 57 months compared with 39 months in the ALS group).

Some of these patients have a long ALS clinical course, in that they usually preserve ambulatory ability, albeit with gait disorders, until we first reported necropsy cases in our laboratory.5

Now, these patients with their clinical course, in that they usually preserve ambulatory ability, albeit with gait disorders, until we first reported necropsy cases in our laboratory.5

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Sasaki replies: We thank Gamez et al for their interest in our article concerning the atypical form of amyotrophic lateral sclerosis (ALS).

Over many years, several researchers have recognised this peculiar distribution of muscular atrophy in clinical practice. The clinical manifestations consist of the muscular atrophy confined to the shoulder girdle and the arms (proximally dominant), absence of deep tendon reflex in the arms, almost normal deep tendon reflex in the legs, and subluxation of the shoulder joints. Some patients progress to bulbar involvement, as Gamez et al cite, many times have been coined to describe this peculiar pattern of the muscular atrophy such as flailing arm, orang utan sign, dead arm sign, suspended form, flail arm syndrome, amyotrophic brachial diplegia syndrome, and incomparable syndrome.

Some researchers classified into a category of motor neuron disease (ALS or spinal progressive muscular atrophy). However, others could not exclude the possible cause of cervical diseases such as dissociated motor loss in the upper extremity.5 In fact, these patients had cervical abnormalities such as cervical root lesions and atrophy of the posterior longitudinal ligament disclosed by cervical radiography, MRI, or myelography. By contrast with clinical awareness of this peculiar pattern of muscular atrophy, no pathological confirmation has been made until we first reported necropsy cases in our articles.1,2 Now, these patients with their peculiar pattern of muscular atrophy are considered to be ALS or a subtype of ALS. In my private opinion, “dangling arm syndrome” or “dead arm sign” seems to be the most suitable term depicting this type of motor neuron disease.

As I agree with Hu et al reporting four important statistical discoveries in this form of ALS, the prevalence percentage of 10% of the whole ALS group, the similar age onset to the rest of ALS, a predominance among men (the male/female ratio was 9:1 in this study), and a longer median survival. It is clinically important to give wider publicity to the existence of this atypical form of ALS to avoid unnecessary surgical intervention for cervical abnormalities.

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Isolated dystarthis

We read with interest the article by Urban et al. Using transcranial magnetic stimulation, the authors demonstrated electrophysiological evidence for a central monoparesis of the tongue in patients with isolated dystarthis from stroke.6,7 As in their patients transcranial magnetic stimulation induced absent or delayed corticocolgual responses at the tongue, the authors ascribed isolated dystarthis to interruption of the corticopontocerebellar pathway. On the whole, their findings are plausible, but we would like to comment on the underlying mechanism of isolated dystarthis.

As in the case of isolated dystarthis reported by Urban et al, all of our patients with isolated dystarthis had lacunar infarctions involving the internal capsule and corona radiata.7 Measurement of cerebral blood flow with IMP-SPECT in these patients disclosed frontal cortical hypoperfusion, particularly in the anterior opucular and medial frontal regions. Anterior opucular lesions produce facio-pharyngoglosso-massaryngeal paresis (anterior opucular syndromes), and damage to the medial frontal regions, including the supplementary motor area, causes speech expression disorders. White matter lesions can disrupt afferent and efferent fibre connections in motor control circuits, leading to dysfunction of these cortices.8 Therefore, we postulated that isolated dystarthis results from interruption of corticospinal/cortico-subcortical networks indispensable for speech output, involving the thalamocortical and corticostriatal fibres as well as the corticobulbar fibres. In fact, lacunar infarctions around the internal capsule-corona radiata are likely to underlie these ascending and descending corticocerebellar tracts.

To assess corticopontocerebellar tract function, Urban et al investigated cerebellar blood flow in patients with isolated dystarthis using HMPAO-SPECT. The authors concluded that the corticopontocerebellar tract is preserved in isolated dystarthis because of no evidence for cerebellar diaschisis on SPECT. Their SPECT findings on cerebellar blood flow were similar to our results. However, we wonder whether cerebral cortical blood flow was preserved in their patients, because our SPECT study suggested frontal cortical dysfunction as an underlying mechanism of isolated dystarthis. Linguo-palatal dystarthis is seen in vascular disease evident in three of seven patients reported by Urban et al and in two of 12 by us. This indicates that isolated dystarthis originates in incoordination of multiple organs necessary for speech function as well as cerebellar dysfunction.

Although interruption of the corticocerebellar pathways is a likely cause of isolated dystarthis, it should be borne in mind that damage to other descending and ascending projections may contribute to isolated dystarthis.


Motor cortical excitability in Huntington's disease

We read with great interest the paper of Okuda et al reporting that intracortical inhibition in the motor cortex is normal in patients with chorea of various origins. At variance with their results we previously found a reduced intracortical inhibition in a group of patients with genetically confirmed Huntington's disease. Hanajima et al suggest that the discrepancies between the two studies may be due to inclusion of patients with various movement disorders (focal dystonia, myoclonus, parkinsonism, restless legs syndrome, Tourette's disorder), but also in Huntington's disease even in the early stage. 1 We think, therefore, that the discrepancy between the two studies may be due to methodological differences. The results strongly depend on the intensities of both a conditioning and a test stimulus. Especially, the intensity of the conditioning stimulus is critical. We used an intensity of 5% less than the active threshold as a conditioning stimulus in our study. Therefore, we used several intensities of the conditioning stimulus before we did not find any change in four patients, two of them already reported, with positive DNA testing but completely asymptomatic.

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intracortical inhibition is often decreased even in normal subjects. The 80% of the thresholds for relaxed muscles must correspond to different values relative to the threshold for active muscles in patients from that in normal subjects. (2) The intracortical inhibition is decreased in a variety of patients with Huntington's disease. This slight abnormality could be detected with their method but not with ours because their method has better sensitivity in detecting an abnormality than ours. Whether it is true, an intracortical inhibition must be normal or slightly disturbed in Huntington's disease.

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Critical closing pressure: a valid concept?

Czosnyka et al recently published a study investigating the clinical significance of critical closing pressure (CCP) estimates in patients with head injury. We see problems both with the theoretical foundation of their CCP concept and with the interpretation of their results.

Firstly, the physiological meaning of both formulae of CCP presented (CCP1 and CCP2, respectively) is questionable. The implication of both presented equations is that the instantaneous value of cerebral blood flow velocity (FV(t)) at a given moment t is equal to arterial blood pressure at the given time (ABP(t)) minus CCP divided by cerebrovascular resistance (CVR):

\[ FV(t) = \frac{(ABP(t)−CCP)}{CVR} \] (1)

At the time of systolic and diastolic pressure (ABP) and cerebrovascular pressure (CVR0), respectively, it follows that systolic and diastolic pressure (FV, FVd) should be equal to (ABP−CCP)/CVR and (ABP−CCP)/CVR0, respectively. However, it fails to explain that the vascular resistance valid for the static pressure/flow connection (CVR0, concerning mean pressures and flows) is different from and is in general much higher than resistances determining dynamic pressure/flow relations (CVR1) as in the case of pulsatile pressure.\footnote{Czosnyka et al.} Therefore, equation 1 cannot be applied to describe dynamic flow. This can best be illustrated using the frequency domain approach (\(ABP=mean \, pressure; \, FV=mean \, flow \, velocity; \, A1=amplitude \, of \, the \, pulsatile \, pressure \, wave; \, F1=amplitude \, of \, the \, pulsatile \, flow \, wave\)):\footnote{Czosnyka M, Smielewski P, Piechnik S, et al. Critical closing pressure: a new concept of cerebrovascular control. J Neurol Neurosurg Psychiatry 1999; 66:606–11.}

\[ FV(t) = \frac{(ABP−CCP)}{CVR} \] (2)

Inserting equations 2 and 3 into the frequency domain equation for CCP2 of the authors results in:

\[ CCP2 = \frac{ABP−A1/F1}{FV} \] (4)

leads to:

\[ CCP2 = \frac{ABP−CVR1/CVR0×(ABP−CCP)}{A1} = \frac{ABP−CVR1/CVR0}{FV} \] (5)

Observe that CCP2 is only in the case \(CVR1=CVR0\) equal to CCP. Under the more realistic assumption that CVR1 is equal to about half of CVR0 it follows for CCP2:

\[ CCP2 = \frac{0.5ABP+0.5CCP}{FV} \] (5)

With decreasing CVR1/CVR0 ratios, CCP becomes more and more dependent on ABP and independent of CCP. In any case, without exact knowledge of the CVR1/CVR0 ratio, equation 4 is useless for a valid CCP calculation.

The second criticism concerns the correlation of the calculated FV values with mean ABP found by the authors (\(r<0.5; \, p<0.05\)). According to the original idea of Burton,\footnote{Czosnyka et al.} CCP represents a certain mean ABP value below which small vessels begin to collapse. CCP should, therefore, be a constant value independent of the actual ABP. On the other hand, this significant correlation can be explained by our equation 5, again indicating the missing physiological basis of the CCP concept of the authors.

Thirdly, it seems doubtful that CCP could be estimated using pressure and flow values from ABP ranges clearly above CCP and flow values clearly above zero flow, respectively. As long as small vessels do not collapse (ABP>CCP) it is not possible to decide whether their actual wall tension is determined more by transmural pressure or by active vasoconstriction. However, the relative contribution of both effects is critical for the limit of CCP.

Finally, I would be interested in the authors' explanation of negative diastolic flow values as seen in Doppler spectra of arteries with a high vascular resistance (peripheral arteries, middle cerebral artery during strong hypocapnia). In the case of ABP<CCP and a small vessel collapse according to the model of the authors, CVR should increase towards \(\infty\) and \(FV\) towards zero (equation 1). Negative flow values could, consequently, not occur.

I suggest that the relation between pulsatile pressure and flow should be better described using the concept of different static and dynamic resistances (CVR0 and CVR1). The driving pressure of the mean FV is more accurately given by cerebral perfusion pressure (CPP=ABP−ICP) rather than by ABP−CPP. Therefore, equation 2 changes to:

\[ FV = \frac{(ABP−ICP)}{CVR} \] (6)

and equation 5 to:

\[ CCP2 = \frac{ABP−(CVR1/CVR0)×CVR1}{FV} \] (7)

Equation 7 explains well the positive correlations found between CCP2 and ABP and between CCP2 and ICP, respectively, without assuming a connection between CCP2 and Burton's concept of "critical closing pressure".\footnote{Czosnyka et al.}

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We thank Diehl very much for the interesting letter provoking some mathematical considerations about cerebral haemodynamics.

We need to emphasise that our primary intention was to investigate Burton's hypothesis in patients with head injury that critical closing pressure (CCP) may be represented by a sum of intracranial pressure (ICP) and the tension in the arterial walls.

CCP=ICP+active tension of arterial walls\footnote{Czosnyka et al.} proposed the mathematical formula taken for calculations:

\[ CCP1 = ABP−ABPpp/FPppy/FPppp \] (8)

(where ABP and FV are mean values of arterial pressure and MCA flow velocity, ABP and FV are systolic values, ABPpp and FPppy are peak to peak amplitudes). A graphical interpretation of this formula has been given in fig 1. CCP1 is an x intercept point of linear regression between subsequent systolic and diastolic values recorded within 6 second intervals of flow velocity (along y axis) and arterial pressure (along x axis). In fact, the concept proposed by Michel et al is very similar. The only difference is that instead of the original waveforms of FV and ABP, first (fundamental) harmonic components were taken for the same graphical construction—that is:\footnote{Czosnyka et al.}

\[ CCP2 = \frac{ABP−A1/F1}{FV} \] (9)

In our paper we confirmed empirically that both CCP1 and CCP2 produced the same values in a group of patients with head injury, therefore the mathematical consideration of Dichtl (equations 1–5) must contain an error!\footnote{Czosnyka et al.}

First of all we cannot see how equation (1) from Dichtl's letter can be derived from any of our formulae. Everyone who has tried to plot momentary values from ABP pulse waveform against momentary values of FV waveform knows that it never plots a straight line (equation (1) implies). I would be surprised if "clouds" of systolic and diastolic values of ABP and FV waveforms (fig 1 in) one can neither see an ellipsoidal shape which is rather seldom regular enough to be approximated by a straight section. Therefore, equation (1) in Dichtl's letter is not correct. In fact, CVR is a frequency dependent variable (represents vascular impedance) and if a linear theory can be applied, division in (1) should be substituted by a convolution with an inverse of Fourier transform of "cerebrovascular admittance".

Definition of CVR0 as FV/(ABP−ICP) is completely artificial and lacks a physiological basis. It is rather taken from the geometrical interpretation of figure 1 in. In our material equivalent of parameter CVR0 (as defined by Dichtl) is 1.007 (SD 0.31) and CVR1 0.972 (SD 0.29), the difference between them was not statistically significant. Therefore, the suggestion that the CVR1/CVR0 ratio is 0.5 is not correct. Real CVR0 should be calculated as (ABP−ICP)/FV. We fully agree that equation (5) proposed by Diehl is "useless for valid CCP calculation". We have not used it and have never suggested anyone could do so.

The second criticism was that our CCP positively correlated with ABP. In our paper it should not be a surprise. When ABP decreases, vasodilatation occurs and arterial wall tension decreases. Therefore presuming ICP was constant, CCP should decrease. A rather weak (though significant) correlation suggests that not all of our patients were pressure reactive or ICP was not always constant.

The final issue concerning negative flow velocities is a trap Diehl has prepared for himself. We never suggested that any factor interpretable as cerebrovascular resistance (CVR0 or CVR1) should be involved in the concept of critical closing pressure. From the definition, closing is a strongly non-linear phenomenon, therefore applying linear theory here is very
High frequency stimulation of the subthalamic nucleus and levodopa induced dyskinesias in Parkinson’s disease

Reduction in the neuronal activity of the subthalamic nucleus leading to diminished excitation of the globus pallidum internum is associated with chorea-ballism in monkeys. Levodopa induced dyskinesias are currently thought to share a similar pathophysiology but recent findings also suggest that abnormal patterns of neuronal firing in the globus pallidum internum may be as relevant. Data from both parkinsonian monkeys and patients with Parkinson’s disease submitted to lesion or functional blockade of the subthalamic nucleus are in keeping with such a general principle, but the threshold to induce dyskinesias in the parkinsonian state is higher than in intact animals. The case recently described by Figueiras-Mendez et al. is extremely interesting as it suggests that functional inhibition of the subthalamic nucleus by high frequency stimulation blocks levodopa induced dyskinesias. This is clearly at odds with the current pathophysiological model of the basal ganglia. Thus, the finding of Figueiras-Mendez et al. rises the intriguing possibility that dyskinesias depend or are mediated by neuronal firing in a given region of the subthalamic nucleus, which is blocked by high frequency stimulation. Measurement of afferent synaptic activity by the technique of 2-deoxyglucose (2-DG) uptake showed an increment in the subthalamic nucleus compatible with increased inhibition from the globus pallidum externum, particularly in the ventromedial tip of the nucleus. This contrasts with the findings in monkeys with chorea induced by pharmacological blockade of the globus pallidum externum, in which 2-DG uptake was maximal in the dorsalateral portion of the subthalamic nucleus, where the sensorimotor region lies. A recent anatomical study also showed that the cortical-subthalamic disease connection is somatotopically segregated, so that fibres from the supplementary motor area project to the most medial portion and fibres from the primary and premotor areas terminate in the lateral region of the subthalamic nucleus. All this heterogeneity may have pathophysiological relevance, one aspect of which could be the findings in the patient reported by Figueiras-Mendez et al. However, before the findings of this case may be used to sustain the postulation on the role of the subthalamic nucleus in the origin of levodopa induced dyskinesias, there is a crucial issue to resolve—namely, the location of the tip of the stimulation electrodes.

There are several points leading us to question the actual site of action of the electrode: (1) Stimulation of the subthalamic nucleus in Parkinson’s disease has been associated with the production of dyskinesias only relieved by reduction in levodopa intake. Moreover, Benabid et al who pioneered this technique, consider the induction of dyskinesias by high frequency stimulation of the subthalamic nucleus as a good indicator of a very positive response to stimulation. Fibre-tracing to the thalamus from the globus pallidum internum are placed dorsocaudally to the subthalamic nucleus and could be blocked by high frequency stimulation. (2) When the recording electrode was placed ventrally, the pattern of neuronal activity was more predominant ventrally than in the subthalamic nucleus in sagittal planes 11 mm or less, neuronal activity is characterised by action potentials of large amplitudes (0.5–1 mV) with low background activity, tonically firing neurons, and absent sensorimotor responses (“driving”). All these characteristics seemed to be present in the patient discussed here. Neuronal activity in the sensorimotor region of the subthalamic nucleus is different from the above but on occasions the distinction may not be easy. Accordingly, it is very important to document in more detail the findings in the case of Figueiras-Mendez et al. Ideally we would like to see the trajectory and length of the different recording tracks, the effects of microstimulation, and the post-surgery MRI with measurement of the tip of the electrodes. If, as assumed, the subthalamic nucleus was indeed correctly targeted in this patient, the pathophysiology of the basal ganglia will need to be revisited.

We thank Obeso et al for their comments regarding our recent report. In summary, they raised some interesting points which need further clarification.

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Recognition of the electrical activity of the subthalamic nucleus was based on the following criteria: (a) high frequency discharge (25 Hz or higher) within the nucleus; (b) a tonic (regular), phasic (irregular) or a rhythmic pattern of discharge; (c) response to voluntary/passive movements; and (d) response to tremor activity. Positive cells were so considered based on the correlation with the EMG and the accelerometer recorded simultaneously. Artificial manual stop testing by one experimenter (confirmed by visual inspection, silence in the EMG, and stoppage in the oscillating accelerometer) and/or spontaneous arrest in the tremor modified the firing frequency and discharge pattern or rhythmic cells corroborating the tremor nature of the cells; (e) the activity of the cells above the subthalamic nucleus. A lower background noise level; (f) the activity of substantia nigra pars reticulata cells when further lowering the microelectrode. These cells discharge at high frequency at regular intervals as identified in patients and primates. All these points were fulfilled by the patient reported.

Considering the questions in the letter by Obeso et al, we make the following comments: (a) Action potentials of low frequency discharge are easily recognised from the rest of the recording cells, and are not very common. The recordings shown in the article have amplitudes less than 0.3 mV and could not be considered large amplitude potentials. We start to record activity from 3 mm before entering the subthalamic nucleus, traverse the length of the subthalamic nucleus, and go further down several mm to encounter substantia nigra pars reticulata cells. Changes in the background activity are clearly recognised and are higher when entering the subthalamic nucleus. Enough cells are recorded along the tracks experimented so as to recognise a large amplitude potential. The
Nitrin oxide in acute ischaemic stroke

The pivotal role of nitric oxide (NO) in cerebral ischaemia has been elegantly highlighted in the recent editorial by O’Mahony and Kendall. Although studies of neuroprotective agents have been largely disappointing in terminating, pharmacological manipulation of NO may play a novel means of protecting the brain from ischaemic insult. One area not discussed in these neuroprotective effects is 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors or “statins” in cerebral ischaemia. Preliminary studies have shown that statins modulate brain nitric oxide synthase and improve activity in a neuroprotective manner. Data from a murine model of ischaemic stroke demonstrate that prophylactic statin therapy reduces infarct size by about 30%, and improves neurological outcome in normocholesterolaemic animals. In this investigation, statin therapy directly upregulated endothelial NO in the brain without altering expression of neuronal NO. Recent findings also suggest that statin therapy influences the activation of inducible NO. Lovastatin has been shown to inhibit cytokine mediated upregulation of inducible NO and production of NO in rat astrocytes and macrophages, and this inhibition may represent a mechanism for suppressing inflammatory responses that accompany ischaemia. Most interestingly, these preliminary findings suggest that statin therapy may modify the friendly and unfriendly faces of brain NO in a synergistically neuroprotective manner. These and other vascular effects of statins in cerebral ischaemia are potentially of great importance in human neuroprotection and ongoing studies include the The Prospective Study of Pravastatin in the Elderly at Risk (PROSPER) study to help clarify their role in human cerebrovascular disease.

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BOOK REVIEWS


That neuroimmunology has come of age is demonstrated by the profusion of volumes published on the subject in recent years. This volume focuses on the central nervous system, and aims to satisfy the curiosity of both the clinician faced with a diagnostic conundrum and the experimental immunologist inquiring into the clinical relevance of his findings. At first sight it seems improbable that both of these goals might be achieved in one volume; this book however, succeeds admirably in what it sets out to do, as much as a result of its literary style as its content. The intrusive authorial voice fell into disfavour in literary circles around the turn of the century because it was thought that it elicited attention to the act of narrating which detracts from realistic illusion, so reducing the emotional intensity of what was being represented. It is a device much favoured by postmodern writers who expose the nature of fictional constructs. The intrusive medical author never dropped out of fashion, although, in these days of evidence based prejudice, authorial omniscience might be considered suspect. The authors of this volume are intrusive in a guiding conversational manner that makes this book by far the most readable of the neuroimmunological texts. The book opens with a highly accessible chapter on immune responses to central nervous system. There follows a chapter that integrates the neurobiology of multiple sclerosis with contemporary issues of aetiology, cell injury, and repair. Next, a chapter on inflammatory demyelinating disease and its syndromes of isolated demyelination, acute disseminated encephalomyelitis and allied conditions, and some of the syndromes of demyelination that are now accepted as part of the range of multiple sclerosis. This book continues with chapters on paraneoplastic disorders of the CNS, stiff man syndrome, neurologival complications of

As Alzheimer's disease becomes of increasing importance to society, basic science research in this field needs to provide the building blocks for both therapeutic interventions and accurate diagnosis. This publication is a collection of papers presented at an international Alzheimer's disease research meeting in Leipzig in 1997. This conference aimed to bring together both clinical and basic science disciplines and this is reflected in the papers selected for this book. There are 31 papers included, covering topics from early symptomatology and cognitive features to immunobiology and theoretical neuronal treatment strategies. The contributors to this book are some of the most authoritative in their field, predominantly based in Europe.

Covering all aspects of Alzheimer's disease research from the correct diagnosis to basic science approaches of treatment is ambitious and well referenced. The only drawback is that in making erudition so readily available, one risks being outshined yet again by one's registrar.

JON SUSSMAN


Organ transplantation, once medical exotica, is now almost routine in the United Kingdom each year are performed cadaveric organ transplants of about 1800 kidneys (in addition to 160 live kidney donors), 700 livers, and 450 heart/lungs (UK Transplant Support Service). Several basic surgical techniques were established at the beginning of the century in canine models. Translocation of these experiments to humans awaited safe and effective immunosuppression. Unsurprisingly, many forms of immunosuppression were radiation (total body or total lymphoid) and non-selective chemical reagents (benzene and tolenue).

Then the antiproliferative drug 6-mercaptopurine (6-MP) was introduced, shortly followed by a derivative, azathioprine, with improved oral bioavailability. Combined with corticosteroids, these allowed the first human solid organ transplants to be performed: in 1954 the first lung transplant in Mississippi and liver transplant in Colorado. Then in 1967 Christian Barnard captured the world's imagination with the first heart transplant. His technique has been modified slightly since, but the increasing success of organ transplantation rests mainly on improved immunosuppression with drugs that selectively suppress lymphocytes by inhibiting lymphokine generation (cyclosporin A, tacrolimus), renal transduction (sirolimus, leflunomide), or differentiation (15-deoxyspergualin) pathways. As a result, over the last 10 years in the United Kingdom, the 1 year survival of grafts has improved from 80% to 90% (kidney), 55% to 75% (liver), and 70% to 90% (heart/lung).

Windics estimates that 10% of transplantation patients have a significant neurological complication. Typically without common being neurotoxicity of immunosuppressive drugs, seizures, and failure to awaken. Yet this is the first text devoted to the neurological aspects of organ transplantation. It is therefore a timely subject because of the increasing number of organ transplant recipients in the excellent Blue Books Of Practical Neurology series. Twenty authors contribute (one Dutch, one Swiss, the rest American) to four chapters on transplantation including failure to awaken, and psychiatric, neuromuscular and demyelinating complications. Especially useful to the neurologist without much experience of transplantation are the comprehen- sive chapters on immunosuppressive drugs and the opportunistic infections associated with them (most commonly Listeria monocytogenes, Aspergillus fumigatus, and Cryptococcus neoformans). The peripheral nerve and plexus injuries associated with transplantation are painstakingly described; astonishingly a signif- icant uilar neuropathy occurs in up to 40% of kidney transplant patients. The Cincinnati Transplant Tumour Registry has recorded information on 10 813 cancers arising de novo in organ allograft recipients worldwide and here are presented the data in the 300 of these with CNS involvement. This is one for the shelves of any neurologist involved in organ transplantation.

CLARE GALTON

ALASDAIR COLES


Volume nine of the Current Issues in Neurodegenerative Disease series examines the interplay between cerebrovascular disease and dementia, particularly Alzheimer's disease. Two hundred pages of what are essentially 20 brief review articles comprise this text, sadly without any illustrations. Each section begins with an introduction to each chapter there is a certain sense of deja vu, although on the positive side each contribution is extremely well referenced.

The book is divided into five sections covering the historical concepts of vascular and Alzheimer's dementias, the arguments for a pure vascular dementia, the role of Alzheimer's disease in the genesis of dementia after stroke, the contribution of white matter changes on neuroimaging to dementia, and finally a short section examining practical questions such as the management of stroke in patients with dementia. Although common conditions such as their own right, stroke and Alzheimer's disease do seem to cross paths more often than would be expected by chance alone, and more often than can be explained by the presence of unexplained angiopathy and recurrent lobar haemorrhages. Perhaps common genetic factors are responsible and here the APOE alleles are discussed. The comprehensive section on deep white matter lesions seeks to explain the connection further — and convinces the reader that there is still a lot which is not well understood. It is in this section particularly that illustrations are greatly missed. Brief mention is made of other conditions which may produce white matter changes and dementia such as CADASIL, cerebral lupus, and the primary antiphospholipid syndrome.

Some typographical errors and mistranslations detract a little further from a book which seems unlikely to appeal to most neurologists, although it will no doubt be a source of reference to those working in the field of cognitive disorders, particularly vascular dementias.

PETER MARTIN


Evolutionary biologists would probably tell us that the enchainment of stories is due to survival having been dependent on the passing of oral culture from one generation to the next. Information put in narrative form not only delights, but is easily recalled. Stories also construct meaning by integrating observation, inference, motive, and consequence in a fashion that informs future action. Our experience of the world is constructed around such narratives. They define us as individuals, family members, professionals, and cultural groups.

This book is a series of essays on psychotherapy, psychiatry, and also medicine that sees the awareness and use of narrative in clinical practice as a construct that can both
deliver effective care as well as act as a conceptual bridge between the different disciplines. One of the great pleasures of being a doctor has always been listening to patient's stories, but the editors of this book fear that this essential art can be overtaken by dull scientific pragmatism. Rather, in the most outstanding chapter, writes a lucid and well reasoned account of the need to search for and maintain narrative meaning in treating psychosis. This avoids the dehumanising effect to both patients and professionals of identifying individuals by their illness as in psychiatries. Every psychiatric library should buy this book for this paper alone, which should be required reading for all practitioners.

The rest of this book is of variable quality. There is a rather prosaic essay on gender issues, and there is repetition in various chapters concerning attachment theory, a useful but over worked paradigm. However, there are two very fine accounts of narrative in psychotherapy by James Phillips and Jeremy Holmes. DUNCAN MCLEAN


In a small accessible and easily digestible volume, the authors address a clinically important field. Faced with slim evidence on which to base clinical recommendations, they acknowledge that their very useful management advice “has often had to be based on practical clinical experience rather than the results of clinical trials or formal research…” This disclaimer seems to have allowed them to mix evidence and opinion, limit references, and confuse the reader regarding the level of evidence. A pity, as the authors, with special expertise in this important area, have made a good start in putting together different aspects of the care of the woman with epilepsy in a practical book that is of direct interest and relevance to neurologists, obstetricians, general practitioners, nurses, midwives, and patients.

Moving on from the general to the particular, the text, although expansive in parts, glosses over some important points. Examples include (a) which oral vitamin K preparations are considered safe in pregnancy (phytomenadione), (b) differential efficacy of various antiepileptic drugs in different syndromes versus side effect and teratogenicity profile, (c) more information on the optimisation of antiepileptic drugs to improve the management of heterogeneous content and trainers—although a clear and consistent management of hyperactivity in childhood, with good practical advice on the use of methylphenidate.

Apart from the chapters on chronic fatigue and the treatment of tardive dyskinesia there is little in this book which is of immediate interest to neurologists. However general psychiatrists wishing to improve their prescribing skills will find this book useful.

SIMON FLEMINGER


The Maudsley prescribing guidelines are produced each year for a local readership, but this, the fifth edition, is the first to go public. The authors and principal contributors, a mixture of pharmacists and psychiatrists with an interest and background in clinical psychopharmacology, are to be complimented on producing a guide of manageable size and ready accessibility.

The book is divided into sections dealing with the treatment of broad groups of clinical disorders—for example, psychosis—special patient populations—for example, elderly people, with further sections on the management of emergencies and the adverse effects of psychotropic drugs. Much of the information is laid out in tabular form. It could become an indispensable resource for a busy on call junior house officer (the dimensions would fit comfortably into the pocket of a clinical white coat, were they still to be worn) but more senior clinicians will find plenty of use for it in the clinic. It does not aim at great erudition, but provides a useful list of references.

There are a few cavils. The section on treatment of anxiety is skimpy (one and a half pages) compared with say the treatment of affective illness (22 pages), or schizophrenia (20 pages). The brevity is only explained by the undeveloped state of that particular area of psychopharmacology. Sections on new treatments such as clozapine and indications for lumbar puncture and indications for EGG seem to have been displaced from some other primer for busy junior doctors. There is no index.

These quibbles apart, prescribing guidelines can be wholeheartedly recommended.

BRIAN TOONE
Motor cortical excitability in Huntington's disease

G ABRUZZESE, R MARCHESE and C TROMPETTO

J Neurol Neurosurg Psychiatry 2000 68: 120-121
doi: 10.1136/jnnp.68.1.120

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