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-limiting course. A postictal phenomenon with focal cerebral hypofunction (similar to Todd’s palsy), rather than ongoing seizure activity, has been postulated.1 Surface EEG is either normal or showing non-specific slow waves.1 Hence, 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 ganglia. As hyperperfusion in ictal cerebral SPECT is closely linked to epileptic activities,4 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 Antiepileptic drugs were withdrawn to facilitate seizure recording.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 diagnostical and statistical manual of mental disorders (DSM-IV) criteria as brief psychotic disorders without marked stressor. HMPAO-SPECT was performed during the psychotic period, which ranged from 2–4 days after the last seizure. Interictal cerebral SPECT, brain MRI, and a Wada test were performed as part of presurgical evaluation.

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 at day 4 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 and continued until 4 weeks after the last seizure. A repeat cerebral SPECT study showed a clear resolution of hyperperfusion signal over the right temporal neocortex and left basal ganglia. Based on these findings, anterior temporal lobectomy was performed and the patient became seizure free and his psychotic features did not recur. The results of these observations are presented here to add to the understanding of the pathogenesis of postictal psychosis.
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 hyperperfusion were identified. Quantitative data at interest of ROIs, were measured on coronal and axial slides containing basal ganglia (BG), mesial (MT), and lateral (LT) temporal lobe structures. Asymmetry index (ASI) was calculated as ((ROI focus−ROI contralateral)/ROI focus+ROI contralateral)×100%. 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 with their interictal study (figure). Quantitative analysis for patient 1 showed changes of ASI during IP and PP over right MT was +75% (-6.46476 to -1.65289); over the right LT was +116.7% (1.07972 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 +3.8% (13.14217 to 12.64158); over right LT was +178.6% (10.4696 to 18.70077); and over left BG was +155.9% (-5.85556 to 3.27522).

Postictal psychosis is a distinct clinical entity associated with temporal lobe epilepsy.7 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 clinical seizure, with partial seizures used to precipitate or interrupt withdrawal of antiepileptic drugs.7 The cluster occurs in patients with poor drug compliance or during video EEG telemetry studies when antiepileptic drugs are not stopped purposefully. The clinical course of postictal psychosis is usually benign and predictable.7 In our patients, the duration of psychotic disturbances lasted from 1 to 7 days, which is in keeping with the good prognosis. Antipsychotic drugs, such as haloperidol and fluphenazine are usually prescribed.7

The underlying mechanism of postictal psychosis is unknown. Postictal cerebral hypofunction has been postulated as an analogue to Todd’s paralysis after seizure.7 8 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.7 8 To conclude, our results are contradictory to the hypofunction theory of Todd’s paralysis in postictal psychosis. We think that these 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.
Previous findings showed that ED-B+FN presents with conformational modifications in its central part and results from deregulation of FN pre-mRNA. The distribution of this isoform was found to be highly restricted in normal adult tissues. By contrast, ED-B+ FN 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.

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 of this 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 upregulated in glioblastomas, was found to be highly expressed in both AVMs and in the vessels of cerebral tissue bordering the malformations, by contrast with the down regulation occurring in the vasculature of the normal brain. The pattern of distribution of structural proteins was consistent with the hypothesis of diffuse activation of angiogenesis, without specific relation to individual vessel types.

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

The present findings indicate that a specific receptor upregulated in glioblastomas, EE, for his technical help and Mr. Tho-

Hashimoto's encephalopathy presenting as "myxoedematous madness"

The neuropyschiatric sequela 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 thyroid hormone. 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 thyroid disease.

The present findings indicate that a specific receptor upregulated in glioblastomas, may present with conformational modifications or from deregulation of FN pre-mRNA. The distribution of this isoform was found to be highly restricted in normal adult tissues. By contrast, ED-B+ FN 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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The present findings indicate that a specific receptor upregulated in glioblastomas, EE, for his technical help and Mr. Thomas Wiley for manuscript revision.

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1 Hatva E, Jääskeläinen J, Hirvonen H, et al. "Thr


became aggressive and threatened them with a saw. The general practitioner was called and suspected that he had bought a new psychoanalyst and was suffering from depression. 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 performance on the Rey figure, which was due to planning rather than visuospatial errors, suggesting a predominantly “dysexecutive” pattern. CT and EEG were both normal, although during the admission, he was apparently healthy and felt well. Behavioural assessment showed persisting deficits in delayed recall of verbal material, verbal fluency, and visuospatial function. Formal psychometric testing, blood tests, and SPECT were repeated, 1 year after the original examinations. Laboratory and neuropsychological results are presented in the table. It is of note that, whereas his naming ability had improved, performance on frontal executive tasks remained impaired. The appearance 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 neuropsychological disturbance, on the background of gradual behavioural and affective change. He was profoundly hypothyroid due to an autoimmune thyroiditis, but there was no clinical evidence of thyroid failure other than the abnormal mental state. The psychiatric component of his illness receded fully, and the antithyroid microsomal antibody titre fell markedly after thyroxine replacement, although his mild neuropsychological deficits remained unchanged. Corticosteroids were not used at any stage. The response to thyroxine does not, in itself, imply that the cerebral illness had an endocrine origin; a recent report described a patient with a subacute encephalopathic illness and compensated hypothyroidism in the presence of increased antimicrosomal antibodies, all of which responded to thyroxine replacement.1 In that case, however, both EEG and SPECT were abnormal, the SPECT showing multiple areas of severely reduced perfusion, which normalised with treatment. By contrast, in the present case the EEG was normal and the SPECT abnormality was marginal and changed little, if at all, with treatment. The evidence for a significant vasculitic component to the illness is, therefore, unconvincing.

The mild and relatively circumscribed neuropsychological deficits coupled with florid psychotic phenomena, also contrast with the profound global disturbance of cognition usually associated with Hashimoto’s encephalopathy. This distinction suggests that microvascular disruption and thyroid hormone depletion may emphasise different aspects of the clinical range in Hashimoto’s encephalopathy. Although the present case would support Asher’s conclusion that the psychiatric features of Hashimoto’s encephalopathy typically respond to thyroid replacement, it additionally suggests that subtle neuropsychological deficits may be apparent even in the absence of obvious cerebral perfusion deficits, and that these may not be fully reversible.

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Table 1 Laboratory and neuropsychological results at presentation (A) and at 12 month follow up (B)

<table>
<thead>
<tr>
<th>Laboratory (units)</th>
<th>A</th>
<th>B</th>
</tr>
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<tbody>
<tr>
<td>Full blood count</td>
<td>Normal</td>
<td>Normal</td>
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<tr>
<td>Erythrocyte sedimentation rate</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Urea and electrolytes</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Liver function tests</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Antithyroid autoantibodies</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>B12 and folate</td>
<td>Normal</td>
<td>Not tested</td>
</tr>
<tr>
<td>VDLR</td>
<td>Negative</td>
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</tr>
<tr>
<td>Thyroid stimulating hormone (mU/L)</td>
<td>1.25600</td>
<td>0.87</td>
</tr>
<tr>
<td>T4</td>
<td>Not tested</td>
<td>7.4</td>
</tr>
<tr>
<td>Free T4 (pmol/L)</td>
<td>1:25600</td>
<td>1:1600</td>
</tr>
<tr>
<td>Antithyroid microsomal antibody titres</td>
<td>25/30</td>
<td>25</td>
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<tr>
<td>Psychometric (normal/predicted range):</td>
<td>10th percentile</td>
<td>16th percentile</td>
</tr>
<tr>
<td>WAIS-R (verbal)</td>
<td>13th percentile</td>
<td>Not tested</td>
</tr>
<tr>
<td>WAIS-R (performance)</td>
<td>27th percentile</td>
<td>Not tested</td>
</tr>
<tr>
<td>FAS verbal fluency (&gt;/=30)</td>
<td>25</td>
<td>23</td>
</tr>
<tr>
<td>Digit span forwards (&gt;/=5)</td>
<td>10/30</td>
<td>16/30</td>
</tr>
<tr>
<td>Rey-Osterreith complex figure (copy) (&gt;/=30)</td>
<td>25.5</td>
<td>24</td>
</tr>
<tr>
<td>Rey-Osterreith complex figure (recall) (&gt;/=30)</td>
<td>Not tested</td>
<td>75%</td>
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</table>

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Alien hand sign in Creutzfeld-Jakob disease

The clinical picture of Creutzfeld-Jakob disease (CJD) includes various movement disorders such as myoclonus, parkinsonism, hemiballismus, 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.

Creutzfeld-Jakob disease, one of the human prion diseases, is characterised by rapidly progressive mental and motor deterioration.1 Involuntary movements occur in above 90% of the patients in the course of the disease, the most common being myoclonus,2 other movement disorders range from tremor to the Rett phenomenon, dystonia, and hemiballismus.3 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”.4 One of the patient’s hands acts as a stranger to the body and is uncooperative. 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,6 oculopontineolabral,7 and corticalenial infection,8 and corticobasal degeneration.9

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 his 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 tiredness of gait and uncontrollable movements. 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

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failing over him”. His wife mentioned bizarre, useless movements of his left hand which were present from the beginning of the disease.

On admission, he was awake, bradyphrenic, and partially collaborative. His consent, haematoxylin, and cytoplasmic components were normal. Prognosm was normal. Prominent dysphagia and dyscalculia were noticed. Immediate recall and short term memory were severely disturbed, whereas long term memory, especially for personal life events, was relatively spared. Abstract thinking was severely affected. Bimanual movements, such as clapping, were extremely difficult.

The cranial nerves were normal as were ocular fundi. The motor examination showed normal. Deep reflexes were symmetric and plantar responses were flexor. The right arm had a dystonic posture. His gait was ataxic on a wide base. At times, the left arm would spontaneously rise in front of the patient during speaking or while using his right hand. He was unaware of these movements until they were brought to his attention. When questioned about their purpose, the patient claimed that these were voluntary. No grasping of either hand or foot was found. The patient had no cortical sensory loss.

The laboratory data including blood chemistry, haematology, and sedimentation rate were normal, as were folic acid, vitamin B12 concentrations, and thyroid function. Venereal disease research laboratory and HIV tests were negative. The cerebrospinal fluid had normal content. Brain CT showed mild cerebral atrophy. An EEG showed severe diffuse slowing at admission. Within a week, repeated EEGs showed triphasic waves with a periodic pattern of 1-1.5 Hz. During the next 2 weeks, the patient developed multifocal myoclonic jerks. Severe dysphasia and cognitive decline were accompanied by confusion and aggression. He became grossly ataxic, and unable to walk and perform any of his daily activities even with help. Transferred to a chronic care hospital, he died few weeks later. Postmortem examination was not allowed.

This short fatal neurological disease manifested by fulminant dementia, myoclonic jerks, and extrapyramidal and cerebellar dysfunction was strongly suggestive of CJD. The periodic EEG pattern reinforced this diagnosis. Our patient’s alien hand was part of the otherwise characteristic clinical picture of CJD, but appeared early in the disease course when no myoclonic jerks were present. We are aware of only one report of alien hand in CJD. MacGowan et al. described two patients with CJD and a myoclonic alien hand syndrome. In one patient the left arm “was noted to have spontaneous movements which appeared purposeful…waned out of her view”. In the second, the alien limb performed complex actions such as unbuttoning her blouse and removing a hair pin. Although our patient had no myoclonus or pyramidal signs when the alien hand appeared, in their patients it was associated with spontaneous or stimulussensitive myoclonus, spastic hemiparesis, and cortical sensory loss.

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 hemispheric 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 a coronary 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 responding “I do not want to”. Another patient’s left arm was at times “elevated in front of his mouth”, 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 aetiology 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 Zardel, Department of Physiology, University of California, Los Angeles, USA. R INZELBERG P NISIPEANU S C BLUMEN R L CARASO Department of Neurology, Hillel Yaffe Medical Center, Hadera, Israel Correspondence to: Dr Dr R Inzelp, Department of Neurology, Hillel Yaffe Medical Center, Hadera, Israel


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 (ESPgan) 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 erroneously 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; 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 uric acid, cholesterol, triglycerides, glucose, creatinine, transaminase, bilirubin, immunoglobulins (Igs), lead, iron, copper, urinalysis, urinary porphyrin, folic acid, and vitamins A, B, D, E, and K. Antinuclear antibodies, antineutrophil cytoplasmic antibodies, antinuclear antibodies, anti-neutrophil cytoplasmic antibodies (ANCA), antithrombin antibodies (AGA), IgM and IgA antireticulum antibodies, specific and non-specific organ autoantibodies, IgA and IgG antithrombin antibodies (AGAs), IgA antidiomene antibodies (EMAs), and IgA antireticular antibodies (ARA), assessed 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

Electrophysiological study suggestive in both episodes of an acute demyelinating peripheral neuropathy confined to the lower limbs. Values were within normal limits as the upper limbs

<table>
<thead>
<tr>
<th>1st Episode</th>
<th>2nd Episode</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tibial</strong></td>
<td><strong>Tibial</strong></td>
</tr>
<tr>
<td><strong>CMAP (µV)</strong></td>
<td>22</td>
</tr>
<tr>
<td><strong>F wave latency (ms)</strong></td>
<td>70</td>
</tr>
<tr>
<td><strong>CMV (ms)</strong></td>
<td>26</td>
</tr>
<tr>
<td><strong>DL (ms)</strong></td>
<td>74</td>
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<tr>
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<td>3</td>
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<tr>
<td><strong>SV (µV)</strong></td>
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<tr>
<td><strong>MCV (ms)</strong></td>
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<td><strong>SV (µV)</strong></td>
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<tr>
<td><strong>SV (µV)</strong></td>
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MVC= motor conduction velocity; DL= distal latency; CMAP= compound motor action potential; SSV= motor sensory conduction velocity; AMP= amplitude; L= left; R= right.

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

An autoimmune pathogenesis in association with strong evidence of a genetic susceptibility 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. 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 celiac disease many immunological perturbations can occur outside the gastrointestinal tract. Crossing of the antigens through a damaged small intestinal mucosa, deposition of immune complexes in target organs, a reduction in immune surveillance, 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 possible 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 study shows two major issues: an acute polynuropathy 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.
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 palmonental, hand grasp, foot grasp, glabellar, rooting, snout, sucking (tactile) and sucking (visual). Neuropsychological measures included the assessment of frontal lobe function (trail-making 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, suicide, and suicide ideation within the past year were also recorded, as were blood pressure and a checklist for chronic physical illness.

Total FRSS scores and scores on FRSS subscales were compared between groups using the Mann-Whitney U test for independent samples. In the peripheral vascular disease group, a correlation matrix for total FRSS score against DSMIV depression, CAMCOG score, behavioural dyscontrol scale score, verbal fluency score (total number of words beginning with F, A, and S) and trail-making test times was examined using the Spearman correlation coefficient, confidence interval, sex, blood pressure, and chronic physical illness. Behavioural dyscontrol scale scores, trail-making A/B test times, and verbal fluency scores were first converted into binary variables according to whether they were at/above or below the median value for the group. CAMCOG score was divided into subjects scoring 69 or above or less than 69. Those associations with a two-tailed significance of 0.1 or less were then entered into a linear regression equation using the significance of 0.15. Further bed-side 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).

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

<table>
<thead>
<tr>
<th>Hand grasp</th>
<th>Foot grasp</th>
<th>Glabellar</th>
<th>Palmonental</th>
<th>Paratonia</th>
<th>Rooting</th>
<th>Snout</th>
<th>Sucking (tactile)</th>
<th>Sucking (visual)</th>
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*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 coexistent disruption of frontal/subcortical brain function may not present with high 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 Mr Paul Baskerville for allowing me to interview patients under their care. The study was carried out as part of a University of London MD thesis. RAHUL RAO Department of Old Age Psychiatry, Maudsley Hospital, Institute of Psychiatry, London Correspondence to: Dr Rahul Rao, Department of Old Age Psychiatry, Guy’s, King’s, and St Thomas Medical School, Job Ward, Thomas Guy House, Guy’s Hospital, St Thomas Street, London SE1 9RT, UK Email: rao@globalnet.co.uk

4. Alexandrova, N.A., Gibson, W.C., Norris, J.W., et al. 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).
density lipoprotein (3.92 mmol/l) and triglycerides (4.30 mmol/l) and low high density lipoprotein (0.73 mmol/l). Serum phenytoin concentration was therapeutic at 74 µmol/l. An ECG was normal.

Ophthalmological consultation and formal visual field testing demonstrated a concentrically constricted field of mild degree in the right eye and tunnel vision in the left eye. The patient consented to overnight video-EEG monitoring and was seen on multiple occasions to move his left arm and/or leg in a normal fashion, at one point using the left arm to readjust his bed covers shortly after arousal from sleep, before glancing briefly at the video camera and completing the task with his right arm. The prolonged EEG was normal.

A formal neuropsychological assessment performed in hospital documented impaired attention, concentration, and working memory, as well as several atypical calculation and spelling errors, the second involving unusual “near miss” letter substitutions or memory, as well as several atypical calculations inattentive, but was able to answer questions.

It is unclear how or when the patient acquired the information needed to mimic a constructional apraxia. Previous bedside neuropsychological evaluations may have served to familiarise him with the format of such testing, acting as an impetus to research the issue of stroke and focal brain deficits (which might also have occurred after his father’s stroke), much in the same way he is now researching conversion disorder, thereby discovering what expected answers should look 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 paresis, supranuclear vertical gaze palsy, difficulty converging, left sided flaccid hemiparesis, and dense, left sided hemianaesthesia. 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 examined, 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 interested in talking 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. He began to anxiously recalled being otherwise. By this time he had a moderate hemiplegia and recognized “a little weakness,” but continued to insist that he was well and able to return to work. By the 6th week after the stroke he was 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 to work. His awareness of his hemiplegia fluctuated within an hour of making such statements the patient might insist that after a week’s exercise he would be ready to return to work. His awareness of his hemiplegia fluctuated for 8 weeks after the stroke before being fixed, but remained shallow after 12 weeks; he no longer planned to return to work and applied for social security disability insurance “because they say I’m disabled.”

The patient’s mood was remarkably cheerful and optimistic. A week after the stroke he was noted to praise extravagantly the hospital staff, “smelled funny” was another reason he wanted the nurses to take it away. Sleep was not disrupted or reduced

Kahn

Sognosia were described as having “euphoric mood.”

The syndrome of anosognosia

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 had no further episodes. In cases of epileptic cardiac dysrhythmia, isolated EEG or ECG recording may prove insufficient and prolonged simultaneous EEG/ECG monitoring may be required.

Cardiac arrhythmias subsequent to epileptic seizures have been recognised for more than 90 years. They provoke diagnostic confusion and may be a mechanism of sudden unexplained death in epilepsy. Whereas sinus tachycardia was noted to accompany more than 90% of epileptic seizures, isolated bradycardia was seen much
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 restored.

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, dysphoria, or diuresis. Often, however, he sustained soft tissue injuries to his face and scalp.

Witnesses reported that the patient would, without warning, suddenly collapse to 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. The onset of the episode was not witnessed and the patient would return to his resting state. Throughout the episode his heart rate was 1.5 mb deletion in chromosome 17p11.2 thought to be epileptic in origin and therefore inappropriate therapy being consid- ered or inappropriate therapy being drawn and erroneous conclusions being drawn and witnesses' accounts of events. Further investigations are required which are often normal unless an episode is captured during monitoring. Recording solely the EEG or the ECG may result in erroneous conclusions being drawn and insufficient or inappropriate therapy being instituted. Distinction between a primary cardiac arrhythmia and a secondary central arrhythmia is possible only with simultaneous EEG/ECG recordings.

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

Hereditary neuropathy with liability to pres- sure palsies (HNPP) is an autosomal domi- nant 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 entrap- ment sites. Respiratory muscle weakness has not been previously reported in HNPP. We describe a patient with HNPP whose 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. At the age of 57, he experienced difficulty in going up stairs. However, he was almost independent in daily life. At the age of 60, he was admitted to the Norfolk Red Cross Hospital as an emer- gency patient with a coma due to CO2 narcosis (PCO2 117.6, PO2 64.0). Responding to mechanical ventilatory support, he com- pletely recovered consciousness within a day. His respiratory condition in the daytime improved to that previously. However, he needed mechanical ventilation during sleep because of nocturnal hypventilation.

The patient had no history of diabetes mellitus, pulmonary disease, or other medical problems. There was no familial history of neurological disorder, including entrapment neuropathies. After a few months, he noted that in his teens he had experienced some episodes of right peroneal and right axillary nerve palsies which resolved themselves over a few months.

In a neurological examination, the patient’s mental state and cranial nerves were normal. Evidence of muscular atrophy and lumbar lordosis was found. The muscular atrophy was prominent in the shoulder girdle, intercostal muscles, paravertebral muscles, and pelvic girdle, and moderate atrophy was present in all four limbs (figure). There was moderate weakness of the shoulder and pelvic girdle and mild weakness of the distal limbs. The thorax showed poor respiratory movement, and the patient showed paradoxical movement of the abdomen in the supine position. Tendon reflexes were hypoactive in all limbs. The patient’s sensations of touch and pain were mildly impaired in the four lower limbs. His position sense was normal. His vital capacity was 1.9 l (55% of the normal mean) in the sitting position, but 1.3 l (38%) in the supine position. The percentage of forced expiratory volume in 1 second was normal (90% predicted) and chest ro- graphy at inspiration and expiration showed poor movement of the diaphragm but no abnormality in the lung field. Routine haematological and serological studies gave normal results. No monoclonal or polyclonal proteins were detected. IgG and IgM antibodies to gangliosides GM1 and GD1b were negative. Analysis of CSF showed 1 lymphocyte/mm3 and 25 mg/dl protein. Motor nerve conduction studies showed pro- longed distal latencies in the right median (8.8 ms (normal value in our laboratory <4.6) and ulnar (6.2 ms (normal <3.6) nerves, and moderate decreased conduction velocities in the right median (54%) and ulnar (54%) nerves (normal>45), ulnar (45 ms (normal>49)), tibial (35 ms (normal>38)), and peroneal (29 ms (normal>41)) nerves. There were moderate decreases in the amplitude of com- pound action potentials in all the nerves tested, and an amplitude reduction of 50% was detected across the cuffural tunnel of the right ulnar nerve. Minimum F wave latencies were prolonged in all the nerves tested. The latency of the right phrenic nerve was slightly...
of myelinated fibres was reduced (5726/mm² normally thin axonal myelin sheaths. The density of the myelin sheath and some abnormality was found. Biopsy showed scattered tomaculous thickening of the myelin sheath and some abnormality was found. The density of myelinated fibres was reduced (5726/mm² normally thin axonal myelin sheaths. A gene analysis disclosed a 53% gene dose of 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 mononeuropathy, and the familial occurrence of asymptomatic entrapment neuropathy was detected by nerve conduction studies. The patient required mechanical respiratory support during the night.

General muscle atrophies, which are most prominent in the trunk are shown. A tracheotomy was performed for nocturnal hypoventilation because the patient required mechanical respiratory support during the night.

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 tomaculous thickening of the myelin sheath and some abnormality was found.

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 hypoventilation in the supine posture and paradoxical movement of the abdomen, which suggested diaphragmatic weakness. 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. Diffuse proximal weakness in our patient is an uncommon finding as for HNPP. Mancardi et al 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.

Spinal accessory neuropathy and internal jugular thrombosis after carotid endarterectomy

Spinal accessory neuropathy is a rare complication of carotid endarterectomy (CEA). 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 unrecognized 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 few published cases. Despite this apparent rarity, a common pathogenetic mechanism for postoperative spinal accessory neuropathy and internal jugular venous thrombosis may 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 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, when 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 right shoulder drooping and minor right scapular winging. Right arm abduction produced more prominent scapular winging and was limited to 90 degrees due to pain and weakness. Electrodagnostic studies were consistent with partial right accessory nerve neuropathy with minor denervation of the right trapezius. Cervical ultrasonography and MRI demonstrated right internal jugular venous thrombosis. The patient was treated with a shoulder support, analgesics, and low dose aspirin. There was no significant clinical change 1 year after CEA. Repeat electrodagnostic studies were consistent with chronic right spinal accessory neuropathy, and repeat ultrasonography showed persistent right internal jugular venous thrombosis.

Spinal accessory neuropathy was first reported as a complication of CEA in 1982. Since then, there have been several case reports and small series. A 1996 review of reports of cranial neuropathy after CEA disclosed only one patient with spinal accessory neuropathy in over 3000 cases. Although the authors did not include several other reports which, taken together, may seem to suggest a somewhat higher incidence, the overall small number of reported cases in proportion to the hundreds of thousands of CEAs that have been done worldwide suggests that clinically significant spinal accessory neuropathy is a rare complication. More frequent spinal accessory neuropathy after CEA may be more frequent. The cause of spinal accessory neuropathy after CEA is usually not well established, but intraoperative nerve stretching or compression from retraction is most often invoked. Delayed onset (after 3 weeks) has been noted in some; for these patients, postoperative inflammation and scarring seem more likely causes. Spinal accessory nerve transection or ischemia/infarction (arterial or venous) are other possibilities. As in our patient, high carotid dissection and retraction have been reported to precede spinal accessory neuropathy. The spinal accessory nerve courses along the internal jugular vein and near the internal carotid artery, typically well above the carotid bifurcation. It is therefore reasonable that a high incision and retraction resulting from a high carotid bifurcation would place the nerve at risk. Whether this realisation may lead to any technical modification to decrease the risk of spinal accessory neuropathy in those with a high bifurcation remains to be determined.

From our search, internal jugular venous thrombosis after CEA has been reported in only one case. As Southcott et al noted, retraction of the internal jugular during CEA may cause thrombosis in venous channels, 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. The presence of induration about the incision site and a palpable supraclavicular cord in our patient led us to suspect venous thrombosis. Internal jugular venous thrombosis may be more frequent. Whether this realisation may lead to the consideration of the possibility of both when either is discovered.

Ischaemic 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 serve to alert the medical community to possible serious adverse effects of energy supplements.

A 33 year old man had a severe aphasia on awakening in the morning of 23 January 1999. 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 CSF examination was normal. There was no coagulopathy. D-dimers were within the normal range (360 ng/ml, normal <500 ng/ml). Creatinine was in the normal range (102 μmol/litre). Transesophageal echocardiography and ECG 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 mall 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 coenzyme Q10 per capsule. 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 ruled out as he recently returned from a transatlantic flight, there was no deep venous thrombosis and D-dimers were normal. However, ephedrine has an indirect sympathomimetic action which can cause arteriole vasoconstriction in addition to other catecholaminergic effects. 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 medicines for multiple uses. The drug is marketed as a weight loss supplement, and as a sports supplement which contains ephedrine, is used in conjunction with other drugs as energy supplement in non-prescription tablets in some countries.

Although no cardiovascular side effects have been reported with the use of creatine monohydrate, this compound, used in association with other drugs as energy supplement may have deleterious side effects. This may be particularly true when used at high doses in combination with sympathomimetic drugs as in our patient. Renal dysfunction has also been reported after oral creatine supplements. Our patient had a slight increase in creatinine concentration although...
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.1

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 hypoaesthesia 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 of 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

(A) Axial T2 weighted SE MR images of a 32 year old woman with left sided cervicofacial dyskinesias show a large left petroclival meningioma compressing the brainstem. (B) Coronal inversion recovery MR scans demonstrate marked displacement and distortion of the brainstem due to the petroclival meningioma. (C) Gadolinium enhanced axial T1 weighted SE MR scans 3 months postoperatively show complete removal of the tumour and normalisation of the displacement of the brain stem.
decreased on the left side. Furthermore, there was mild left dysdokinesia. Neurography of the facial nerve was normal on both sides. Needle myography of the left frontalis and orbicularis 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 cavae Meckeli 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 transtemporal supratentorial and infratentorial presigmoidal approach. The postoperative course was uneventful, and there were no new deficits. The facial palsy improved slightly as well as the trigeminal hypoaesthesia. 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 craniofacial 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 supposed 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.4 Alternatively, enhanced excitability of brainstem interneurons has been suggested.5 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.6

Our case provides further evidence that functional impairment by compression and distortion of the brain stem may cause hyperkinetic cervicofacial movement disorders. It is not 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 MRI imaging to rule out a surgically treatable cause.

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4 Krauss JK, Seeger W, Jankovic J. Cervical dystonia associated with the petroclival meningioma and the segmental hyperkinetic cervicofacial movement disorders. It is important to know 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 MRI 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 strength 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 infections;1 therefore, treatment with transfer factor has been suggested in patients with selective deficits in cell mediated immunity such as some refractory neoplasms and chronic infections. Moreover, it has been used in the treatment of uveitis.1 Administration of dialysable leukocyte extract has seemed to be free of hypersensitivity, long lasting side effects, or complications, except for transitory hyperpyrexia.1

We report on a patient in whom multiple cerebral white matter lesions developed after taking dialysable leukocyte extract orally for 14 months. 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 in the 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 tities (355 UI/ml, normal <200 UI/ml), and anticardiolipin IgG (30 UI/ml, normal 12 UI/ml). Negative results were obtained for HIV antibody and serum immunoglobulins, venereal disease laboratory test, erythrocyte sedimentation rate, fibrinogenemia, C reactive protein, rheumatoid factor, Wäaler-Rose, protein electrophoresis, antinuclear, anti-DNA, anti-neutrophil, anti-smooth muscle, and antineutrophil cytoplasmic antibody, lupus anticoagulants, 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, Coxsackie, 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.

Cell, protein, and glucose concentrations in CSF were normal. No oligoclonal bands or antibody against CMV, Herpes simplex, Varicella zoster, Epstein-Barr virus, Coxsackie, 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 tities (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 casual. Despite the absence of biopsy, we reasonably excluded...
the diagnosis of vasculitis or neuro-Behçet's disease although in the absence of biopsy. In fact, the clinical, laboratory, and MRI findings were not typical and a low titre of antiphospholipid 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 the 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.1 In addition, CSF without oligoclonal banding argues against a diagnosis of multiple sclerosis, whereas it is commonly found in acute disseminated encephalitis.1 On the other hand the possibility that acute disseminated encephalitis may recur has been accepted9 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 autoantigenic 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.1 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 infections1 led us to postulate in this patient a clinical, autoimmune range. Some findings suggest that acute disseminated encephalitis and multiple sclerosis 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 autoantigenic reactivity is only temporary and direct against a single antigen in acute disseminated encephalitis and multiple antigens in multiple sclerosis.

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 disease1—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, dysgraphaesthesia on sensory testing, and a manneristic gripping handshake. There were no extrapyramidal

Brain CT, axial section: dense calcific deposits in the basal ganglia, thalamus, and orbitofrontal cortex consistent with Fahr's disease.
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' intentions. 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, cerebellar dentate nucleus, and orbitofrontal cortex, consistent with Fahr’s disease (figure). SPECT CT showed increased activity in the basal ganglia relative to the cerebral cortex. A fine banded karyotype was normal. Serum calcium was 1.55 mM (normal 2.15–2.55 mM), phosphate 1.69 mM (normal 0.70–1.34 mM); calcium was 1.55 mM (normal 2.15–2.55 mM); pH 7.4 (normal 7.38–7.45); serum creatinine 0.55 mg/l (normal 0.60–1.20 mg/l); platelets 165 × 10^9/l (normal 150–350 × 10^9/l); hemoglobin 11.3 g/dl (normal 12.0–16.0 g/dl); hematocrit 34% (normal 37–47%); ESR 30 mm/h (normal 0–20 mm/h). Postoperatively, the patient presented an impairment on the Tower of London test, which measures executive function, and in a task assessing the understanding of others’ intentions. 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.

Asperger’s syndrome is a subtype of pervasive developmental disorder of unknown aetiology. Evidence for involvement of specific brain regions in pervasive developmental disorder are scarce and inconclusive.1 Although the tempo-orbital region is the most often involved in pervasive developmental disorders2 abnormal functioning of the frontallobar cortex is suspected from replicated findings of executive function deficits and from occasional findings of frontal hypometabolism or abnormal macroscopic brain morphology.3 Abnormal cell counts and morphology in the cerebellar hemispheres have also been reported, but the relation of these findings to autism is controversial.4

Fahr’s disease consists of symmetric calcifications, located mainly in the basal forebrain and cerebellum, which are of various aetiologies. Cognitive and behavioural abnormalities may be present when calcifications occur early in development. A fortuitous association between pervasive developmental disorder and hypoparathyri[oma]nia, given the paucity of published cases, is plausible in the present patient. Nevertheless, our case suggests that abnormal phospho-calcium metabolism could produce an autistic syndrome when brain calcifications cause specific neuropsychological deficits, due to their localisation. For example, errors of social judgement may be related to calcifications of the orbitofrontal cortex, whereas dysfunction of frontal-basal ganglia circuits may contribute to repetitive and ritualistic activities. Additionally, developmental lesions of the basal ganglia and cerebellum may contribute to the abnormalities of sensory attention, procedural learning, and motor intention in this patient.

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.5 By contrast, this case, similarly to some others6 suggests that dysfunction in key brain circuits may result in behavioural and cognitive abnormalities clinically 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?
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 reflexes, 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 cranioocular injury. Responsi-

ble 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 topographical anatomy seemed 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 palsies 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 lesion, 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.

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 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 run 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 palsies 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 lesion, 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.
CORRESPONDENCE

Toluene induced postural tremor

We read with interest the article by Miyagi et al and comment on the medical treatment of toluene induced tremor. Microdialysis experiments in rats have shown that inhalation of toluene increases extracellular γ-amino butyric 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. Degeneration of certain cerebellar pathways is probably responsible for the loss of this dopaminergic innervation. Dopamine agonists could therefore be of potential interest in the treatment of toluene induced tremor. This hypothesis was explored in a recently described case, 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 absence from inhalant misuse, and (d) mild cerebellar atrophy and marked low signal intensity in globus pallidus, thalami, red nuclei, and substantia nigra on T2 weighted MRI. As our patient’s tremor was progressive, medical treatment with a dopamine agonist was considered. One particular agent (amantadine) caught our attention because it had proved successful in the treatment of postural tremor associated with heredodegenerative disorders in which the dentatorubro-olivary system is affected. In addition, there is evidence that catecholaminergic pathways are also involved in this type of ataxias, supported by the observation that amantadine hydrochloride abolishes the tremor in patients with tuberous sclerosis complex in children with tuberous sclerosis.

We think that there are two problems with this study that make the physician cautious about adopting the risk 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 test in a general population of patients with tuberous sclerosis complex is understood well.

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

Nabbout et al 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.

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 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 and upper limbs and little or no effect of either a bulbar nature or in the lower limbs. Thus Hu et al coined the term “familial amyotrophic lateral sclerosis” 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 al 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 diplaiga syndrome.

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

Probable 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 Volkmann in 1886 and known in Franco-German literature as Vulpen-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. 1

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 slight or no functional impairment of the bulbar muscles or legs. Hu et al also made four important statistical discoveries.

(1) The prevalence of this form of ALS constituted 10% of the ALS group as a whole (p=0.051). (2) The age of onset of this form was similar to the rest of ALS. (3) There was a small predilection 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, for more than 5 years after the onset of symptoms. On a personal level, we also note two findings characteristic of these patients. In the initial stages of the illness, there is no effect on the diaphragm and the respiratory muscle failure occurs much later than in the typical form of ALS. This can be seen in the follow up of the results obtained in the respiratory function tests (VC, FImax, and PFImax).

We do not know the reason for either the characteristic distribution of weakness or muscle atrophy. A meticulous study shows that there is an atrophy of the deltoides (especially the upper pars spinata) and a loss of strength in the external rotation of the shoulder (infraespinatus, supraespinatus, and teres minor). As a consequence, the upper limbs adopt a characteristic position, with the shoulders slumped, and the arms, forearms, and hands in pronation.

The atrophy and weakness of the infraspinatus and the supraespinatus, that act as an active ligament in scapulohumeral articulation, would explain the presence of subluxation of the shoulder joints in these patients.

Finally, we are in complete agreement that the atrophy of cervical spondylosis and ALS can cause difficulty in diagnosis. The problem lies in the fact that cervical spondylosis is a common condition. It is found in 83.5% of men and 80.7% of women over the age of 65. The faster progressive deterioration of the symptoms, the appearance of bulbar signs, and the absence of sensory symptoms and signs would favour the diagnosis of ALS.1

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

Over many years, several researchers have recognized 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, in line with the opinion of other authors. However, we consider that this peculiar distribution of the muscular atrophy such as “dangling arm, oran gon utan sign, dead arm sign, suspectio interna” in amytrophic bulbar diplegia syndrome, bicipital palsy and man-in-the-barrel 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.1 In fact, these patients had cervical abnormalities such as cervical lateral spondylosis and ossification of posterior longitudinal ligament disclosed by radiographic, MRI, or myelography. By contrast with clinical awareness of these peculiar patterns of muscular atrophy, no pathological counterpart 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 our private opinion, “dangling arm syndrome” or “dead arm sign” seems to be the most suitable term describing this type of motor neuron disease.

As I agree with Hu et al in 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 dysarthria

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 dysarthria from stroke.1 As in their patients transcortical magnetic stimulation induced absent or delayed corticomedial responses at the tongue, the authors ascribed isolated dysarthria to interruption of the corticomedial pathways. On the whole, the patients’ results are plausible, but we would like to comment on the underlying mechanism of isolated dysarthria.

As in the case of isolated dysarthria reported by Urban et al, all of our patients with isolated dysarthria had lacunar infarctions involving the internal capsule and corona radiata.2 Measurement of cerebral blood flow with IMP-SPECT in these patients disclosed frontal cortical hypoperfusion, particularly in the anterior opercular and medial frontal regions. Anterior opercular lesions produce facio-pharyngo-glossomasticatory paresis (anterior opercular syndrome), 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 major language areas, resulting in dysfunction of these cortices.3 Therefore, we postulated that isolated dysarthria results from interruption of 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 undergo this ascending and descending organisation.

To assess corticopontocerebellar tract function, Urban et al investigated cerebellar blood flow in patients with isolated dysarthria using HMPAO-SPECT. The authors concluded that the corticopontocerebellar tract is preserved in isolated dysarthria 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 dysarthria. Lingual paresis was evident in three of seven patients reported by Urban et al and in two of 12 by us. This indicates that isolated dysarthria originates in incoordination of multiple organs necessary for speech calculation as well as cerebellar dysfunctions. Although interruption of the corticomedial pathways is a likely cause of isolated dysarthria, it should be borne in mind that damage to other descending and ascending projections may contribute to isolated dysarthria.


References

We have two completely different interpretations of the results of paired magnetic stimulation. We also consider that methodological differences are very important in paired magnetic stimulation. 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 have no difficulty in showing normal inhibition, but have much difficulty in showing reduced or absent inhibition because of such marked dependence of the results on the intensities of stimuli. Therefore, we used the intensity of the conditioning stimulus before we confirmed inhibition in studies of patients. We used an intensity of 5% less than the active threshold as a conditionalIntensity in the study of chorea. We did not need to change the intensity of the conditioning stimulus because we always obtained a normal inhibition with this intensity. We consider that this is very important. If using a supra-threshold (active threshold) conditioning stimulus, a facilitatory effect must often superimpose on the intracortical inhibition. This makes the interpretation difficult. Was the intensity of 80% of the resting threshold below the active threshold in their patients? In our experience, 80% of the resting threshold was sometimes above the active threshold. These factors must be considered in interpreting the results of paired magnetic stimulation.

Such a methodological problem is inherent in human studies because we have no direct way of detecting the threshold of the motor cortex. Our two results must be true. We may have two completely different interpretations of these results. (1) The intracortical inhibition is normal in Huntington's disease. Abbruzzese et al showed the reduced inhibition because they used a high intensity conditioning stimulus with which the degree of the
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 instantaneus value of cerebral blood flow velocity (FV(t)) at a given moment is equal to arterial blood pressure at the given time (ABP(t)) minus CCP divided by cerebrovascular resistance (CVR):

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

At the time of systolic and diastolic pressure values (ABPp, ABPd), respectively, it follows that systolic and diastolic pressure (FVs, FVd) should be equal to (ABPs-CCP)/CVR and (ABPd-CCP)/CVR, respectively. However, it is known 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. Therefore, equation 1 cannot be applied to describe dynamic flow. This can be best 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):

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

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

CCP2=ABP-A1/F1×FV (4)

leads to

CCP2=ABP-CCV1/CCV0×(ABP-CCP) =ABP-(1-CCV1/CCV0)×(ABP-CCP) (5)

It is clear that CCP2 is only in the case CVR1=CCV0 equal to CCP. Under the more realistic assumption that CVR1 is equal to about half of CVR0 it follows for CCP2:

CCP2=0.5ABP×0.5CCP

With decreasing CVR1/CCV0 ratios, CCP2 becomes more and more dependent on ABP and independent of CCP. In any case, without exact knowledge of the CVR1/ CCV0 ratio, equation 4 is useless for a valid CCP calculation.

The second criticism concerns the correlation of the calculated CCPs with mean ABP found by the authors (ρ=0.5; p<0.05). According to the original idea of Burton, 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 vasoconstruction. 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 ABPd<CCP and a small vessel collapse according to the model of the authors, CVR should increase towards zero 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) than by ABP-CCP. Therefore, equation 2 changes to:

FV=(ABP-ICP)/CVR0 (6)

and equation 5 to

CCP2=ABP-(1-CCV1/CCV0)×(ABP-CVR0)ICP (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”.1

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Czosnyka et al reply:

We thank Diehl very much for the interesting letter providing 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 Aaslid1 proposed the mathematical formula taken for calculations:

CCP=ABP×ABPP/FV; FV=FVp/FVpp

(where ABP and FV are mean values of arterial pressure and MCA flow velocity, ABPs and FVs are systolic values, ABPP and FVpp are peak to peak amplitudes). A graphical interpretation of this formula has been given in fig 1. CCP 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 formula 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:

CCP=ABP×A1/F1×FV

In our paper we confirmed empirically that both CCP1 and CCP2 produced the same values in a group of normal subjects after head injury, therefore the mathematical consideration of Diehl (equations 1–5) must contain an error!

First of all we cannot see how equation (1) from Diehl’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 (as equation (1) implies). We have never suggested anyone could do so.

The final issue concerning negative flow values 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 pressure 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 animals.1 Levodopa induced dyskinesias are currently thought to share a similar pathophysiology but recent findings also suggest that abnormal fluctuations of neuronal firing in the globus pallidum internum may be as relevant.2 Data from both parkinsonian monkeys and patients with Parkinson's disease submitted to lesion3 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.4 The case recently described by Figueiras-Mendez et al.5 rises extremely interesting as it suggests that functional inhibition of the subthalamic nucleus by high frequency stimulation blockades levodopa induced dyskinesias. This is clearly at odds with the current pathophysiological model of the basal ganglia.6 Thus, the finding of Figueiras-Mendez et al.7 rises the intriguing possibility that dyskinesias depend or are reduced in levodopa intake.8 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 and; subsequently, reversing to the thalamus from the globus pallidum internum are placed dorsocaudally to the subthalamic nucleus and could be blocked by high frequency stimulation.9 The difference in the recording electrode position was not related to 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”).10 All these characteristics seem 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.11

Very importantly, it is very important to document in more detail the findings in the case of Figueiras-Mendez et al.12 Ideally we would like to see the trajectory and length of the different recording tracks, the effects of microstimulation, and the postsurgery 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.

low background activity found in our recordings is only due to the better signal-to-noise ratio of the electrodes used. “Good recording electrodes” depend on many variables such as tip size, tip profile, insulation material, impedance, manufacture, etc. The signal-to-noise ratio of the cells in question has the same ratio as the subthalamic nucleus cell shown by Hutchinson et al. (b) In our report, cells discharged tonically, but also other cells discharged phasically. They were well differentiated by a profuse burst activity and identified by statistical means (autocorrelation and interval histograms).

(c) Motor responses and tremorgenic cells in line with the above mentioned criteria were found along the trajectory of the electrode. Unfortunately, this point was not mentioned in the paper. It would surely have changed the opinion of Obeso et al. In the mentioned patient, a total of eight neurons were recognized as belonging to the subthalamic nucleus in the right hemisphere, with a mean frequency of 74 Hz (range 38–109 Hz). Four of them responded to passive and/or voluntary movements and one was considered tremorgenic. The stimulating electrode was placed in the lateralis 11. One track was performed. In the left hemisphere, two tracks were performed. One track was abolished by the poor responding activity of the cells recorded. In the other track, nine neurons were recorded in the subthalamic nucleus (always following the above mentioned criteria) with a mean of 69 Hz (range 17–98 Hz). Five cells responded to passive and/or voluntary movements. One of them was also positive to tremor. The stimulating electrode was placed in lateralis 11. Another track was performed. The stimulating electrode was always tested in the surgery before cementing it and, only when the symptoms are considered of unquestionable benefit it is left in the chosen place. The final position of the electrodes, assessed by ventriculography, was as follows: (a) posteroanterior: 15 mm behind the mean point of intercomissural line, (b) height: 6.5–6.5 mm below the intercomissural line, and (c) lateral: 12 mm for the right hemisphere, and 11.5 mm for the left hemisphere.

**Nitrates in acute ischemic 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, pharmacological manipulation of NO may represent a novel means of protecting the brain from ischaemic insult. One area not discussed in the recent editorial is the neuroprotective effect of 3-hydroxy-3-methylglutaril coenzyme A reductase inhibitors or “statins” in cerebral ischaemia. Preliminary studies have shown that statins modulate brain nitrergic nerve terminals, and neuronal activity in a neuroprotective manner. Data from a murine model of ischemic 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 regulated endothelial NO in the brain without altering expression of neuronal NO. Recent findings also suggest that statin therapy influences the activity 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 by which statins suppress 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 strategies are the The Prospective Study of Pravastatin in the Elderly at Risk (PROSPER) study will 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 calling attention to the act of narrating might detract from realistic illusion, so reducing the emotive 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 response in the CNS. 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 examines 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. The chapters on demyelinating disease are drawn to a close by a discussion of existing and experimental therapies for multiple sclerosis.

The book continues with chapters on para-neoplastic disorders of the CNS, stiff man syndrome, neurologically 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 for such a compact book (315 pages), and although the editors succeed in collecting an interesting series of papers around these themes, they make no claims to be comprehensive in their scope. The papers included range from original research reports to reviews of the current literature. The review papers are generally excellent, concise, clear, well referenced, and illustrated—for example, there are excellent reviews of Alzheimer's disease with vascular pathology (Pasquier et al), and Lewy body disease (McKeith et al), great updates on neuropathology (Jellinger and Bancher, Braak et al), and several worthy reviews of treatment strategies for Alzheimer's disease including NSAIDS (Möller), antioxiands, and radical scavengers (Rösler et al). I found the review by Reisberg et al on ontogenetic models in the understanding of the management of Alzheimer's disease particularly interesting. However, the papers of original research are of more limited interest to the general reader. Although, as mentioned, the quality of illustrations is good, there is some variability in the definition of abbreviations and occasional lapses into other European languages.

Certainly, I think this book would be of value for investigators interested in the neuropathology, immunopathology, and molecular biology of Alzheimer's disease. It would make an excellent addition to libraries as a reference text for many researchers of varied interests.

CLARE GALTON


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/lung (UK Transplant Support Service). Transplantation was established in 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. Until recently, non-specific forms of immunosuppression were radiation (total body or total lymphoid) and non-selective chemical reagents (benzene and tolenuene). 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 1963 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 transplant (sirolimus, levunolimuce), or differentiation (15-deoxyerupergulin) 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).

Wijdicks estimates that 10% of transplantation patients have a significant neurological complication. The most 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 for another title in the excellent series. The peripheral nerve and plexus 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.

ALASDAR 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, written by any illustration. Each brief contribution to each chapter there is a certain sense of deja vu, although on the positive side each contribution is extremely well referenced.

Each bifurcated 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 clinical concern in 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 unproved 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.


Evolutionary biologists would probably tell us that the enchantment of stories is due to survival having been dependent on the passing of oral culture from one generation to the next. Information put into narrative form not only delights, but is easily recalled. Stories also construct meaning, including 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 the awareness of the 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. However, in the outstanding chapter, writes a lucid and well reasoned account of the need to search for and maintain narrative meaning in treating psychosis. This avoidance of dehumanising effect to both patients and professionals of identifying individuals by their illness as in schizophrenia. Every psychiatric library should buy this book for this paper alone, which should be required reading for psychiatric training.

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 overworked paradigm. However, there are two very fine accounts of narrative in psychosynthesis concerning attachment theory, a useful psychiatric library should buy this book for this narrative meaning in treating psychosis. This pragmatism. Roberts, in the most outstanding chapter has always been listening to patient's stories, One of the great pleasures of being a doctor... Women and Epilepsy By TIM BETTS and PAM CRAWFORD. (Pp 84, gratis from the British Epilepsy Association). Published by Martin Dunitz, London, 1998. ISBN 1-85317-680-X.

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, family practitioners, and trainees.

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 (phytonadione), (b) differential efficacy of various antiepileptic drugs in different syndromes versus side effect and teratogenicity profile, (c) more information on the availability of available evidence to support the statement "no monotherapy human abnormality reported" with certain new antiepileptic drugs in pregnancy, (d) the need to consider the problem of pregnancy prevention well before the menopause (not only with enzyme inducing drugs such as valproate has also been implicated), (e) discussion of differences (and available formulations) between synthetic and natural progesterone, (f) strand of pregnancy when various malformations are detectable on scanning, and (g) time to closure of the neural tube (different from the 21-56 days they quoting as the "most sensitive time of the fetus to the induction of malformations by exogenous agents.").

Despite these comments (made with an eye on the next edition) I would recommend this book to all those involved in the care of women with epilepsy.

LINA NASHEF


Childhood Epilepsies and Brain Development is the fruit of a symposium held in 1997 to try and bridge the chasm between those working in the clinic or at the bedside and those in the laboratory. Both groups must collaborate and communicate to improve the management of children (and other patients) with epilepsy. The book is essentially a collection of monographs of heterogeneous content and style and the result, perhaps not surprisingly, is that some of the component parts are better than others. The most outstanding chapter will clearly be of particular interest to those who treat children and their families. The chapters on infantile spasms and Lennox-Gastaut syndrome are informative and provide some new but speculative insights into the pathogenesis of spasms. However, it was surprising that severe myoclonic epilepsy of infancy did not merit a specific chapter. In view of the unique electroclinical evolution and natural history of the syndrome. The crucial issue of the cognitive and behavioural sequelae of early and frequent seizures on the immature brain, which is probably of most concern to both clinicians and families, is succinctly addressed in two chapters—although a clear and consistent working relationship... One chapter on anticonvulsants... This book is laid out in tabular form. It could become an important primers for busy junior doctors. There is no index.

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, psychoses—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 psychiatric 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 a difficult tradition, 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). The brevity is only partly explained by the undeveloped state of that particular area of psychopharmacology. Sections on general indications to and contraindications to and indications for ECG 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
High frequency stimulation of the subthalamic nucleus and levodopa induced dyskinesias in Parkinson's disease

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