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. Surface EEG is either normal or showing non-specific slow waves. 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 ganglion. As hyperperfusion in ictal cerebral SPECT is closely linked to epileptic activities, our findings support a contrary explanation for postictal psychosis.

Prolonged video-EEG telemetry study was performed in patients who underwent presurgical evaluation for epilepsy surgery. Antiepileptic drugs were withdrawn to facilitate seizure recording. A diagnosis of temporal lobe epilepsy was based on analysis of the electroclinical events and, if applicable, postoperative outcome after anterior temporal lobectomy. Psychosis was diagnosed according to the fourth edition of the diagnostics and statistical manual of mental disorders (DSM-IV) criteria of 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 hyperfusion 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 hypoperfused area over the left hemisphere. An antipsychotic agent (thioridazine) was
started after the cerebral SPECT. His psychotic symptoms resolved 2 weeks later with full recovery.

Cerebral SPECT performed during the interictal period (IP) and during postictal psychosis (PP) were analysed visually and areas of hyperperfusion were identified. Quantitative data at intervals of Regions Of Interest (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 \((\text{ROI focus−ROI contralateral)/ROI focus+ROI contralateral})\times200\%$. 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 $+116.78\%$ (1.07927 to 12.55764); and over the left BG was $+206.8\%$ (2.07373 to 2.21574). Quantitative analysis for patient 2 showed changes of ASI during IP and PP over right MT was $+3.8\%$ (13.14217 to 12.64158); over right LT was $+178.6\%$ (10.4696 18.70057); and over left BG was $+159.5\%$ (-5.85565 to 3.27522).

Postictal psychosis is a distinct clinical event associated with temporal lobe epilepsy. The diagnosis of postictal psychosis requires a close temporal relation between bouts of complex partial seizures and the onset of psychosis. The psychosis usually develops after a cluster of seizures, partial were used precipitated by abrupt withdrawal of antiepileptic drugs. The cluster occurs in patients with poor drug compliance or during video EEG monitoring studies and antiepileptic drugs are generally assumed to be responsible. The clinical course of postictal psychosis is usually benign and unpredictable. In our patients, the duration of psychotic disturbances lasted from 2 to 10 days, which is in keeping with the good prognosis. Antipsychotic drugs, such as haloperidol and fluphenazine are usually prescribed.

The underlying mechanism of postictal psychosis is unknown. Postictal cerebral hypo-function has been postulated as an analogue to Todd’s paralysis after seizure. 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.

To conclude, our results are contradictory to the hypothesis function of Todd’s paralysis is 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.

Characterisation of the employed Abs and distribution of the recognized isoforms.

<table>
<thead>
<tr>
<th>Anti-FN mAb†</th>
<th>Anti-TN Ab fragments†</th>
</tr>
</thead>
<tbody>
<tr>
<td>IST-4</td>
<td>IST-9</td>
</tr>
<tr>
<td>Recognised isoforms</td>
<td>Total FN</td>
</tr>
<tr>
<td>Distribution of the isoform ($)</td>
<td>Widespread</td>
</tr>
<tr>
<td>IST-12</td>
<td>IST-11</td>
</tr>
<tr>
<td>Total TN</td>
<td>Type III repeat C Isoform</td>
</tr>
<tr>
<td>Total TN</td>
<td>Widespread Absent in adult tissues</td>
</tr>
</tbody>
</table>
| Tissue samples were obtained after neuro-surgical resections of ruptured AVMs. All 10 patients had experienced an intracerebral haemorrhage as the first clinical manifestation of their disease. There was no drug history before bleeding. Control specimens from two right gyri recti and one cerebellar tonsil were obtained, respectively, from operations for ruptured aneurysms of the anterior communicating artery or for Arnold Chiari disease.

Immunohistochemical evaluations were performed on $5\,\mu m$ thick cryostat sections using a protocol reported previously. Owing to the limited amount of available material, only in a few cases was some fresh tissue retained to allow western blots. Distribution of FN and TN isoforms was investigated using three monoclonal antibodies (mAbs) or two Ab fragments, obtained by phage display technology, respectively. These Abs, prepared in our laboratory, were found to work on fresh frozen material. According to the previous characterisations the BC-1 mAb and the TN-11 Ab fragments are specific for isoforms occurring almost exclusively in fetal tissues and in tumours, with the recognised TN isoform being typically associated with anaplastic gliomas (table).

These isoforms were processed identically to the other specimens, but the primary antibody was substituted with a specific immunoglobulin of recombinant antibodies. The antibodies were blocked using the specific antigens. The antigens were recombinant protein containing the epitope produced in $E\,Coli$. For the mAb BC-1 we used the recombinant protein containing the type-III repeats 7B–8–9. For the mAb IST-4 we used the recombinant protein containing the type-III repeats 2–8. For the recombinant antibodies TN-11 and TN-12 the recombinant type-III repeat C and the recombinant fragment containing the BG repeat were used respectively.

All 10 AVMs were found to contain large amounts of FN and TN, as shown by intense immunostaining with the use of the IST-9 / IST-4 mAbs and the TN-12 Ab fragment. The staining was localised either in the endothelium or the subendothelial layer. A positive response was found in several artery-like vessels and in a few vessels with thinner walls. The antibodies were used respectively.

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

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

Immunohistochemical evaluations were performed on $5\,\mu m$ thick cryostat sections using a protocol reported previously. Owing to the limited amount of available material, only in a few cases was some fresh tissue retained to allow western blots. Distribution of FN and TN isoforms was investigated using three monoclonal antibodies (mAbs) or two Ab fragments, obtained by phage display technology, respectively. These Abs, prepared in our laboratory, were found to work on fresh frozen material. According to the previous characterisations the BC-1 mAb and the TN-11 Ab fragments are specific for isoforms occurring almost exclusively in fetal tissues and in tumours, with the recognised TN isoform being typically associated with anaplastic gliomas (table).

One of the 10 examined specimens was found to contain portions of cerebral tissue surrounding the angiomatous nidus. In all these cases the wall of several vessels exhibited intense staining with the use of the TN-11 Ab fragment. Using the BC-1 mAb some of these vessels exhibited some staining (figure). In the control specimens (brain and cerebellum) both the FN isoform containing the ED-B sequence (ED-B+FN), and the type III repeat C TN isoform were absent despite the widespread distribution of total FN and TN in the vascular walls.
Previous findings showed that ED-B+FN presents with conformational modifications in its 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 MIB-1 showed endothelial proliferation in arterioles, venules, and capillaries of the cerebral tissue neighbouring AVMs.

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

Hashimoto’s encephalopathy presenting as “myxoedematous madness”

The neuropsychiatric sequelae of hypothyroidism range from lethargy and mental slowing to the florid psychotic illness referred to as “myxoedematous madness”. The last condition is characterised by frank hypothyroidism accompanied by psychosis, and may respond completely to thyroxine. More recently described is a syndrome of subacute encephalopathy, associated with high titres of thyroid autoantibodies, raised CSF protein, EEG abnormalities, and perfusion deficits in the presence of normal structural neuroimaging. In most cases, the encephalopathy occurs without any gross change in circulating concentrations of thyroid hormones, suggesting that an inflammatory process is responsible for the cerebral dysfunction. In the absence of pathological data, the evidence for a specific pathogenic mechanism is largely circumstantial: a small vessel vasculitis and immune complex deposition have both been suggested.

Although none of the published cases of Hashimoto’s encephalopathy has described psychosis as a primary feature, it is possible that “myxoedematous madness”, a condition first described in detail by Asher in 1949, lies in a range of encephalopathic phenomena mediated by autoimmune mechanisms. This suggestion would certainly be consistent with the range of clinical presentations of other autoimmune cerebral vasculitides. As autoimmune thyroiditis is the commonest cause of hypothyroid failure in this country, it is likely that these conditions have been present in at least some of Asher’s original 14 cases. Although most had florid myxoedematous features at psychiatric presentation, this may simply reflect the difficulty of diagnosing subclinical thyroid disease before rapid laboratory assays became widely available. Many features of the present case, however, favoured an endocrine rather than an inflammatory mechanism, suggesting that the condition of “myxoedematous madness”, though rare, remains a valid diagnostic entity.

A 63 year old market stallholder without medical or psychiatric history was brought to a local psychiatric hospital by police. His business had been in decline for several months, and his family had noticed uncharacteristic emotional lability. In the weeks preceding admission he had experienced delusions and hallucinations, and had lost all previous uncharacteristic behaviour. He had reported a vision of the crucifixion, and hearing the voice of his dead mother. He claimed that his house was occupied by the devil, drove around aimlessly in his car, and appeared constantly fearful and withdrawn. On the day of admission he had made a bonfire in the garden and burned his wife’s clothes, family photographs, furniture, and business papers. When his wife and son tried to intervene he...
became aggressive and threatened them with a saw. The general practitioner was called and suspected he had bought a new psychotic, and a severe depressive illness. Police assistance was requested because of the patient’s continuing violent behaviour.

On admission he was unkept but cooperative and appeared apathetic. 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 mildly naming deficit, and poor word finding. His performance on the Rey figure, which was due to planning rather than visuospatial errors, suggesting a predominantly “disexecutive” pattern. CT and EEG were both normal. His disease manifested widely, but mild cortical hyperperfusion. Thyrotopract (2 mg twice daily) was started on admission, and thyroxine (75 μg once daily) added 1 week later. His mental state and behaviour stabilised, leading to discharge after 2 months.

At 6 months follow up the patient had stopped neuroleptic drugs, but continued taking thyroxine. He reported feeling “back to normal”, had bought a new psychic, and was working as a part-time shop assistant. He still had subtle word finding difficulties, and was referred to the regional memory clinic for further evaluation, which took place 6 months later. Behavioural examination was consistent with a mild neuropsychological deficit, and he 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 recovered fully, and the antithyroid microsomal antibody titre fell rapidly progressive mental and motor deterioration. The response to thyroxine does not, in itself, imply that the cerebral illness had an autoimmune thyroiditis.4

Other movement disorders included in the differential diagnosis of diseases which present with an alien hand.

**Alien hand sign in Creutzfeldt-Jakob disease**

The classical picture of Creutzfeldt-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.


<table>
<thead>
<tr>
<th>Laboratory (units)</th>
<th>A</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full blood count</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<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>Antinuclear antibody</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>
<td>56.4</td>
</tr>
<tr>
<td>Thyroid stimulating hormone (mU/L)</td>
<td>7.4</td>
<td>Not tested</td>
</tr>
<tr>
<td>Free T4 (pmol/L)</td>
<td>1:25000</td>
<td>1:1600</td>
</tr>
<tr>
<td>Antithyroid microsomal antibody titre</td>
<td>25/30</td>
<td>25</td>
</tr>
<tr>
<td>(normal predicted range):</td>
<td>10th percentile</td>
<td>18th percentile</td>
</tr>
<tr>
<td>(normal predicted range):</td>
<td>13th percentile</td>
<td>Not tested</td>
</tr>
<tr>
<td>(normal predicted range):</td>
<td>27th percentile</td>
<td>Not tested</td>
</tr>
<tr>
<td>(normal predicted range):</td>
<td>10/30</td>
<td>16/30</td>
</tr>
<tr>
<td>(normal predicted range):</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>(normal predicted range):</td>
<td>25.5</td>
<td>24</td>
</tr>
<tr>
<td>Rey-Osterreith complex figure (copy) (36)</td>
<td>Not tested</td>
<td>75%</td>
</tr>
</tbody>
</table>

### Table 1

Laboratory and neuropsychological results at presentation (A) and at 12 month follow up (B)
The laboratory data including blood chemists, haematology, and sedimentation rate were normal, as were folic acid, vitamin B12, immunoglobulins, 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 involuntary movements. 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 facility, he died few weeks later. Postmortem examination was not allowed.

This short fatal neurological disease manifested by bulimic dementia, myoclonic jerks, and extra pyramidal 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 differed 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...wanneled out of her view”. In the second, the alien arm 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 stimulcus sensitive myoclonus, spastic hemiparesis, and cortical sensory loss.
Coeliac disease associated with peripheral neuropathy in a child: a case report.

Coeliac disease

Nervous system involvement in paediatric coeliac disease. In both cases, however, these were chronic axonal polyneuropathies presenting during a gluten free diet. 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, wallerian 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 cell mediated 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 in 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 pathogenetic mechanisms of damage to the nervous system. Although we ruled out a vitamin deficiency it is still questionable whether a toxic neuropathy can be the case.

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

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

Coeliac disease

Nervous system involvement in paediatric coeliac disease.

Epilepsy and cerebral calcifications.

Autigliadin antibodies in the various stages of coeliac disease. Nervous system involvement in paediatric coeliac disease. It is known that in 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 surveil-lance, 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 pathogenetic mechanisms of damage to the nervous system. Although we ruled out a vitamin deficiency it is still questionable whether a toxic neuropathy can be the case.

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

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

AGATA POLIZZI
Neurosciences Group, Institute of Molecular Medicine, Department of Clinical Neurology, University of Oxford, Oxford, UK

Correspondence to: Dr Agata Polizzi, Division of Paediatric Neurology, Department of Paediatrics, University of Catania, Viale A Doria 6, 95125 Catania, Italy email: rupo@ctonline.it

3 Papadatos B, Di Capua M, Gambazarra M, et al. Nervous system involvement in paediatric coe-
4 Simonati A, Battistella PA, Guariso G, et al. Coeliac disease associated with peripheral neu-

Frontal release signs in older people with peripheral vascular disease

A growing body of research examining neurological aspects of clinically “silent” cerebrovascular disease suggests that neurological signs indicative of generalised organic brain damage may occur in the absence of completed stroke. These soft signs include primitive reflexes (frontal release signs), representing an anatomical and functional deafferentation of cortical from subcortical structures. Primitive reflexes are known to occur in a wide variety of dementias, including Alzheimer’s disease and vascular dementia. It is likely that the presence of undetected cerebrovascular disease accompanying peripheral vascular disease is underestimated, as peripheral vascular disease is known to be a risk factor for transient ischaemic attacks. A study assessing 373 older patients with peripheral vascular disease found that 72 of the 144 patients who had not experienced a transient ischaemic attack or stroke were found to have a degree of carotid stenosis of between 60% and 99%.

In the present study, the prevalence of primitive reflexes was examined in a group of people with peripheral vascular disease and a non-vascular control group. Independent predictors of these reflexes were also examined in peripheral vascular disease. Both groups were drawn from the same geographical area. All were interviewed and examined outside hospital by myself. Interviewees were community residents from the catchment area of an inner city London teaching hospi-

Twenty five consecutive non-amputees on the waiting list for femoropopliteal bypass operation were compared with 25 postoperative patients who had undergone elective hip or knee replacement and a period of rehabilitation. All participants were aged 65 and over at the time of interview. Patients with peripheral vascular disease all had clinical and Doppler proved evidence of peripheral ischaemia. Controls were interviewed between 6 months and 1 year after their operation. Both groups had no history of stroke or transient ischaemic attack.

A more detailed description of instruments is provided elsewhere. All subjects were
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 palmenucle, hand grasp, foot grasp, glabellar, rooting, plantar, and visual/tactile sucking reflexes. Neuropsychological measures included the assessment of frontal lobe function (trailmaking tests A and B, behavioural dyscontrol scale, and the controlled word association test) and generalised cognitive impairment (CAMCOG). Depression was assessed using the Hamilton rating scale for depression, 15 item geriatric depression scale, and diagnostic criteria for DSM IV major depressive disorder. Family history of depression, wish to die, and suicidal ideation within the past year were also recorded, as were blood pressure and a checklist for chronic physical illness.

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 DSMSIV depression, CAMCOG score, behavioural dyscontrol scale score, verbal fluency score (total number of words beginning with F, A, and S) and trailmaking test times was examined using the Spearman correlation coefficient, corrected for ties. Age, sex, blood pressure, and chronic physical illness. Behavioural dyscontrol scale scores, trailmaking 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 60 or above or less than 60. Those associations with a two tailed significance of 0.1 or less were then entered into a linear regression equation using the stepwise method.

Patients with peripheral vascular disease had a higher mean score on the frontal release signs scale than controls (3.8 (SD 4.6) vs 1.7 (SD 1.0)), Mann-Whitney U=144.500, Z=-3.33, two tailed p=0.001, as well as on glabellar and rooting reflexes (table). Only one variable (trailmaking B test time) was significant at a level of 0.1 or less. A higher mean score on the frontal release signs scale was associated with a lower CAMCOG score, behavioural dyscontrol scale score, verbal fluency score, and a higher mean score on the frontal release signs scale.

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 these two diseases may manifest clinically as a single entity. Blood pressure, age, 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 raoo@globelink.co.uk


Factualistic clock drawing and constructional apraxia

A 45 year old man presented with a 1 day history of headache, possible seizures, and left sided weakness. On the day of presentation the patient’s wife had twice found him, inexplicably, on the floor. After the second such episode she brought him to hospital for evaluation. Examination disclosed a complete left hemiplegia and hemianesthesia, although muscle tone was documented to be normal and the plantar responses downgoing bilaterally. Brain CT was normal and routine blood examination was unremarkable. There were no further seizure-like episodes and the patient was transferred to this hospital 10 days later, hemiplegia unchanged, for possible angiography and further investigations.

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

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

On transfer to this hospital the patient was alert, orientated, and cooperative. Although up to date on current affairs and able to describe the investigations performed at the transfer ring hospital, he scored only 23/30 on a mini mental state examination, with absent three word recall, impaired registration, and poor copying of a two-dimensional line drawing. Further bedside neuropsychological testing showed other findings indicative of con tructional 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 clock hands, were placed on the right hand side of the clock outline (figure A).

Copying of three dimensional line drawings was also significantly impaired (figure B). When asked to select a clock, he did so only minimally to the right of the midpoint (58% of the distance from the left side). A detailed cranial nerve examination suggested an incongruent and inconsistent left hemianopsia to confrontation testing but was otherwise normal, including bilaterally symmetric optokinetic nystagmus. Motor examination showed paralysis of the left arm and leg, with bilaterally symmetric bulk, tone, and deep tendon reflexes. The plantar response was flexor bilaterally. Sensory examination showed decreased pinprick and absent light touch, joint position sense, and vibration sense on the entire left side. There was also impaired perception of a tuning fork’s vibration on the left side of the forehead, with a distinct demarcation in the midline. The rest of the physical examination was unremarkable.

Brain CT and MRI, CSF examination, and routine EEG were normal. Routine haematological and metabolic analyses plus erythrocyte sedimentation rate, serum lactate, prothrombin time, partial thromboplastin time, fasting serum glucose, HbA1c, serum Ig survey, and thyroid stimulating hormone were all within normal limits. A hypercoagulability profile was negative. A lipid profile showed mild hyperlipidaemia with increased low
density lipoprotein (3.92 mmol/l) and triglycerides (4.30 mmol/l) and low high density lipoprotein (0.73 mmol/l). Serum phenylalanine 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 reversals (for example, “anixety”, “excecu- tion”), unusual “near miss” letter substitutions or reversals (for example, “anixety”, “excecu- tion”), unusual “near miss” letter substitutions or reversals (for example, “anixety”, “excecu- tion”).

The clinical and laboratory findings described above indicate beyond any doubt the non-organic nature of this patient’s left hemiplegia/hemianesthesia. His seizure-like episodes at presentation are presumed to have been non-epileptic in origin (as had been suspected during his previous admission to hospital) although this cannot be definitively proved.

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

During follow up, the patient admitted to feeling tremendous occupation related stresses, and described how he had come to adoption of the evidence that he should be able to move his left side. Six months later he was ambulatory but otherwise not significantly improved. He had been assessed by a psychiatrist but had refused psychiatric follow up, electing instead to be followed up by a psychologist. He understood his diagnosis to be “conversion disorder” and reported that he was actively collecting information on the subject via the internet.

Outpatient brain SPECT and visual and somatosensory evoked potentials performed 1 year after discharge demonstrated no hemispheric abnormalities. The patient remained off work and was receiving disability funding. He walked with a limp favouring his left side and complained of persistent decreased sensation on the left side. Forced choice sensory testing of finger and arm movement on the left demonstrated performance to be worse than chance (68% wrong choices). Motor bulk, tone, and reflexes were symmetric and plantar responses down-going. He drew a clock normally at the 1 year follow up.

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, acute, left sided, hyperacute thalamic bleed with mass effect and oedema. The patient was extubated 2 days later and 4 days after the stroke he was described as being drowsy and inattentive, but was able to answer questions...
appropriately. Neurological examination showed contralateral gaze preference, supra-nuclear vertical gaze palsy, difficulty converging, left sided flaccid hemiparesis, and dense, left sided hemianesthesia. Deep tendon reflexes were absent on the left and Babinski’s reflex was obtained 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 moved to a room nearer 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. Several times previously he had been acutely recalled being otherwise. By this time he had a moderate hemiplegia and recognised “a little weakness,” but continued to insist that he was well and able to return to work. By the 6th week after stroke the patient more consistently acknowledged that he was weak on the left side of his body. A request for disabled housing “so that I won’t be a burden to my family” seemed to indicate an appreciation of his impaired performance. This was confirmed 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 stroke before becoming fixed, but remained shallow after 12 weeks; he acknowledged that his left arm belonged to him. By this time he had a moderate hemiplegia and recognised “a little weakness,” but this insight was fleeting; his awareness of his hemiplegia fluctuated. Brain CT 30 days after stroke showed a large right thalamic hemorrhage with mass effect and oedema, with oedema extending into the cerebral peduncle. This was consistent with the presence of decreased cerebral blood volume at the posterior margin of the right thalamus without any evidence of decreased cerebral blood volume within the right parietal, frontal, or temporal cortex.

This is a case of anosognosia of hemiplegia and mania co-occurring in a patient with a large right thalamic hemorrhage. Although anosognosia and mania are not generally thought of as occurring together, when Babinski introduced the term anosognosia he used it as one of his examples in a case in which the patient, though not confused, was “a little overexcited,” and in a later paper he presented a case in which there was “a certain agitation, which expresses itself by exaggerated loquacity, a decrease in attention, and a tendency to erotic ideas.”

The patient’s mood was remarkably cheerful and optimistic. A week after the stroke he was told that his left hand was paralyzed. He expressed no concern over the potential impact of the lesion.

The patient was transferred to a room nearer to the nurses’ station, and he used the nurses as one of his examples. Moreover, Heinstein and Kahn noted that euphoria was common in patients with anosognosia. Moreover, although Cutting emphasised that apathy is the mood more usually associated with anosognosia, 10% of his patients with anosognosia were described as having “euphoric mood.”

Right sided thalamic lesions are known to produce both anosognosia and mania, but the relation of each to the pathology is unclear. Only some of the patients with right hemispheric lesions are manic or agnostic. These two syndromes may be related to dysfunction of different neural networks and are only spread out in time when a disease process affects both networks.

Evaluation 1 month after stroke showed many deficits and a few strengths. Inattention to the left hemiparesis was marked. By 2 months after stroke he no longer distinguished between double simultaneous stimulation, but, although he could see to the left, was still missing targets in his left visual hemifield. Visual integration, both with and without the requirement of construction, was severely impaired. He was able to correctly recognise and produce facial emotional information. Simple attention was intact, but attentional control (backward span and mental control) was impaired. Visualmotor tracking was slow and he had significant problems with conceptual shifting (both auditory and visual). Language processing difficulties included very poor reading ability, impaired confrontation naming, and impaired performance on a verbal task of fluency and initiation. Auditory comprehension was mildly impaired. Vocabulary scored formally in the borderline impaired range, as did abstract verbal reasoning. On tests of praxis he demonstrated a tendency to use the hand as object. Memory performances remained intact. His initial recall of two paragraphs scored formally within the low average range and after a 30 minute delay, he was able to recall most of the information initially encoded, scoring formally within the average range.

Structural brain MRI on admission to the emergency room showed a large right thalamic hemorrhage with mass effect and oedema, with oedema extending into the cerebral peduncle. This was consistent with the presence of decreased cerebral blood volume at the posterior margin of the right thalamus without any evidence of decreased cerebral blood volume within the right parietal, frontal, or temporal cortex.

This is a case of anosognosia of hemiplegia and mania co-occurring in a patient with a large right thalamic hemorrhage. Although anosognosia and mania are not generally thought of as occurring together, when Babinski introduced the term anosognosia he used it as one of his examples in a case in which the patient, though not confused, was “a little overexcited,” and in a later paper he presented a case in which there was “a certain agitation, which expresses itself by exaggerated loquacity, a decrease in attention, and a tendency to erotic ideas.”

The patient’s mood was remarkably cheerful and optimistic. A week after the stroke he was told that his left hand was paralyzed. He expressed no concern over the potential impact of the lesion.

The patient was transferred to a room nearer to the nurses’ station, and he used the nurses as one of his examples. Moreover, Heinstein and Kahn noted that euphoria was common in patients with anosognosia. Moreover, although Cutting emphasised that apathy is the mood more usually associated with anosognosia, 10% of his patients with anosognosia were described as having “euphoric mood.”

Right sided thalamic lesions are known to produce both anosognosia and mania, but the relation of each to the pathology is unclear. Only some of the patients with right hemispheric lesions are manic or agnostic. These two syndromes may be related to dysfunction of different neural networks and are only spread out in time when a disease process affects both networks.

Another possibility is that these syndromes are aetiologically related. Could anosognosia be a manifestation of mania? Although it is easy to conceive how elevated mood might facilitate anosognosia of hemiplegia (or other types of anosognosia), it is difficult to explain the presence of denial of ownership and disliking of the left arm (other anomognosic phenomena) on the basis of euphoria. Moreover, Starkstein et al., finding that similar frequencies and severities of major and minor depression were present in patients with and without anosognosia, suggest that a particular mood state may not necessarily influence anosognosia.

Several explanations have been proposed to explain the phenomenon of anosognosia. All the models invoke dysfunction of the cerebral cortex, especially the parietal cortex, in some way. It is interesting that this case’s functional MRI failed to demonstrate decreased CBV in the parietal lobe.

In summary, we present a case of mania accompanying anosognosia of hemiplegia with a right thalamic hemorrhage. The coexistence of mania and anosognosia may be more common than previously appreciated. The association with anosognosia implies that the mechanisms implicated in the pathogenesis of secondary mania may be similar to those of anosognosia. The absence of evidence of abnormal parietal, temporal, or frontal lobe function by functional MRI in this case is intriguing.

ELIZABETH LIEBSON
Department of Psychiatry, Tufts, New England Medical Center, 750 Washington Street, Box 1007, Boston, MA 02111, USA. Telephone 016 617 636 1633; eliebson@opal.tufts.edu


Epileptic cardiac asystole

A patient is reported on with habitual episodes of collapse and loss of consciousness associated with EEG evidence of focal epileptiform discharges. Simultaneous ECG recordings disclosed 25 seconds of cardiac ventricular asystole occurring 24 seconds after the onset of electrical seizure activity. After changes to antiepileptic medication and the insertion of a permanent cardiac pacemaker he has had no further episodes. In cases of epileptic cardiac dysrhythmia, isolated EEG or ECG recording may prove insufficient and prolonged simultaneous ECG/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 lost.

16 Channel ictal EEG (eight channels illustrated with ECG) showing electrographic seizure onset and subsequent bradycardia and asystole.
restored and he found himself lying on the floor. On recovery there was no confusion, drowsiness, dysphasia, or diuresis. Often, however, he sustained soft tissue injuries to his face and scalp.

Witnesses reported that the patient would, without warning, suddenly collapse to the ground where he would remain unresponsive, inaccessible, and motionless for 90 to 120 seconds. On two occasions he appeared confused and disoriented 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. At the end of the episode his heart rate would return to normal and within 2 minutes he would have fully recovered. Unusually during one reported episode of unconsciousness he was seen to briefly extend the fingers of both hands.

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

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

Cardiovascular and neurological examination was normal as were MRI and routine interictal EEG. Sixteen channel ambulatory EEG using an Oxford Instruments digital EEG receiver was performed continuously for 340 hours before an episode was captured. Interictally rare spikes were seen over the right frontocentrotemporal region during sleep. The patient started to have dyspnoea on exertion at the age of 44. At the age of 47, he noticed 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 Sir Charles Red Cross Hospital with his respiratory rate being 30 breaths per minute. The respirator had to induce tachycardia and more caudal region stimulation to cause bradycardia. 1

It had been hypothesised that there is laterisation with respect to central autonomic cardiac control with an increase in heart rate seen after an intracarotid injection of amobarbital and inactivation of the left hemisphere and a decrease in heart rate on right hemispheric inactivation. Experimental stimulation of the rostral posterior insular cortex in anaesthetised rats has been shown to induce tachycardia and more caudal region stimulation to cause bradycardia. 

Interictally patients with epilepsy seem no significantly more often than tachycardia and bradycardia or inappropriate therapy being 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.

FERGUS J RUGG-GU NN
JOHN S DUNCAN
SHELDON J M SMITH
Epilepsy Research Group, University Department of Clinical Neurology, Institute of Neurology, The National Hospital for Neurology and Neurosurgery, Queen Square, London WC1N 3BG, UK

Correspondence to: Professor John S Duncan, National Society for Epilepsy, Pall Mall St Peter, Gerrards Cross, Bucks SL9 ORJ, UK
email j.s.duncan@ion.ucl.ac.uk

Respiratory insufficiency in a patient with hereditary neuropathy with liability to pressure palsies (PNP-2) gene

Hereditary neuropathy with liability to pressure palsies (HNPP) is an autosomal dominant disorder, the molecular basis of which is a 1.5 Mb deletion in chromosome 17p11.2 including the peripheral myelin protein-22 (PMP-22) gene. HNPP typically presents recurrent pressure palsy of peripheral nerves, such as the axillary, median, radial, ulnar, or peroneal nerves, at common entrapment sites. Respiratory muscle weakness has not been previously reported in HNPP. We describe a patient with persistent respiratory failure and proximal muscle weakness who had recurrent pressure palsies of peripheral nerves.

The patient presented with an episode 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 limbs. His position sense was normal. His vibration sense was normal (4.6 m/s (normal value in our laboratory)). The patient started to have dyspnoea on exertion at the age of 44. At the age of 47, he noticed 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 Sir Charles Red Cross Hospital with his respiratory rate being 30 breaths per minute. The respirator had to induce tachycardia and more caudal region stimulation to cause bradycardia.
ing of the myelin sheath and some abnor-
bidity for his technical help with the sural nerve

tissue showing scattered tomaculous thickening of the myelin sheath and some abnor-

eral muscle atrophies, which are most prominent in the trunk are shown. A tracheotomy was performed for nocturnal hypoventilation because the

response to this treatment. General muscle atrophies, which are most prominent in the trunk are shown. A tracheotomy was performed for nocturnal hypoventilation because the

Our patient recalled experiencing recur-

Spinal accessory neuropathy and internal jugular thrombosis after carotid endarterectomy

Spinal accessory neuropathy is a rare compi-

We thank Dr T Yamamoto from the University of

ience of the diaphragm. Although the prolon-
gation of distal latency in the phrenic nerve was mild considering the severity of respira-
tory failure, assessment of axonal loss is not possible with phrenic nerve stimulation. In fact, phrenic nerve latency is not necessarily associated with pulmonary dysfunction in HMSN.1

Diffuse proximal weakness in our patient is an uncommon finding as for HNPP. Mancardi et al8 reported on three patients with progres-
sive 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 respira-
tory function in HNPP.

We thank Dr T Yamamoto from the University of

5 Mancardi GL, Mandich P, Nassani S, et al. Progres-

1 Chance PF, Alderson MK, Lepping KA, et al. DNA deletion associated with hereditary neu-

2 Eichacker PQ, Sprio A, Sherman M, et al. Respira-


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

Spinal accessory neuropathy is a rare compi-

Spinal accessory neuropathy is a rare compi-

Spinal accessory neuropathy is a rare compi-

Spinal accessory neuropathy is a rare compi-

Spinal accessory neuropathy is a rare compi-

Spinal accessory neuropathy is a rare compi-

Spinal accessory neuropathy is a rare compi-

venous thrombosis is often asymptomatic, or presents with non-specific pain, it is probably unrecognised in many cases.1 Concurrent ipsilateral spinal accessory neuropathy and internal jugular venous thrombosis after CEA is expected to be rare, and this is underscored by the lack of published cases. Despite this apparent rarity, a common pathogenetic mechanism for postoperative spinal accessory neuropathy and internal jugular venous thrombosis may well be present, at least in some cases, which may lead to the consideration of the possibility of both when either is discovered.

We report on a patient who developed right spinal accessory neuropathy and internal jugular venous thrombosis after right CEA. A 59 year old man underwent right CEA for possibly symptomatic stenosis. Angiography had shown 90% stenosis of the right internal carotid. The operation was done under general anaesthesia. The carotid bifurcation was unusually distal, necessitating a long dissection and high retraction. No immediate postoperative complications were evident. The next day, the patient complained of mild pain at the operative site, but 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, and 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 tests were consistent with chronic right spinal accessory neuropathy, and repeat ultrasonography showed persistent right internal jugular venous thrombosis. Symptomatic spinal accessory neuropathy was first reported as a complication of CEA in 1982.1 Since then, there have been several case reports and small series.1 A 1996 review of reports of cranial neuropathy after CEA disclosed only one patient with spinal accessory neuropathy in over 3000 cases.1 Although the authors did not include several other reports2 which, taken together, may suggest to some a somewhat higher incidence, the overall small number of reported cases in proportion to the hundreds of thousands of CEA cases that have been done worldwide suggests that clinically significant spinal accessory neuropathy is a rare complication. More than 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.3 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 cervical dissection and retraction have been reported to precede spinal accessory neuropathy.1,4

The spinal accessory nerve courses along the internal jugular vein and near the internal carotid artery, typically well above the carotid bifurcation. It is thought 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 is uncertain.

From our search, internal jugular venous thrombosis after CEA has been reported in only one case.5 As Southcott et al noted, retraction of the internal jugular during CEA may cause injury to the venous system, 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 more than 6 weeks after neck dissection, often with recanalisation after several months.3 The presence of induration about the incision site and a palpable supraclavicular cord in our patient led us to suspect venous thrombosis. Although the symptoms of internal jugular venous thrombosis may often be asymptomatic. Potential symptoms of internal jugular venous thrombosis include headache, dysphagia, and anterolateral neck pain, tenderness, and swelling. In addition to perivenous induration, fever and leukocytosis may occur.7 Common pathogenetic mechanisms for spinal accessory neuropathy and internal jugular venous thrombosis may include intraoperative traction, haematoma, and postoperative inflammation and scarring. Although the onset of either spinal accessory neuropathy or internal jugular venous thrombosis in our patient cannot be determined precisely, it is likely that both developed at about the same time. The delayed worsening of the spinal accessory neuropathy in this case suggests postoperative scarring or inflammation. The lack of improvement after a year, as in some other cases of spinal accessory neuropathy after CEA, implies considerable axonal injury, but does not clarify the manner of injury.

GEORGE WOODWARD
RAM VENKATESH
Department of Neurology, University of Kansas, and Neurology Section, VA Eastern Kansas Health Care System, VA, USA

Correspondence to: Dr George Woodward, Neurology Section (111), VA Medical Centre, Leavenworth, Kansas 66048, USA. Telephone 001 913 682 2000 extension 2441; fax 001 913 758 4225.


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 alert the 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 and EEG were also normal except for a patent foramen ovale.

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

Although a paradoxical embolism through a patent foramen ovale in this patient cannot be excluded as 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 and is an energy supplement in non-prescription medicines for multiple uses. Ephedrine, MaHuang extract and creatine have been reported to cause vasoconstriction in addition to other catecholaminergic effects. Both ischaemic and haemorrhagic stroke associated with ephedrine use have been reported.1 Acute myocardial infarction and acute psychosis have also been reported after taking ephedrine and other sympathomimetic drugs.1 Ephedrine and its metabolites are natural products that are used in non-prescription medicines for multiple uses. Ephedrine is an active ingredient in many over the counter weight loss, energy, and dieting aids. 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 creatine 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 effect of energy supplements, particularly when used in multiple combination.

K VAHEDI
V DOMIGO
P AMARENCO
M-G BOUSSER
Service de Neurologie, Hôpital Lariboisière, Paris, France

Correspondence to: Dr K Vahedi, Service de Neurologie, Hôpital Lariboisière, 2 Rue A Paré, 75010 Paris, France
e-mail vahedi@ccr.jussieu.fr


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 dysaesthesia 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 dysdiadochokinesia.

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

An MRI study showed a large gadolinium enhancing tumour within the left cerebellopontine angle extending to the cavaux Meckelii with marked displacement of the brainstem to the contralateral side (figure A and B). Cerebrovascular angiography showed a discrete blush of the tumour as typically seen in meningiomas. The tumour was totally removed by a combined transpetrosal supratentorial and infratentorial presigmoidal approach. The 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 grimming and the cervical dystonia indicates a causal association between the petroclival meningioma and the segmental hyperkineitic 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. Asymmetrical 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.1 Acoustic neurinomas and anaplastic pontocerebellar glioma can be associated with facial myokymia and spastic parietic facial contracture.2,3 Also, cervical dystonia due to tumours of the cerebellopontine angle have been reported recently.1,2

The pathophysiological mechanisms responsible for dystonic movement disorders caused by structural or functional lesions of the brainstem are not fully understood. The possibility of denervation supersensitivity of cranial nerve nuclei has been proposed previously. Alternatively, enhanced excitability of brainstem interneurons has been suggested. This pathophysiological mechanism is supported by the findings of blink reflex studies in patients with blepharospasm, spasmodic dysphonia, and cervical dystonia. Tosola 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.4

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 finding that such movement disorders are accessible to surgical treatment of the underlying pathology. Therefore, patients with cranial or cervical dystonia or choreic dyskinesia should undergo MR imaging to rule out a surgically treatable cause.


Acute multifocal cerebral white matter lesions during transfer factor therapy

Transfer factor is an active substance of unknown structure present in dialysable leucocyte 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 leucocyte extract increases macrophage activation and interleukin (IL) 1 production and enhances leucocyte 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 in some refractory neoplasms and chronic infections. Moreover, it has been used in the treatment of uveitis.1 Administration of dialysable leucocyte extract has seemed to be free of hypersensitivity, long lasting side effects, or complications, except for transitory hyperpyrexia.2

We report on a patient in whom multiple cerebral white matter lesions developed after taking dialysable leucocyte extract orally for uveitis. A 28 year old man was admitted to the hospital because of headache, mental confusion, and right hemiparesis. He had had recurrent bilateral uveitis from the age of 12 to 14 with relapse of right eye. In January 1995 retinal vasculitis was diagnosed at fundoscopy and in July 1995 he started oral transfer factor as dialysable leucocyte 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 tites (355 UI/ml, normal <200 UI/ml), and anticardiolipin IgG (30 UI/ml, normal 12 UI/ml). Negative results were obtained for VDRL and for syphilis, antinuclear factors, lupus anticoaugulants, cryoglobulins, anti-DNA, anti-smooth muscle, and antineutrophil cytoplasmic antibody. No oligoclonal bands or antibody against CMV, Herpes simplex, V aricella zoster, Epstein-Barr virus, Cox sackie, Encephalitis, Enterovirus or Borrelia burgdorferi were present. Polymerase chain reaction search for Herpes simplex 1 and 2, V aricella 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, V aricella zoster, Epstein-Barr virus, Cox sackie, Encephalitis, Enterovirus or Borrelia burgdorferi were present. Polymerase chain reaction search for Herpes simplex 1 and 2, V aricella zoster, CMV, Epstein- Bar 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 tites (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 leucocyte extract therapy and appearance of cerebral white matter lesions in our patient supports the possibility that the association of the two events might not be causal. Despite the absence of biopsy, we reasonably excluded

THOMAS POHLE JOACHIM K KRAUSS
Department of Neurosurgery, Inselspital, University of Bern, Berna, Berna, Switzerland

JEAN-MARC BURGUNDIER
Department of Neurology

Correspondence to: Dr J K Krauss, Department of Neurosurgery, University Hospital, Klinikum Mannheim, Theodor-Kutzer-Ufer 1-3, 68167 Mannheim, Germany. email: joachim.krauss@nch.m.u.uni-heidelberg.de

1 Hemifacial spasm was seen in patients with blepharospasmus, spasmodic dysphonia, and cervical dystonia. Tosola 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.

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

3 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 tites (355 UI/ml, normal <200 UI/ml), and anticardiolipin IgG (30 UI/ml, normal 12 UI/ml). Negative results were obtained for VDRL and for syphilis, antinuclear factors, lupus anticoaugulants, cryoglobulins, anti-DNA, anti-smooth muscle, and antineutrophil cytoplasmic antibody. No oligoclonal bands or antibody against CMV, Herpes simplex, V aricella zoster, Epstein-Barr virus, Cox sackie, Encephalitis, Enterovirus or Borrelia burgdorferi were present. Polymerase chain reaction search for Herpes simplex 1 and 2, V aricella zoster, CMV, Epstein- Bar virus, and JC virus in the CSF was negative.

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

5 The close temporal relation between assumption of dialysable leucocyte extract therapy and appearance of cerebral white matter lesions in our patient supports the possibility that the association of the two events might not be causal. Despite the absence of biopsy, we reasonably excluded...
the diagnosis of vasculitis or neuro-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 anticytodioplin antibodies is found in 2% of healthy subjects.

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. In addition, CSF without oligoglonal banding argues against a diagnosis of multiple sclerosis, whereas it is commonly found in acute disseminated encephalitis. On the other hand the possibility that acute disseminated encephalitis may recur has been accepted and on the basis of the patient’s clinical picture and CSF, we favoured such a diagnosis.

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

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

FRANCESCO G FOSCHI  
LORENZO MARSIGLI  
MAURO BERNARDI  
Semestica Medica, Dipartimento di Medicina Interna,  
Epatologia e Cardioangiologia, Università di Bologna,  
Policlinico Sant’Orsola, Bologna, Italy

FABRIZIO SALVI  
Dipartimento di Scienze Neurologiche, Ospedale Bellaria, Bologna, Italy

MARIO MASCALCHI  
Cattedra di Radiologia, Università di Pisa, Italy

GIOVANNI GASBARRINI  
Cattedra di Medicina Interna, Università Cattolica del Sacro Cuore, Roma, Italy

GIUSEPPE F STEFANINI  
Divisione di Medicina Interna, Ospedale di Fanzara (Ravenna), Italy

Correspondence to: Dr Francesco Giuseppe Foschi, Semestica Medica, Dipartimento di Medicina Interna, Epatologia e Cardioangiologia, Università degli Studi di Bologna, Policlinico Sant’Orsola, via G Massarenti 9, 40138 Bologna, Italy. Telephone 0039 51 308943; fax 0039 51 308966; email fgfoschi@tin.it


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

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

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

Neurological examination showed bilateral hyperreflexia, mild impression of fine finger movements, dysgraphaesthesia on sensory testing, and a manneristic gripping handshake. There were no extrapyramidal signs. A CT scan showed multiple calcifications of the basal ganglia and thalamus, which were confirmed on a MRI scan. The patient was treated with calcium carbonate and daily vitamin D and calcium supplements.

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 infections led us to postulate in this patient a cell mediated immunological mechanism. Therefore, an immunological cross reaction between viral antigens (or other foreign material contained in vaccines) and various parts of the nervous system resulting in acute disseminated encephalitis might have occurred. As already noted, dialysable leucocyte extract contains a multitude of immunostimulating or potentially activating substances so it is impossible to pinpoint which one could have been responsible for the demyelinating effect seen in our patient. This notwithstanding, our finding indicates that neurological surveillance is worthy in patients assuming dialysable leucocyte extract therapy.

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 sequential reasoning. 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). Since CT shows increased activity in 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 0.70–1.45 mM). Ionised calcium was 0.80 mM at pH 7.4 (normal 1.10–1.34 mM); urinary calcium was 0.8 mM (normal 2.5–6.3 mM). Serum parathyroid hormone was below 0.6 pmol/l. Serum calcium was 1.55 mM/l (normal 2.15–2.55 mM). Hypertrophic atlantoaxial ligaments: an unusual cause of compression of the upper cervical spinal cord (figure). The laboratory tests were normal, confirming the absence of rheumatoid arthritis, metabolic disease, or gout. Surgical removal via a transtoral approach with a minimal bony resection was direct and provided sufficient space to obtain spinal cord decompression. It was followed by a posterior C1–C2 fusion. Macroscopically, the lesion had no capsule and resembled a hypertrophic ligamentum flavum. Microscopically, it was non-inflamatory, hypocellular, and ligamentary pieces found within the mass fibres and almost disintegrated. The patient regained normal neurological function. Over a 3 year follow up period there was no recurrence.

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

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

The craniovertebral junction can be affected by several pseudotumorous masses extradurally located, such as rheumatoid panus, hypertrophic non-union of odontoid fracture, post-traumatic cicatrix, synovial cysts, tumorous calcium pyrophosphate dihydrate crystal deposition, tophaceous gout, calcification of the posterior longitudinal ligament, synovial disease-like pigmented villonodular synovitis, and synovial chondromatosis. 1–8 Hypertrophy of the atlantoaxial ligaments as a consequence of degenerative disease was recently recognised as an individual entity. Only five previous cases have been published. 9–12 We add another case to the short series available in the literature, emphasising that as the cause of the spinal cord compression is amenable to surgical removal, symptomatic patients should be diagnosed and treated without delay.

A 66 year old woman presented with a rapid development of progressive spastic tetraparesis and an unremarkable medical history. There was no osteolysis or instability on plain cervical radiography and C.T. A bone scan with “Tc was unremarkable. Magnetic resonance imaging showed a retro-odontoid extradural mass that was homogeneous and isointense on T1 weighted signal, demarcated no enhancement after intravenous gadolinium contrast, and was compressing the upper cervical spinal cord (figure). The laboratory tests were normal, confirming the absence of rheumatoid arthritis, metabolic disease, or gout. Surgical removal via a transtoral approach with a minimal bony resection was direct and provided sufficient space to obtain spinal cord decompression. It was followed by a posterior C1–C2 fusion. Macroscopically, the lesion had no capsule and resembled a hypertrophic ligamentum flavum. Microscopically, it was non-inflamatory, hypocellular, and ligamentary pieces found within the mass fibres and almost disintegrated. The patient regained normal neurological function. Over a 3 year follow up period there was no recurrence.

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

ALEJANDRA TERESA RABADAN
Department of Neurosurgery, Instituto de Investigaciones Medicas “Alfredo Lanari”, Facultad de Medicina, Universidad de Buenos Aires, and Equipo de Neurocirugia de Buenos Aires, Argentina

GUSTAVO SEVLEVER
Department of Pathology, Cliniica Bax terrica, Buenos Aires, and Equipo de Neurocirugia de Buenos Aires, Argentina

Correspondence to: Dr Alejandra T Rabadan, Bill-inghurst 1976 PB, 1425 Buenos Aires, Argentina. Telephone 0054 1 902 4417;fax 0054 1 903 892;email rabadan @ movi.com.ar

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

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

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 left ambient cistern in addition to the previous lesion (figure). Brain MRI, taken 3 days later, demonstrated an intraparenchymal lesion, at 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 cranioeccrival injury. Responsible lesions for sensory impairment, detectable by neuroimaging studies, almost always accompany associated neurological deficits.

To our knowledge, a selective injury at the spinothalamic or trigeminothalamic tracts due to closed head injury has not been highlighted in the neurological literature.

The MR images in our case showed a discrete lesion at the left dorsolateral midbrain. Topographical study at this lower midbrain level showed that the lateral and ventral spinothalamic and ventral trigeminothalamic tracts pass at the surface of this level by carrying a superficial somatosensory sensory input. The lesion shown in our MR images seemed to be localised to these tracts. The medial lemniscus for the deep sensation and lateral lemniscus and nucleus of inferior colliculus associated with hearing function in 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 precondionned with narrow tentorial incisura, which may have been the case in our patient.

The concept of tentorial coup injury against the midbrain is not new. It usually accompanies various degrees of conscious disturbance and other long tract signs, sensory deficits as well as cerebellar and cranial nerve palsy due to the midbrain lesion or other associated intracranial lesions.

The clinical manifestation of our patient may represent one of the mildest forms of the midbrain contusion. The next time 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 al1 and comment on the medical treatment of toluene induced tremor. Microdialysis experiments in rats have shown that inhalation of toluene increases extracellular γ-aminobutyric acid (GABA) concentrations within the cerebellar cortex2 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.3 Degeneration of certain cerebellar pathways is probably responsible for the loss of this dopaminergic innervation.4 Dopamine agonists could therefore be of potential interest in the treatment of toluene induced tremor. This hypothesis was explored in a recently described case,5 which showed remarkable clinical and iconographic similarities with that described by Miyagi et al: (a) long history of chronic toluene inhalation, (b) marked postural tremor, (c) progressive worsening of the symptoms despite abstinence from inhalant misuse, and (d) mild cerebral atrophy and marked low signal intensity in globus pallidi, thalami, red nuclei, and substantia nigra on T2 weighted MRI. As 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 in a group of 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 ataxia, supported by loss of dopaminergic terminals of these neurotransmitters in the CSF of patients with heredodegenerative ataxias.6 In our patient, amantadine hydrochloride (100 mg twice daily) abolished the tremor and ataxia. He was rechallenged to amantadine hydrochloride, which resulted in relapse of the tremor and ataxia. The tremor and ataxia resolved after treatment with a dopamine agonist.6

3 Bjornaess S, Naalsund LU. Biochemical changes in different brain areas after toluene inhalation. Toxicology 1989;49:36.

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

Nabbout et al7 have attempted to identify the risk factors for the progression of subependymal nodules into giant cell astrocytomas (SEGAs) in tuberous sclerosis complex. In attempting to develop screening strategies that avoid iatrogenic morbidity, patient inconvenience, and excess cost, it is essential that the natural history of these lesions in the general population of patients with tuberous sclerosis complex be understood well.

We think that there are two problems with this study that should make the physician cautious about applying the factors identified by Nabbout et al.8 as a basis for a screening programme. The first is that this study was performed in a population that had been referred to a tertiary medical centre, and then had been further selected by virtue of having had at least 3 years tertiary centre follow up and needing two MR scans of the head. The prevalence of astrocytomas and risk factors, and hence the positive predictive value of any screening tool in a general population of patients with tuberous sclerosis complex is likely to be different from those described in the highly selected group studied in this paper. The second is that the authors have made a potentially misleading decision to exclude more than half their study sample because they do not have lesions close to the foramen of Monro. It is not certain that all SEGAs arise from lesions close to the foramen. They may arise in the fourth ventricle. Furthermore, the late presentation of many lesions in the lateral ventricles has, in the past, precluded accurate determination of their point of origin. In a study selects 24 of 60 patients who had met their entry criteria but does not state how many of the included 36 patients had no subependymal nodules or nodules that were not “near the foramen of Monro”. Exclusion of these cases is given for what constitutes proximity to the foramen. The authors were apparently not blinded at the point when they selected which patients had lesions near to the foramen and therefore there is an obvious issue of potential selection bias.

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

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

FINBAR J K O’CALLAGHAN
ANDREW LUX
JOHN OSBORNE

Department of Clinical Pharmacology and Neurology, College of Medicine, PO Box 35, Al-Rhad, Muscat-123, Sultanate of Oman

YOLANDE HANSENS

Drug Information Services, Hospital Pharmacy

Correspondence to: Dr. Dirk Deleu, College of Medicine, PO Box 35, Sultan Qaboos University, Al-Rhad, Muscat-123, Sultanate of Oman email deleu@omanel.net


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 al9 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 al10 coined the term ‘flail arm syndrome’, to describe a subgroup of patients affected by ALS that predominantly showed signs of lower motor neuron disease in the upper limbs, without significant functional involvement of other regions on clinical presentation. This subgroup of patients was clinically characterised by the display of progressive atrophy and weakness affecting the proximal muscles in the upper limb muscles in a more or less symmetric manner.

Recently, along these lines, Katz et al11 described a series of patients affected by ALS from an adult onset motor neuron disorder restricted to the upper limbs, with severe proximal and varying degrees of distal involvement, calling it amyotrophic brachial diplegia syndrome. Other terms used to describe this form of ALS have been dangling arm syndrome, suspended form, oranganut 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.

Probably all these terms used to define this variation of ALS are synonyms for an older, well-known condition, the scapuloumaplo-phrenic form, or the chronic anterior poliomyelitis reported by Vulpian in 1886 and known in Franco-German literature as Vulpin-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 scapuloumaplophrenic distribution (over 45 years of age) generally leads to ALS as a matter of course. Be that as it may, the truth is that this atypical form of amyotrophic lateral sclerosis behaves differently from typical ALS. The comparative study with the rest of the ALS group supplied important clinical findings, such as little or no functional impairment of the bulbar muscles or legs. Hu et al also made four important statistical discoveries. (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 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 (FVC, PImax, and PEmax).

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 deltoideus (upper arm muscle) 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 infraespinatus and the supraespinatus, that act as an active ligament in scapuloumaplophrenic articulation, would explain the presence of subluxation of the subclavian joints in these patients.

Finally, we are in complete agreement that the presence 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 55. 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.


Isolated dystarthis

We read with interest the article by Urban et al. Using transcranial magnetic stimulation, the authors demonstrated electrophysiologically evidence for a central monoparesis of the tongue in patients with isolated dystarthis from cervical spondylosis. As in their patients transient magnetic stimulation induced absent or delayed corticospinal responses at the tongue, the authors ascribed isolated dystarthis to interruption of the corticospinal path. On the whole, the results are plausible, but we would like to comment on the underlying mechanism of isolated dystarthis.

As in the case of isolated dystarthis reported by Urban et al, all of our patients with isolated dystarthis had lacunar infarctions involving the internal capsule and corona radiata. Measurement of cervical blood flow with IMP-SPECT in these patients disclosed frontal cervical hypoperfusion, particularly in the anterior opercular and medial frontal regions. Anterior opercular lesions produce facio-pharyngo-glossal muscular 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 with motor and language areas, resulting in dysfunction of these cortices. Therefore, we postulated that isolated dystarthis results from interruption of corticospinal/subcortical networks indispensable for speech output, involving the thalamocortical and corticostriatal fibres as well as the corticobulbar fibres. In fact, lacunar infarctions around the internal capsule-corona radiata are likely to underlie this ascending and descending projection system.

To assess corticopontocerebellar tract function, Urban et al investigated cerebellar blood flow in patients with isolated dystarthis using HMPAO-SPECT. They showed that the cortex disclosed the corticopontocerebellar tract is preserved in isolated dystarthis because of no evidence for cerebellar diaschisis on SPECT. Their SPECT findings on cerebellar blood flow were similar to our results. However, we wonder whether cerebral cortical blood flow was preserved in their patients, because our SPECT study suggested frontal cortical dysfunction as an underlying mechanism of isolated dystarthis. Linguo-palatal paresis and contractions with cerebral language areas, including in three of seven patients reported by Urban et al and in two of 12 by us. This indicates that isolated dystarthis originates in incoordination of multiple organs necessary for articulation as well as speech production. Although interruption of the corticobulbar pathways is a likely cause of isolated dystarthis, it should be borne in mind that damage to other descending and ascending projections may contribute to isolated dystarthis.
Motor cortical excitability in Huntington’s disease

We read with great interest the paper of Hanajima et al reporting that intracortical inhibition of the motor cortex is normal in patients with chorea of various origins. At variance with the results we previously found1 a reduced intracortical inhibition in a group of patients with genetically confirmed Huntington’s disease. Hanajima et al suggest that the discrepancies between the two studies1,2 may be due to selection issues as they included patients with early stage Huntington’s disease to “study the pathophysiology of chorea unaffected by other disorders movement.” They postulated that our cases, because of the reported coexistence with a dystonic rating scale, had a more advanced stage of the disease possibly with coexisting dystonia or rigidity. These assertions deserve some comments.

The mean disease duration of our nine patients with Huntington’s disease was 6.2 (4.1) years which is actually shorter than the duration of the six patients reported by Hanajima et al (8.3 (5.9) years). Most of our patients could be considered in an early stage of the disease, in contrast to the Unified Huntington’s disease rating scale, and none presented dystonia, rigidity, or any other additional movement disorder. In this regard, however, it should be pointed out that bradykinesia is often associated with chorea in patients with Huntington’s disease3 and may even precede the appearance of choreic dyskinesias.4 Chorea itself is often reduced in the more advanced Huntington’s disease stages.5 It is unlikely, therefore, that any neuropsychiological approach can test purely chorea even in the early Huntington’s disease stages. In addition, different mechanisms are involved in Huntington’s disease and other choreas as suggested by the lack of impairment of somatosensory evoked responses and long latency stretch reflexes in the second.5

We were not really surprised at the results of Hanajima et al as we do share their opinion that patients with Huntington’s disease may be characterised by large individual differences in the involvement of motor cortical areas. Actually, three patients in our study showed an amount of intracortical inhibition within the confidence limits of the control population. We also think that the impairment of intracortical inhibition is likely to develop during the progression as we did not find any change in four patients, two of them already reported,6 with positive DNA testing but completely asymptomatic.

The discrepancies between the two studies are more likely to be explained, at least in part, by some methodological differences. For instance, the amplitude of the control response was larger in our set (approximately 1.0 mV compared with 0.3 mV in the study of Hanajima et al). This may induce a different sensitivity of the test, and the amount of intracortical inhibition in our normal controls is greater (see also7) than in the study of Hanajima et al.

When interpreting the results of studies with paired transcranial magnetic stimulation pathophysiologically it should be kept in mind that similar changes of intracortical inhibition have been shown in patients with various movement disorders (focal dystonia, myoclonus, parkinsonism, restless legs syndrome, Tourette’s disorder), but also in different diseases such as amyotrophic lateral sclerosis.8 We think, therefore, that the impairment of intracortical inhibition cannot be regarded as the marker of a specific pathophysiological mechanism, but is likely to reflect a non-specific imbalance of inhibitory and facilitatory circuits within the motor cortex.


The authors reply: We are very grateful for the response of Abbruzzese et al to our paper. We completely agree with their opinions.

The discrepancy between the two studies1,2 may not be mainly due to the different stage of the disease between our two groups of patients. Although the duration of the disease is one factor to judge the disease stage, the severity of the disease (stage of the disease) is also positively correlated with CAG repeat number.

We may have to take CAG repeat number into consideration in comparisons. Unfortunately, however, we have no way to do such comparisons between these two studies. We could say, at least, that the intracortical inhibition was normal even at the same stage of the disease as that of the patients of Abbruzzese et al, if studied with our method.

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 stimulation. Therefore, we used the same intensities of the conditioning stimulus before we confirmed inhibition in studies of patients.1 We used an intensity of 5% less than the active threshold as a conditional stimulus, below the resting threshold in our experience. 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 in the results 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
involuntary contraction is often decreased in Huntington’s disease. The 80% of the threshold for relaxed muscles must correspond to different values relative to the threshold for active muscles in patients from that in normal subjects. (2) The involuntary contraction is described by Michel et al’s concept of “critical closing pressure”. This slight abnormality could be detected with their method but not with ours because their method has better sensitivity in detecting an abnormality than ours. Whether is true, the involuntary contraction must be normal or slightly disturbed in Huntington’s disease.

R HANAJIMA
Y UGAWA
Department of Neurology, Division of Neuroscience, Graduate School of Medicine, University of Tokyo, 7–3–1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan

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

Firstly, the physiological meaning of both formulae of CCP presented (CCP1 and CCP2, respectively) is questionable. The implication of both presented equations is that the instantaneous value of cerebral blood flow velocity (FV) 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) = (ABP(t)−CCP)/CVR (1) At the time of systolic and diastolic pressure values (ABPs, 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 does not follow 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 pressures.4 Therefore, equation 1 cannot be applied to describe dynamic flow. This can best be illustrated using the frequency domain approach (ABP=mean pressure; FV=mean flow velocity; A1=amplitude of the pulsatile pressure wave; F1=amplitude of the pulsatile flow wave): FV(t) = (ABP−CCP)/CVR0 (2) F1 = A1/CVR1 (3) Inserting equations 2 and 3 into the frequency domain equation for CCP2 of the authors

CCP2=ABP−A1/F1=FV

leads to

CCP2=ABP−CCP×CVR1/CVR0×(ABP−CCP)=ABP−CVR1×CVR0/CVR1

CVR0×CVR1

where CCP2 is only in the case of CVR1×CVR0 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 FV values with ABP found by the authors (r=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 vasconstrictor function. 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 at FV values with a high vascular resistance (peripheral arteries, middle cerebral artery during strong hypocapnia). In the case of ABP<CCP and a small vessel collapse according to the model of the authors, CVR should increase towards CVR0 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

and equation 5 to

CCP2=ABP−(1/CVR1×CVR0)+CVR1/CVR0

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”.

Rolf R Diehl
Department of Neurology, Krupp Hospital, Alfred-Krupp-Straße, 45117 Essen, Germany

4 Czosnyka et al reply: We thank Diehl very much for the interesting letter providing some mathematical considerations about cerebral haemodynamics. We need to emphasize 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 Aaslid proposed the mathematical formula taken for calculations:

CCP1=ABP−ABPPp×FVp×FVp=ABP−ABPPp×FVp×FVp

(where ABP and FV are mean values of arterial pressure and MCA flow velocity, ABPs and FVs are systolic values, ABPPp and FVp are peak to peak amplitudes). A graphical interpretation of this formula has been given in fig 1. CCP1 is an x intercept point of linear regression between subsequent systolic and diastolic values recorded within 6 second intervals of flow velocity (along y axis) and arterial pressure (along x axis).

In fact, the 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:

CCP2=ABP−A1/F1×FV

In our paper we confirmed empirically that both CCP1 and CCP2 produced the same values in a group of normal patients 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). This means “clouds” of systolic and diastolic values of ABP and FV waveforms (fig 1 in) one can rather see an ellipsoidal shape which is very seldom regular enough to be approximated by a straight section. Therefore, equation (1) in Diehl’s letter is not correct. In fact, CVR is a frequency dependent variable (represents vascular impedance) and if a linear theory can be applied, division in (1) should be substituted by a convolution with an inverse of Fourier transform of “cerebrovascular admittance”.

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

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

The final issue concerning negative flow velocities is a trap Diehl has prepared for himself. We never suggested that any factor interpretable as cerebrovascular resistance (CVR0 or CVR1) should be involved in the concept of critical closing pressure. From the definition, closing 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 monkeys.1 Levodopa induced dyskinesias are currently thought to share a similar pathophysiology4 but recent findings also suggest that abnormal patterns of neuronal firing in the globus pallidum internum may be relevant.2 Data from both parkinsonian monkeys and patients with Parkinson’s disease submitted to lesion3 or functional blockade of the subthalamic nucleus2 are in keeping with such a general principle, but the threshold to induce dyskinesias in the parkinsonian state is higher than in intact animals.3 The case recently described by Figueiras-Mendez et al1 is extremely interesting as it suggests that functional inhibition of the subthalamic nucleus by high frequency stimulation blockade of levodopa induced dyskinesias. This is clearly at odds with the current pathophysiological model of the basal ganglia.2 Thus, the finding of Figueiras-Mendez et al1 rises the intriguing possibility that dyskinesias depend or are mediated by neuronal firing in a given region of the subthalamic nucleus, which was blocked by high frequency stimulation. Measurement of afferent synaptic activity by the technique of 2-deoxyglucose (2-DG) uptake showed an increment in the subthalamic nucleus, which was compatible with increased inhibition from the globus pallidum externum, particularly in the ventromedial tip of the nucleus.3 This contrasts with the findings in monkeys with chorea induced by pharmacological blockade of the globus pallidum externum, in which 2-DG uptake was maximal in the dorsolateral portion of the subthalamic nucleus, where the sensorimotor region lies. A recent anatomical study4 also showed that the cortical-subthalamic nucleus con-
nection is somatotopically segregated, so that fibres from the supplementary motor area project to the most medial portion and fibres from the primary and premotor areas terminate in the lateral region of the subthalamic nucleus.5 All this heterogeneity may have pathophysiological relevance, describing one aspect of which could be the findings in the patient reported by Figueiras-Mendez et al.1 How-
ever, before the findings of this case may be used to sustain the hypothesis that dyskinesias depend or are mediated by neuronal firing in a given region of the subthalamic nucleus, there is a crucial issue to resolve—namely, the location of the tip of the stimulation electrodes. There are several points leading us to question the actual site of action of the electrode: (1) Stimulation of the subthalamic nucleus in Parkinson’s disease has been associated with the production of dyskinesias only with the reduction of levodopa intake.6 Moreover, Benabid et al who pioneered this technique, consider the induction of dyskinesias by high frequency stimulation of the subthalamic nucleus as a good indicator of a very positive response to stimulation.7 The finding of Figueiras-Mendez et al8 to lesioning to the thalamus from the globus pallidum internum are placed dorsocaudally to the subthalamic nucleus and could be blocked by high frequency stimulation. (2) When the recording electrodes are placed dorsoventrally to the subthalamic nucleus in sagittal planes 11 mm or less, neuronal activity is characterised by action potentials of large amplitudes (0.5–1.5 mV) with low background activity, tonically firing neurons, and absent sensorimotor responses (“driving”). All these characteritics seemed to be present in the patient discussed here. Neuronal activity in the sensorimotor region of the subthalamic nucleus is different from the above but on occasions the distinction may not be easy. (3) Very importantly it is difficult to document in more detail the findings in the case of Figueiras-Mendez et al1 Ideally we would like to see the trajectory and length of the different recording tracks, the effects of microstimulation, and the post surgery MRI with measurement of the tip of the electrodes. If, as assumed, the subthalamic nucleus was indeed correctly targeted in this patient, the pathophysiology of the basal ganglia will need to be revisited.

J A OBSEO
G LINAZASORO
J CURIDI
E RAMOS
Centro de Neurologia y Neurocirugia Funcional, Clínica Quiron, San Sebastian, Spain

J A OBSEO
M C RODRIGUEZ-OROZ
Hospiten, Tenerife, Spain

Correspondence to: Professor J A Obeso, 30 Cíutz Artea, Cruzar Mayor, 31180 Navarre, Spain.

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 the cells fired phasically 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.

For 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 voluntary movements, and the three engaged in tremulous movements were not tested in the surgery before cementing the electrode, assessed by ventriculography. It always tested in the surgery before cementing the electrode was placed in laterality 11. One track was performed. In the left hemisphere, two tracks were performed. One track was performed 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 laterality 12. The trajectory stimulated electrode is 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) posterointeranterior: 1.5 mm behind the mean point of intercommissural line, (b) horizontal: 6.5–6.5 mm below the intercommissural line, and (c) lateral: 12 mm for the right hemisphere, and 11.5 mm for the left hemisphere.

ROBERTO FIGUEIRAS-MÉNDEZ, FERNANDO MARIN-ZARZA, JOSE ANTONIO MOLINA, FÉLIX JAVIER JIMÉNEZ-JIMÉNEZ, MIGUEL ORTÍ-PAREJA, CARLOS MAGARINOS, MIGUEL ANGEL LÓPEZ-PINO, VICENTE MARTINEZ.

Correspondence to: Correspondence to: Dr F Jiménez-Méndez, C Corregidor, Jose de Pasamonte 24 3ºD, E 28030 Madrid, Spain.


connective tissue disorders, organ specific autoimmunity, sarcoidosis, and cerebral vasculitis.

Each chapter is an appropriate length and well referenced; the wood is always clearly visible between the trees. This book is sufficiently readable and small to be recommended as holiday reading. Its only drawback is that in making erudition so readily available, one risks being outshined yet again by one's registrar.

JON SUSSMAN


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 seminal 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 (Pascuier 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 (Mölter), antioxidants, and radical scavengers (Röser et al). I found the review by Reisburg 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


Volume nine of the Current Issues in Neurodegenerative Disease series examines the interplay between cerebrovascular disease and dementia, particularly Alzheimer's disease. Two hundred pages of what are essentially 20 brief review articles comprise this text, sadly without any illustrations. Each chapter is a reasonably comprehensive, if not exhaustive, overview of research into the topics covered, but the introduction to each chapter is a certain sense of deja vu, although on the positive side each contribution is extremely well referenced.

The brief essays are divided into five sections covering the historical concepts of vascular and Alzheimer's dementia, the arguments for a pure vascular dementia, the role of Alzheimer's disease in the genesis of dementia after stroke, the contributions of white matter changes on neuroimaging to dementia, and finally a short section examining practical questions such as the management of stroke in patients with dementia.

Although common conditions 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 in narrative form not only delights, but is easily recalled. Stories also construct meaning through interwoven observation, inference, motive, and consequence in a fashion that informs future action. Our experience of the world is constructed around such narratives. They define us as individuals, family members, professionals, and cultural groups.

This book is a series of essays on psychotherapy, psychiatry, and also medicine that sees the awareness and use of narrative in clinical practice as a construct that can both...
deliver effective care as well as act as a conceptual bridge between the different disciplines. One of the great pleasures of being a doctor has always been listening to patient's stories, but the editors of this book fear that this essential art can be overtaken by dull scientific pragmatism. Rather, in the most outstanding chapters, writes a lucid and well reasoned pragmatism. Roberts, in the most outstanding theoretical art can be overtaken by dull scientific pragmatism. Apart from the chapters on chronic fatigue and the treatment of tardive dyskinesia there is little in this book which is of immediate interest to neurologists. However general psychiatrists wishing to improve their prescribing skills will find this book useful.

SIMON FLEMINGER


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

The book is divided into sections dealing with the treatment of broad groups of clinical disorders—for example, psychosis—special patient populations—for example, elderly people, with further sections on the management of emergencies and the adverse effects of psychotrophic drugs. Much of the information is laid out in tabular form. It could become an indispensable resource for a busy on call senior 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 their clinics. It does not aim at great erudition, but provides a useful list of references.

There are a few cavils. The section on treatment of anxiety is skimpy (one and a half pages) compared with say the treatment of affective illness (22 pages) or schizophrenia (58 pages). The brevity is only partly explained by the undeveloped state of that particular area of psychopharmacology. Sections on new indications to and contraindications for lumber puncture and indications for EEG 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


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 older 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 the whole (the chapters) are better than the whole (the book). 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 answer does not emerge. The chapters covering basic neurophysiology, neuroanatomy, and neuropathology, are erudite and fascinating but at times are barely comprehensible. Further work is needed, including answering the fundamental question—why does the first seizure occur—before the clinician and basic scientist are able to talk the same language—of the patient with epilepsy.

The concept of Childhood Epilepsies and Brain Development is innovative and commendable and whilst the majority of the monographs are interesting and informative, the overall impression is that the individual parts (the chapters) are better than the whole (the book). The lack of an index is a strange omission, perhaps due to a prolonged editorial atypical absence, and although this militates against it becoming a well thumbed reference text, the book is an erudite addition to the mossy fibre-like sprouting of the epileptological literature. RICHARD E APPLETON


Difficult clinical problems in psychiatry come in many forms. Diagnosis often causes difficulty, particularly in cases which demand some assessment of the role of physical illness in symptom formation. Perhaps for most psychiatrists practising in community settings risk assessment comes high on their list of concerns. Unsurprisingly, given the psychopharmacological expertise of the editors, this book is particularly interested in treatment resistance. The first 6 chapters give excellent reviews of the management of clinically relevant topics—for example, refractory schizophrenia or the difficult panic patient. The emphasis is very much on psychopharmacological management.

The second half of the book is more of a mixed bag, both in terms of the areas covered and quality of the chapters. The remaining chapters covering all aspects of the assessment and management of anorexia nervosa and chronic fatigue are followed by a thorough revision of the pharmacological management of substance misuse. Then come two weak chapters on behavioural disturbances in old age and the violent patient in the community. This last chapter will be of particular interest to community psychiatrists but is not one that I would recommend because some aspects of the practical management of violence are missing—for example, a documented risk-benefit analysis, good failsafe communication, or deciding when to detain. One of the last chapters is a very good account of the management of hyperactivity in childhood, with good practical advice on the use of methylphenidate.

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

DUNCAN MCLEAN


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

Moving on from the general to the particular, the text, although expansive in parts, glosses over some important points. Examples include (a) which oral vitamin K preparations are considered safe in pregnancy (phytomenadione), (b) differential efficacy of various antiepileptic drugs in different syndromes versus side effect and teratogenicity profile, (c) more information on the interpretation of available evidence to support the statement “no monotherapy human abnormality reported” with certain new antiepileptic drugs in pregnancy, (d) the need to consider drug prevention well before the menopause (not only with enzyme inducers 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 21-5th week they quote 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

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

JOSEP GAMEZ, CARLOS CERVERA and AGUSTIN CODINA

J Neurol Neurosurg Psychiatry 2000 68: 118-119
doi: 10.1136/jnnp.68.1.118b