Cerebral metabolism during vegetative state and after recovery to consciousness

One way to approach the study of consciousness is to explore lesional cases in which impairment of consciousness is the prominent clinical sign. Vegetative state is such a condition wherein awareness is abolished whereas arousal persists. It can be diagnosed clinically soon after a brain injury and may be reversible (as in the following case report) or progress to a persistent vegetative state or death. The distinction between vegetative state and persistent vegetative state is that the second is defined as a vegetative state that has continued or endured for at least 1 month.

We present a patient who developed a vegetative state after carbon monoxide poisoning and in whom we had the opportunity to measure brain glucose metabolism distribution during the vegetative state and after recovery to consciousness. Using 18F-fluorodeoxyglucose (FDG) PET and statistical parametric mapping (SPM) we compared both patient's sets to a normal control population. Our findings offer an insight into the neural correlates of "awareness", pointing to a critical role for posterior associative cortices in consciousness.

A 40 year old right handed woman attempted suicide through CO intoxication and was found unconscious. She was treated with hyperbaric oxygen but evolved to a vegetative state diagnosed according to the following criteria: (1) spontaneous eye opening without evidence of awareness of the environment; (2) no evidence of reproducible voluntary behavioural responses to any stimuli; (3) no evidence of language comprehension or expression; (4) intermittent wakefulness and behaviourally assessed sleep-wake cycles; (5) normal cardiorespiratory function and blood pressure control; (6) preserved pupillary, oculocephalic, corneal, and vestibulo-ocular reflexes. Brain MRI performed 14 days after admission was normal. Electroencephalography showed a 6 Hz basal activity with more pronounced slowing on the left parietal regions. Auditory evoked potentials were normal. Somaesthetic evoked potentials of the median nerve showed normal latency and amplitude of P14 and N20 potentials without any late cortical components. After remaining in a vegetative state for 19 days the patient regained consciousness. Her sequelae consisted of a bilateral spastic paresis of upper and lower limbs. Neuropsychological examination 1 month after admission showed an attention deficit with moderate impairment of short term memory. One year after the accident she showed a spastic gait with altered fine motor function, most prominent on the right, a slurred speech, and minor short term memory disturbances. FDG-PET was performed during the vegetative state (day 15 after admission) and after recovery to consciousness (day 57).

The control population consisted of 48 drug free, healthy volunteers, aged from 18 to 76 years (mean: 42 (SD 21) years).

The study was approved by the ethics committee of the University of Liège. Informed consent was obtained by the husband of the patient and for all control subjects. Five to 10 mCi FDG was injected intravenously; PET data were obtained on a Siemens CTI 951 R 16/31 scanner in bidimensional mode. Arterial blood samples were drawn during the whole procedure and cerebral metabolic glucose rates (CMRGlu) were calculated for all subjects. PET data were analysed using SPM software (SPM96 version; Welcome Department of Cognitive Neurology, Institute of Neurology, London, UK). The use of SPM to assess between subject (rather than within subject) variability is unlikely to alter the relevance of our results given their high degree of significance. Data from each subject were normalised to a standard stereotactic space and then smoothed with a 16 mm full width half maximum isotropic kernel. The analysis identified brain regions where glucose metabolism was significantly lower in each patient scan compared with the control group. The resulting foci were characterised in terms of peak height over the entire volume analysed at a threshold of corrected p<0.05.

During the vegetative state, average grey matter glucose metabolism was 36% lower than in controls (4.5 ± 7.3 (SD 1.4) mg/100 g/min). No substantial change in mean CMRGlu was found after recovery (4.7 ± 4.10 mg/100 g/min). During the vegetative state, significant regional CMRGlu decreases were found in the left and right superior parietal lobule; the left inferior parietal lobule; the precuneus; the left superior occipital, superior and middle temporal gyri; and the premotor and precentral and prefrontal cortex (figure, yellow colour). After recovery, metabolic impairment was confined to the left and right precentral and postcentral gyri and premotor cortices (figure, blue colour).

This case report offers an insight into the neural correlates of human consciousness (at least, external awareness as it can be assessed at the patient's bedside). Given that global glucose utilisation levels remained essentially the same, the recovery of consciousness seems related to a modification of the regional distribution of brain function rather than to the global resumption of cerebral metabolism. The main decreases in metabolism seen during the vegetative state but not after recovery were found in parietal areas, including the precuneus. This is in agreement with postmortem findings in persistent vegetative state, in which involvement of the association cortices is reported as a critical neuroanatomical substrate and with PET studies in postanoxic syndrome, in which the parieto-occipital cortex showed the most consistent impairment.

The functions of these areas are manifold: lateral parietal areas are involved in spatial perception and attention, working memory, mental imagery, and language, whereas the precuneus is activated in episodic memory retrieval, modulation of visual perception by mental imagery, and attention. Our data point to a critical role for these posterior associative cortices in the emergence of conscious experience.

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Localisation of voxels in which cerebral glucose metabolism was impaired during vegetative state (in yellow) and after recovery to consciousness (in blue), compared with the control population. SPM(Z) threshold was set at voxel level corrected p<0.05 and projected on the patient's co-registered MRI, normalised to the stereotaxic space of Talairach.
Electrical inexcitability of nerves and muscles in severe infantile spinal muscular atrophy

Spinal muscular atrophy (SMA) is one of the most common fatal autosomal recessive disorders, characterised by progressive degeneration of anterior horn cells. Before the advent of genetic testing, the diagnosis of SMA was based on clinical, histopathological, and electrophysiological features. In 1992, the International SMA Consortium defined diagnostic criteria of proximal SMA based on clinical findings.1 In SMA type I (severe; Werdnig-Hoffmann disease), affected persons have onset of symptoms before 6 months of age and are never able to sit without support. Electromyography demonstrates denervation features. In early 1995, the candidate gene, the survival motor neuron (SMN) gene, was identified, making the confirmation of SMA by DNA analysis possible.

With the availability of a genetic test for SMA, many investigators are refining the diagnostic criteria published by the Consortium. Studies involving hundreds of patients worldwide have disclosed a subset of patients who fulfil at least one exclusion criterion defined by the Consortium.2 We identified an infant with severe SMA who fulfilled two exclusion criteria and also showed abnormalities of nerves as well as muscles. This report will further delineate the wide range of phenotypes for this particular gene mutation.

A 2945 g male infant was born at term. First fetal movements were noted at 13 weeks of gestation. Chorionic villus sampling at 10 weeks of gestation disclosed normal chromosomal decreases. Decreased fetal movement and polyhydramnios were noted at about 34 weeks of gestation. At delivery, the infant was cyanotic with no respiratory effort and was subsequently intubated. On physical examination, the infant had no spontaneous movements. He opened his eyes with brief fixation but no following. Tongue fasciculations were present. Other cranial nerves seemed intact. Mild flexion contractures of both elbows, knees, and ankles were noted. Tone was flaccid in the upper extremities and lower limbs, and there was no movement response to painful stimuli. Deep tendon reflexes were absent.

Brain MRI disclosed mild diffuse cortical atrophy. His EMG was severely abnormal, with widespread fibrillations and absent voluntary motor units except in the genioglossus, where mildly neurogenic motor units with decreased recruitment were seen. Stimulation of the median, ulnar, peroneal nerves with a maximal stimulus resulted in no clinical or electrical response. The biceps brachii and rectus femoris muscles were electrically inexcitable by direct needle stimulation. Median, ulnar, and sural sensory potentials were not obtainable. DNA testing showed a homozygous deletion of exons 7 and 8 of the telomeric SMN gene, all three siblings showed a large deletion in the region that includes all alleles of the multiplex markers Ag1-CA and C212, localised at the 5’ end of the two SMN gene copies. It has been postulated that the severity of disease may be correlated to the extent of a deletion involving the SMN gene and the multicyclop markers.3,4 The infant in our report with SMA type I showed electrical inexcitability of motor nerves as well as the characteristic alteration of the SMN gene.

Although it has been shown for some time from histological studies that sensory systems are involved in SMA, electrophysiological sensory findings have been previously reported only once.5 Sensory nerve conduction velocity was tested in an infant with severe SMA and showed no recordable potential, but the infant in our report also exhibited universal absence of sensory potentials. In both cases, DNA analysis disclosed the 5q deletion. It is unclear whether this finding represents a distinct entity or merely the severe end of classic Werdnig-Hoffmann disease. The diagnostic criteria produced by the International SMA Consortium currently lists “absence of recordable sensory action potentials” as an exclusion criterion.1 Our finding of absent sensory potentials in a 5q deletion established case of SMA indicates further need for revision of the Consortium criteria. Studies involving large numbers of patients with SMA have identified cases of SMA variants.6 These patients were diagnosed as infantile SMA by the presence of proximal weakness and atrophy, hypotonia, and evidence of neurogenic alterations in EMG and muscle biopsy. In addition, these patients also exhibited one of the exclusion criteria defined by the Consortium—for example, diaphragmatic weakness, involvement of the CNS, or arthrogryposis. Although these patients did not show the typical SMA deletion and were therefore probably not linked to chromosome 5q, they could have had point mutations. The infant in our report showed no respiratory effort after birth, indicating diaphragmatic weakness. He did, however, possess the characteristic SMN gene alterations. This finding suggests that diaphragmatic weakness should be reclassified as an exclusion criterion by the Consortium.

Review of the literature disclosed no previous reports of electrically inexcitable muscles in SMA. This phenomenon is known to occur in a few other neuromuscular conditions such as periodic paralysis and critical illness polyneuropathy. Fibrillations, as seen in the subacute stage by measurement of acetylcholine receptor antibodies and candidate cDNAs.


Acute overdosage and intoxication with carbidopa/levodopa can be detected in the subacute stage by measurement of 3-0-methyldopa

Although the effects of a chronic overdose with levodopa are well known, few cases of acute intoxication have been described.1,2 A particular problem in establishing a diagnosis of levodopa overdosage is the observation of only half life in the circulation of levodopa.3 If there is a delay in bringing an acutely intoxicated patient to hospital, perhaps due to late discovery, the blood concentration of levodopa could already be normal (responsible to the peak levodopa concentration in Parkinson’s disease therapy) after 6–8 hours. Depending on the extent of the overdosage, the time could be even shorter. This report describes the clinical effects and the plasma concentrations of levodopa and specific metabolites over a period of 132.5 hours after ingestion of 30 tablets of carbidopa/levodopa (50 mg/200 mg tablets).

A 76 year old patient had a pre-existing mild akinetic rigid Parkinson’s syndrome, which had been treated for the past 1.5 years with 3x1 tablets of carbidopa/levodopa (50 mg/200 mg) a day without a substantial response. The weight of the patient was 74 kg. A known chronic obstructive airway disease was treated with a home oxygen appliance. At about 8.30 pm, the patient had attempted suicide by taking 3x1 tablets of carbidopa/levodopa. At about 10.00 hours the patient appeared psychically altered, crying without reason, anxious, and depressed. After about 30 minutes he was increasingly inadequate, withdrawn, and subeuphoric, and was experiencing visual hallucinations; he was restless, tossing and turning, and getting out of bed. He did not represent peak dose dyskinesia or other extrapyramidal clinical features. At 10.00 pm he showed bilaterally maximally dilated pupils. The muscle stretch reflexes were lively, there were no pyramidal tract signs, and he did not show any signs of Parkinson’s syndrome or dyskinesia. Arterial hypotension and sinus tachycardia could be registered.

After an empty box of Striaton (carbidopa/levodopa, 50 mg/200 mg) was found in the patient’s flat, 1 g of carbon was given by stomach tube after gastric lavage. The patient was carried out before the diagnosis of intoxication had been made; it showed a pronounced subcortical arteriosclerotic encephalopathy with reduced brain volume. The patient was moved to the medical intensive care unit and observed for 24 hours. The ECG showed a P pulmonale, but no other unusual features. Echocardiography showed normal right and left ventricular function with suspicion of right ventricular hypertro-
Movement disorder is a prominent feature of Huntington's disease and consists of involuntary and voluntary components as well as associated bradykinesia. Pharmacological treatment is problematic because of the side effects of the drugs used, which may further compromise cognitive functioning and mobility. Patients are often not subjectively aware of their movements but may be considerably disabled by them and carers are often distressed and enquire about treatment options. If drug treatment is considered it is important to achieve the maximum improvement in movements with the minimum of negative side effects. This paper describes the effect of olanzapine on movements when other treatment options had been ineffective or limited by side effects.

Huntington's disease is a hereditary progressive neurodegenerative disorder. It consists of a triad of symptoms comprising motor, psychological, and cognitive abnormalities. The motor component consists of involuntary choreiform movements and involuntary oculomotor abnormalities. The motor, psychological, and cognitive abnormalities of Huntington's disease treated with these drugs. The atypical antipsychotic clozapine is a new antipsychotic drug. It is a thienobenzodiazepine structurally very similar to clozapine. Unlike clozapine it is not associated with the potentially serious side effect of agranulocytosis and therefore frequent blood monitoring is not necessary.

This report describes the progress of a man who has Huntington's disease. He developed a marked movement disorder and was unable to tolerate both sulpiride and risperidone but had symptomatic improvement when treated with olanzapine. He is a man in his early 50s who had a confirmationary genetic test for Huntington's disease in 1994, after the development of clinically obvious motor symptoms. It is likely that the onset of symptoms had occurred a few years previously as he had experienced difficulties in concentration and memory, which he never before had. The patient described the onset of symptoms a few years previously as he had experienced difficulties in concentration and memory, which he never before had. The patient described the onset of symptoms and was unable to tolerate both sulpiride and risperidone but had symptomatic improvement when treated with olanzapine.

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This was started at a dose of 1 mg twice daily, increasing to a dose of 1 mg four times a day over a period of 2 weeks, stopped after a brief period. He developed hypotension (blood pressure 100/60 mm Hg), complaining of dizziness after the initial dose. His blood pressure remained stable, although low, after this and as there was improvement in his movements the drug was continued. However, he decided to stop the risperidone after 4 months because of his subjective experience of slowed thinking and occasional dizziness. A repeated trial of sulpiride was carried out in March 1997. Sulpiride was started at a dose of 200 mg twice a day and increased to a total daily dose of 1000 mg over 2 weeks. He was on sulpiride for 4 weeks with no improvement in his movements; so it was discontinued. The patient continued to experience low mood and after the discontinuation of sulpiride, his antidepresant drug was changed to lofepramine commencing at 70 mg once a day and increasing after a few days to 140 mg daily. There were no changes noted in his movements during this change.

Although the patient was subjectively unaware of the extent of his movements his everyday life continued to be problematic. A trial of olanzapine was then performed in May 1997. Olanzapine was started at a dose of 10 mg at night and 20 mg at morning; 06/97: before olanzapine, 140 mg lofepramine daily; 06/97: 5 mg olanzapine at night, 140 mg lofepramine daily.

In the absence of a cure for Huntington’s disease, it is very important that any interventions considered enhance the quality of life of the patient and improve overall functioning. It may not always be in the best interests of the patient to use drug treatments for the movement disorder. In those patients who have severe movements, however, a trial of treatment may be appropriate and continued if a clear benefit has been achieved. Neurological monitoring and the patient’s own perception of the effect of the drug must be taken into account.

The mechanism by which olanzapine may have beneficial effects is unclear. Olanzapine has been shown to have high affinity for a large number of receptors including D1, D2, D4, 5HT2A, 5HT2C, 5 HT3, o1-adrenergic, histamine H1, and 5 muscarinic receptors. This binding profile is similar to clozapine, another atypical antipsychotic drug, but substantially different from the conventional antipsychotic haloperidol. Preferential loss of D2 projection neurons which are involved in a feedback loop normally active in the suppression of involuntary movements is thought to be the pathological basis of chorea in patients with Huntington’s disease. The D2 antagonist properties of olanzapine may explain its possible benefits in the improvement of chorea. However, the effect at other receptors such as D4 may also be important, as D4 receptor density has been shown to be raised in Huntington’s disease, therefore the D4/D2 ratio of activity may also be relevant. Differences in binding profile across a range of receptors may explain clinical differences in outcome when comparing different antipsychotic drugs. This case report indicates that olanzapine may be a useful addition to the treatments for movement disorder, for some patients, and controlled trials of its use in Huntington’s disease would be welcome.

### Patient characteristics

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age at surgery</th>
<th>Sex</th>
<th>Years with PD</th>
<th>H and Y*</th>
<th>UPDRS off+</th>
<th>PD and levodopa</th>
<th>Pallidotomy side</th>
<th>Transient side effects</th>
<th>Medication additional to levodopa</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>66</td>
<td>M</td>
<td>8</td>
<td>2/5</td>
<td>57/NP</td>
<td>R</td>
<td></td>
<td>Slight facial paresis, swallowing problems, drooling</td>
<td>Trypsin, temazepam, alprazolam, apomorphine</td>
</tr>
<tr>
<td>2</td>
<td>43</td>
<td>F</td>
<td>7</td>
<td>2/2.5</td>
<td>25/7</td>
<td>L</td>
<td></td>
<td>Slight dysarthria</td>
<td>Trihexifenyl</td>
</tr>
<tr>
<td>3</td>
<td>45</td>
<td>M</td>
<td>15</td>
<td>2/3</td>
<td>55/15</td>
<td>L</td>
<td></td>
<td>Facial paresis</td>
<td>Perigolide, amantadine</td>
</tr>
<tr>
<td>4</td>
<td>50</td>
<td>M</td>
<td>12</td>
<td>2/2.2</td>
<td>45/22</td>
<td>L</td>
<td></td>
<td>Slight dysarthria</td>
<td>Selegiline, biperiden</td>
</tr>
<tr>
<td>5</td>
<td>53</td>
<td>M</td>
<td>14</td>
<td>2.5/4</td>
<td>69/36</td>
<td>R</td>
<td></td>
<td>Facial paresis, hypophonia</td>
<td>Pergolide, selegeline</td>
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<tr>
<td>6</td>
<td>58</td>
<td>M</td>
<td>13</td>
<td>2.5/3</td>
<td>40/27</td>
<td>L</td>
<td></td>
<td>Facial paresis, aphaenia</td>
<td>Selegiline, biperiden</td>
</tr>
<tr>
<td>7</td>
<td>61</td>
<td>F</td>
<td>15</td>
<td>2.5/4</td>
<td>55/NP</td>
<td>L</td>
<td></td>
<td></td>
<td>Clozapine, temazepam, cisapride</td>
</tr>
</tbody>
</table>

*H and Y=Hoehn and Yahr; †UPDRS off=unified Parkinson’s disease rating scale part 3 (motor examination), in a standardised off state, 12 hours without antiparkinson medication; N=not performed.


### Transient hiccups after posteroventral pallidotomy for Parkinson’s disease

Hiccup is defined as an abrupt intermittent, involuntary, contraction of the diaphragmatic and external (inspiratory) intercostal muscles, with inhibition of expiratory intercostal activity. This results in a sudden inspiration, abruptly opposed by closure of the glottis. Hiccup may result from various structural or functional disorders of the medulla, the afferent or efferent nerves to the respiratory muscles, and the gastrointestinal tract. Newson Davis performed a study of hiccup with electrophysiological techniques and concluded that hiccup is served by a supraspinal mechanism distinct from that generating rhythmic breathing. The principal site of interaction of the hiccup discharge with other descending drives to the respiratory motoneuron is at the spinal level. Neurogenic hiccup is particularly associated with structural lesions of the medulla oblongata.

Since 1994 we have performed 66 pallidotomies for Parkinson’s disease in 60 patients. So far, we have seen transient hiccups in seven patients after the operation (table). Our target coordinates for the posteroventral globus pallidus at the border of the medial and lateral segments are 2–3 mm anterior to the midcommissural point, 5 mm below the intercommissural line and 22 mm lateral to the midline of the third ventricle. Ventriculography was performed for target coordinates developed for Huntington’s disease.
localisation. Patients started with a short schedule of corticosteroids (5 days) the night before surgery.

The hiccups started immediately after the operation or the next day, were intermittent, and the bouts of hiccup of six patients, with a duration of hours, resolved within 3 days after the procedure. One patient complained of yawning more often and frequent bouts of hiccup for 6 months.

Five patients were men. All patients were right handed. The mean age at surgery was 54 years and the mean duration of Parkinson’s disease was 12 years. All patients were taking levodopa. In four patients the hiccups appeared after a left sided pallidotomy; Patient 2 had a right sided thalamotomy 4 years before the pallidotomy. Patient 5 underwent a left sided pallidotomy 10 months before the right sided pallidotomy which caused the hiccups. The pallidotomies improved parkinsonism in the “off” state (table), contralateral dyskinesias, and pain accompanying Parkinson’s disease. Six patients had transient adverse events: four patients had a transient facial paresis postoperatively and two a slight transient dysarthria.

Three patients had transient adverse events: four patients had a transient facial paresis postoperatively and two a slight transient dysarthria (table). Two patients had choricac move- ments after the pallidotomy at the contralateral side which resolved spontaneously within 2 hours and is associated with a favourable surgical outcome.3

Postoperative MR scans were obtained in the first six patients, and showed that in five patients the lesions were located in the posterior part of the globus pallidus pars externa (GPe) and interna (figure). In patient 5 the lesion was situated slightly more anterior in the GPe and putamen. In patient 3 there was a small separate lesion more dorsal, probably an infarct.

We never encountered hiccups in 150 other stereotactic procedures for Parkinson’s disease, such as thalamotomies or deep brain stimulation electrode implantation in the thalamus and therefore it is unlikely that medication or positive contrast medium ven- triculography with Iohexol evoked the hic- cups. A possible cause for the transient hiccups could be the lesion in the ventral medial segment of the globus pallidus or pressure, due to oedema, on an adjacent structure like the internal capsule or putamen. We could not find other reports of hiccups as an adverse event after functional stereotactic surgical interventions, nor after lesions of other aetiology involving the striatum.3 Based on our experience we hypothesise that the globus pallidus or a neighbouring structure may be involved in a supramedullary system involved in triggering hiccups.

Letters, Correspondence, Book reviews, Correction

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5 Bathia KP, Marsden CD. The behavioral and motor consequences of focal lesions of the basal ganglia in man. Brain 1994;117:859–76.

Psychological adjustment and self reported coping in stroke survivors with and without emotionalism

Emotionalism after stroke is common, occurring in 10%–20% of a community sample.1 Psychological factors in its cause or mainte- nance have not been studied; research has tended to concentrate instead on location of the stroke lesion. We suspect that one reason for this neglect of psychological aspects of

Five months after left sided pallidotomy, MRI of patient 6: (A) transversal slice at the level of the anterior commissure and (B) 6 mm more ventral.

emotionalism is that most people do not make a distinction between emotionalism, and pathological crying and laughing. As a result all disorders of emotionality after stroke are stereotyped as being related to brain damage and therefore psychologically meaningless.

None the less, many patients with emotionalism describe their crying as provoked by emotionally congruent experiences, which makes the tearfulness seem understandable.1 In two previous studies1 4 we have shown that stroke patients with emotionalism have more symptoms of psychological disorder than do patients without emotionalism. In the present study, we explored further the psychological characteristics of stroke patients with emotionalism. Our aim was to determine whether they differed from patients without emotionalism in their psychological reactions to stroke, or in the coping strategies they reported.

Post-traumatic stress disorder is also char- acterised by recurrent episodes of intrusive and uncontrollable emotion, and we were therefore interested in whether patients with emotionalism also experienced intrusive and uncontrollable thoughts typical of post-traumatic stress disorder. Because emotionalism is often described as uncontrollable, we were inter- ested in the possibility that patients were more generally helpless, powerlessness, or uncontrollability in their responses to stroke. Again, because of the reported uncontrollability of emotionalism, we postulated that patients with emotionalism would report a more external locus of control than those without emotionalism.

Participants were adults admitted to local general hospitals after stroke, and were inter- viewed within 1 month of admission. Exclusion- es were due to poor physical health, cogni- tive impairment, communication difficulties, or lack of consent. Approval for the study was obtained from the local research ethics com- mittees.

All participants completed a standardised measure of distress—the general health ques- tionnaire, GHQ-12;1 a widely used measure of intrusive thoughts of the sort encountered in post-traumatic stress disorder—the impact of events rating scale;3 a measure of cognitive coping—the mental adjustment to stroke scale (O’Rourke S, Dennis M, MacHale S, Slattery J. The development of the mental adjustment to stroke scale: reliability, patient outcome and associations with mood and social activity, manuscript in preparation); and a measure of beliefs about responsibility for recovery from illness—the recovery locus of control scale.3 All the measures are self report questionnaires.

A total of 177 stroke patients were screened, of whom 112 were excluded. The 65 participants (29 men, 36 women) had a mean age of 71.8 years (range 43 to 88 years). Nineteen (29.2%) patients met our criterion for emotionalism,4 a rate similar to that found in other studies. Their scores on the study measures are compared with the scores of patients without emotionalism in the table. It might be that these associations with emotionalism were accounted for by the greater general levels of distress experienced by those with emotionalism. We therefore undertook analysis of covariance with GHQ-12 and presence of emotionalism as the co- variates, and each of the other test items in turn as the independent variable. The results showed an association, after adjustment for GHQ-12 score, between emotionalism and the impact of events subscales intrusion
Comparison of stroke survivors with and without emotionalism, assessed in hospital 1 month after stroke

<table>
<thead>
<tr>
<th>GHQ-12*</th>
<th>Cognitive impairment subscale</th>
<th>Impact of events scale intrusion subscale**</th>
<th>Impact of events scale avoidance subscale*</th>
<th>MASS Fighting subscale</th>
<th>MASS Anxious preoccupation subscale**</th>
<th>MASS Fatalism subscale*</th>
<th>MASS Avoidance subscale</th>
<th>MASS Helplessness/hopelessness subscale**</th>
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</thead>
<tbody>
<tr>
<td>(F=15.33, p=0.001)</td>
<td>3.2 (2.4)</td>
<td>3.5 (3.3)</td>
<td>3.9 (4.6)</td>
<td>4.7 (4.6)</td>
<td>4.91 (4.6)</td>
<td>22.2 (2.8)</td>
<td>20.0 (1.9)</td>
<td>1.7 (0.8)</td>
</tr>
<tr>
<td>(Mean (SD))</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
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<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
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</table>

**p=0.05, *p<0.01, t tests.

MASS = Mental adjustment to stroke scale.

We thank those patients who participated in the study and the staff of local hospitals and the Leeds Stroke Database for their invaluable help. We also thank Dr Louise Dye for her statistical advice.

Paraneoplastic stiff limb syndrome

Stiff man syndrome (SMS) is a rare, severe progressive motor disorder characterised by painful spasms, symmetric axillary muscle rigidity, and uncontrollable contractions leading to distorted posturing. The disorder has been associated with the autoantigens, glutamic acid decarboxylase (GAD), and amphiphysin, which are cytoplasmic proteins in neurons of the CNS. A large series of patients with SMS found that most have autoantibodies against GAD, whereas amphiphysin is presumably the predominant autoantigen in paraneoplastic SMS. Recently, Borron et al presented four patients with a stiff leg syndrome marked by progressive rigidity and spasms of the lower extremities. This group of patients tested negative for anti-GAD antibody by immunoprecipitation and demonstrated distinct electrophysiologic features. By contrast, another report described two patients with stiff leg syndrome who tested positive for anti-GAD antibody. Finally, in presenting a group of 13 patients, Barker et al proposed that the nomenclature "stiff limb syndrome" refers to the focal form of SMS when one or more distal limbs are involved; two of their patients were also anti-GAD antibody positive, but none were tested for antibodies to amphiphysin or identified as having an underlying neoplasm. We present a patient clinically consistent with the stiff limb syndrome who was found to have autoantibody to GAD and breast cancer.

A 68 year old woman presented with a 1 month history of painful spasms in her legs. Cramps were associated with tactile stimuli and emotional upset. Within weeks, inversion began at the left and then right ankle, making ambulation difficult. Her medical history was significant for Graves’ disease treated with thionamides and radioactive iodine therapy, and hyperlipidaemia. She was a chronic smoker. General examination was noteworthy for lymphadenopathy in the right axilla. Her mental status was worse during periods of lower extremity spasms, during which she became anxious, diaphoretic, and tachycardic. Cranial nerve and motor evaluations were unremarkable, but assessment of the left leg, due to painful spasms elicited by light touch, was difficult. Inversion and plantar flexion were essentially fixed at the left ankle but could be overcome on the right. Deep tendon reflexes were 3+ in the upper and lower extremities, with sustained clonus at the right ankle. Sensory examination showed the exception of hyperaesthesia in the distal lower extremities, and coordination testing were grossly normal. No hyperlordosis or myoclonus was noted. Gait was limited due to ankle posturing.

The laboratory evaluation was noteworthy for a CSF with increased IgG indices (2.5, 3.4; normal, 0.2–0.8) and oligoclonal bands (5, 5) but no pleocytosis. Serological testing for anti-Hu, anti-Yo, and anti-Ri antibodies was unremarkable, and the haemoglobin A1C was 6.6 (5.6–7.7%). Skin biopsy at three sites on the patient’s leg showed diminished epidermal nerve fibre density and terminal axonal swelling distally, consistent with a small fibre sensory neuropathy. The patient would not tolerate EMG. Magnetic resonance images of the brain and the entire spinal cord were normal. Fine needle aspiration of a soft tissue right axillary mass showed no evidence of metastatic adenocarcinoma. On an open surgical procedure, infiltrating duct carcinoma of the breast was identified. Anti-GAD antibodies were not detected by chemical assay and immunoprecipitation, but antibodies to amphiphysin were not detected by immunocytochemistry, immunoprecipitation, or western blotting (Dr P De Camilli, Yale University).

Ongoing therapy with clonazepam and a trial of oral dexamethasone did not improve the lower extremity symptoms. The patient’s ankle posturing continued a slow progression to marked inversion, with spontaneous extension of hallucis longus. The patient died 18 months after symptom onset. Gross necropsy attributed the cause of death to aspiration pneumonia. Neuropathological examination showed a grossly normal cord and spino-cord. Microscopically, the lumbar cord had mild reactive gliosis in the anterior horns but no evidence of inflammation. Sections of the frontal cortex, pons, and medulla showed mild diffuse reactive astrogliosis.

Stiff man syndrome is increasingly recognised as a heterogeneous disorder. Other case reports have documented patients with “focal” disease involving either lower, upper extremity posturing, which contrast...
with the “diffuse” axial and subsequent proximal muscle distribution of the classic disorder.’ Our patient differs from those reported with stiff leg syndrome in that an occult malignancy was present. Unfortunately, we were unable to obtain electrophysiological studies for comparison. The search for a paraneoplastic process was based on the findings of axillary lymphadenopathy and an abnormal CSF. Our patient is only the second reported patient with paraneoplastic SMS associated with anti-GAD antibody; the other reported patient with paraneoplastic SMS had abnormal CSF. Our patient is only the second reported patient with paraneoplastic SMS. Occasionally, multiple levels, as in the syndrome of sensory neuronopathy-encephalomyelitis. Our patient’s findings were not entirely consistent with criteria for classic SMS in that an apparent encephalopathy and a small fibre neuropathy were identified—for example, her dysautonomia (tachycardia and relative hypertension) during spasms may have been a manifestation of involvement of small fibres. The role of autoantibodies in the pathogenesis of SMS and cancer is unclear. Via its probable function in endocytosis, amphiphysin has been postulated to play a part in the regulation of growth factor internalisation; however, the absence of an autoimmune response to this autoantigen in our patient suggests that other mechanisms of oncogenesis in SMS exist. Given anecdotal evidence of improvement in paraneoplastic SMS after treating the underlying malignancy, we suggest that all patients with SMS, diffuse or focal, be screened for occult cancer.

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Changes in the symptoms of poisoning in relation to each course of haemodialysis. Scales in the vertical axis represent the arbitrary measurements of severity of each symptom; the numbers indicating day(s) after onset; ^ = haemodialysis).
Tetrodotoxin (TTX) was demonstrated by thin layer chromatography, high performance liquid chromatography, and cellulose acetate membrane electrophoresis. Toxicity was assayed by using Institute of Cancer Research strain adult male mice and the toxicity score was 25 mouse units (MU)/g in fish muscle (1 MU/g in the CR strain mice). Tetrodotoxin exerts its effect through binding with and blocking the voltage dependent sodium channel. The voltage clamp experiments showed that tetrodotoxin diminishes the sodium inward current responsible for the depolarization of excitable membrane. The gating properties of the sodium channel, such as the activation and inactivation mechanism, are not altered—that is, the sodium channel is not permanently damaged and its function recovers when the bound toxin is released. In uraemia, ion conductance through the sodium channel is also impaired. Sodium permeability through excitable membranes is reduced and small inward sodium current and reduced action potential amplitudes are noted in experimental uraemic neuropathy. By contrast with the effects of tetrodotoxin, uraemia changes the basic property of the sodium channel by an increased inactivation and an impaired activation mechanism. The excitability of peripheral nerves will be more significantly depressed when these two conditions coexist. The synergistic effect of uraemia and tetrodotoxin is obvious in this incident in which the patient and her husband ingested roughly an equal amount of tetrodotoxin (about 200 µg, calculated from toxic score times the weight of ingested fish). The amount is about 10% of the estimated lethal dose in humans—2200 µg/60 kg body weight (body weights of the patient and her husband were 54.5 and 62 kg respectively)—and caused no clinical evidence of poisoning in the healthy person. It was of interest that the CNS was relatively spared from the toxicity as the EEG showed a posterior dominant, promptly reactive alpha rhythm and the patient retained consciousness when the symptoms were at their most severe.

One of the most striking clinical features in our patient was the response to haemodialysis. Despite the small amount of toxin ingested, the dramatic improvement of her clinical condition was most likely attributed to the rapid elimination of absorbed toxin in the course of haemodialysis, rather than spontaneous recovery. The physical and chemical properties of tetrodotoxin are also supportive to this hypothesis. It has a low molecular weight (C, H, N, O), is water soluble, and not significantly bound to protein—all these features are often found in toxins amenable to haemodialysis. Traditionally, the management of tetrodotoxin intoxication is mainly supportive, such as gastric lavage to remove unabsorbed toxin and machine assisted ventilation when respiration is severely affected. We suggest that haemodialysis may be an effective method in the treatment of tetrodotoxin intoxication.

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Relation between critical illness polyneuropathy and axonal Guillain-Barré syndrome

The clinical entity critical illness polyneuropathy occurs almost exclusively in patients in critical care units and has been characterised as a complication of sepsis and multiple organ failure. Critical illness polyneuropathy may be a common cause of the difficulty in weaning patients from the ventilator, particularly those who show intractable ventilator dependence. All the measures used to prevent ventilator dependence and eliminate multiple organ failure are the main steps needed now to deal with critical illness polyneuropathy. Knowledge of this type of polyneuropathy is of help in making decisions about respiratory technique, nursing care, prognosis, and overall management. Moreover, recognition of critical illness polyneuropathy indicates the need for physiotherapy, rehabilitation, and other supportive measures as the patient recovers. Bolton et al have made an important positive contribution to the care of patients with critical illness polyneuropathy. The actual aetiology, however, has yet to be determined. The pathogenesis needs to be clarified to treat patients more effectively.

Critical illness polyneuropathy invariably occurs at the peak of critical illness and sepsis, but in Guillain-Barré syndrome there is a brief period of recovery after a relatively minor illness or inoculation. Except for differences in the predisposing causes, as Bolton et al reported, it is difficult to distinguish critical illness polyneuropathy from Guillain-Barré syndrome on purely clinical grounds. In both, polyneuropathy runs a monophasic course, the onset being relatively acute but with subsequent improvement in most instances. The clinical features also are similar; evidence of muscle weakness in all four limbs, occasional involvement of facial muscles and frequent involvement of the muscles of respiration, the depression or absence of deep tendon reflexes, and some evidence of distal sensory loss.

The first step by Bolton et al in determining exact aetiology was to differentiate critical illness polyneuropathy from Guillain-Barré syndrome. In reviewing the patients with critical illness polyneuropathy and Guillain-Barré syndrome who were studied in their EMG laboratory, they found marked differences between the two types of polyneuropathies. Patients with Guillain-Barré syndrome had greater slowing of the speed of impulse conduction, and, in the initial stages, abnormal spontaneous activity in the muscle was absent, indicative of a predominantly demyelinating polyneuropathy. The CSF was only mildly increased in patients with critical illness polyneuropathy, but it was much increased in patients with Guillain-Barré syndrome. Comprehensive studies done at necropsy and nerve biopsy of patients with critical illness polyneuropathy showed the presence of primary axonal degeneration of the motor and sensory fibres, mainly distally, with no evidence of inflammation. Zochodne et al (excluding Bolton) therefore concluded that the two types of polyneuropathies most probably are separate entities.

Guillain and colleagues enumerated the clinical and spinal fluid features of presumed acute flaccid paralysis without regard for the underlying physiology or pathology. Classic pathological studies of Guillain-Barré syndrome, however, have identified prominent demyelination and inflammatory infiltrates in the spinal roots and nerves. Guillain-Barré syndrome often has been considered to be synonymous with the pathological designation of acute inflammatory demyelinating polyneuropathy, and the physiological abnormalities consistent with demyelination have been taken as supportive evidence for the diagnosis of Guillain-Barré syndrome. Feasby et al have drawn attention to patients who were clinically considered as having Guillain-Barré syndrome, but who were characterised electrophysiologically as having early axonal degeneration of the motor and sensory nerve fibres. The evidence included a rapid fall in compound muscle action potentials and sensory nerve action potentials, and no evidence of demyelination. Such patients often had severe paralysis and made a slow recovery, presumably reflecting the need to regenerate axons rather than remyelination. Pathological findings are consistent with axonal degeneration without demyelination. Feasby et al termed this pattern axonal Guillain-Barré syndrome and suggested that there is a fundamental difference in the underlying pathophysiology, resulting in primary axonal damage rather than demyelination. Griffin et al then confirmed the existence of the acute motor-sensory axonal neuropathy (AMSAN) pattern of Guillain-Barré syndrome described by Feasby et al.

Infection caused by the gram negative bacterium Campylobacter jejuni, a leading cause of gastroenteritis, is a well-recognised cause of Guillain-Barré syndrome.
of acute diarrhoea, commonly precedes the development of Guillain–Barré syndrome. There is a close association between axonal Guillain–Barré syndrome and antecedent C jejuni infection. The antecedent infectious symptom was diarrhoea in three of five previously reported axonal Guillain–Barré syndrome described by Feasby et al. Observations by Griffin et al confirmed that C jejuni infection was the antecedent of Guillain–Barré syndrome. The antecedent infectious symptom was diarrhoea in three of five previously reported axonal Guillain–Barré syndrome.

Recently, a new technology known as repetitive transcranial magnetic stimulation (RTMS) has been developed. In 1994, the use of magnetic stimulation in clinical psychiatry was suggested. Since then, it has been used in the study or treatment of obsessive-compulsive disorder, conversion disorder, schizophrenia, and particularly, depression.

Our pilot study aimed to assess the possible adverse effects of this treatment in chronic schizophrenic patients with severe negative symptoms; to evaluate if direct RTMS of the prefrontal cortex might improve negative symptoms or cognitive impairments in patients with chronic schizophrenia; and thirdly, to note if RTMS might modify the deficit in prefrontal cortical activity, often reported to underlie the UKU side effects established in schizophrenia, specially under conditions of task activation.

Six right-handed patients with chronic schizophrenia were identified at the outpatient psychiatric service of the Hospital Clinic of Barcelona. There were two men and four women (mean age 39).

Exclusion criteria included alcohol or substance abuse, psychosis, any kind of mental retardation, severe extrapyramidal symptoms, or any brain abnormality on imaging study. All patients were taking neuroleptic drugs, but no other psychotropic medications were continued at the beginning of the treatment. During the RTMS, psychotropic medications were continued at the initial dosage.

All patients were admitted to hospital. Inpatients underwent the UKU side effects scale, the positive and negative syndrome scale (PANSS), and a neuropsychological battery, the day before beginning the treatment and at the end of the treatment. The UKU scale was also administered after each session.

An equivalent neuropsychological battery was used on both occasions, which consisted of the block design test of the Wechsler intelligence scale, the trail making tests A and B, the FAS verbal fluency test, and two subtests of the Wechsler memory scale (the visual memory reproduction and the verbal paired associates subtests).

A brain SPECT study was performed, using a rotating dual head gamma camera, fitted with high resolution fanbeam collimators. Two """"TT-HMPAO SPECT scans with cognitive activation, such as the Wisconsin card sorting test (WCST), were performed on each patient (24 hours before the beginning of the treatment and 24 hours after the last session).

RTMS was given with a Mag Pro magnetic stimulator, 5 days a week, during 2 weeks, at the initial dosage. All patients were studied on both occasions, which consisted of the Wisconsin card sorting test (WCST), the Trail making test A and B, the FAS verbal fluency test, and two subtests of the Wechsler memory scale (the visual memory reproduction and the verbal paired associates subtests). Two patients who initially did not perform any categories on WCST, after the RTMS, showed hypofrontality on the initial neuroimaging. The results after RTMS indicated no changes in the hypofrontality.

Negative symptoms showed a general decrease for all patients (table). Significance (p<0.02) was noted on the PANSS negative symptoms subscale. These patients seemed to be more sociable than when originally seen. Nevertheless, clinical effects of the RTMS were subtle and difficult to distinguish from those derived from the supportive environment of the psychiatric ward.

With regard to the neuropsychological battery, we found a general improvement in all post-treatment scores (table), but only delayed visual memory achieved significance (p<0.05). This feature might be basically explained by improvement of attention, specifically of the maintenance of attention, which allows the correct function of the working memory. To avoid these methodological limitations regarding the power of our conclusions, it is certain that there has been an improvement in the attentional capability.

We found that all patients (except one, who was always within the normal range) diminished their number of perseverative answers and errors on WCST (items characteristically altered in schizophrenia) after the RTMS. However, significance was not achieved on any WCST scores.

Two patients who initially did not perform any categories on WCST, after the treatment, achieved one category, a possible indication of improvement of the abstract thinking. This change leads us to consider a research strategy previously reported, in which the WCST is used as a screening test for selecting schizophrenic patients. These patients achieving low category scores would be compared to higher category scorers in an effort to identify a subgroup most likely to benefit from RTMS.

Taking into account these mild improvements together, and the lack of changes in

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<th>Test</th>
<th>Mean (SD)</th>
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<tr>
<td>Block design</td>
<td>Pre 49 (11.9) NS</td>
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<td>Trail making test A</td>
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<td>Delayed visual reproduction</td>
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Pre=preatreatment; Post=post-treatment; PANSS=positive and negative scale; PG=general psychopathology scale; NG=negative scale; P=positive scale.
hypofrontality after treatment, we are consid-
ering extending the treatment course to 20
sessions, each at 30 Hz for 1 second, at 90% of
motor threshold. It was also suggested that
other positions of the coil and other kinds of
coils might give better results.

The clinical change in our cohort after the
RTMS could be attributed to both the treat-
ment and the supportive environment of the
psychiatric ward, and even to enhance
compliance to medication during hospital
admission. We are aware that the small sam-
ple size and lack of controls compel a very
careful interpretation of the results.

Nevertheless, in the light of these, we suggest
further controlled studies of the efficacy of
RTMS in negative symptoms of schizophrenia,
not only as an add on technique but also
as a sole therapeutic procedure. Research on
RTMS also requires some controlled studies
aimed to the complexity of the methodology
dosage, duration, and localisation), as this
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of motor threshold. It was also suggested that
coils might give better results.

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3 Spence SA. Free will in the light of neuropsy-
4 Crow TJ. Schizophrenia as a transcortical
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The authors reply:
We appreciate Persaud’s comments regarding the
alien hand syndrome, “the perceived
malevolence of the affected limb towards its
victim, and the question of whether with loss of
the conscious sense of voluntary control over
our bodies, our minds... consider the possibility
that if ourselves are not in control then someone
or something else must be.” We would offer that
the value of our particular case is that it was
due to a central deafferentation—therefore
the term “sensory alien hand syndrome”. As

Sensory alien hand syndrome

The case report by Ay et al of alien hand syn-
drome and review of the literature neglected
the intriguing issue of why in every case so far
reported the patient seems to be terrified of
the alien limb. Not believing that you are any
more in control of a limb is not likely to be a
pleasant experience.

Those with alien hand syndrome seem to
jump to extremely negative conclusions con-
cerning the intent of the limb. Typically, as in
the report of Ay et al, the common belief is
that the limb has deeply malevolent inten-
tions towards the victim.

It is this aspect of alien hand syndrome that
I suggest also needs incorporating into its
neurological explanations, and which pro-
vides a clue as to why our everyday
experience of being in charge of our bodies,
and so initiating all personal action, itself has
a neurological basis. In other words, while the
brain is the source of all our conscious and
experiences, there is also a part of our nervous
system which is responsible for our belief that
we have free will over our behaviour. Patients
with alien hand syndrome think that they are
no longer in control of a limb because the
part of the brain that gives us the sensation
of control over our bodies has been damaged.

When that happens, our limbs seem to act
independently of us.

Research conducted in the 1980s has
found that the same electrical brain wave
changes that characteristically precede all
limb movements, occur several 100 ms before
we seem to consciously decide to move a limb. If our conscious decision to act is
preceded by brain changes that anticipate
action, then our “decision” to choose how
to behave or “freedom”, as in free will, is in fact
illusory. Our choices have in a sense been
decided beforehand by our brains.

Spence1 asserts that evidence such as this,
combined with phenomena such as alien
hand syndrome, means that philosophers
have to reconsider whether we have free will.
He argues that these data suggest that our
sense of agency is illusory and it follows that
most of us share in common the useful delu-
sion that we have free will. Patients with alien
hand syndrome have lost this experience in
relation to a particular limb. There is a sense
then that those who experience the syndrome
are closer to the reality of how much we are
responsible for our actions than the rest of us.
This is because consciousness and the function
of the part of the brain that normally works to
make us think that we have conscious freedom of will. They develop the experience,
therefore, of becoming mere remote specta-
tors to the actions of the alien limb.

Defenders of human “free will” argue what
happens before the brain itself decides to act
is still unknown, and there may be a role for
our autonomous body. But even these free
will guards concede the neurological
research indicates that whatever happens before
the brain is roused, must occur before our
conscious awareness.

Yet in alien hand syndrome the patient thinks
that the hand has hostile motivations; it is
invariably the case that the patient not
only thinks that the limb is “not self” but
finds that the limb behaves towards the self in
a destructive and aggressive manner. This
could be explained by the apparent deaffer-
entation—therefore, of becoming mere remote specta-
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that if ourselves are not in control then someone
or something else must be.” We would offer that
the value of our particular case is that it was
due to a central deafferentation—therefore
the term “sensory alien hand syndrome”. As
opposed to the idea that “we know our limbs belong to us because they obey us”, we know that our limbs belong to us because they provide us with sensory input that is recognised as self. Many patients with movement disorders or psychoses lose control of their limbs but still have no difficulty in realising them as self. Indeed even in “phantom limb” there is sense of self due to central processes in the absence of a limb. Our patient, as do others with peg-syndrome and primary abnormalities of central sensory systems, shows perhaps that it is central sensory processes that are the key to identifying “self”. We know our limbs not because they obey us but because they have a pattern of sensory excitation that accompanies our own limb movements. When this pattern never reaches specific cortical regions, then the limb is not perceived as self; called “amorphogenesis” by Denny-Brown and Banker. Selective deafferentation by the centrally deafferented limb in “sensory” or “posterior” alien hand syndrome, or kinaesthetic stimuli due to movement of the limb as in the “anterior” or “forearm-attached” syndrome, is perceived as due to another person or thing without critical questioning. This raises the most interesting question of what brain region is deafferented in the anterior alien hand syndrome whose processing is intact. It is not our clinical experience nor the conclusions based on published reports that all patients suffering with alien hand syndrome are deafferented by the affected limb. In one author’s experience (BHP), two patients with alien hand syndrome and related intermanual conflict were irritated by but not terrified by their opposing limbs simultaneously. Conversely, a patient reported by Heilman’s group with persistent alien hand syndrome referred to it as “my little sister”. Similar to our experience, they suggest that a pre-existing personality type may be necessary given that most patients with collosal infarcts or tumours do not emphasise this complaint.

Unlike our case of limited duration, the persistence of alien hand syndrome depends on mesial frontal dysfunctional. These patients rarely deny that the affected limb belongs to them. Instead, they understand it in terms of their “anarchic hand”. Hence, although the initial syndrome may result in disjoined and terrifying perceptions, it seems that the brain quickly re-establishes its control by presently unknown adaptive capacities. Furthermore, why it almost exclusively involves the left body side in right handed people remains unknown. Studying this syndrome in greater detail may yield additional insights into the pathophysiology of denial and misidentification.

Vasomotor reactivity is exhausted in transient ischaemic attacks with limb shaking

The article of Baumgartner and Baumgartner entitled “Vasomotor reactivity is exhausted in transient ischaemic attacks with limb shaking” provides interesting new information regarding the nature of involuntary limb movements contralateral to haemodynamic failure from severe carotid artery occlusive disease. The authors evoke an “exhausted cerebral vasoreactivity in the hemispheres opposite the involuntary limb movements”. In their report, involuntary movements affected only the limbs, and displayed no tonic contraction, tonic-clonic jerking, or Jacksonian march and no epileptic activity during attacks. These findings led the authors to strongly argue against seizures as the cause of limb shaking in these transient ischaemic events.

In contradistinction, a 72 year old right handed man admittted to our hospital with a 3 month history of episodic weakness and numbness of the right arm. The patient then had six discrete stereotypic episodes of right arm weakness and clumsiness that were also associated with right side speech arrest. In speaking. Several episodes of dysarthria, numbness and weakness of the right arm and leg (MRC grade 4/5) were seen, unrelated to posture, some of which occurred when the patient was supine. Muscle weakness was characterised by slight tremulousness and asterixis-like movements of the outstretched right arm. There was a return to baseline functioning between events. Video/EEG monitoring, however, showed low voltage spikes in the left central-parietal head regions contralateral to the facial twitching and the right arm and right leg weakness. Although ongoing clinical and EEG seizure activity stopped after 2 mg intravenous lorazepam, they reoccurred after loading with phenytoin. Because angiography disclosed a greater than 95% stenosis of the left internal carotid artery (while the patient was treated with phenytoin at a concentration of 16.5 mg/l), the patient was anticoagulated with heparin, but episodes continued. It was only after a left carotid endarterectomy that all episodes resolved, tremulousness, and EEG epileptiform activity stopped. They have not recurred over the past 5 years.

The literature includes several cases of focal motor inhibitory seizures causing weakness. Although it is impossible to prove a negative, it could be argued that although no epileptiform or other evidence of seizure activity is present in a particular case, the abolition of ongoing clinical and EEG evidence of inhibitory motor activity by intravenous diazepam argues in favour, at least in part, of an ictal contribution. The fact that in virtually all reported cases, abnormal movements are more definitively resolved by carotid endarterectomy, argues for an underlying ischaemic aetiology that induces focal seizures. There are few reports that clearly delineate the interaction and association of inhibitory focal motor seizures and transient ischaemic attacks, as there are few sequential trials of antiepileptic drugs or anticoagulation (under EEG monitoring) and finally carotid endarterectomy. Several authors support the concept of an inhibition of motor function in parietal and secondary somatosensory regions by seizure activity which then interrupts the sensory feedback loop to motor integration with inhibition of subcortical and cortical areas.

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BOOK REVIEWS


To the MRCP candidate neurology is one of the more daunting specialties. The unfamiliar nerve conduction study and the frankly mysterious EEG can distress an otherwise well rounded junior house officer. Despite the fact that much of neurology is commonly seen on a general medical ward—strokes, dementias and so forth—the general perception is of an unimaginable list of eponymous syndromes and obscure signs. Rather than dwell on the last, in this book Dr Smith tries to address the commoner complaints as examination style questions each with a "simple clinical les-


This book, after a short introduction to some of the fundamental features of the disease goes on to provide some 117 illustrations of aspects of the disease from Cruveihier's plates to histopathological specimens and also a heavy leaning to imaging particularly magnetic resonance imaging, as might be expected. There is no doubting the aesthetic impact of this short book. In addition, the fact that these illustrations emanate from a well established figure in the multiple sclerosis world and are likely to be a representative set of personal teaching slides from a successful academic career all vouch for the provenance and informative nature of the atlas. However the place of such a book within a neurologist's library has to be questioned. There are a plethora of high quality textbooks devoted to all aspects of multiple sclerosis all well illus-


Transcranial colour duplex sonography is an ultrasound technique which is becoming increasingly available for the non-invasive imaging of intracranial structures, particularly the basal cerebral arteries. There are now four principal components to the technique: B mode ultrasound which can be used to image the brain parenchyma; colour coded Doppler which provides a colour image of the basal vessels; spectral analysis of pulsed wave Doppler which is used to derive blood flow velocities; and latterly "power" Doppler which is also providing information following analysis of the amplitude rather than the frequency of the reflected ultrasound beam. In addition, echocontrast agents are now available which can increase the signal to noise ratio and thus help to ameliorate some of the detrimental acoustic effects of the skull.

Acoustic imaging etc will certainly provide a more detailed current knowledge on pathogenesis is followed by a good account of some of the more common techniques used to treat single suture synostosis. Understandably, in a book of this type there is space only for an overview of the treatment and complications of multi-


This is volume 47 of a series entitled Neurological Disease and Therapy, series editor W C Koller. This volume is edited by an American surgeon and two British neuro-

All articles are from Southampton. The book begins with a pathophysiological
introduction setting the scene for the five main disease sections covering developmental/genetic disease, spinal cord injury, tumour, and the effect of neurological and systemic disease on the spinal cord. This chapter covers a wide area from multiple sclerosis to motor neuron disease to vascular disease to metabolic diseases. Then follows a section on investigation considering imaging, neurophysiology, and urodynamics. Finally, there is a miscellaneous section covering clinically important entities such as pain, sexual problems, and terminal care associated with spinal cord disease but also including a highly specialised chapter on the role of spinal cord injury in pregnancy.

This is an ambitious attempt at being comprehensive. The editors themselves worry that the emphasis favours surgical conditions. Although this might be the case, many surgeons to the neurologist or rheumatologist, care for spinal disease often falling between several specialties. Therefore, it is of benefit to the clinician to have all aspects of spinal disease in one volume. The standard and style of the individual chapters varies, that on motor neuron disease being up to date and topical, malignancies being covered in depth. That on sexual problems associated with spinal cord disease is excellent for the practical and a must for both doctors dealing with spinal disease and for patients themselves who are often uninformed (our fault, not theirs). The chapter on depression will be food for thought for many doctors who enjoy recreational diving, for although studies have not yet shown adverse affects on the quality of life in those who dive frequently but without incident, the evidence for cumulative neurological damage from neurophysiological, imaging, and pathological studies is compelling.

The quality of illustration is high. Perhaps unsurprisingly, this is particularly evident in the imaging section (where there is a rather spectacular sagittal T2 weighted MRI of a intramedullary arteriovenous malformation). In addition to imaging many of the chapters also make good use of schematic diagrams and line drawings to enhance the text.

Drs Engler, Cole, and Merton end their preface by commenting that “Our main hope, however, is that the chapters will read as a series of views on the spinal cord and its disease, so that a surgeon may learn about what is outside the field of surgery”. While I agree that educating surgeons is an admirable aim, I think that the authors rather undersell themselves and that this book’s main strength, as I have said above, is that it will appeal to all disciplines that deal with spinal cord disease, bringing together neurological, rheumatological, and surgical disease that is often covered in separate textbooks.

GILLIAN HALL


This is the second time that I have been asked to review a book on this topic. The first time I approached the task with some scepticism—were neurological diseases in women really so different from those in men that they warranted their own text book? But I rapidly became a convert to the cause, being reminded that there are issues specific to females that influence both disease, investigation, and treatment (pregnancy, breast feeding, menopause, to name the most obvious) and that not all neurological diseases attack the sexes equally. There are also wider socioeconomic and legal issues that play a part in the complete disease picture which many of us neglect too often but which this book is careful to address (see below). Leaving content aside for a moment, this is a beautifully presented book; clearly headed and with wide use of well constructed tables. It encourages one to read on. It seems up to date and well referenced.

The contributors (40 in total) are exclusively American, and east coast American at that with only occasional forays westward. The text is divided into three sections. The first, entitled General Issues in Women includes an anatomical chapter considering the sex differences of regional brain structure and function. More novel for this type of text, it contains two thoughtful chapters considering women’s health within the context of lifestyles and women’s health and its relation with the law. This chapter considers issues such as coercive approaches to preventing foetal harm, those relating to informed consent to medical treatment, and difficult choices with neurological implications. The law and the case examples are exclusively American but the issues are universal. This opening section leaves no doubt that this is a book that has taken female issues extremely seriously.

The second section looks at neurological diseases as they affect females at different life stages, from birth through menarche, pregnancy, and menopause, to the elderly woman. As well as considering genetic diseases that strike at a particular age, these chapters consider the influence of changing physiology and hormonal balance on neurological disease. The third section is the most conventional. Each chapter considers a neurological disease representing these diseases with emphasis on their effect on women and there is, by necessity, some overlap between this and the previous section. As a non-American, I would feel more comfortable to believe that the high number of female patients with peripheral nerve injuries secondary to physical beatings, knife wounds, or gunshot wounds reflected the country of origin of this book!

If pushed to criticise, the indexing could be more complete and certain conditions considered in more detail, in particular, paraplastic conditions associated with breast and gynaecological malignancies. However, that aside, I think this a rather special book and not only a good addition to any neurological library but a useful purchase for anyone interested in female medical issues.

GILLIAN HALL

CORRECTION


During the editorial process the descriptions of the histograms in figure 4 (p 614) were wrongly ascribed. The corrected figure is reproduced below.