Cerebral metabolism during vegetative state and after recovery to consciousness

One way to approach the study of consciousness is to explore lesions 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 wakeness 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. Somesthetic 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 sequela consisted of a bilateral spastic paresis of upper and lower limbs. Neurological examination one 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 pronounced 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 glucose costes (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 ± 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 postcentral and precentral 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.

**LETTERS TO THE EDITOR**

Cerebral metabolism during vegetative state and after recovery to consciousness

We present a patient who developed a vegetative state and persistent 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]fluoro-deoxyglucose (FDG) PET and statistical parametric mapping (SPM) we compared both patient’s sets to a normal control population. PET data were obtained 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 ± 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 postcentral and precentral 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.

**LETTERS TO THE EDITOR**

Cerebral metabolism during vegetative state and after recovery to consciousness

We present a patient who developed a vegetative state and persistent 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]fluoro-deoxyglucose (FDG) PET and statistical parametric mapping (SPM) we compared both patient’s sets to a normal control population. PET data were obtained 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 ± 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 postcentral and precentral 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.
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. 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 with SMA have disclosed a subset of patients who fulfil at least one exclusion criterion defined by the Consortium. We identified an infant with severe SMA who fulfilled two exclusion criteria and also showed instability of all 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 flexure contractures of both elbows, knees, and ankles were noted. Tone was flaccid in both arms and lower limbs, and there was no movement response to painful stimulus. 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 unit activity was seen. Sensory responses were absent. Nerve conduction studies (NCS) were not obtainable. Review of the literature disclosed no previous reports of electromyographically 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 infant in our report, are commonly seen in acute denervation and are thought to be caused by perturbation of the sarcocellular membrane, rendering it unstable. One possibility may be that the acute denervation in SMA type I can result in abnormal function of the membrane to make it electrically inexorable. Further electrophysiological studies at the cellular level are required to delineate this interesting finding.

A.LICE A. Kuo
Department of Pediatrics

STEFAN-M PULST
DAWN S ELIASHIV
CAMERON R ADAMS
Division of Neuropathology, Cedars-Sinai Medical Center, Los Angeles, CA, USA

Correspondence to: Dr Cameron R Adams, Department of Neuropathology, Cedars-Sinai Medical Center, 8631 West Third Street, Room 1145, East Tower, Los Angeles, CA 90048, USA.

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

Although the effects of a chronic overdose with levodopa are well known, few cases of acute intoxication have been described. A particular problem in establishing a diagnosis of levodopa overdose is the relatively short half life in the circulation of levodopa. 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 nonexpressing. The patient we report only once.

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 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 tablets) 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 30 tablets of carbidopa/levodopa. At about 9.00 pm, he appeared psychically altered, crying without reason, anxious, and depressed. After about 30 minutes he was increasingly inadequate, with closed eyes, 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 treatment was carried out before the diagnosis of intoxication had been made; it showed a pronounced subcortical arteriolesclerosis 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 can 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 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 increasing difficulties with voluntary movement. The degree of the involuntary movements is variable but in some patients can be very marked. Progression over time of the movement disorder in Huntington's disease can be monitored using the quantitative neurological examination (QNE). This measure has three subscales, an eye movement scale, a motor impairment scale (MIS) quantifying voluntary motor movements and a chorea scale measuring involuntary movement.

Pharmacological control of the symptoms has been shown to be effective with dopamine antagonists, but their use is limited because of the side effects. Clinically the most problematic of these are sedation, cognitive slowing, increased mobility problems, and hypotension. The inability of traditional dopamine antagonists to improve functional capacity, despite ameliorating motor disturbances, is likely due to suppression of voluntary motor activity.

Tardive dyskinesia has occasionally been reported in patients with Huntington's disease treated with these drugs. The atypical antipsychotic clozapine has been shown to be effective in improving the movement disorder. However, in a double blind randomised trial of clozapine which included patients who were already receiving traditional antipsychotic medication, a small group who had not received drug treatments for their movement disorder, chorea was reduced in those who were antipsychotic naive only and the authors concluded that clozapine was of little additional value in Huntington's disease. Olanzapine is a new atypical antipsychotic drug. It is a thienobenzodiazepine structurally very similar to clozapine. Unlike clozapine it is not associated with the potentially serious side effects 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 sulphiride and risperidone but had symptomatic improvement when treated with olanzapine.

He is a man in his early 50s who had a confirmatory 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. Work, attributed at the time to stress, leading to the loss of employment. In addition his family, watching family videos of a few years earlier, thought that there were some early signs of his movement disorder. However there was no known family history of Huntington's disease which might have led to an earlier diagnosis. By May 1995 his involuntary movements were becoming more noticeable, although control of voluntary movement was good. A trial of sulphiride commencing at 200 mg twice daily and increasing over 1 week to 800 mg daily was undertaken with a subsequent decrease in the frequency and extent of involuntary movement recorded in case notes; unfortunately the QNE was not repeated at this time. However, the patient experienced a subjective slowing of his cognitive processes, concurrently became depressed, and decided to stop the treatment within 3 weeks. Paroxetine, a selective serotonin reuptake inhibitor antidepressant, was started at a dose of 20 mg a day, which led to an improvement in his low mood. His involuntary movements continued to cause difficulties in his daily living. He was unable to sit comfortably in a chair and when out of door he felt that he was disengaged from the environment and was knocking into them. He agreed to a trial of
risperidone. This was started at a dose of 1mg twice daily, increasing to a dose of 1mg 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 antidepressant drug, but substantially different to the conventional antipsychotics haloperidol.1 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.1 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.

Quantitative neurological examination scores showing the progress of the movement disorder. 06/95: before trial sulpiride, no medication; 05/96: before risperidone, 20 mg paroxetine daily; 07/96: 1 mg risperidone four times daily and 20 mg paroxetine daily; 03/97: before retrial sulpiride, 20 mg paroxetine daily; 04/97: 400 mg sulpiride in the morning and 20 mg paroxetine; 04/97: before olanzapine, 140 mg lofepramine daily; 06/97: 5 mg olanzapine at night, 140 mg lofepramine daily.

Patient characteristics

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age at surgery</th>
<th>Sex</th>
<th>PD</th>
<th>H and Y*</th>
<th>UPDRS off#</th>
<th>Pallidotomy</th>
<th>Pallidotomy side</th>
<th>Transient side effects</th>
<th>Medication additional to levodopa</th>
</tr>
</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>L</td>
<td>Slitght facial paresis, swallowing problems, drooling</td>
<td>Tranylcypromine, remoxapine, alprazolam, apomorphine</td>
</tr>
<tr>
<td>2</td>
<td>43</td>
<td>F</td>
<td>7</td>
<td>2/2.5</td>
<td>22/NP†</td>
<td>L</td>
<td>L</td>
<td>Slitght dysarthria</td>
<td>Trihexyphenidyl</td>
</tr>
<tr>
<td>3</td>
<td>45</td>
<td>M</td>
<td>15</td>
<td>2/3</td>
<td>55/L</td>
<td>L</td>
<td>L</td>
<td>Facial paresis</td>
<td>Pergolide, amantadine</td>
</tr>
<tr>
<td>4</td>
<td>50</td>
<td>M</td>
<td>12</td>
<td>2/2</td>
<td>45/22</td>
<td>L</td>
<td>L</td>
<td>Slitght 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>L</td>
<td>R</td>
<td>Facial paresis, hypophonia</td>
<td>Pergolide, selegeline</td>
</tr>
<tr>
<td>6</td>
<td>58</td>
<td>M</td>
<td>13</td>
<td>2.5/3</td>
<td>48/27</td>
<td>L</td>
<td>L</td>
<td>Facial paresis, aphasis</td>
<td>Selegiline, biperiden</td>
</tr>
<tr>
<td>7</td>
<td>61</td>
<td>F</td>
<td>15</td>
<td>2.5</td>
<td>55/NP†</td>
<td>R</td>
<td>L</td>
<td></td>
<td>Clonazapate, temazepam, cipride</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; SNMP=not performed.


Transient hiccup 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 abnormally strong expiratory efforts.1 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.1,2 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.2 The principal site of interaction of the hiccup discharge with other descending drives to the respiratory motoneurons 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
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 dyskinesia, 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. The pallidotomies 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. 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.

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. Psychological factors in its cause or maintenance 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 emotionalism is that most people do not make a distinction between emotionalism, and pathological crying and laughing. As a result all disorders of emotionalism 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. In two previous studies 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 characterised by recurrent episodes of intrusive and uncontrollable emotion, and we were therefore interested in whether patients with emotionalism also experienced thoughts typical of post-traumatic stress disorder. Because emotionalism is often described as uncontrollable, we were interested in the possibility that patients were more generally helpless and more generally passive 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 interviewed within 1 month of admission. Exclusions were due to poor physical health, cognitive impairment, communication difficulties, or lack of consent. Approval for the study was obtained from the local research ethics committees.

All participants completed a standardised measure of distress—the general health questionnaire, GHQ-12; a widely used measure of intrusive thoughts of the sort encountered in post-traumatic stress disorder—the impact of events rating scale; 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. 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, 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 covariates, 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...

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.
**Comparison of stroke survivors with and without emotionalism, assessed in hospital 1 month after stroke**

<table>
<thead>
<tr>
<th></th>
<th>No emotionalism (n=45)</th>
<th>Emotionalism (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GHQ-12*</td>
<td>3.2 (2.4)</td>
<td>5.3 (3.5)</td>
</tr>
<tr>
<td>Recovery locus of control scale**</td>
<td>33.2 (5.3)</td>
<td>34.1 (5.7)</td>
</tr>
<tr>
<td>Impact of events scale intrusiveness subscale**</td>
<td>2.9 (4.6)</td>
<td>9.2 (6.6)</td>
</tr>
<tr>
<td>Impact of events scale avoidance subscale*</td>
<td>4.7 (4.6)</td>
<td>9.9 (6.1)</td>
</tr>
<tr>
<td>MASS Fighting spirit subscale</td>
<td>49.1 (4.0)</td>
<td>48.6 (2.2)</td>
</tr>
<tr>
<td>MASS Helplessness/hopelessness subscale**</td>
<td>22.2 (2.8)</td>
<td>25.2 (4.0)</td>
</tr>
<tr>
<td>MASS Anxious preoccupation subscale*</td>
<td>20.0 (1.9)</td>
<td>21.3 (2.2)</td>
</tr>
<tr>
<td>MASS Avoidance subscale</td>
<td>1.7 (0.8)</td>
<td>1.9 (0.8)</td>
</tr>
<tr>
<td>MASS = Mental adjustment to stroke scale. **F = 15.33, p = 0.001, and avoidance (F = 11.84, p = 0.003); the mental adjustment to stroke scale subscales helplessness/hopelessness (F = 11.7 1, p = 0.00 1) and anxious preoccupation (F = 8.05, p = 0.006). The associations with fatalism (F = 14.79, p = 0.052) and avoidance (F = 0.06, p = 0.80) on the mental adjustment to stroke scale were no longer significant after adjustment for GHQ-12 score.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

This study confirms earlier work by showing that stroke survivors with emotionalism have more harmful mood symptoms (here rated by the GHQ-12) than do those without emotionalism. It goes further however, in showing that they also have more intrusive thoughts about their lives—thoughts similar to those reported by people with post-traumatic stress disorder. This unpleasant remembering is probably responsible for their higher ratings on anxiety and preoccupation. It is compatible with our finding in a previous study that irritability is associated with emotionalism, as irritability is a common response to threatening intrusive memories of the sort encountered in post-traumatic stress disorder. It may not be that emotionalism is a direct manifestation of post-traumatic stress disorder, although that condition has been described after stroke,\(^2\), but the analogy raises the possibility that an abnormality in processing emotionally distressing stimuli is an important cause of emotionalism. If correct it suggests possible treatment strategies along the lines of those used in post-traumatic stress disorder.

A corollary is our finding of increased feelings of helplessness and hopelessness, coupled with avoidance—at least as a cognitive coping strategy reported on one of our measures. Avoiding coping may perpetuate the symptom of emotionalism, by preventing habitation to the social stimuli which provoke it. Alternatively it may lead to a reduction in social support, exacerbating coexistent mood disturbance. Thus, it may be that avoidance coping is not an integral part of emotionalism, but rather that it is an important maintaining factor.

We predicted that patients with emotionalism would have more “external” scores on the locus of control measure, reflecting their sense of lack of personal control over crying. They did not, perhaps because the emotional expression, although not apparently controlled by external resources, is none the less perceived as having psychological meaning, so that responsibility for it cannot readily be devolved to others.

Our study used a relatively weak between-groups design, the number of patients was not large, and we cannot be sure that all co-founders were dealt with. None the less, our results suggest that future research into emotionalism could profitably concentrate not just on seeking its biological correlates, but should also explore the psychological factors which might contribute to its cause or continuation.

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 Dyer for her statistical advice. This study was completed as part of work for the degree of DClinPsych at Leeds University (SE).

STEVEN ECCLES
ALLAN HOUSE
Division of Psychiatry and Behavioural Sciences in Relation to Medicine, University of Leeds, Leeds, UK.

PETER KNAPP
Stroke Outcome Study, Research School of Medicine, Leeds, UK.

Correspondence to: Dr Allan House, Division of Psychiatry and Behavioral Sciences in Relation to Medicine, University of Leeds, 15 Hyde Terrace, Leeds LS2 9LT, UK.


**Paraneoplastic stiff limb syndrome**

Stiff man syndrome (SMS) is a rare, severe progressive motor disorder characterised by painful spasms, symmetric axial muscle rigidity, and uncontrollable contractions leading to distorted posturing. The disorder has been associated with the autoantigens, glutamic acid decarboxylase (GAD), and amphiophisyn, which are cytoplasmic proteins in neurons of the CNS. A large series of patients with SMS found that most have autoantibodies against GAD, whereas amphiophisyn is presumably the predominant autoantigen in paraneoplastic SMS.\(^5\) Recently, Bloodworth 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 electrophysiologica features. By contrast, another report described two patients with stiff leg syndrome who tested positive for anti-GAD antibody.\(^6\) Finally, in presenting a group of 13 patients, Barker et al.\(^7\) proposed that the nomenclature...
with the "diffuse" axial and subsequent proximal muscle distribution of the classic disorder.1 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 upper limb rigidity in the setting of breast cancer and additionally mounted an immune response to amphiphysin.2 Paraneoplastic processes can affect any component of the nervous system and, occasionally, multiple levels, as in the syndrome of sensory neuronopathy-encephalomyelitis. Our patient's findings were not entirely consistent with criteria for classic SMS3 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.4 Via its probable function in endocytosis,2 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,4 we suggest that all patients with SMS, diffuse or focal, be screened for occult cancer.

ISAAC E SILVERMAN
Department of Neurology, Johns Hopkins University, Baltimore, USA

Correspondence to: Dr I E Silverman, Johns Hopkins Hospital, Pathology 509, 600 North Wolfe Street, Baltimore, MD 21287, USA. Telephone 001 410 955 6626; fax 001 410 614 1008; email isilver@jhmi.edu

1 Solimena M, Folli F, Aparisi R, et al. Autoanti-
2 Folli F, Solimena M, Cofelli R, et al. Autoanti-
6 McCarthy BG, Hsieh S-T, Stocks A, et al. Cuta-
8 Rosin L, De Camilli P, Butler M, et al. Stiff-man syndrome in a woman with breast cancer: an uncom-
mon central nervous system paraneo-
10 David C, McPherson PS, Mundigl O, et al. A role of amphiphysin in synaptic vesicle endocy-

Tetrodotoxin intoxication in a uraemic patient

Tetrodotoxin intoxication results from inges-
ting puffer fish or other animals containing the toxin. Clinical presentation is mainly acute motor weakness and respiratory paralysis. Death is common in the worst affected victims. Although the severity of the symp-
toms generally depends on the amount of toxin ingested, it may be influenced by the victim's medical condition, as described in this report. The patient was a 52 year old uraemic woman. The uraemia was of unde-
fined aetiology. Over the past 3 years she has received regular haemodialysis. One day both she and her husband, a healthy 55 year old man, ate a fish soup. About 3 hours after the meal she developed a headache and a lingual and circumoral tingling sensation and numb-
ness at the distal parts of all four limbs. She was dizzy and unsteady, had difficulty in swallowing, and became very weak. She was taken to the emergency service and was placed on machine assisted ventilation as res-
piratory distress and cyanosis developed. Her husband remained asymptomatic throughout the
treatment.

The patient's condition kept on deteriorat-
ning, developing eventually into a comatous-
like state with no spontaneous or reflexive eye opening or limb movement within 30 min-
utes of intubation. On neurological examina-
tion, the pupillary light reflex was absent and oculocephalic manoeuvre elicited no oculon-
motor movements. All four limbs were areflexic and Babinski's signs were absent. Brain CT and laboratory studies of arterial blood gas (under assisted ventilation), electrolytes, liver func-
tion, blood glucose, and CSF study were unremarkable. An examination of renal function indicated chronic renal insufficiency with mild azotaemia (urea nitrogen 70 mg/dl, cre-
tatine 9.1 mg/dl). An EEG, recorded 18 hours after the onset of symptoms when the neurological condition was unchanged, showed posterior dominant alpha waves intermixing with trains of short duration, dif-
fuse theta waves. When brief noxious stimuli were applied to the sternum, they were replaced transiently by beta activities. The findings suggested that the profound neuro-
logical dysfunction might be peripheral in origin. The patient was given a course of haemodialysis according to the set schedule for uraemia at 21 hours after onset of the symptoms. Her condition improved dramati-

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; 1= haemodialysis).
Critical illness polyneuropathy
Axonal Guillain-Barré syndrome

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 characterized as a complication of sepsis and multiple organ failure.1 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 dependency and multiple organ failure are the main methods now used to deal with critical illness polyneuropathy. Knowledge of this type of polyneuropathy is of help in making decisions about respiratory techniques, 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.2 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.2 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 impairment.

The first step by Bolton et al.2 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 polyneuropathy. 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 not 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 on 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.2 Zochodne et al.3 (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 one form of acute flaccid paralysis without regard for the underlying pathology or physiology. Clinical 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. The pathological abnormalities consistent with demyelination have been taken as supportive evidence for the diagnosis of Guillain-Barré syndrome. Feasby et al.4 (excluding Bolton) 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 apparently reflecting the need to regenerate axons rather than remyelination. Pathological findings are consistent with axonal degeneration without demyelination. Feasby et al.5 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.6 confirmed the existence of the acute motor-sensory axonal neuropathy (AMSAN) pattern of Guillain-Barré syndrome described by Feasby et al.5.

Infection caused by the gram-negative bacterium Campylobacter jejuni, a leading cause
of acute diarrhoea, commonly precedes the
development of Guillain-Barré syndrome. The
close association between axonal Guillain-Barré syndrome and
to: Dr Nobuhiro Yuki, Department of Neurology, Dokkyo University School of Medicine, Japan. Correspondence to: Dr Nobuhiro Yuki, Department of Neurology, Dokkyo University School of Medicine, Kitakobayashi 880, Mibu, Shimotsuga, Tochigi 321–0293, Japan.

Repetitive transcranial magnetic stimulation in the treatment of chronic negative schizophrenia: a pilot study

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 related to hyperactivity of the CBF in schizophrenia, typically under conditions of task activation.

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

Exclusion criteria included alcohol or substance abuse, first-degree family history of schizophrenia or bipolar disorder, or a history of a significant neurological illness, taking anticonvulsant medications, electroconvulsive therapy within 6 months, and significant abnormal findings on laboratory examination.

All patients were taking neuroleptic drugs, but a stable dose for at least 3 months was required. All patients were studied off benzodiazepines for at least 1 week before beginning the treatment. The RTMS, psychotropic medications were continued at the initial dosage.

All patients were admitted to hospital. Inpatients underwent the UCUK scale effect size, 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 UCUK scale was also administered after each session.

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

A brain SPECT study was performed by rotating a dual head gamma camera, fitted with high resolution fanbeam collimators. Two 99mTc-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 motor threshold, determined by an activator or vasodilator medications, electroencephalography, we found a general improvement in all RTMS patients (except one, who was always within the normal range) diminishing 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 working memory. This, along with other improvements and methodological limitations regarding the power of our conclusions, it is certain that there has been an improvement in the attentional capacity.

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.

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

Table Neuropsychological tests and PANSS scores

<table>
<thead>
<tr>
<th>Test</th>
<th>Mean (SD)</th>
<th>Block design</th>
<th>Trail making test</th>
<th>Immediate visual reproduction</th>
<th>Delayed visual reproduction</th>
<th>Immediate verbal paired associates</th>
<th>Delayed verbal paired associates</th>
<th>PANSS-P</th>
<th>PANSS-N</th>
<th>PANSS-PG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre</td>
<td>49 (11.95)</td>
<td>NS</td>
<td>38.8 (14.3)</td>
<td>50.5 (4.82)</td>
<td>54.8 (11.2)</td>
<td>53.8 (11.84)</td>
<td>54 (7.46)</td>
<td>59.5 (10.03)</td>
<td>8.8 (1.17)</td>
<td>37.67 (11.15)</td>
</tr>
<tr>
<td>Post</td>
<td>41 (10.03)</td>
<td>NS</td>
<td>38.5 (4.5)</td>
<td>41 (10.03)</td>
<td>46.18 (8.23)</td>
<td>47 (8.23)</td>
<td>54 (7.26)</td>
<td>16.83 (7.28)</td>
<td>31.67 (8.20)</td>
<td>37.67 (11.15)</td>
</tr>
<tr>
<td>PANSS-PG</td>
<td>3.0 (11.4)</td>
<td>p&lt;0.05</td>
<td>3.0 (11.4)</td>
<td>3.0 (11.4)</td>
<td>3.0 (11.4)</td>
<td>3.0 (11.4)</td>
<td>3.0 (11.4)</td>
<td>3.0 (11.4)</td>
<td>3.0 (11.4)</td>
<td>3.0 (11.4)</td>
</tr>
</tbody>
</table>


hypofrontality after treatment, we are considering 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 treatment and the supportive environment of the psychiatric ward, and even to enhance compliance to medication during hospital admission. We are aware that the small sample 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 form of intervention may prove to be an economical and convenient therapy in treating several psychiatric disorders.

E COHEN
M BERNARDO
J MASANA
F J A RRUFAT
V NAVARRO
Department of Psychiatry
J VALLS-SOLÉ
Department of Neurophysiology
T BOGET
N BARRANTES
S CATARINÉU
M FONT
Department of Psychology
F J LOMENA
Department of Nuclear Medicine, Institut d’Investigacions Biomèdiques August Pi Sunyer, Hospital Clinic i Provincial, Universitat de Barcelona, Spain

Correspondence to: Dr M Bernardo, Servicio de Psiquiatría, Hospital Clínic i Provincial, Villarroel 170, 08036 Barcelona, Spain. Telephone 00343 2275400, ext 2405; fax 00 343 2274747; email bernardo@medicina.ub.es


**CORRESPONDENCE**

Sensory alien hand syndrome

The case report by Ay et al. of alien hand syndrome 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 concerning the intent of the limb. Typically, as in the report of Ay et al., at some common belief is that the limb has deeply malevolent intentions towards the victim.

It is this aspect of alien hand syndrome that I suggest also needs incorporating into its neurological explanations, and which provides 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 conscious and experiential 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.

Research2 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.

Spence2 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 delusion 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 these brain changes in the part of the brain that normally functions to make us think that we have conscious freedom of will. They develop the experience, therefore, of becoming mere remote spectators to the actions of their bodies.

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 own autonomy there. But even these free will guardians concede the neurological research indicates that whatever happens before the brain is roused, must occur below 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 above hypothesis that if we lose our conscious sense of voluntary control over our bodies, our minds have to come up with an explanation for the location of our actions. We decide that if ourselves are not in control, then someone or something else must be; therefore, we no longer have a sense of the limb belonging to us.

Because to lose control over our bodies is one of the most terrifying experiences, our attempt to explain this finding occurs in the context of fear. It may be that our apprehension leads us to misinterpret innocent reflexive acts of our hands, such as scratching or rubbing, as malevolently inspired. Plus it could be that our interpretation of spurious possession in turn helps us to disassociate from the fact that only this is beyond our conscious awareness.

It may therefore be that we need to believe in our own free will and personal control over our actions, because if we did not, the experience of our bodies acting as if we merely came along for the ride, too frightening. Also, we may no longer believe that our bodies or its relevant parts belong to us. All neurologists who have reported alien hand syndrome remark on how psychologically disturbing the symptom is for the patient. Psychiatrists would be interested in the parallels between alien hand syndrome and the non-physical experiences. So the fact that every case, plus the fact that the two diseases may share corpus callosum pathology, could go some way to explaining why schizophrenic symptoms are frightening to the patient. So it seems we know that our limbs belong to us because they obey us. When they seem to stop responding to our wills, we conclude that our limbs are no longer our own, and try to fend them off. Hence it would seem that one of the prices we have had to pay for awareness of ourselves to evolve as a function of the brain, is the delusion that we are responsible for all our actions. If we had conscious awareness of ourselves, but no sense of free will, our bodies would feel alien to us.

The philosophical importance of alien hand syndrome is that it shows emphatically via neurology that it is possible to drive a wedge between consciousness and the experience of free will. The brain had to develop the sensation of free will after developing consciousness, because being without the sensation of free will produces extremely negative emotional experiences. So the fact that every case, so far reported of alien hand syndrome imputes negative intent to the alien limb might not be an incidental finding, but a core aspect of the disorder.

R PERSAUD
The Maudsley Hospital, Croydon Mental Health Services, Westways Rehabilitation Unit, 49 St James’s Road, West Croydon, Surrey CR9 2RR, UK. Telephone 0044 181 700 8512; fax 0044 181 700 8504; email rajendra@btinternet.com


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... decide 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 paralysis lose control of their limbs but still have no difficulty in recognising 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 anosognosia 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 there is a pattern of sensory innervation that accompanies our own limb movements. When this pattern never reaches specific cortical regions, then the limb is not perceived as self; called "amorposynthesis" by Denny-Brown and Banker. Selective deafferentation by the centrally deafferented limb in “sensory” or “motor” alien hand syndrome, or kinaesthetic stimuli due to movement of the limb as in the “anterior” or “mirror alien hand 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 wherein the patient is no longer able to move a limb that he or she believes another person is controlling.

It is not our clinical opinion nor the conclusions based on published reports that all patients suffering with alien hand syndrome are teriffied by the effected limb. In one author's experience (BHP), two patients with alien hand syndrome and related intermural conflict were irritated by but not teriffied by their opposing limbs simultaneously vying for a cigarette or book. In the other patient was amused but rather indifferent to his affected left side. The most terrifying situation we have heard is when the patient identified his affected left side as belonging to his mother. As 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 positively emotional state may be necessary given that most patients with colloidal infarts or tumours do not emaphisise this complaint.

Unlike our case of limited duration, the persistence of alien hand syndrome seems dependent on mesial frontal dysfunction. 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 disjointed 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.

HAKAN AY FERDINANDO S BUIANNONE DEAN A LEWALTER J KOROSHEITZ Department of Neurology, Stroke Service, Massachusetts General Hospital, Harvard Medical School, 32 Fruit Street, Boston MA 02114, USA

BRUCE H PRICE Department of Neurology, McLean Hospital, 115 Mill Street, Belmont MA 02178-9106, USA


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 perception that 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 male, admitted 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 associated with violent attacks in speaking. Several episodes of dysphasia, 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. Most observations were 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 min 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 disappeared, 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, argue 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 antiseizure 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.

PETER W KAPLAN John Hopkins Bayview Medical Center, 4940 Eastern Avenue, Baltimore, MD 21224, USA


Baumgartner and Baumgartner reply: We are grateful for the response of Kaplan to our short report. We agree that somatic inhibitory seizures may mimic transient ischaemic attacks (TIAs). Such TIAs are associated with negative symptoms such as sensorimotor deficits and difficulty with speaking, EEG evidence of seizure activity, and cessation of the TIAs after the administration of an anticonvulsant drug.1 Limb shaking TIAs, however, differ from TIAs related to inhibitory seizures in several ways. (1) They are associated with positive phenomena (limb shaking), and the involuntary movements do not affect the facial muscles. (2) Patients with attacks of shaking movements of the limbs have no EEG evidence of epileptic activity, and involuntary movements do not stop after administration of anticonvulsive therapy. (3) Although the patient presented by Kaplan had a 95% stenosis of the left internal carotid artery, it is unclear whether haemodynamic failure was present or not, because no studies evaluating the haemodynamic reserve of the homolateral hemisphere were presented. This is in accordance with the finding that the involuntary movements as well as the sensorimotor deficits of Kaplans’ patient were not related to posture. (4) The pathogenesis in these TIAs might be due to dis inhibition of subcortical control mechanisms as a result of ischaemia.

In our opinion, it is not clear whether the asterixis-like movements of the outstretched right arm of Kaplan’s patient are due to epileptic seizures, because unilateral asterixis of the outstretched arm has been reported with contralateral vascular lesions affecting almost all cerebral structures, and the pathogenesis in these TIAs might be due to dis inhibition of subcortical control mechanisms as a result of ischaemia. 

RALF W BAUMGARTNER Department of Neurology, University Hospital of Zurich, Switzerland

IRIS BAUMGARTNER Division of Angiology, University Hospital of Bern, Switzerland

Correspondence to: Dr Ralf W Baumgartner, Neurologische Klinik, Frauenklinikstrasse 26, CH-8091 Zurich, Switzerland. Telephone 044 416 21 00, fax 044 1 255 48 30; email StruB@neuro.uzh.ch


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 senior 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-

The “grey case” section, for instance, includes questions on multiple sclerosis, cluster headache, and HSV encephalitis, while broadening the topics to include postinfective demyelination, chronic hemi-

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 senior 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-

The “grey case” section, for instance, includes questions on multiple sclerosis, cluster headache, and HSV encephalitis, while broadening the topics to include postinfective demyelination, chronic hemi-


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 scanning 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-


This monograph is the latest to be produced by the American Association of Neurological Surgeons as part of their Neurosurgical Topics series. It begins by tracing the history of cal-

Craniosynostosis is a topic which is covered very well in standard paediatric neuro-


Transcranial colour duplex sonography is an ultrasonic 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 used to generate an image depicting flow without the subtraction of noise. The results of this approach form the basis of the discussion of the anatomy, pathology and clinical application. The book is well documented with 610 illustrations and 18 tables and provides a comprehensive overview of this developing technique.

This volume of 400 pages and liberal colour diagrams and prints is edited by three exponents of the technique. Thirty one chapters contain by chapters on areas which may be expected to be a popular choice for some pharmaceutical companies.

BOOK REVIEWS

NEIL ROBERTSON


This is a volume of 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-

PETER MARTIN

Letters, Correspondence, Book reviews, Correction

J Neurol Neurosurg Psychiatry, Volume 67, Number 1, 1 July 1999. Downloaded from http://jnnp.bmj.com/ on October 1, 2022 by guest. Protected by copyright.

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 Disease 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 their 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, paraneoplastic 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

The reader may be interested in the following:


CORRECTION

Hanna PA, Jankovic J, Vincent A. Comparison of mouse bioassay and immunoprecipitation assay for botulinum toxin antibodies. J Neurol Neurosurg Psychiatry 1999;66:612–16. During the editorial process the descriptions of the histograms in figure 4 (p 614) were wrongly ascribed. The corrected figure is reproduced below.

Figure 4 Correlation of clinical response (grade 0 or 1 response indicates non-responders, grade 2 response indicates reduced response, and grade 3 or 4 are responders) with response to test injections.

Hanna PA, Jankovic J, Vincent A. Comparison of mouse bioassay and immunoprecipitation assay for botulinum toxin antibodies. J Neurol Neurosurg Psychiatry 1999;66:612–16. During the editorial process the descriptions of the histograms in figure 4 (p 614) were wrongly ascribed. The corrected figure is reproduced below.

Figure 4 Correlation of clinical response (grade 0 or 1 response indicates non-responders, grade 2 response indicates reduced response, and grade 3 or 4 are responders) with response to test injections.