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 [F]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 paraparesis of upper and lower limbs. Neuropsychological testing 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 prominently 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 97).

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 ± 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.

STEVEN LAUREYS
CHRISTIAN LEMAIRE
PIERRE MAQUET
Cyclotron Research Centre, University of Liège, Sart Tilman, 4000 Liège, Belgium

CHRISTOPHE PHILLIPS
Institute of Cognitive Neurology, University College London, Alexandra House, 1 Queen Square, London WC1N 3AR, England, UK

GEORGE FRANCK
Department of Neurology, CHU Liège Sart, Tilman B-33, 4000 Liège, Belgium

Correspondence to: Dr Pierre Maquet, Cyclotron Research Centre (B30), University of Liège, Sart Tilman, 4000 Liège, Belgium Telephone 0032 43 66 36 87; fax 0032 43 66 29 46; email maquet@pet.crc.ac.be

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.2

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 fulfill at least one exclusion criterion defined by the Consortium.3 We identified an infant with severe SMA who fulfilled two exclusion criteria and also showed inexcitability 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 the thoracic 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 units with decreased recruitment were seen. Stimulation of the median, ulnar, tibial, 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 multi-copy 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 with the extent of a deletion involving the SMN gene and the multicopy markers.4 5 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 known for some time from histological studies that sensory systems are involved in SMA, electrophysiological sensory findings have been previously reported only once.6 Sensory nerve conduction velocity was tested in an series 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 sensory conduction potentials” as an exclusion criterion.7 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 series of patients with SMA have identified cases of SMA variants.8 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 reconsidered as an exclusion criterion by the Consortium.

A review of the literature disclosed no previous reports of electromechanical inexcitability of muscles in SMA. This phenomenon is known to occur in a few other neuromuscular conditions such as periodic paralysis and critical illness polynuropathy. 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 sarcolemmal 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 inexcitable. Further electrophysiological studies at the cellular level are required to delineate this interesting finding.

ALICE 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 3-3′-methyldopa

Although the effects of a chronic overdose with levodopa are well known, few cases of acute intoxication have been described.9 10 A particular problem in establishing a diagnosis of levodopa overdosage is to differentiate it from the usual half life in the circulation of levodopa.9 11 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 (and responsible for 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 3×1 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 30 tablets of carbidopa/levodopa. About 40 hours later he appeared psychically altered, crying without reason, anxious, and depressed. About 30 minutes he was increasingly inadequate, restless, and subeuphoric, and was experiencing visual hallucinations; he was restless, tossing and turning, and getting out of bed. He did not report peak dose dyskinesia or extra-pyramidal 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 admitted 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-
noradrenaline, which stimulates the sympathetic nervous system. Acute overdose of levodopa is caused by absent light reaction, at the time of the maximal bilateral mydriasis, with symptoms of hypotension, tachycardia to the raised concentrations of levodopa, and rise in blood pressure. Clinical manifestations are variable but in some patients can be quite dramatic. 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 movement, and a chorea scale measuring involuntary movement.

Distribution into muscles rather than metabolism may largely determine the plasma half life of levodopa and explain why this was only slightly altered with overdose. The measured peak concentration of 66 763 ng/ml is about 30 times higher than the peak concentration to be expected after taking one 400 mg tablet of carbidopa/levodopa (50 mg/200 mg). It is apparent that the 30 tablets did not interfere with absorption or lead to a gastrointestinal paralysis due to the high dose of levodopa; the relation between amount ingested and plasma concentration seems to be linear, at least in this dose range.

We conclude from these findings that in cases of suspected intoxication, by some hours previously, it could be important to measure the concentration of 3-o-methyldopa, so as not to overlook an overdosage with levodopa, which may be due to a suicide attempt. In addition to the diagnostic uncertainty in relation to the immediate treatment in movements with the minimum of distress and enquire about treatment options. The treatment is problematic because of the side effects, the potential 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 conformational 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 was designated by the peripheral conversion of levodopa into noradrenaline, which stimulates α-adrenergic receptors in the dilator iridi. There is no indication from animal experiments of a specific activation of dopamine receptors. The arterial hyper tension measured initially can also be attributed to the high systemic concentrations of noradrenaline, and the tachycardia to the raised concentrations of adrenaline and dopamine. As seen in the figure, the only indicator which can show a levodopa intoxication in the subacute stage is the concentration of 3-o-methyldopa. The metabolite 3-o-methyldopa results from the oxidative conversion of levodopa, which explains the delayed peak of the 3-o-methyldopa concentration. The half-life of 3-o-methyldopa in plasma was calculated at 16.7 hours in this patient. On the other hand, the plasma half life of levodopa was 111 minutes; this is slightly longer than normal, and can be explained by assuming a rate limited metabolism of levodopa when the substrate concentration for the enzymes metabolising it is raised.
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 mg 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 experience low mood and after the discontinuation of sulpiride, his antidepressant 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 a problem. He felt that activities he wanted to pursue or events he felt able to attend were becoming more limited and activities he wanted to pursue such as travelling abroad by air were problematic. A trial of olanzapine was then instituted. He was started on 5 mg a day in the morning and 5 mg at night and 2mg of clozapine; 04/97: before olanzapine, 140 mg lofepramine daily; 06/97: 5 mg clozapine at night, 140 mg lofepramine daily.

Hiccups is defined as an abrupt intermittent, involuntary contraction of the diaphragmatic and external (inspiratory) intercostal muscles, with inhibition of expiratory intercostal muscles. Hiccups may result from various structural or functional disorders of the medulla, the afferent or efferent nerves to the respiratory muscles, and the gastrointestinal tract. Hiccups 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 pallidectomies 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 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.

Patients had transient adverse events: four patients had a transient facial paresis postoperatively and two a slight transient dysarthria. 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.

Two patients had choreatic movements after the pallidotomy at the contralateral side which resolved spontaneously within 2 hours and is associated with a favourable surgical outcome.

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 ventriculography with Iohexol evoked the hiccups. 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 supramedulary system involved in triggering hiccups.

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.
MASS = Mental adjustment to stroke scale.

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. Avoidant 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 avoidant 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 their own resources, is none the less perceived as having psychological meaning, so that responsibility for it cannot readily be devolved to others.

Our study using a relatively weak between-groups design, the number of patients was not large, and we cannot be sure that all confounders 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 Dye 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 Behavioural 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 spasm, symmetric axial 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, Barker 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’s disease treated with thymectomy and radiation therapy, and hyperlipidaemia. She was a chronic smoker. General examination was noteworthy for lichenophasydomenopathy 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. Sensor examination revealed the exception of hyperesthesia 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 the right parotid gland revealed abundant metastatic adenocarcinoma. On an open surgical procedure, infiltrating duct carcinoma of the breast was identified. Anti-GAD antibodies were present in the patient’s serum 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 skipped inversion and brief presentation 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 spinal 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 astrocytosis.

Stiff man syndrome is increasingly recognised as a heterogeneous disorder. Other case reports have documented patients with "focal" disease involving either lower or 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 had upper limb rigidity in the setting of breast cancer and additionally mounted an immune response to amphiphysin. 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 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 onconeogenesis 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.

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 is Silverman@jhu.edu


Tetrodotoxin intoxication in a uraemic patient

Tetrodotoxin intoxication results from ingesting 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 symptoms 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 undefined 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 4 hours after the meal she developed a headache and a lingual and circumoral tingling sensation and numbness 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 respiratory distress and cyanosis developed. Her husband remained asymptomatic throughout this time.

The patient’s condition kept on deteriorating, developing eventually into a comatous-like state with no spontaneous or reflexive eye opening or limb movement within 30 minutes of intubation. On neurological examination, the pupillary light reflex was absent and oculocephalic manoeuvre elicited no ocular 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 function, blood glucose, and CSF study were unremarkable. An examination of renal function indicated chronic renal insufficiency with mild azotaemia (urea nitrogen 70 mg/dl, creatinine 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, diffuse theta waves. When brief noxious stimuli were applied to the sternum, they were replaced transiently by beta activities. The findings suggested that the profound neurological 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-
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 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 or treat sepsis 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 patients breathe with respirators and in the use of 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. 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 illne but or infection. 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 involvement.

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 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 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 critical illness polyneuropathy. Critical illness polyneuropathy has been considered as having axonal Guillain-Barré syndrome, but who were characterised electrophysiologically as having early axonal degeneration of the motor and sensory nerves. Guillain-Barré syndrome often has been considered to be synonymous with the pathological designation of acute inflammatory demyelinating polyneuropathy, and physiological abnormalities consistent with demyelination have been taken as supportive evidence for the diagnosis of Guillain-Barré syndrome. Feasby et al. (excluding Bolton) drew 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 nerves. 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, probably 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., caused by the gram negative bacteria Campylobacter jejuni, a leading cause
of acute diarrhoea, commonly precedes the development of Guillain-Barré syndrome. There is a close association between axonal Guillain-Barré syndrome and C jejuni infection. The antecedent infectious symptom was diarrhoea in three of five patients with anoxal Guillain-Barré syndrome described by Feasby et al. Observations by Griffin et al. confirmed that AMSAN follows C jejuni infection. Serum samples from patients with axonal Guillain-Barré syndrome subsequent to C jejuni enteritis often have anoxal class autoantibodies to gangliosides GM1, GM1b, GD1a, or GaINAc-GD1a in the acute phase of the illness, and there is molecular mimicry between these gangliosides and the lipopolysaccharides of C jejuni isolates from patients with Guillain-Barré syndrome. This ganglioside mimicry may trigger high production of the IgG anti-ganglioside antibodies, and these autoantibodies may cause motor nerve dysfunction in patients with GBS.

Interestingly, Hagensen et al. reported a case of “C jejuni bacteremia and subsequent Guillain-Barré syndrome” that occurred in a patient with chronic graft versus host disease and axonal Guillain-Barré syndrome. Because there was acute flaccid paralysis associated with sepsis, some physicians might have diagnosed critical illness polyneuropathy. Conversely, the existence of this case strongly suggests that some diagnostic of critical illness polyneuropathy should actually be axonal Guillain-Barré syndrome or AMSAN. Our hypothesis of the nosological relation between critical illness polyneuropathy and Guillain-Barré syndrome is shown in the figure. Serum IgG antibodies against GM1, GM1b, GD1a, or GaINAc-GD1a could be used as immunological markers for axonal Guillain-Barré syndrome. To examine the aetiology of critical illness polyneuropathy and its nosological relation to axonal Guillain-Barré syndrome, it is necessary to investigate whether patients with critical illness polyneuropathy have anti-ganglioside antibodies during the acute phase of the illness.

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 referred to as “hypofrontality”, specifically under conditions of task activation.

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

Exclusion criteria included alcohol or substance abuse disorder in the past 5 years, focal neurological signs, systemic neurological illness, taking cerebral metabolic activator or vasodilator medications, electroconvulsive therapy within the past 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. During the RTMS, psychotropic medications were continued at the initial dosage.

All patients were admitted to hospital. Inpatients underwent the UKU 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 UKU scale was also administered after each session.

An equivalent neuropsychological battery was used on both occasions, which consisted of the block design of the Wechsler adult 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 by rotating a dual head gamma camera, fitted with high resolution fanbeam collimators. Two Tc-99m-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 beginning of the treatment and 24 hours after the last session. The FAS verbal fluency test, and two subtests of the Wechsler memory scale, were used in the study or treatment of schizophrenia. The remainder of the patients 

*Table* Neuropsychological tests and PANSS scores

<table>
<thead>
<tr>
<th>Test mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Block design</td>
</tr>
<tr>
<td>Pre 49 (11.5)</td>
</tr>
<tr>
<td>Post 50 (8.69)</td>
</tr>
<tr>
<td>Trail making test A</td>
</tr>
<tr>
<td>Pre 38.6 (14.1)</td>
</tr>
<tr>
<td>Post 42.6 (14.1)</td>
</tr>
<tr>
<td>Trail making test B</td>
</tr>
<tr>
<td>Pre 38.3 (4.5)</td>
</tr>
<tr>
<td>Post 41 (10.03)</td>
</tr>
<tr>
<td>Immediate visual reproduction</td>
</tr>
<tr>
<td>Pre 50.5 (4.82)</td>
</tr>
<tr>
<td>Post 54.8 (11.2)</td>
</tr>
<tr>
<td>Delayed visual reproduction</td>
</tr>
<tr>
<td>Pre 46.18 (2.3)</td>
</tr>
<tr>
<td>Post 53.8 (11.8)</td>
</tr>
<tr>
<td>Immediate verbal paired associates</td>
</tr>
<tr>
<td>Pre 54 (7.46)</td>
</tr>
<tr>
<td>Post 59.5 (10.03)</td>
</tr>
<tr>
<td>Delayed verbal paired associates</td>
</tr>
<tr>
<td>Pre 8.8 (1.17)</td>
</tr>
<tr>
<td>Post 8.8 (1.17)</td>
</tr>
<tr>
<td>PANSS-PG</td>
</tr>
<tr>
<td>Pre 36.5 (11.47)</td>
</tr>
<tr>
<td>Post 31.67 (8.26)</td>
</tr>
<tr>
<td>PANSS-N</td>
</tr>
<tr>
<td>Pre 31.67 (8.26)</td>
</tr>
<tr>
<td>Post 27.83 (8.47)</td>
</tr>
<tr>
<td>PANSS-P</td>
</tr>
<tr>
<td>Pre 16.83 (7.28)</td>
</tr>
<tr>
<td>Post 15.33 (7.55)</td>
</tr>
</tbody>
</table>

All patients tolerated the RTMS well, with minimal side effects (mild headache and tinnitus).

Preliminary SPECT of one patient was reported to be normal, showing no evidence of hypofrontality. The remainder of the patients showed hypofrontality on the initial neuropsychological battery. 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 sociaizable than when originally seen. Nevertheless, clinical effects of 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 working memory. Taking into account the 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, 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 working memory. Taking into account the 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.

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 working memory. Taking into account the 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.

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 working memory. Taking into account the 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.

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 working memory. Taking into account the 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.

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 working memory. Taking into account the 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.

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 working memory. Taking into account the 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.

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 working memory. Taking into account the 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.

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 working memory. Taking into account the 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.

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 working memory. Taking into account the 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.
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 this small sam-
ple size and lack of controls compel a very
careful interpretation of the results. Neverthe-
less, in the light of these, we suggest furth-
er controlled studies of the efficacy of
RTMS in negative symptoms of schizophre-
nia, 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 ARRUFAT V NAVARRO
Department of Psychiatry
J VALLS-SOLÉ
Department of Neurophysiology
T BOGET N BARRANTES S CATARINEU M FONT
Department of Psychology
F J LOMENA
Department of Nuclear Medicine, Institute 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 2275477; email bernardo@medicina.uib.es

1 Barker AT, Jalous R, Freeston IL. Non-
invasive magnetic stimulation of the human
2 George MS, Wassermann EM. Rapid-rate tran-
scranial magnetic stimulation and ECT. Con-
3 Pascual-Leone A, Catala MD, Pascual-Leone
AP. Lateraled effect of RTMS on the prefron-
502.
4 Elliot R, Sahakin B. The neurophysiology of
schizophrenia: relations with clinical and neu-
robiological dimensions. Psychiatr Med 1995;28:
581–94.
5 Wolkin A, Sanfilipo M, Wolf AP, et al. Negative
symptoms and hypofrontality in chronic schizophre-
nia. Arch Gen Psychiatry 1992;49:
959–65.
6 Lingasoe O, Atifors UG, Bech P, et al. The
UKU side effects scale. Acta Psychiatr Scand
1987;76(suppl 334):1–100.

CORRESPONDENCE

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, in
the report of Ay et al at position 10, 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 seat of our conscious decisions and experi-
ences, there is also a part of our nervous sys-
tem 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.

Spence’ 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 the brain normally functions as
the part of the brain that normally works to
make us think that we have conscious free
will. They develop the experience, therefore,
becoming mere remote specta-
tors 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 assumption that
we lose our conscious sense of voluntary con-
trol over our bodies, our minds have to come
up with an explanation for the location of
action of our movements. 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 apprehen-
sion leads us to misinterpret innocent reflex-
exive acts of our hands, such as scratching
or rubbing, as malevolently inspired. Plus it
could be that our interpretation of spurious
possibilities in turn the phenomenon itself 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 believe in
the experience of our bodies acting as if we
merely came along for the ride, too frighten-
ing. 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 security phobia. So that in the end, plus the fact that the two diseases may share
corpus callosum pathology, 1 could some way to explaining why schizophrenic symp-
toms 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 had to pay for becoming aware of ourselves to evolve as a function
of the brain, is the delusion that we are
responsible for all our actions. If we had con-
scious 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 sen-
sation of free will after developing conscious-
ness, because being without the sensation of
free will produces extremely negative emo-
tional 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.

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

Letters, Correspondence, Book reviews, Correction

J Neurol Neurosurg Psychiatry: first published as 10.1136/jnnp.67.1.126 on 1 July 1999. Downloaded from http://jnnp.bmj.com/ on April 5, 2022 by guest. Protected by copyright.
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 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 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 “amorphosynthesis” by De Renzi and Battaglini.

letters, Correspondence, Book reviews, Correction

131


Baumgartner and Baumgartner reply:

We are grateful for the response to Kaplan to our short report. We agree that somatic inhibitory seizures may mimic transient ischemic 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 (1) They are associated with positive phenomena (limb shaking), and the involuntary movement do not affect the speech or language. (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 anticonvulsant therapy.3 (3) Although the patient pre-


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”2 provides interesting new information regarding the existence 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”4. 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 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 also associated with speech arrest in the middle of 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. Motor examination was characterised by slight tremulousness and asterixis-like movements of the outstretched right arm. There was a return to baseline functioning between events.1 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. EEG and SEP were characterised by slight tremulousness and asterixis-like movements as well as the sensorimotor cortex and activity stopped. They have not recurred over the past 5 years.

The literature includes several cases of focal motor inhibitory seizures causing weakness.1 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 raises doubts 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 re-


Baumgartner and Baumgartner reply:

We are grateful for the response to Kaplan to our short report. We agree that somatic inhibitory seizures may mimic transient ischemic 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 (1) They are associated with positive phenomena (limb shaking), and the involuntary movement do not affect the speech or language. (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 anticonvulsant therapy.3 (3) Although the patient pre-


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”2 provides interesting new information regarding the existence 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”4. 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 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 also associated with speech arrest in the middle of 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. Motor examination was characterised by slight tremulousness and asterixis-like movements of the outstretched right arm. There was a return to baseline functioning between events.1 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. EEG and SEP were characterised by slight tremulousness and asterixis-like movements as well as the sensorimotor cortex and activity stopped. They have not recurred over the past 5 years.

The literature includes several cases of focal motor inhibitory seizures causing weakness.1 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 raises doubts 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 re-


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 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 hem-

In summary, this is a creditable first edition. I look forward to the second.

STEFAN MARCINIAK


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-

and informative nature of the atlas. However the detrimental acoustic e

There follows a discussion of the different autologous donor sites and synthetic materi-

of 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-

the technical chapters on instrumentation, signal processing, echocontrast agents, har-

The clinical section covers the examination technique, normal reference values, the main categories of cerebrovascular disease, and also contains chapters on areas which may be less immediately suitable for ultrasound study. For example, the findings in head trauma, tumours, psychiatric disorders, and movement disorders are the subject of separate chapters. Although I have no problem with enthusiasm for this technique a little pragmatism would not go amiss. A more bal-

As with any book with multiple authors there is some variation in style and overlap, particularly in the introductions and conclu-

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 display amplitude flow. 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-

In summary, this is a creditable first edition. I look forward to the second.

NEIL ROBERTSON


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-

The reconstruction of traumatic and post-

surgical calvarial defects occupies the bulk of this volume, and is dealt with very e-

merely with enthusiasm for this technique a little pragmatism would not go amiss. A more bal-

As with any book with multiple authors there is some variation in style and overlap, particularly in the introductions and conclu-

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 display amplitude flow. The

neurology lends itself best to this section of the written exam-

ation but it is let down by the poor quality of some of the images in this book. This is especially unfortunate, as other images in the same section are remarkably impressive. The Sturge-Weber skull radiograph and central pontine myelinolysis MRI are beautiful. In summary, this is a creditable first edition. I look forward to the second.

ROBERT MACFARLANE


Transcranial colour duplex sonography is an ultrasound technique which is becoming

Stefan Marciniak

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 Diseases 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 to 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!