Emotion processing in the minimally conscious state

As a newly described condition distinct from coma or the vegetative state, minimally conscious state (MCS) is characterised by a threshold level of consciousness, and diagnostic criteria have recently been proposed. In MCS, cognitively mediated behaviour occurs inconsistently, but is reproducible or sustained enough to be differentiated from reflexive behaviour. It is clinically essential to distinguish this condition from persistent vegetative state (PVS), due to a potentially more favourable outcome. So far, whether patients in MCS can process emotion is unknown.

Cortical processing has been described in PVS using auditory and visual functional paradigms with positron emission tomography. However, to date hardly any functional imaging studies are available in patients in MCS. We used fMRI to assess brain activity induced by an emotional stimulus in a patient in MCS.

A 17 year old man was riding his bicycle when he was hit by a train. The accident resulted in head trauma and immediate coma, progressing to MCS over the course of 4 months, when he was admitted to our institution. This research protocol was approved by the Institutional Ethics Committee. At the time of the fMRI study, 5 months after the accident, the patient localised noxious stimuli, had spontaneous eye opening, detectable sleep/wake cycles, sustained visual fixation, and contingent smiling, thus meeting criteria for MCS. A structural MRI study showed mild cortical atrophy and dilated ventricles. Auditory evoked potentials showed decreased conduction velocities at brainstem level. The patient increased his level of awareness 2.5 months after the functional study was conducted. Auditory evoked potentials after recovery were within normal range, while MRI showed much less ventricle dilatation. Six months after recovering full consciousness, he was able to chat normally and feed himself. Currently we are restesting the patient with the same paradigm.

Non-familiar voice v silence and mother’s voice v non-familiar voice recognition were tested in an fMRI block design with 30 seconds per epoch. The patient listened to his mother reading a story, followed 30 seconds later by an age matched voice reading the same story, for 30 seconds with silence epochs in between. Blood oxygen level dependent images were acquired using a T2 weighted gradient echo planar sequence on a General Electric Signa CVI, 1.5T system with real time imaging processing of multislice and multi-phase images during patient stimulation and rest periods. The Medx 3.4 Sensor System was used to carry out fMRI post-processing, including motion correction and Gaussian smoothing. An uncorrected significance threshold of P<0.001 was used because amygdala and insula activation was expected, owing to emotional voice processing. Activated clusters were localised following co-registration with an anatomical T1-IR volume.

Subtraction of the phrases read by the age matched voice from silence was the control experiment, showing a significant focus of activation in the transverse and superior temporal gyrus, which spread to the planum temporale; more anterior activation was found in the superior (right) and inferior (left) insula (fig 1A). The subtraction of the mother’s phrases from the age matched voice disclosed a strong activation of the amygdala and insula spreading to the inferior frontal gyrus; there was also weaker activation of the transverse temporal gyrus, temporal operculum, and planum temporale (fig 1B,C). Activation was lower on the right hemisphere in both comparisons, non-familiar voice v silence and familiar voice v non-familiar.

To the best of our knowledge, our results provide for the first time anatomical evidence for the response of an MCS patient to a familiar voice, in which both amygdala and insula appear to play a major role.

The activation pattern of the control experiment agrees with previous studies. Our results showed that the mother’s voice activates the extended amygdala, an emotionally related structure, and a directly connected area such as the insula, perhaps acting jointly as limbic integration cortex. Although residual cerebral activity was unequivocal in our case, representing fragmentary cognitive processing, it should not be assumed that it depicts a fully integrated system required for normal levels of awareness; however, our findings highlight the legal and ethical implications of careless bedside chatter. Whether functional imaging represents a reliable method to evaluate neural processing in MCS patients, in whom cognitive output is extremely difficult to assess, remains to be seen.

References


Figure 1 Brain areas of activation produced by non-familiar voice subtracted from silence in coronal view (control experiment, A). Brain areas of activation produced by mother’s voice subtracted from non-familiar voice in coronal view (B), and in axial view (C)
Neurosyphilis presenting with gummatous oculomotor nerve palsy

Although epidemiological studies suggest that the incidence of primary syphilis is rising, neurosyphilis remains an uncommon manifestation of *Treponema pallidum* infection. In addition, the MRI appearances of this treatable neurological condition are not well known. Many patients with neurosyphilis are asymptomatic, but manifestations include subacute basal meningitis, a meningovascular syndrome of small deep cerebral and cranial nerve infarctions, chronic gummatous inflammation with focal intracranial mass lesions, chronic comportmental dementia of general paresis, and chronic sensory-ataxic myelopathy of tabes dorsalis. We report a case in which a meningeval form of neurosyphilis presented with rapid evolution of a pupil-involving oculomotor nerve palsy to highlight the clinical, CSF, and MRI features and good response to treatment.

Case report

The patient was a 54 year old right handed homosexual man with a history of syphilis of unknown stage, treated with penicillin 25 years previously. He was well until 6 weeks prior to admission when he sustained minor head trauma in an automobile accident, followed by intermittent headaches, fatigue, photophobia, and anorexia. Four days before admission he developed worsening and persistent drooping of the right eyelid and double vision. On examination, his mental status was remarkable only for psychomotor slowing. The right pupil was round but enlarged at 6 mm and sluggishly constricted to 5 mm with direct and consensual light stimulation as well as near vision. The left pupil was round and 4 mm and constricted briskly to 2 mm with direct and consensual light stimulation. The right eye showed a moderate ptosis of the upper lid, and the globe was deviated laterally in primary gaze with markedly impaired adduction and elevation. In the left eye, ptosis was absent and ocular motor function was normal. Other cranial nerve, sensory, motor, and reflex functions and gait were normal with the exception of a slight decrease in vibration and position sense in the feet. There were no signs of meningeval irritation. Head computed tomography (CT) and CT angiography revealed no blood in the subarachnoid space nor evidence of intracranial aneurysm. MRI of the head (fig 1) showed a sphericoid contrast-enhancing lesion at the root of the right oculomotor nerve, which extended towards the cavernous sinus. Incidentally noted were right cerebellar and right frontal developmental venous anomalies. CSF examination revealed normal opening pressure at lumbar puncture, 344 white blood cells (WBCs) (95% lymphocytes), 14 red blood cells (RBCs), protein of 167 mg%, and glucose of 71 mg%. CSF VDRL and serum RPR titres were unchanged. At 6 months, no additional improvement in oculomotor nerve functions was seen but fatigue had subsided. Repeat MRI 7 months after hospital admission showed complete resolution of the oculomotor nerve abnormality.

Discussion

Neurosyphilis is known to cause oculomotor nerve palsies either in the meningeval phase, due to slow vessel vasculitis with resultant nerve infarction, or in granulomatous basal meningitis, due to inflammation of the nerve or its investiture; however, the literature on syphilitic mass lesions around the oculomotor nerve is sparse. Vogel et al. reported a case of oculomotor nerve paralysis associated with MR findings similar to ours that also resolved with penicillin treatment. Standaert et al. described an enhancing penicillin-responsive lesion based in the interpeduncular cistern that compressed the ventral midbrain. The oculomotor nerve lesion in our patient was coexistent to adjacent brain on T1 and T2 sequences, with brisk enhancement after intravenous injection of gadolinium contrast. We believe the lesion was a manifestation of meningeval syphilis in the form of an oculomotor nerve gumma. A gumma is a focally accentuated, exuberant granulomatous response of the meninges, typically with sparse treponemal organisms. Nonetheless, treatment of the underlying infection quiets the inflammatory process and can, as in our patient, lead to significant reversal of neurological deficit. We add our case to the growing literature on MR correlates of neurosyphilis and encourage a search for neurosyphilis when an unexplained mass lesion is present in the basal subarachnoid space. Neurosyphilis, albeit rare, still deserves inclusion among eminently treatable causes of a rapidly developing oculomotor nerve palsy.

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References


High dose cyclophosphamide for severe refractory myasthenia gravis

Myasthenia gravis (MG) exemplifies autoimmune disease. Most patients require immuno-modulating treatment, including steroids, chemotherapy, or intravenous immunoglobulin (Ig), in addition to anticholinesterase

References

treatment. Drachman et al. published the beneficial effects of high dose cyclophosphamide in three patients with severe refractory myasthenia. We recount our experience of three myasthenic patients treated in a similar way.

Materials and methods
All patients participated in studies approved by the Drexel University College of Medicine and signed informed consent. These three patients with severe (class IVb) refractory MG includes all patients treated. Patients received cyclophosphamide 50 mg/kg (adjusted ideal body weight)/day over four consecutive days. Patients received antibacterial, antifungal, and antifungal prophylaxis. Haemorrhagic cystitis prophylaxis included Mesna and forced diuresis. Packed red cells and platelets were transfused to maintain haemoglobin >8.5 g/dL and platelets >10 x 10^9/L, respectively. Patients received filgrastim (G-CSF) (5 μg/kg/day) starting day 10 until their absolute neutrophil count (ANC) reached 10 x 10^9/L for two consecutive days.

Results
Patient 1 was diagnosed with seronegative MG at 30 years of age by a positive tensilon test and a decremental response on repetitive stimulation. Initial treatment included pyridostigmine and plasmapheresis, but worsening symptoms prompted thymectomies at 12 and 18 months later. Her thymic pathology revealed thymic hyperplasia. Additional treatment with only transient responses included low dose oral cyclophosphamide, intravenous Ig, azathioprine, methylprednisolone, and continued pyridostigmine with plasmapheresis. She required 27 intubations between initial diagnosis and immunomodulatory treatment at 41 years of age.

Patient 2, previously reported, suffered myasthenic symptoms at 12 years of age, initially treated with pyridostigmine. She received her first thymectomy at age 18 years and continued on pyridostigmine and occasional steroids. By 36 years of age, she was steroid dependent. Between ages 38 and 41 years she required 11 intubations and only transiently responded to intravenous Ig and plasmapheresis. A second thymectomy was performed at age 39 and cyclosporine (CsA) was initiated. She continued on prednisone 25 mg qod, scheduled intravenous Ig every 3–4 weeks, and intermittent plasmapheresis. The CsA and Cellecept were maintained but poorly tolerated. At 41 years of age, she underwent high dose cyclophosphamide without stem cell rescue.

Treatment course
Patient 1 had 13 days of neutropenia, required three units of packed red cells, and three platelet transfusions. Patient 2 had 9 days of neutropenia, required two units of packed red cells, and three platelet transfusions. Patient 3 had 11 days of neutropenia, required five units of packed red cells, and two platelet transfusions. Patients 1 and 3 experienced MG flares requiring intravenous Ig and plasmapheresis, but neither required intubation.

Neurological follow up
Patient 1, intubated 27 times before treatment, required a single intubation during 48 months of follow up. To control less severe exacerbations, the daily activity and time to peak improvement. Long term follow up is necessary and increase life quality among people with MG refractory compared to conventional treatment. Patients 1 and 3 had multiple exacerbations. As this treatment targets IgG production, exacerbations following treatment are expected. Patient 1, who required 27 intubations before treatment and only once since, and who has in the past 6 months stopped oral cyclophosphamide, may yet to enjoy the maximum benefit of this treatment. Patient 2, one year after treatment, has an improving activity level. The intervals between exacerbations are increasing: 5, 8, and 11 weeks. It is 26 weeks since her last exacerbation.

Recently, Drachman et al. published a single institution case series of three patients with refractory MG who were also treated with high dose cyclophosphamide. In this series, one patient had AChR antibody negative MuSK antibody positive myasthenia. Their mean disease duration was 10.3 months (range: 3–15 years); one required intubation and median follow up was 24 (range: 7–40) months. In comparison, in the three patients described here, two had antibody negative myasthenia and the mean disease duration was 16.3 months (range: 9–29) years. All required multiple intubations: 27, 2, and 11, and our median follow up is 25 (range: 13–48) months. During follow up, patient 3’s serum AChR levels remained detectable and did not correlate with her clinical course. Drachman et al. reported a decline in antibody levels in their patients treated in a similar way, although AChR antibody titres and MuSK antibodies persisted in their patients even after 2 years. This suggests that long term remissions in MG may be possible even without achieving complete immunosuppression. High dose cyclophosphamide has the potential to significantly reduce symptoms and increase life quality among people with MG refractory compared to conventional treatment. Long term follow up is necessary to evaluate the duration effect and time to maximum benefit. High dose cyclophosphamide treatment warrants further study as a treatment for severe refractory MG.

Table 1 Patient characteristics before high dose cyclophosphamide treatment

<table>
<thead>
<tr>
<th>Age/sex</th>
<th>Patient 1 41/female</th>
<th>Patient 2 56/male</th>
<th>Patient 3 41/female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of MG (y)</td>
<td>11</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>MG severity class</td>
<td>NB</td>
<td>NB</td>
<td>NB</td>
</tr>
<tr>
<td>AChR antibodies</td>
<td>Undetectable</td>
<td>Undetectable</td>
<td>Detectable</td>
</tr>
<tr>
<td>Previous treatment</td>
<td>Pyridostigmine</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Thymectomy(ies)</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>iv Ig (no. of infusions)</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Prednisone</td>
<td>10-100 mg qd, duration 3 years</td>
<td>40-100 mg qd, duration 7 years</td>
<td>10-60 mg qd, duration 4 years</td>
</tr>
<tr>
<td>Plasmapheresis (no. of procedures)</td>
<td>2/17</td>
<td>14</td>
<td>16</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>50 mg/d, duration 7 months limited by nausea/vomiting</td>
<td>200 mg qd, duration 2 months limited by nausea/vomiting</td>
<td>50-150 mg qd, duration 15 months</td>
</tr>
<tr>
<td>Oral cyclophosphamide</td>
<td>100 mg qd, 28 months</td>
<td>250-500 mg qd, duration 7 months</td>
<td></td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>30-125 mg bid, duration 7 months</td>
<td>100 mg qd, duration 1 year</td>
<td></td>
</tr>
<tr>
<td>Cellecept</td>
<td>250-500 mg qd, duration 7 months</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MG: myasthenia gravis; iv, intravenous; Ig, immunoglobulin; qd, four times daily; bid, twice daily.

Discussion
The patients discussed have all suffered from severe refractory MG, which requires multiple intubations. All underwent thymectomy: patients 1 and 3 repeat thymectomies. Patient 2 had an early and sustained response to immunotherapy. The three patients treated in a similar way, published the case series of three patients with refractory MG who were also treated with high dose cyclophosphamide. This suggests that long term remissions in MG may be possible even without achieving complete immunosuppression. High dose cyclophosphamide has the potential to significantly reduce symptoms and increase life quality among people with MG refractory compared to conventional treatment. Long term follow up is necessary to evaluate the duration effect and time to maximum benefit. High dose cyclophosphamide treatment warrants further study as a treatment for severe refractory MG.

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Acute head drop after cervical hyperflexion injury

Head drop is familiar to neurologists, but not widely appreciated by neurosurgeons. There are multiple causes of this condition in which the patient is unable to hold their head up because of weakness of the neck extensor musculature. It predominantly results from primary muscle pathologies in the neck extensor muscles, with occasional evidence supporting a neurogenic aetiology.1,2 I describe three patients in whom acute head drop closely followed cervical hyperflexion injury, and suggest that the cause is bilateral traction neuropathies in the cervical dorsal rami.

Patient A was an 84 year old man who enjoyed excellent health prior to falling backwards, striking his occiput on a wall and sustaining forced flexion of the cervical spine. He complained of posterior cervical pain but, when seen in casualty for closure of an occipital laceration, was found to be neurologically intact. Cervical x rays showed only degenerative disease in the mid-lower cervical spine and loss of lordosis. Over 2 weeks the pain in his neck resolved, but he became aware of a difficulty holding his head up as the day progressed and, later, of ache in his neck extensor muscles. He was referred to neurosurgery as a possible case of delayed instability. Cervical x rays demonstrated 5° of forward angulation at C4/C5, which did not change with neck flexion, but were otherwise unchanged. He remained neurologically intact but complained of some progression of the angulation and development of neural injury, posterior segmental fixation at C4/5 with a Harthill rectangle and sublaminar wiring was advised. Surgery was remarkable only for the absence of significant ligamentous injury or abnormal mobility. Unfortunately, his head ptosis recurred after 2 months. x Rays showed that the sublaminar wire at C5 had “cheese-wired” through the bone and allowed removal of the wire. He regained neurologically intact. After some discussion, he was advised to extended fixation from C3–C7, producing good alignment, albeit with restricted neck movements. However, he had ongoing problems with neck pain because of prominence of the metalwork due to profound atrophy of the paraspinal muscles. Three months later, he again developed head drop because of “cheese-wiring”, and the Harthill rectangle was extended to D2 in the skin, necessitating a third procedure to remove it. At this stage, a muscle biopsy was performed showing end-stage atrophy and fibrosis although no comment could be made as to aetiology. The patient was lost to further investigation or surgery and was managed in a Philadelphia collar in the long term. Despite all the above, the malalignment at C4/5 never progressed, nor did any neurological deficits develop.

Patient B was a fit 72 year old man who sustained a flexion/extension whiplash injury during a road traffic accident (RTA). In the accident, he had minor neck pain but was neurologically intact and had cervical x rays showing only minor degenerative changes and loss of lordosis. He was managed with analgesics and a soft collar. Several days later, he returned to casualty complaining of ache in his neck and progressive difficulty in holding up his head throughout the day. Neurological examination remained normal. Cervical x rays showed angulation into 7° of flexion at C5/6, but were otherwise unchanged. He was referred to neurosurgery and at review was strikingly reminiscent of patient A. He had to hold his chin up with a hand to look ahead, had pain in the back of his neck, which developed over the day unless he used his collar, and was neurologically normal, including in the cervical dermatomes. Magnetic resonance imaging (MRI) of his neck revealed normal soft tissue anatomy. A neurological opinion confirmed the normal examination, other than head ptosis. There was no evidence of inflammatory, autoimmune, or endocrine disease clinically or biochemically, the Tension test was negative, and serum creatine kinase was normal. There were no features of Parkinson’s disease or amyotrophic lateral sclerosis (ALS). Electroneuromyography (EMG) studies over the following 6 weeks showed the neck muscles performed 3 weeks after injury were normal in the ventral muscles, but there were typical features of acute partial denervation in the neck extensors bilaterally, particularly in a band in the mid-to-lower cervical spine with more normal EMGs above and below this. However, electrophysiological examination of the limbs was abnormal also and consistent with an asymptomatic peripheral neuropathy. The patient declined muscle or nerve biopsy.

In view of patient A’s course and the evidence in patient B of acute denervation that might recover, patient B was managed expectantly. He was “cheese-wired” to maintain range of neck movement and encourage use of the neck extensor muscles. He was given a Philadelphia collar, which was worn by day once he became aware of head ptosis. This was removed to recover to normal over 4 months, including recovery of the spinal alignment at C5/6, and the Philadelphia collar was withdrawn. There has been no recurrence of head ptosis.

Patient C, a 54 year old man, was similar to patient B. He suffered a whiplash injury in an RTA and developed head ptosis and angulation at C5/6 on cervical x rays 2 weeks later. Investigation and management mirrored patient B. His cervical dermatomes and segmental denervation of his neck extensor muscle EMG, which suggests partial denervation, but otherwise was normal clinically, biochemically, and electrophysiologically. We did not suggest muscle or nerve biopsy as it was clear he would be managed conservatively. With physiotherapy and external bracing, patient C made a complete recovery in 2 months, including recovery of spinal alignment at C5/6. There was no recurrence of head ptosis.

Although there are reports of head drop in conditions predominantly affecting neural rather than muscular elements,1,4 Umaphati et al4 cite Braun et al,5 who treat refractory torticollis by dissecting multiple cervical dorsal rami without generating significant functional deficits, as evidence that focal denervation of neck extensor muscles is unlikely to cause head ptosis. This surgical denervation, however, is unilateral and the denervated muscles are not grossly abnormal because of secondary changes resulting from the underlying condition. The cat neck extensor muscle biventer cervicis (analogous to human semispinalis capitis) has tendinous insertions defining serially arranged compartments, each receiving segmental innervation from a cervical dorsal ramus. The muscle only generates useful tension if all compartments are co-stimulated; unstimulated compartments act as weak springs in series and dissipate the muscle.” There is some evidence for similar architecture in human neck extensors: they receive innervation from several cervical dorsal rami6 and have tendinous insertions producing several at least partially serial compartments.7 Denervation of one compartment bilaterally would produce significant weakness and fatigability in such compartmentalised muscles. Additionally, the deeper muscles only traverse one motion segment and are innervated by one posterior primary ramus. Segmental denervation of either type of muscle would lead to angulation at a motion segment, limited by degree of intact joints, ligaments, and disc space.

Whiplash injury can cause neuropaxia of cranial nerve XI, XII, and branches of the cervical plexus,8,9 and there are other reports of traction neuropathies in the neck. In the present cases, the close temporal relationship of the head drop to a forced flexion injury and the EMG findings suggesting acute denervation of neck extensor muscles are consistent with a neurogenic mechanism.

Despite dystonia of neck flexor muscles can be expected to recover in patients B and C, there were normal EMG findings in the ventral neck muscles but abnormal findings in the neck extensors.

Neuropaxia of dorsal primary rami would be expected to recover in patients B and C. Equally, muscle tearing may simply have made him more prone to traction neuropaxia after whiplash and his eventual recovery is consistent with the proposed mechanism.

It is unclear why this syndrome has not been described before. Perhaps most whiplash injuries produce insufficient neuropaxia to provoke head drop unless patient factors adversely affect the transmission of forces to the nerves or their susceptibility to injury. In non-predisposed individuals, sufficient fibres would have been torn to produce head drop without also producing soft tissue abnormalities of the neck. This is not the case. Only two of the cases were investigated to exclude primary neuro-muscular disorders. These were excluded in patient C. Although patient B had evidence of a pre-existing peripheral neuropathy, this may simply have made him more prone to traction neuropaxia after whiplash and his eventual recovery is consistent with the proposed mechanism.

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We report a case of acute disseminated encephalomyelitis (ADEM) temporally associated with *Campylobacter* gastroenteritis.

The association of Campylobacter infection and Guillain-Barré syndrome is well recognised.

**References**


**Acute disseminated encephalomyelitis temporally associated with *Campylobacter* gastroenteritis**

The association of Campylobacter infection and Guillain-Barré syndrome is well recognised.
surface components of the peripheral nerves, resulting in myelin destruction and axonal degeneration. Furthermore, patients with ADEM often have peripheral nervous system involvement and there have been occasional cases of ADEM associated with Guillain-Barré syndrome. Our patient did not have any clinical features suggestive of peripheral nervous system involvement. However, nerve conduction studies were not performed and a degree of sub-clinical neuropathy cannot therefore be excluded.

We describe the first identifiable case of ADEM temporally associated with Campylobacter gastroenteritis alone. Our patient made an excellent recovery associated with therapy with high dose methylprednisolone.

Acknowledgements
We are most grateful to Dr D Connolly for reviewing the MRI imaging.

References
Evidence for an association between the CSF HVA:5-HIAA ratio and aggressiveness in frontotemporal dementia but not in Alzheimer’s disease

In their recent paper, Soderstrom et al confirmed their preliminary data suggesting that the CSF HVA:5-HIAA ratio was associated with psychopathic traits and, in particular, violent and aggressive behaviour with childhood onset and adult expression. These findings might indeed reflect changed dopaminergic activity, possibly as a result of serotonergic dysregulation. We hypothesise that their findings might be applicable to other brain disorders characterised by specific behavioural disturbances, including aggression and agitation. Indeed, since several studies have found associations between altered serotonergic neurotransmission and aggression in persons with dementia, we could propose that the CSF HVA:5-HIAA ratio might be associated with aggression in persons with dementia as well. To test this hypothesis, we performed an interim analysis on 102 out of 103 patients who were included in a prospective and longitudinal study on neurochemical and genetic correlates of behavioural and psychological signs and symptoms of dementia (BPSD). The data presented further support a general application of the interesting findings of Soderstrom et al.

Patients with various neurodegenerative forms of dementia were included in this prospective study, and were followed up by means of a neuropsychological and behavioural assessment every six months. In any case of death, brain autopsy was performed for neurochemical analysis as well as for neuropathological confirmation of the clinical diagnosis. All subjects and their caregivers gave informed consent to participation in the study, which was approved by the local ethics committee.

At baseline, behaviour was assessed by means of a battery of behavioural assessment scales which included the Behavioural Pathology in Alzheimer’s Disease Rating Scale (Behave-AD) and the Cohen-Mansfield Agitation Inventory (CMAI). Lumbar puncture was performed between 9 and 10 am on the first 11 ml of CSF were collected in several polypropylene vials that were immediately frozen in liquid nitrogen and stored at −80°C. Neurochemical analysis was carried out on the CSF fraction containing 6.75 ml by means of high performance liquid chromatography and electrochemical detection according to a method recently described. Routine investigation of the CSF included cell count, total protein and glucose analysis, and agar gel electrophoresis of proteins. For this interim analysis, HVA and 5-HIAA levels were determined in the CSF of 13 participants with frontotemporal dementia (FTD) and 89 participants with probable Alzheimer’s disease (AD). Spearman Rank Order was used for correlation analysis between the CSF HVA:5-HIAA ratio and BPDS, applying SigmaStat Software (SPSS Science, Erkrath, Germany).

In the AD patient group, no significant correlations were found between the CSF HVA:5-HIAA ratio and Behave-AD clusters, total and global scores, or CMAI clusters (aggressive, physically non-aggressive, and verbally agitated behaviours) and total scores. In persons with FTD, however, the CSF HVA:5-HIAA ratio correlated significantly with the Behave-AD aggressiveness cluster score (r = 0.386; p = 0.033) and with the CMAI verbally agitated behaviour cluster score (r = 0.564; p = 0.041). Despite small sample sizes, effects of treatments were ruled out by comparing the CSF levels of HVA (t-test: p = 0.691), 5-HIAA (p = 0.370), and the CSF HVA:5-HIAA ratio (p = 0.157) between six untreated subjects with FTD and seven subjects with FTD who were receiving atypical antipsychotics.

Our preliminary results revealed an association between aggression and the CSF HVA:5-HIAA ratio in participants with FTD but not in those with AD. More refined neurochemical analyses, including the determination of all catecholamines and serotonin in an extended population of FTD patients, are scheduled. This will allow further testing of the hypothesis that altered serotonergic modulation of dopaminergic neurotransmission leads to BPDS and in particular to aggression. Meanwhile, our findings suggest that the association between the CSF HVA:5-HIAA ratio and aggression as observed by Soderstrom et al. is not limited to violent and aggressive behaviour with childhood onset and adult expression, but may indicate an underlying pathophysiological mechanism that may be common to aggressive symptomatology in other brain disorders, such as frontotemporal lobe dementia.

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References

Extensive radiculopathy: another false localising sign in intracranial hypertension

We read with interest the review by Lamrê on false localising signs. Among the various false localising signs described in patients with intracranial hypertension (ICH), radiculopathy is an important manifestation which is probably under recognised. Many authors have documented subtle features of radiculopathy in patients with isolated intracranial hypertension (IH). The usual manifestations of radiculopathy in these cases were acral paraesthesias,2 and backache and radicular pain.3 Rarely, motor deficits due to radiculopathy caused by ICH have been described.4

Obied et al reported two patients with extensive radiculopathy due to ICH5: one individual had IH and the other had cerebral sinus venous thrombosis. Both persons had papilloedema, marked visual impairment, and flaccid areflexic quadraparesis with normal MRI of brain, brainstem, and cervical spinal cord. The electrophysiological findings were consistent with radiculopathy. Both individuals initially received intravenous immunoglobulin for Guillain–Barre syndrome, without benefit, but they responded well to lumbo-peritoneal shunting. We also encountered two such cases with angiographically proven cerebral venous sinus thrombosis.6

The most likely mechanism at the basis of radiculopathy appears to be similar to that of other cranial neuropathies in ICH—that is, mechanical compression of nerve roots, due to elevated CSF pressure distending the subarachnoid space. Documented enlargement of spinal subarachnoid space and distended root pouches in a patient with radicular pain and areflexia due to IH supports this view. Radiculopathy secondary to ICH has been reported almost exclusively in patients with IH or cerebral venous sinus thrombosis. Other causes of ICH may not induce a diffuse increase in pressure in both intracranial and intraspinal compartments, and are unlikely to manifest as radiculopathy. The constellation of flaccid-areflexic quadriparesia and papilloedema may be misdiagnosed as Guillain–Barre syndrome with papilloedema.7 Careful analysis of the evolution of symptoms, estimation of CSF pressure, and appropriate vascular imaging should help to correctly identify the cause of ICH.

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References
Role of entacapone in later Parkinson’s disease not yet established

The study by Brooks and Sagar, along with a number of previous others, demonstrates benefits for the catechol-O-methyltransferase (COMT) inhibitor entacapone when compared with placebo in Parkinson’s disease (PD). However, this is insufficient evidence to justify the authors’ conclusion that “it appears logical to employ levodopa combined with entacapone routinely”. The important issue is not whether entacapone is more efficacious than placebo, but whether it is more or less clinically effective and cost effective than the other available treatments for patients with PD that is no longer adequately controlled by levodopa alone. Other available agents—including dopamine agonists and monoamine oxidase type B (MAO-B) inhibitors—have also shown efficacy when compared with placebo. The paper would have benefited from a balanced discussion of the merits of entacapone compared with these other available treatment options.

Such a discussion is likely to be inconclusive, however, as there is a dearth of reliable evidence on the best treatment for PD, at any stage of the disease, since very few trials directly comparing active treatments have been undertaken. Companies are reluctant to undertake such trials, as it is not in their commercial interests to risk studies that might show their product to be inferior to that of a competitor. For this reason, independently funded trials—such as the current PD MED trial in the UK—should be supported to provide the reliable evidence on comparative efficacy needed to enable clinicians to make informed treatment decisions. Analysis, presentation and interpretation of the results of independent studies are also likely to be more objective than those of commercial studies. The potential for bias in commercial trials has recently been highlighted by systematic reviews and journal editors—for example “systematic bias favours products which are made by the company funding the research” and “scientific studies can be manipulated in many ways to give results favourable to companies.”

There are problems with the trial reported by Brooks and Sagar, and these are common to many PD trials, which are generally of poor methodological quality. In a progressive condition such as PD, it is important to evaluate the long term effects of treatment, and six months follow up is inadequate. The outcome measures used should reflect the impact of treatment on the patients’ own perceptions of their functioning and quality of life, not that of clinicians as with the Unified Parkinson’s Disease Rating Scale (UPDRS). It is unclear how well the data obtained from on-off diaries correlates with global quality of life measures. The intention to treat (ITT) analysis was not performed, since patients who withdrew from treatment were excluded from the analysis—ITT analysis requires such patients to be followed up and included in the analysis according to the arm to which they were allocated even if they have withdrawn from allocated therapy. Nearly 50% more patients (24.1% v 16.5%) dropped out of the entacapone arm than from the placebo arm and, in progressive diseases such as PD, dropout bias tends to favour the active treatment. Thus, although COMT inhibitors are welcomed additions to the treatment options in PD, large, rigorously conducted comparative trials, assessing the long term impact on patient-rated measures of overall quality of life, are still needed to define their role in routine clinical practice.

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Competing interests: We are investigators in the PD MED trial and thus have a vested interest in obtaining objective evidence on the best treatment for PD. CC has received honoraria for lectures, consultancy fees, and travel expenses from the manufacturers of many of the drugs discussed.

References

Portal-systemic shunts, manganese, and Parkinsonism

I read with interest the article by Yoshikawa and colleagues.1 The authors reported the case of a 44 year old woman with hereditary haemorrhagic telangiectasia (Rendu-Osler-Weber disease) involving the liver, who had raised serum concentrations of manganese, hyperintense areas in the basal ganglia on T1 weighted magnetic resonance images, and levodopa unresponsive parkinsonism. Naturally, I agree that the parkinsonism in this case is most probably related to portal-systemic (portal-venous) shunts. There are, however, two points that deserve clarification.

First, it is not entirely clear whether their fig 2 (left panel) shows portal-systemic or arterovenous shunts. The authors say that the figure shows a selective angiogram of the superior mesenteric artery. If that were the case, there should not be a “feeding artery” involved in the intrahepatic shunts (as they state in the legend to fig 2). Instead, the figure would show the portal venous phase of the angiogram and show a feeding artery (the hepatic artery) and arterovenous (not portal-systemic) shunts. Interestingly, there is evidence to suggest that both types of shunt are of potentially toxic substances (for example, manganese) passing directly from the gut to the systemic circulation through portal-systemic shunts could be rapidly cleared by a normal liver as long as the hepatic artery flow is adequate.

Second, Yoshikawa and colleagues claim that the parkinsonism of their patient was induced by manganese. While this is a reasonable working hypothesis, the authors provide no direct evidence supporting such a statement. The fact that manganese was raised does not necessarily imply that manganese played a key role in the pathogenesis of parkinsonism. Indeed, their patient lacked various clinical features often seen in cases of manganese induced parkinsonism (for example, cock walk and propensity to fall backwards).

Levodopa unresponsive parkinsonism is a well known manifestation of chronic non-Wilsonian hepatocerebral degeneration.2 Although blood concentrations of ammonia were within the normal range in the case reported by Yoshikawa and colleagues, the possibility of manganese induced Parkinsonism occurring particularly after meals was not investigated.

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References

Authors’ reply

We are pleased to have an opportunity to comment on the important issues raised by Dr de la Fuente-Fernández regarding a case of hereditary haemorrhagic telangiectasia.
with parkinsonism. Raised serum manganese combined with the abnormal findings in cranial magnetic resonance imaging and abdominal angiography were the rationale for our conclusion that the parkinsonism in our patient was induced by manganese that had accumulated because of portal-systemic shunting.

About the angiogram: the angiogram of the superior mesenteric artery presented in our manuscript showed a dilated feeding artery, a dense mottled hepatogram, and early filling of the hepatic vein. These findings concerned the arterial phase. The intrahepatic arteriovenous shunts were definite diagnostic evidence of hereditary haemorrhagic telangiectasia but not of portal-systemic shunts. We therefore agree with Dr de la Fuente-Fernández that we should have presented another angiogram in the portal phase showing a hypoplastic portal vein with abnormal vessels between the mesenteric and inferior vena cava to confirm the portal-systemic shunt.

About the parkinsonism: after the failure of treatment by levodopa, we took other measures to relieve the parkinsonism; for example, we persuaded the patient to avoid manganese-rich foods such as blueberries. Fortunately, her serum manganese gradually decreased below the normal upper limit during the next six months, and her neurological symptoms became less prominent. Alleviation of parkinsonism in inverse proportion to serum manganese concentrations suggests that the parkinsonism in this case may have been caused by manganese accumulation, and that the patient was in the early stage of manganese intoxication in which neurological symptoms were incomplete and partially reversible.

About transient hyperammonaemia: we searched for cases of hyperammonaemia related parkinsonism, and finally found a case with portal-systemic encephalopathy and parkinsonism which disappeared after treatment of the portal-systemic shunting.1 The mechanism of parkinsonism in that case is not openly to debate, as hyperammonaemia is generally thought to cause disturbance of consciousness or negative ammonaemia is generally thought to cause

References

Parkinsonism and persistent vegetative state after head injury
Matsuda et al recently reported three patients with a persistent vegetative state (PVS) after severe head injury who, after recovering from prolonged disturbance of consciousness, presented parkinsonian features (mainly rigidity and hypokinesia) which improved after levodopa treatment.1 MRI studies showed lesions in the dorsolateral midbrain and cerebral peduncles suggesting axonal injury involving the dopaminergic system (substantia nigra and subthalamic area). Similar observations were made in a series of 125 patients with severe vegetative state following head injury (survival time 1–10 years). Nineteen of 49 patients surviving in fully developed or mild recovery stages of PVS initially presented with severe to moderate, mainly symmetrical, parkinsonian symptoms (amnesia, rigidity, hypokinesia, convergence disorders). Following levodopa treatment, 11 patients showed incomplete and full improvement of both the PVS and parkinsonism, while four patients showed complete recovery from both syndromes. However, in 15 patients—despite good recovery from the initial PVS and other neurological symptoms (spasticity, frontal and cerebellar symptoms), and long term levodopa treatment—a progressive parkinsonian syndrome (rigidity, hypokinesia) developed in six patients. This was associated with unilateral or bilateral resting tremor. In MRI studies done in 34 patients, 32 showed unilateral or bilateral lesions in the midbrain involving both the dorsolateral tegmentum and the cerebral peduncles.2

Neuropathological studies were undertaken in 32 patients surviving without essential improvement of the PVS for at least two months after head injury. Parkinsonian syndromes were severe in seven, moderate in five, and mild in four. In addition to older haemorrhages or necroses in the putamen (n = 6), globus pallidus and thalamus (n = 8), all brains revealed multiple lesions in the rostral brain stem with unilateral or bilateral focal lesions in the substantia nigra, with vascular lesions in the lateral and caudal midbrain in seven, and symmetrical post-anoxic cellular depletion and gliosis or unilateral necroses in the substantia nigra in one case each. In nine cases, there was a good correlation between the severity of clinical parkinsonian signs and the severity and extent of nigral lesions; three patients showed severe parkinsonian signs associated with only mild nigral damage, but there was severe bilateral damage to the globus pallidus in two. In four patients the expression of clinical parkinsonian signs was more severe than the anatomical lesions, in particular the damage to the substantia nigra. The distribution pattern of the brain stem lesions correlated with the sequelae of transtentorial shifting caused by increased intracranial pressure; direct or “primary” traumatic lesions to the oral brain stem usually cause acute death, as seen in two young men with rupture of the diencephalon and acute haemorrhage into the substantia nigra or midbrain following severe and acute fatal head injuries. However, in rare patients with long term survival following head injury, symmetrical necrosis of the substantia nigra without a clinical parkinsonian syndrome has been reported.3

The clinical phenotype of post-traumatic parkinsonism often resembles that of post-encephalic parkinsonism, both showing akinesia, rigidity, hypomimia, rare tremor, and optomotor and vegetative disorders. Both the lesion pattern and the therapeutic efficacy of long term levodopa treatment suggest a dysfunction of the striato-nigral dopaminergic system which, however, may show progressive decompensation in some patients with long lasting PVS after severe head injury.

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REFERENCES

Authors’ reply
We greatly appreciate the thoughtful comments offered by Dr Jellinger, and his interest in our report of three cases in a persistent vegetative state (PVS) after severe head

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injury, who recovered from a prolonged disturbance of consciousness after they were given levodopa. Jellinger et al. reports that in cases of prolonged post-traumatic coma the brains showed multiple lesions of primary and secondary traumatic origin and that the highest incidence of lesions was found in the rostral brain stem. These were considered to be almost exclusively of secondary origin, resulting from cerebral and peripheral circulatory disorders, post-traumatic oedema, and increased intracranial pressure. Primary (direct) traumatic lesions to the rostral brain stem usually cause acute death. In contrast to this report, the brain stem injuries in our cases suggested by MRI may have been the primary traumatic lesions. All these cases showed high intensity lesions in the dorsolateral midbrain on T2 weighted MRI. These findings implied that the midbrain was injured by tentorial compression induced by translatory and rotatory acceleration when the cranium was struck in its sagittal axis, or by posterostral damage. MRI findings, particularly in the acute stage, are useful for evaluating primary brain damage. Furthermore, another distinctive feature of our cases was that the anatomical distribution of the lesions was not multifocal but was localised in the cerebral peduncle or the dorsolateral midbrain, implying diffuse axonal injury involving the substantia nigra or the ventral segmental area. The neuroradiological findings, the clinical features of extrapyramidal dysfunction, and the efficacy of levodopa treatment all strongly suggest that the dopaminergic pathways were selectively damaged and caused defects in the nigrostriatal, mesocortical, or mesolimbic system. As Dr. Jellinger indicates, progressive decompensation in levodopa treatment is a considerable problem. However, not all our patients have required permanent medication, an example is case 1 in our report, whose recovery was sustained even after the levodopa treatment was discontinued. Some patients may need levodopa only as a trigger and withdrawal of medication involves ethical problems.

In recent neuropathological and neuroradiological studies on PVS after traumatic brain injury, the most common structural abnormalities were diffuse axonal injury involving the corpus callosum, the dorsolateral aspect of the rostral brain stem, and the thalamus. Although the clinical features will vary in such cases, a take-home message which we learned from our three cases is that in any group of patients with PVS after severe head injury there may be some whose dopaminergic systems may have been selectively damaged; such individuals may respond to levodopa treatment. It is necessary to accumulate a great deal more clinical experience and data to elucidate the pathogenesis and pathophysiological mechanism of post-traumatic PVS. We respect Dr. Jellinger’s careful observations and descriptions of his cases of prolonged post-traumatic coma, and look forward to further views from him on this topic.

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References

BOOK REVIEWS

Year book of neurology and neurosurgery 2003

Every year, countless journals publish myriad neurology and neurosurgery papers. There is immense attraction in the notion of a single volume yearbook that selects and comments upon the most. How well does the Yearbook of neurology and neurosurgery succeed in informing about significant advances in knowledge over the past year in neurosurgery? For 2003? The editors draw their selection from a survey of 500 journals, with something from most of those with big impact. Thirty seven associate editors assisted by reviewing the various subspecialty areas; of these all except 11 come from North America, of whom 9 are neurosurgeons rather than neurologists, an intriguing imbalance.

Papers selected cover every conceivable subspecialty, and sometimes the inconceivable. New gene mutations abound, illuminating case histories are provided, we learn that the visual cortex is hyper-excitable in migraineurs, and about informed consent in neurosurgery, and we are treated to pictures of new cranial remodelling devices for treating craniosynostosis. To provide a critical review of such a diversity of subject matter would be an impossible task. All one can do is to congratulate the editors for high-lighting a selection of topics that opens one’s eyes to the dazzling diversity of our specialty. Nevertheless, you would not go to a yearbook for a comprehensive review of developments in a particular subspecialty. Therefore, this is essentially armchair reading, and none the less useful for that.

Each article is summarised in half a page or so under the headings introduction (or background), methods, results, and conclusion. This is followed by a brief editorial comment—often interesting and pithy. At least some of this signed editorial comment is derived verbatim, or with only minor paraphrasing, from editorial comment in the journal originally publishing the chosen paper. So whose opinion are you really reading in the yearbook?

Although interestingly informative outside one’s subspecialty, one does need to ask whether the concept of a single volume yearbook isn’t becoming submerged by the sheer volume of potentially eligible papers published each year. And, although this 2003 yearbook arrived on my desk in December 2003, it predominantly covers papers published in 2001, with some from early 2002, and an occasional hangover from 2000. So, it isn’t that up to date. I guess libraries will buy it, partly out of habit. But for individuals, £74 is a steep price for neurological coffee table reading.

M Donaghy

Reference

Catatonia: a clinician’s guide to diagnosis and treatment

This nicely produced book reviews one of the historically most interesting, but clinically still very important, disorders of neuro-psychiatry. Catatonia, described by Kahlbaum in the latter half of the 19th century, was hijacked by Kraepelin to be incorporated into his concept of dementia praecox, and almost disappeared from the literature in the first half of the 20th century, being finally eclipsed by the introduction of effective psychotropic drugs thereafter. But, as Fink and Taylor explore here, catatonia as a diagnosis is still a diagnostic challenge, with causes far beyond schizophrenia and a syndrome with effective treatment, notably, but not exclusively electroconvulsive therapy (ECT).

For those interested in the cerebral basis of psychiatry, a condition with the main presenting signs of mutism, immobility, negativism, posturing, stereotypy, and echo- phenomena cannot fail to attract attention, and the many faces of catatonia (title, chapter 3) are an olla podrida of neuro- psychiatry. It is refreshing to find reference to Leonardo’s work and the many words in a text from American authors, who are thoroughly appreciative of the European literature on their subject, and shyly critical of DSM-IV. Their overall conclusions are clear: Catatonia is a common subtype, neurollepetic malignant syndrome is malignant catatonia, catatonia is not usually associated with schizophrenia, and it is a syndrome of motor dysregulation with a good prognosis—if identified and treated early. This book is a pleasure to read, but should be on the imperative reading list for all psychiatric trainees to inform them about the history of their discipline, the importance of neuropsychiatry, and how to write clearly.

M R Trimble

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New Oxford textbook of psychiatry, vols 1 and 2

The New Oxford textbook is the latest and largest from the Oxford textbook of psychiatry’s stable. The book was originally published in 2000 and has recently appeared in paperback. This is the best modern British textbook of psychiatry. It is over 2000 pages long and comes in two stout volumes. The international editorship is led by Michael Gelder, Emeritus Professor of Psychiatry at Oxford, with Spanish (Jaun Lopez-Ibor) and American (Nancy Andreasen) co-editors. The book is inevitably based on a myriad of individual contributions although the choice of contributor and standard of editing is exemplary.

The first volume covers general issues and the scientific basis of psychiatry, including a number of reviews of neurobiology. Interestingly, psychodynamic contributions have a separate section. The remainder of the first volume is taken up with coverage of the clinical syndromes of adult psychiatry, including substantial coverage of dementia.

The second volume includes review of special topics with a number of articles on aspects of the psychiatry and medical conditions. This includes a useful chapter on neurological disease by Maria Ron, and on epilepsy (Marco Iacoboni). The remaining part of the second volume addresses the psychiatric subspecialties as well as having a substantial section on psychiatric treatments, both pharmacological and non-pharmacological. This text is my first personal first choice when I encounter a problem in the clinic that I want to look up—and I am rarely disappointed by what it says. This is a Rolls Royce of a textbook. There is a tendency to think of books as large as this one (particularly at a price of £125 even for the paperback) as suitable only for libraries. This would be a mistake. Despite its size and price this book’s accessibility and comprehensiveness would make it the first choice as a postgraduate handbook, not only for psychiatrists but for neurologists and neurosurgeons too.

The parallel brain: the cognitive neuroscience of the corpus callosum

Roger Sperry’s research on the cognitive abilities of split-brain patients following callosal section is a landmark in the study of brain-behaviour relationships. His studies firmly established the role of the corpus callosum in inter-hemispheric information transfer. What have we learned more recently about the role of the corpus callosum in cognition? In this book Eran Zaidel (originally one of Sperry’s students) and neurologist Marco Iacoboni present 22 chapters based on a 1996 NATO Advanced Science Institute that attempt to answer this question. The central focus is on the classic problem of why reaction time to respond to a light flashed in either visual field differs according to whether the ipsilateral or contralateral hand is used to respond (known as the Poffenberger effect, after the psychologist who described it in 1912). This is thought to reflect callosal information transfer between the hemispheres; the book uses anatomical, physiological, and behavioural perspectives to address the question of what information is transferred and how the transfer might be affected by injury. Any chapter is accompanied by commentaries and editorial comment, giving a flavour of the debates and controversies in the field.

Perhaps reflecting the long interval between the original conference of this book, more recent studies that use functional neuro-imaging techniques to investigate callosal function are relatively poorly represented. However, there is still much of interest in this otherwise comprehensive volume. The chapters generally have a basic scientific focus, but chapters on multiple sclerosis, dyslexia and alexia, schizophrenia, and attention deficit hyperactivity disorder also contain much that will interest the practicing clinician.

M Sharpe

Magnetic resonance imaging in stroke

This book does much more than its title would suggest. Although mainly concerned with magnetic resonance imaging (MRI) in stroke, the text actually covers single photon emission computed tomography (SPECT) and positron emission tomography (PET) imaging as well and tends to be one of the best chapters ever written on computed tomography (CT) in stroke. The approach and content reflect the predominance of neurologists among the editors and authors, with only a few radiologists, and is really aimed at practitioners who need to understand more about imaging and its role in patient characterisation, decision making, and assessment of treatments. The scene is set in the first chapter with a discussion of the limitations of clinical diagnosis of stroke and the specific role that imaging can play in diagnosing the type and cause of stroke. There is a superb chapter on CT in acute stroke, which exemplifies how the role of imaging in any diagnostic process should be evaluated. Separately, there is a chapter on CT evaluation of cerebral blood flow, a useful and practical introduction to MRI, discussion of conventional structural MR techniques such as T2, FLAIR, and gradient echo sequences, and a section on MR angiography. Much of the rest of the book (about half of it) is given over to diffusion and perfusion MRI, including its evaluation in animal models, concepts of identifying the ischaemic penumbra, evaluation of transient ischaemic attacks, selection of patients for new therapies and drug development trials, and finally a chapter on MR spectroscopy and a (very short) chapter on functional MRI after stroke.

Although written by MR enthusiasts, the text is tempered with some discussion of the drawbacks of MR, such as poorer patient accessibility (compared with CT) and problems of metallic foreign bodies. It also makes the point that, despite the huge interest in MR diffusion and perfusion imaging, the precise thresholds of defining reversibly damaged tissue and tissue at risk are yet to be determined. Some aspects of stroke MRI are not dealt with in much detail, for example classification or interpretation of white matter lesions (frequently found in stroke patients), or the identification and interpretation of microhaemorrhages on MR and how they might influence decisions regarding stroke treatment, or on using diffusion imaging to identify lesions in patients with milder strokes or at a few hours after acute stroke (that is, not just the first few hours). There is very little on practical issues (perhaps reflecting the neurolinguistic rather than the radiological approach) such as how one assesses a stroke patient who is unable to speak prior to MR to make sure that it is safe for the patient to go into the magnet, and how one manages the patient while in the magnet with respect to factors such as oxygenation.

Some of the authors express personal views that not all readers will agree with. For example, in the chapter on assessment of a transient ischemic attack (TIA), the authors suggest that the definition of a TIA should be changed to one based on the presence or absence of certain imaging features. Although this clearly represents a personal opinion expressed by the authors, and a decision to changing a classification that is so fundamental to stroke epidemiology and clinical practice is that only those with access to an MR scanner with diffusion imaging would be able to correctly diagnose a TIA using this new classification. Not only that, but the diagnosis of a TIA might be dependent on the ability of the local radiologist or clinician to spot subtle features of recent ischaemia on diffusion images and the timing of scanning after symptom onset.

I found it a little disappointing that a proportion of the perfusion images were presented in black and white when this is one technique which really requires colour display for proper interpretation and appreciation.

In summary, this is a useful textbook, particularly for neurologists or stroke physicians who need to understand more about imaging and its role in patient characterisation, decision making, and assessment of treatments in acute stroke. It’s not just about MR and everybody with an interest in stroke should read the chapter on clinical efficacy of CT in acute cerebral ischaemia (in less than 250 pages it is easily digestible and yet also a useful reference. At £80.00 I think compared with other books on MR and on stroke it represents good value for money.

G Rees

Cortex and mind: uniting cognition

Joaquin Fuster is a distinguished American neuroscientist whose work has explored the neurophysiology of cognition, largely in animals, but with the ultimate goal of understanding how the human mind is implemented in the brain. His own research has focused particularly on the neuronal mechanisms of working memory, revealing “memory” cells in the prefrontal cortex that help to retain the information an animal must “keep in mind” if it is to act appropriately after a delay—like the position of a covered well containing a treat. At the level of the prefrontal memory cells are a key component of an extensive cortical network required to maintain working memory, which also involves
cognitive neuroscience, including perception, language, the inner world of memory and emotions, and the breakdown of the mind in certain neuropsychiatric disorders. Within these acts, each examines a particular feature of the mind and illustrates how Shakespeare dissected and explored it in his own laboratory—the theatre. The scene opens with a quotation of a chosen play and a brief synopsis of the plot before moving on to discuss the hard neuroscience underlying this cognitive phenomenon as revealed by the latest neuroimaging techniques. For example, in discussing the role of the frontal lobes in attention shifting and the planning of behaviour, the example is chosen of Prince Hal, the wayward, youthful heir of Henry IV who purposely turns from the influence of Sir John Falstaff and his frivolous drinking companions in order to develop the resolve and strength of character which will later serve him well as King Henry V. This transformation is compared with the case of Phineas Gage, the 19th century rail worker who survived a dramatic penetrating injury to his cranium but consequently displayed a remarkable alteration in his personality. Recent computed tomography reconstructions of Gage’s skull and Antonio Damasio have clearly delineated the passage of the three foot tamping iron through the frontal cortex—the area “responsible for the functioning of what we call a moral sense”.

The concept is an entertaining one and the authors have worked hard to bring it to life. The target audience presumably consists of people with no specialist knowledge of either Shakespeare or neurology and, if this is so, the reader will be rewarded with new and his or her interest. The rich neuroscience tableaux ranges from Chomsky and language to the functional imaging of hallucinatory experiences in schizophrenia, while the bite-sized chunks of Shakespeare successfully convey the bard’s penetrating insight into the human psyche. The suggestion is that scientists, too, need to step outside the laboratory to find inspiration for their hypotheses. Lavish illustration with exquisite resonance imaging (fMRI), positron emission tomography, and single photon emission computerised tomography images, alongside numerous performance photos from well-known theatrical productions, give the book an enticing, coffee table appeal.

However, the book suffers from the contrivances undergone in order to link the Shakespearean poetry to the scientific project. Take, for example, the use of Macbeth’s grasping at an illusory dagger to introduce a discussion of the cerebellar control of complex motor acts, or the soliloquy from Hamlet’s murderous uncle, Claudius, which begins “O, my offence is rank, it smells to heaven” as a cue to show fMRI pictures of “areas of the brain that become active with smell”. In addition, the simplistic, rather than simplified, portrayal of functional imaging is coupled with brain images that are often unlabelled and poorly explained, giving the impression of a gaudy backdrop used to impress rather than to inform. Despite that, everyone will certainly find this book to be a revelation of the rich and diverse contributions of MPTP to our understanding of PD, genetic and environmental factors, and the drug classes employed in treatment as well as the complications of treatment, including dyskinesia and motor fluctuations. Proper attention is given to the management of psychosis and cognitive decline, with discussion of the relationship of these features in PD to dementia with Lewy bodies and Alzheimer type pathology. Future avenues of treatment, including neuroprotection and gene therapy, are also covered in this near encyclopaedic compendium, which is highly recommended for all those who treat patients with PD in neurology, geriatrics, and old age psychiatry departments, as well as research scientists in the field, and it should be required reading for all neurological trainees.

R Pearce

Principles and practices of emergency neurology—handbook for emergency physicians


This is a handbook based on an earlier larger book, Emergency neurology: principles and practice, in response to enquiries from emergency medicine residents about whether a handbook, based on this main text, would be available. This is the result. Whether it is justified in calling itself a handbook is hard to say. The area covers three of my hands (small). It runs to over 400 pages with approximately 50 authors. It covers neurological examination and neurodiagnostic...
testing, common neurological presentations, for example headache and weakness, specific neurological conditions, for example multiple sclerosis and cerebrovascular disease, neurological trauma, paediatric neurological emergencies, pregnancy related neurological emergencies, neurotoxicology, and brain death. So, it attempts a comprehensive coverage. The editors consider it to be symptom based, although this is not always achieved. It has many tables, good illustrations, and management of algorithms with “pearls and pit falls” at the end of every chapter.

The neurological examination is done poorly, particularly the cranial nerves. This needs to be done with pictures of the lesions, their causes, and the anatomy, based around the common emergency presentations in A&E. Although many specialists would disagree with some of the advice given, most of the text is reliable and clear. (For instance, in the chapter on myasthenia gravis, it states “useful gauges include pulse oximetry, peak expiratory flow and PCO2 measurement”, which are all poor gauges of impending ventilatory failure and vital capacity is the most important measurement in this respect.)

The most disappointing feature is that the chapters are not adequately focused on emergency conditions. The chapter on movement disorders covers virtually the whole spectrum of chronic movement disorders without specifically concentrating on the common emergency presentations, such as drug induced dystonia with oculogyric crisis and hemiballisms, which are likely to come to A&E. Unfortunately the editors and authors have failed to produce a sufficiently concise account of emergency conditions to make this book really useful. It needs to be much briefer and appropriately focused to achieve its aim and it would be better as a pocket this book really useful. It needs to be much more comprehensive and affect which are re-represented cortically and which propel our very being.

D E Bateman

Duchenne muscular dystrophy, 3rd edn

Quite simply, this monograph is essential reading for anybody involved with this devastating condition, and indeed for those involved with any form of muscular dystrophy, whether in the clinic or in the laboratory. Duchenne muscular dystrophy (DMD) is the archetypal dystrophy. It is because the clinical course is so stereotyped that it was the first of the dystrophies to be defined clearly, over a century ago. The historical journey from the first clinical descriptions to our present state of knowledge forms the core of this book, with side branches relevant to the identification of other specific forms of dystrophy, particularly the limb girdle dystrophies. The nihilist may suggest that all of this knowledge has as yet failed to find a cure, but for the clinicians intimately involved with these patients we can now do more than ever to provide an improved quality of life. There is of course great hope that “genetic engineering” will lead to a cure, but patients and their families cannot live on hope alone and Professors Emery and Muntoni have elegantly summarised present management options.

The second edition was published in 1986, a matter of months before the identification of the gene involved in the disease process and its protein product dystrophin. Within a few years it became apparent that dystrophin and dystrophin associated proteins have a fundamental role in various forms of muscular dystrophy, and for a while it looked as if there might be a common mechanism of membrane fragility due to dysfunction of these membrane associated proteins. Then abnormal cytosolic proteins were found in some forms of limb girdle dystrophy and it became clear that there was no simple single disease mechanism. Despite that, altered function of membrane proteins is clearly of fundamental importance in many dystrophies and Muntoni has been at the forefront of recent discoveries relating to altered glycosylation of the membrane protein z-dystroglycan in various forms of congenital and adult onset limb girdle dystrophies.

There is no need to describe the individual chapters in detail. In brief, the monograph covers the history of the disease (Emery being a noted medical historian), clinical features, differential diagnosis, muscular pathology, pathogenesis, genetic counselling, and management. Emery is retired from clinical practice but the clinical setting is kept up to date by his being joined by Muntoni for this timely third edition.

All those involved in the management of DMD will find something of value in this book. Some patients and families may also want to dip into it. Those interested in the history of medicine will find it an excellent example of modern genetic and molecular techniques, will find it a fascinating story.

Let us hope that a fourth edition, detailing the successes of genetic engineering, will not be too far off, but in the meantime there is much that can be done to alleviate the consequences of this truly awful condition.

D Hilton-Jones

Mental and behavioral dysfunction in movement disorders

It was not long ago that the basal ganglia were confidently asserted to have no influence on cognition, and to have only motor functions. This was the province of neuropsychiatry of movement disorders. The main themes, cognition in movement disorders, and affects which are re-represented cortically and which propel our very being.

M Trimble

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CORRECTIONS
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In the review by Rockwood in the May issue of JNNP (K Rockwood. Size of the treatment effect on cognition of cholinesterase inhibition in Alzheimer’s disease. J Neurol Neurosurg Psychiatry 2004;75:677–85) there is an incorrect entry on the x axis each of the tables in figure 1. The sixth entry should read 0.25, instead of 0.3. The corrected table can be viewed at http://www.jnnp.bmjournals.com/cgi/content/full/75/5/677/DC1

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The authorship list of the letter entitled emotion process in the minimally conscious state, by Bekinschtein et al (JNNP May 2004;75:788), was incorrectly printed as T Bekinschtein, J Niklison, L Sigman, F Manes, R Leiguarda, J Armony, A Owen, S Carpintiero, L Olmos. The correct order is as follows: T Bekinschtein, R Leiguarda, J Armony, A Owen, S Carpintiero, J Niklison, L Olmos, L Sigman, F Manes.