LETTERS TO THE EDITOR

Behavioural status during the intracarotid amobarbital procedure (Wada test): relevance for surgical management

Presurgical evaluation in many epilepsy programmes often includes the intracarotid amobarbital procedure (IAP). Sodium amytal is injected into the internal carotid artery to produce a temporary “pharmacological paralysis” of hemispheric function. Traditionally, the IAP has been employed in patients with refractory frontal lobe epilepsy being considered for anterior temporal lobectomy. In these cases it is used to determine cerebral dominance for language, to assess the risk of severe postsurgical amnesic syndrome, to predict postsurgical material specific memory changes. More recently, the use of the IAP has been extended to complement EEG localisation and radiological data by lateralisng temporal lobe dysfunction.

There are a number of potential implications for the selection of temporal lobectomy, this outcome may have the potential application of the IAP in the surgical management of extratemporal cases.

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Reversal of tetrabenazine induced depression by selective noradrenaline (norepinephrine) reuptake inhibitor

Tetrabenazine (TBZ), a synthetic benzoxazine, was first introduced as a neuroleptic agent in 1960, and is now widely used in the treatment of hyperkinetic movement disorders such as chorea, tics, or tardive dyskinesia. The side effect profile is mainly characterised by the triad of drowsiness/fatigue, parkinsonism, and depression; depression is found in about 15% of patients treated with TBZ. We here report on the rapid reversal of depressive symptoms in a patient treated with TBZ for orofacial dystonia by administering the new and highly selective noradrenaline (norepinephrine) reuptake inhibitor (SNRI) reboxetine.

On admission, the 64-year-old woman presented with perioral and lingual hyperkinetias as well as intermittent and involuntary movements of her lower jaw, which had lasted for about 2 years, causing her considerable impairment in her daily life. No history of neuroleptic treatment or Parkinson's disease was evident. Her cranial CT and blood chemistry were normal. We diagnosed a segmental dystonia, which improved dramatically after a short term of a tetrabenazine medication (60 mg a day). This successful treatment response, however, was accompanied by a severe depressive syndrome, which was characterised by a mixed anxiety-depressive mood, low self esteem, a complete loss of drive, and intermittent suicidal ideations. After switching from TBZ to tiapride, the patient recovered from depression, but her neurological status worsened significantly. The re-exposure to TBZ again ameliorated hyperkinesia, but provoked a depressive relapse. A comedication with reboxetine (6 mg/day), a new and selective noradrenaline reuptake inhibitor, finally led to a stable remission of the depressive symptoms within a week, without any worsening of the dystonic syndrome.

Tetrabenazine (TBZ) is known to act as a monoamine depleting and dopamine receptor blocking drug.1 In more detail, TBZ binds to and inhibits specifically the human vesicular monoamine transporter isoform 2 (vHvMAT2). Whereas the indolamine serotonin forms a similar affinity for both vHvMAT1 and hVvMAT2, catecholamines such as noradrenaline exhibit a threefold higher affinity for hVvMAT2. As these specific transporters are responsible for packaging monoamine neurotransmitters into presynaptic secretory vesicles for release by exocytosis, the inhibition of hVvMAT2 by compounds such as tetrabenazine thus results in consecutive noradrenaline depletion.

Alterations of noradrenergic neurotransmission—that is, a neuronal noradrenaline depletion—can therefore be postulated to form one major origin of TBZ induced depression.2 From this assumption, brain-specific catecholaminergic activity enhancers (CAEs) such as phenylethylamine have been shown to antagonise TBZ induced depression-like behaviour in rats.3 Modulating this altered noradrenergic neurotransmission pattern by the administration of selective noradrenaline reuptake inhibitors such as reboxetine may thus provide a new, specific, and fast acting tool in the management of depression caused by TBZ and related (neuroleptic) compounds.

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Spinal sulcal artery syndrome due to spontaneous bilateral vertebral artery dissection

In young adults vertebral artery dissection (VAD) is an important cause of brain infarction.1 A known mechanism is microtrauma due to abrupt head movements, for example, chiropractic manoeuvres. In addition a pathogenic role of connective tissue diseases, cystic media necrosis, fibromuscular dysplasia, migraine, and inflammatory diseases has been postulated.2 In VAD initial neck pain is often reported, which may be slight. Lesions caused by VAD are cerebellar or brainstem infarcts, unilateral or bilateral thalamic infarcts (top of the basilar syndrome), or infarctions in the posterior cerebral artery territory due to intra-arterial embolism or haemodynamic decompensation when collaterals are insufficient.3 Lesions of the cervical spinal cord are rare because of its good collateral supply.4 We report on a patient with a syndrome of the spinal sulcal artery (incomplete Brown-Séquard syndrome) caused by spontaneous bilateral VAD.

A 43-year-old man with a history of arterial hypertension presented with left sided numbness sparing the face, which had evolved suddenly while he was walking. In addition, he reported on dull right sided neck pain irradiating into the occiput, which had been initiated by a head rotation while he was working at a computer 2 weeks before. The neck pain had spontaneously ceased 6 days later. Neurological examination disclosed dissociated sensation defect on the left with an indistinct level around C4 to C6. Below this level on the left he had a marked hypalgesia and nearly a loss of temperature sense. The right limbs were warmer than the left ones. In addition, we found mild right sided motor system deficits. Cranial nerve function was intact, despite a right sided Horner's syndrome. According to chest radiography phrenic nerve function was preserved. Routine laboratory findings including CSF analysis were normal. The hemiparesis and the different temperature sensation in the limbs resolved completely within 3 weeks.

Tibal nerve somatosensory evoked potentials (SSEP) had regular N22 and P40 latencies and amplitudes. Central motor conduction time (CMCT) and transcranial magnetic stimulation was prolonged to the right abductor digitii minimi (9.2 ms) and tibialis anterior (23.1 ms). The CMCT to the left target muscles was normal. Duplex sonography showed increased flow velocity on the level of the cervical vertebrae 3 to 5 with a maximum of 214 cm/s in the right and 197 cm/s in the left vertebral artery. Colour mode showed irregular narrowings of the lumen indicating dissections.

Cervical MRI showed a spinal cord infarction at the level C2 (figure). The circumference and dorsal part of the cord were not affected. In digital subtraction angiography (DSA) both vertebral arteries had string signs in the V1 and V2 segments with collateral flow to the distal V2–4 segments via the threocerebral trunk (cervical ascendant artery) and the costocervical trunk also. The anterior spinal artery was incompletely contrasted by unilateral spinal branches of the right vertebral artery. They originated at the level of dissection. The intradural origins of the anterior spinal artery (ASCA) and the posterior spinal artery (V4 segment) were not visible.

Bilateral spontaneous VAD is not rare, but often missed. In most cases, microtrauma preceding the dissection can be recalled by the patients. Due to the mild mechanical impact, the action of predisposing factors might be postulated. Among these may be changing type III collagen, migraine, fibromuscular dysplasia, infections in the near past, and inflammatory vasculopathy.5 Magnetic resonance imaging with typical semilunar mammalian central artery and in addition magnetic resonance angiography (MRA) with complementary documentation of an angiographic narrowing or tapering occlusion have a high sensitivity and specificity in cases of internal carotid artery dissection.6 By contrast, mural haematomas of the VA especially in the V1 and the V3 segments are often not detectable by MRI. In cases of unclear non-invasive findings, DSA is still the method of choice.7

In addition to consecutive brain infarctions, cervical spinal cord infarctions and nerve root compression syndromes may occur in cases of unilateral or bilateral VAD. Probably as a result of the pial collateral network and the dual posterior spinal artery, spi-
A transient occlusion of these spinal branches is a likely consequence. This unusual type of arterial medullary supply may explain why VAD causes spinal cord infarction. Contrary to Pullicino, who described upper limb atrophies due to cervical spinal cord infarction involving the anterior horns, the present case shows a unilateral involvement of commissural, spinothalamic, pyramidal, and vasococontractor tracts. To our knowledge, such a spinal artery syndrome caused by bilateral spontaneous VAD has not yet been described. In conclusion, differential diagnosis of acute spinal symptoms in young adults should include spontaneous unilateral or bilateral VAD with cervical spinal cord ischaemia.

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Spanish families with cavernous angiomas do not share the Hispano-American CCM1 haplotype

Cerebral cavernous malformations are vascular malformations mostly located in the CNS. Their frequency is estimated close to 0.5% in the general population. Cerebral cavernous malformations occur as a sporadic or hereditary condition. From the Hispano-American population, familial forms were reported with a high frequency. CCM1, a hitherto unidentified gene mapping on chromosome 7 was shown to be involved in all families with cerebral cavernous malformations of Hispano-American descent with a strong founder effect. Around 50% of non-Hispano-American families showed linkage to CCM1 but no common haplotype was found. A recent study showed linkage of cerebral cavernous malformations to two additional loci. No Spanish family with cerebral cavernous malformations has been analysed so far.

We report herein a genetic linkage analysis conducted on nine Spanish families with cerebral cavernous malformations. All procedures were approved by an ethics committee. The families were unrelated and originated from different regions of Spain (south west (CVE2, 3, 4, 10, 17, 25), central (CVE24), south east (CVE28), and north east (CVE29). Seventy seven subjects including 55 potentially informative meioses and 12 spouses gave their informed consent. They were examined by a board certified neurologist, underwent cerebral MRI, and blood samples were taken. Magnetic resonance imaging was used to establish status for linkage analysis. Thirty four members had MRI diagnosis of cavernomas and were considered as affected. Among them, 14 experienced neurological symptoms (cerebral haemorrhage n=6, seizures n=8). Nineteen members with normal cerebral MRI were considered as healthy. Twelve members without MRI investigation had an unknown status.

Analysis of pedigrees was consistent with an

(A) Pedigrees of the nine families with cerebral cavernous malformations. Black symbols=symptomatic patients with cavernous angiomas on MRI; half filled symbols=asymptomatic members with cavernous angiomas on MRI; empty symbols=asymptomatic members with normal MRI; question mark=members with unknown status. (B) Comparison of the Hispano-American CCM1 haplotype and the haplotypes segregating with the disease phenotype within Spanish families. Polymorphic markers are shown on the left. Numbers indicate the sizes in base pairs. Primers used to amplify D7S2409 were different from those in the Hispano-American families resulting in a different size of the amplified fragment. M65B was not studied in the Hispanic-American families. Family CVE24 was not informative for D7S646. For families CVE17 and CVE29, the two haplotypes of the affected siblings are indicated. ND=not determined.
autosomal dominant pattern of inheritance (figure A).

Eight polymorphic microsatellite markers spanning the CCM1 interval were selected for linkage analysis. Four were chosen from the Genethon linkage map (D7S2410, D7S2409, D7S1813, and D7S558), and three from the Cooperative Human Linkage Center (D7S1813, D7S1789, D7S558). The last one (M65B) was identified by SL based on sequencing data of a bacterial artificial chromosome (Gembank HSAC0000865, BAC RG085C05). The length of the genetic interval flanked by markers D7S2410 and D7S689 is 4 centimorgans (cM). Marker distances between D7S2410 and D7S2409, D7S1813 and D7S1789, and D7S558 and D7S689 have been estimated to be 2.2 cM, and 1.8 cM, respectively.1 Oligonucleotide sequences are available through the Genome Data Bank (John Hopkins University, Baltimore). Genotyping and linkage analysis (LINKAGE package version 5.1) were performed as previously described.2

Lod scores were calculated in the five families having a sufficient number of potentially informative meioses—that is, CVE1 (eight), CVE4 (five), and CVE28 (seven). Lod scores higher than 0 were calculated for three families (CVE3, 4, and 28) for at least one marker. Due to incomplete informativity of three markers within family CVE4, lod scores did not reach the level of 3. In family CVE10, lod scores were close to 1 for four markers (D7S2410, D7S1789, D7S558, and D7S689). For family CVE25, lod scores were close to 0 for all markers. In this family, two affected and one asymptomatic sibling with normal standard MRI inherited the same haplotype from their affected father. When the data of all examined families were pooled, a maximum combined lod score of 5.92 was obtained for marker D7S2410 at α = 0.0001.

In seven families (CVE2, 3, 4, 10, 24, 25, and 28), all affected members inherited an haplotype that was not shared by their healthy relatives (figure B). In family CVE17, both affected siblings inherited a distinct haplotype from their affected mother. When the data of all examined families were pooled, a maximum combined lod score of 5.92 was obtained for marker D7S2410 at α = 0.0001.

None of the families shared a common haplotype (figure B). In addition, the extended Hispano-American haplotype was not segregating with the disease phenotype in any of the nine families including the four families with suggested linkage to CCM1. However, two out of nine families (CVE2 and 3), the D7S646 (185bp) and D7S558 (107bp) alleles segregating with the disease phenotype were identical to the ones observed in the Hispano-American haplotype. Consequently, we analysed the frequency of this combination of alleles within a panel of 80 haplotypes of 40 healthy white subjects. Frequency was 17% compared with 25% in our Spanish sample. Therefore, this finding might be attributed to a random distribution of these alleles.

In conclusion, linkage analysis of Spanish families with cerebral cavernous malformations did not show any evidence for Hispano-American haplotype sharing or a founder effect. Although our sample was limited in size and does therefore not formally exclude the possibility of a Hispano-American haplotype in additional Spanish families with cerebral cavernous malformations, this haplotype is more likely not predominant in Spain, and the strong founder effect seen in all published Hispano-American families with cerebral cavernous malformations might be specific for this population.

Hydrocephalus caused by metastatic brain lesions: treatment by third ventriculostomy

Metastasis to the brain occurs in 20%–40% of cancer patients.1 About 20% of these metastases are located in the posterior fossa, cerebellum, and brainstem. Metastatic disease to periventricular brain tissue can obstruct the production of cerebrospinal fluid (CSF) produced in the ventricles to the subarachnoid space where it is normally absorbed by arachnoid granulations. This typically causes an obstructive or non-communication hydrocephalus. A shunt has been customarily placed to drain CSF from a lateral ventricle through a pressure regulating valve and into the atrium or peritoneal or pleural cavity. However, even though this technique has been successful in relieving the hydrocephalus, it has a about a 50% chance of infection or failure from blockage.4

Another option for the treatment of obstructive hydrocephalus is third ventriculostomy, a minimal invasive endoscopic neuurosurgical procedure. In performing third ventriculostomy, a hole is created in the floor of the third ventricle, allowing CSF inside the ventricle to drain out to the CSF space surrounding the brain. Although third ventriculostomy has a low operative morbidity and a high probability of success, hydrocephalus is only commonly used on patients with aqueductal stenosis and the pediatric population. To avoid placing shunts in patients with inoperable metastatic brain tumours who typically have only a few months to live, we have offered the patients third ventriculostomy as a palliative procedure.

We performed third ventriculostomy on several patients with hydrocephalus due to metastatic tumours of the posterior fossa or thalamus. They typically presented with symptoms of acute hydrocephalus in addition to any local mass effect of the tumour. Postoperatively, five patients were relieved of hydrocephalic symptoms and follow up brain imaging studies disclosed decreased ventricular size. These five patients had a median hospital time of 6.5 days and median survival of 9.5 weeks after the operation. In one patient the hospital stay was prolonged by care of their primary disease. However, most of our patients who underwent this operation for hydrocephalus caused by other diseases were discharged from the hospital within 1 to 48 hours from the procedure. There were no operative complications. All five patients had no evidence of redevelopment of hydrocephalus up to the last visit clinic.

Two out of five patients had successful results from their third ventriculostomy. One patient (case 1) showed no change from his initial neurological exam after the procedure, but his mental status deteriorated on post operative day 6. Brain CT showed no change in the size of his ventricles compared with the scan obtained on the day of admission. The patient’s family requested comfort care only and the patient died 2 days later. In the second case (case 2) the patient had improvement in his neurological examination and ventricle size by CT scan immediately after the operation, but had recurrent symptoms of hydrocephalus 11 days later. After placement of another ventriculoperitoneal shunt, his examination returned to baseline.

Every patient except the person described in case 4 received brain radiation therapy after the palliative procedure. One patient (case 3) underwent a course of radiation treatment prior to the operation. Another (case 5) had radiation to her orbit in the distant past after enucleation for retinoblastoma. Even though previous radiotherapy may be considered a contraindication for third ventriculostomy by some authors, it did not seem to affect the success of third ventriculostomy in our patients. Carcinomatous meningiomas which could have caused a communicating hydrocephalus was not grossly evident on examination, on any of the brain imagings, or during endoscopy. However, tumours in contact with CSF space can also cause a communication hydrocephalus by raising CSF protein which can obstruct distal CSF space and arachnoid granulations.

Our success rate of about 70% (five of seven) for third ventriculostomy in periventricular metastatic disease is consistent with the results obtained with third ventriculostomy for adult patients with secondary hydrocephalus.5 This is comparable with the alternative shunting with an implanted shunt which has a year revision rate as high as...
Neuronal activity alters local blood flow in brain tumour adjacent to the activating cortex

Characteristics of blood flow in brain tumours have been studied extensively; these studies are important for diagnosis of malignancy and therapy monitoring. Our study is the first to consider how activity dependent changes of regional cerebral blood flow (rCBF) alter tumour blood flow in the brain tumour adjacent to the activating cortex.

Such an interaction between cortical blood flow and tumour blood flow may be of value for evaluating mechanisms of neurological symptoms associated with brain tumours.

Neuronal activation causes an increase of regional cerebral blood flow (rCBF) in the activating cortical area. Near infrared spectroscopy (NIRS) demonstrates the increase in rCBF during neuronal activity as increases in oxygenated haemoglobin (oxy-Hb) and total haemoglobin (total-Hb) with a decrease in deoxygenated haemoglobin (deoxy-Hb) & NIRS is an optical method to measure concentration changes of oxy-Hb, deoxy-Hb, and total-Hb (oxy-Hb+deoxy-Hb) in cerebral vessels by means of the characteristic absorption spectra of haemoglobin in the near infrared range.

In the present study, we measured changes of oxygenation and haemodynamics in the brain tumour adjacent to the activating cortex by means of NIRS. We found transient decreases in oxy-Hb and total-Hb in the tumour during neuronal activation, suggesting that the local blood flow of the tumour was decreased by a transient increase of rCBF induced by neuronal activation.

The patient was a 35 year old right handed man who presented with complaints of headache and dizziness. A neurological examination showed no abnormalities and a decline in language functions. A postcontrast CT showed a well defined large enhancing tumour (4x5 cm) compressing the left frontal lobe. Computed tomographic angiography showed that the branches of the left middle cerebral artery supplied the tumour (figure A). The patient underwent a left frontal craniotomy for removal of the tumour; the pathological diagnosis was meningioma. The NIRS measurement was performed before the operation.

We measured haemodynamic changes in the brain tumour during neuronal activation in the left frontal lobe induced by cognitive

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### Table 1 Clinical characteristics of patients who underwent third ventriculostomy for obstructive hydrocephalus

<table>
<thead>
<tr>
<th>Case No</th>
<th>Age (y), Sex</th>
<th>Diagnosis</th>
<th>Result*</th>
<th>Postoperative stay in hospital(days)</th>
<th>Survival time (weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>70, M</td>
<td>Lung mixed adenocarcinoma and squamous cancer metastasis to thalamus</td>
<td>Improved</td>
<td>17</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>46, F</td>
<td>Ovarian adenocarcinoma metastases to cerebrum and medulla</td>
<td>Improved</td>
<td>9</td>
<td>13</td>
</tr>
<tr>
<td>3</td>
<td>38, F</td>
<td>Breast ductal carcinoma metastases to brainstem and cerebellum</td>
<td>Improved</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>4</td>
<td>75, M</td>
<td>Rectal adenocarcinoma metastasis to cerebellum</td>
<td>Failed</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>39, F</td>
<td>Breast adenocarcinoma metastasis to cerebellum</td>
<td>Improved</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>6</td>
<td>60, M</td>
<td>Lung adenocarcinoma metastasis to thalamus</td>
<td>Failed</td>
<td>6</td>
<td>6*</td>
</tr>
<tr>
<td>7</td>
<td>64, M</td>
<td>Osteopagial carcinoma metastatic to cerebellum</td>
<td>Improved</td>
<td>7+</td>
<td>1+</td>
</tr>
</tbody>
</table>

*Results are considered improved if the patient had resolution of symptoms and follow up imaging showed hydrocephalus improved or resolved.

†Patient is currently alive.


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The patient was a 35 year old right handed man who presented with complaints of headache and dizziness. A neurological examination showed no abnormalities and a decline in language functions. A postcontrast CT showed a well defined large enhancing tumour (4x5 cm) compressing the left frontal lobe. Computed tomographic angiography showed that the branches of the left middle cerebral artery supplied the tumour (figure A). The patient underwent a left frontal craniotomy for removal of the tumour; the pathological diagnosis was meningioma. The NIRS measurement was performed before the operation.

We measured haemodynamic changes in the brain tumour during neuronal activation in the left frontal lobe induced by cognitive
tasks. We monitored concentration changes of oxy-Hb, deoxy-Hb, and total-Hb, using an NIRO-500 instrument (Hamamatsu Photonics KK, Japan). The optodes were placed at an interoptode distance of 3.5 cm on the left forehead so that the centre of the two optodes was placed at the centre of the tumour. With an interoptode distance of 4 cm, correlations of oxy-Hb and total-Hb were examined by NIRS and rCBF measured by PET suggested that the reliable penetration depth of near infrared light into brain tissue is about 1.3 cm; thus the present NIRS measurement area was restricted in the tumour. The patient was seated and had his eyes open during the NIRS measurement. Informed consent was obtained from the patient.

To activate the left frontal lobe, we used the following four tasks: (1) semantic verbal fluency, which entails naming as many items in a semantic category (for example, animals) as possible; (2) confrontation naming, which involves naming ordinary items presented by the tester; (3) backward digit span, a working memory task which involves reporting of digits (2 to 8) in the reverse order; and (4) ELA task, which entails producing a short descriptive passage aloud. The speech responses of the patient to the tasks were normal.

Figure B shows an example of changes in oxy-Hb during the naming task. After the beginning of the task, oxy-Hb and total-Hb decreased to negative values during the task, and deoxy-Hb also decreased. These changes returned to the control level gradually after the end of the task. The other tasks also caused similar changes of oxy-Hb, total-Hb, and deoxy-Hb.

The rCBF in the left frontal lobe is generally increased by all the tasks used in the present study. Indeed, our NIRS activation study using the cognitive tasks showed increases in oxy-Hb and total-Hb in the left frontal lobe in most normal adults—for example, increases in oxy-Hb and total-Hb—were found in 92.5% of young adult subjects (mean (SD) 28.8 (4.4) years) during the episode. These increases in oxy-Hb and total-Hb were found only during the tasks; consequently, these changes were probably not due to changes in systemic blood pressure, which can alter tumour blood flow. Based on these assumptions, we suggest that the increase of rCBF in the left frontal lobe induced by the tasks stole the local blood flow of the brain tumour through the cortical branches, leading to the decrease of local blood flow in the tumour. The present report suggests that activity-dependent increase in rCBF can steal blood flow from the adjacent tissues including non-activating cortex. Recent NIRS activation studies have shown that cognitive tasks cause decreases in oxy-Hb and total-Hb in the left frontal lobe in some normal subjects; these decreases indicate a decrease in rCBF. Although the physiological mechanisms of the decrease in rCBF during neuronal activity have not yet been elucidated, we hypothesize that a stealing of blood flow is one of the mechanisms. The present report supports this hypothesis.

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Migraine aura masquerading as Balint’s syndrome

Migraine is a common neurological disorder with a prevalence of 0.5% to 2% in the general population. In one fourth of total migraineurs, headache is preceded by an aura.1 We describe a patient with recurrent episodes of migraine in whom headache was preceded by a constellation of visual symptoms, which constituted salient components of Balint’s syndrome. This syndrome, consisting of a triad of simultagnosia, optic ataxia, and oculomotor apraxia, is seen with bilateral lesions of occipitoparietal cortices affecting connections between visual cortical regions and the frontal eye field.2

A 29 year old female teacher presented with an 8 year history of paroxysmal alternating hemianomic and throbbing headache which was often associated with nausea, photophobia, and occasionally vomiting. Headache used to last for about 4 to 18 hours and would respond to either ergot drugs or sumatriptan, especially if taken before the onset of the episode. Occasionally these visual symptoms were not followed by headache. The patient would not lose contact with the environment during or after the visual symptoms. Her mother and two younger sisters were also having paroxysmal episodes of common migraine.

Her general physical and neurological examination in between the episodes was unremarkable. Neurological symptoms during the aura disclosed that she was unable to see simultaneously all the objects in the visual field (simultagnosia). She did omit several words while reading a paragraph. However, she could comprehend and read each and every word individually. On being shown a complex picture comprising multiple subunits she was not able to comprehend and perceive the entire picture but was able to perceive parts of the picture individually (seeing in piecemeal).

These aforementioned features were consistent with simultagnosia. Besides simultagnosia, she had optic ataxia as evidenced by her inability to coordinate hand eye movements. Optic ataxia was tested as follows: each eye was tested separately and the hand ipsilateral to the eye being tested was used. The target stimulus was a 5 mm long pin with a width 5 mm wide placed at prospected locations. The patient was asked to touch this pin with her index finger without shifting her gaze from the fixation point. The patient had difficulty in performing this test but had no problems in reaching out to her own body parts or an auditory stimulus with her eyes closed. These features were consistent with optic ataxia. Moreover, gaze apraxia was evident by her inability to look at an object on command. However, she could do it spontaneously. In addition, she had impaired smooth pursuit and voluntary saccades in all directions. Reflex eye movements were normal. Visual acuity during the episode was 6/6 bilaterally. Visual field was normal during the episode as demonstrated by the confrontation method. Ophthalmological examination, including perimetry performed during a symptom free period, was normal.

There was no clinical evidence of Gerstmann syndrome, prosopagnosia, object agnosia, or colour agnosia. Her cranial CT and magnetic resonance angiography were unremarkable. Electroencephalography was also non-contributory. The frequency of visual aura symptoms and headache decreased considerably after the patient was started on flunarizine at a daily dosage of 10 mg at bed time. The visual impulses, after being recorded by the primary visual cortex (Brodmann area 17), are interpreted and integrated in visual association areas 18 and 19. Brodmann area 19, in turn, is connected with the angular gyrus and frontal eye field via association fibres. Any lesion in the visual association areas or their connections would result in impaired integration of visual impulses despite normal visual acuity.

The visual symptom complex in this case possibly represents an aura of migraine. The pathogenesis of migraine aura has been a debatable issue.3 In this case it is suggested that the parasympathetic process of migraine aura results in a disconnection syndrome by...
involving visual association areas and their
association pathways. Optic ataxia, gaze
apraxia, and simultagnosia seem to represent
a dissociation of visual information from the
frontal eye field and dorsal parietal regions.

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“Can’t you use another vaccine”? postrabies vaccination encephalitis
A healthy 39 year old man was bitten on the
ankle by his own apparently normal dog. After
the incident the dog disappeared into the
forest and was not seen again. Three days later
the patient was seen at a provincial hospital in
Vietnam and started on an alternate day regi-
men of suckling mouse brain postrabies expo-
sure vaccine (SMBV). After the second
dose, he felt unusually lethargic although he
was still able to work. After the third dose, he
became unrousable, and was transferred to the
Centre for Tropical Diseases, Ho Chi Minh
City, the referral hospital for infectious dis-
 ease in southern Vietnam. On admission, he
was afebrile, confused, had slurred speech, and
his Glasgow coma score was 13. He had mild
spastic weakness of his left face, left arm, and
both legs. Full blood count and results from
routine biochemistry and chest radiography
were all normal. The CSF: blood glucose ratio
was 0.47 (63/140 mg%), the protein content
was raised (78 mg/dl), and there was one
lymphocyte/ml in the CSF. Screens for malaria
toxoplasmosis, cryptococcus, and neurocyst-
oses in southern Vietnam. On admission, he
deteriorated with a
Glasgow coma score of 10, and was inconti-
nent of urine and faeces with generalised
spastic paraparesis. Methylprednisolone (500
mg/ day) was given for 5 days followed by a
reduced dose (10 mg/ day) for 4 weeks followed by a
reducing course of prednisone for a presump-
tive diagnosis of postvaccination encephalitis.
The SMBV was stopped. Within 72 hours of
starting steroids there was a dramatic im-
provement in his neurological state. An MRI
examination performed 4 weeks later showed
a marked decrease in both size and number of
brain lesions and no new lesions (figure B).
After 6 weeks he was discharged talking, eat-
ing, walking, and continent but with some
persistent emotional liability and mild
memory impairment. A follow up MRI ex-
amination 5 weeks after discharge showed further
improvement, apart from minor
abnormalities in the basal ganglia, and general-
ised increase in ventricular size, consist-
ent with residual cerebral atrophy.

Rabies is caused by an RNA virus, a mem-
ber of the Rhabdoviridae family, it infects
mammals and can be transmitted to humans
by contact, generally from an animal excre-
ting the virus in the saliva. Rabies manifests as
an acute encephalomyelitis, the development
of which is almost invariably fatal. The distinc-
tion between rabies and postvaccine
cephalitis is difficult and may be helped by
antigen detection via a skin biopsy; however,
this technique is not available in Vietnam.1
Paralytic rabies could not be excluded in this
patient and hence steroids were not used ini-
tially. Steroids have been reported to increase
mortality in experimental animals with ra-
bies, and it has been suggested that they may
abrogate the immune response to the postex-
posure vaccine, thus precipitating uncontrol-
trolled rabbies.2

There are three types of postexposure vac-
cine in use world wide. The Simple type (STV)
is obtained from inactivated virus pre-
aped on adult animal nerve tissue; it is inex-
pen sive and relatively easy to produce. In
India 3 million people receive postexposure
courses of STV (phenolised sheep brain)
antirabies vaccine each year.3 These produce
neurological reactions, including postvacci-
nation encephalomyelitis, in up to 1 in 220
courses, with a 3% mortality.1 Clinical forms
include a reversible mononeuropathies multiplex,
and meningeoencephalitic and encephalomy-
elitic reactions. Myelin basic protein and
related neural proteins from the nervous
tissue of the animal on which the virus
was cultivated stimulate an autoimmune reaction
in the human nervous system.

Tolerance has been improved by the devel-
opment of the suckling mouse brain vaccine
(SMBV).4 The attenuated virus is cultured on
immature mouse brain tissue, which contains
little myelin, thus reducing the risk of complica-
tions. SMBV is inexpensive (US$1.5 per
treatment course) and easily manufactured
locally; it is the most widely used postrabies
vaccine in Vietnam. Rare neurological reac-
tions do occur with SMBV, Complications of
the CNS have been reported to occur after
vaccination with an incidence of 1:27000
treated people, with a 22% mortality5
The mortality was particularly high (90%) if
there was extensive CNS involvement. The
type of vaccine available is the human diploid
cell tissue culture vaccine (HDCV), which
are both safe and efficacious. However, the recom-
ended regimen is not affordable in most
developing countries.

When we approached the Rabies Labora-
tory, Ministry of Agriculture and Fisheries,
United Kingdom for advice in this case their
response was: “why do you use the SMBV,
can’t you use another vaccine”. Worldwide
about 10 million people each year receive
rabies vaccine after exposure; at the Centre
for Tropical Diseases we treat 3000 people
with dog bites annually. The cost of an
HDCV in Vietnam, administered in its
present regimen (1ml given for 5 days on days
0, 3, 7, 14, and 28 with an optional booster on
day 90) is US$ 125, making the use of this
vaccine unaffordable.

This is the first report to show the demyeli-
nating CNS lesions on MRI, and their
resolution after steroid therapy. It is relatively
rare for patients to survive if they develop
severe CNS effects after postexposure rabies
vaccination. Although the incidence of reac-
tions to SMBV is very much lower than STV,
this report confirms that it does still occur.
Both SMBV and STV are widely used
together throughout the developing world, and
would be the vaccine administered to travellers
exposed to animal bites in such countries.
This case stresses the need for high dose ster-
oids in postexposure vaccine encephalitis and
the urgent need for the development and deplo-
moy of a safe, and critically, an
affordable postrabies exposure vaccine regimen.

The economic low dose multisite intradermal
regimen using the HDCV provides an ex-
ample of how this goal may be achieved although
it is not yet widely accepted. Such a vaccine
regimen (0.1 ml HDCV given at multisite
injections on days 0, 7, 28, and 90) could be
made affordable, and offers excellent protec-
tion without the risks of postexposure
immune mediated edematitis.6

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Brain MRI in May 1997. (A) T2 weighted
image showing multiple areas of high signal in the
cerebral white matter. Bilateral subcortical
and periventricular lesions are seen. (B) Brain
MRI in July 1997, T2 weighted image shows
resolution of the white matter lesions.
Leukoencephalopathy associated with khat misuse

The leaves of the tree Catha edulis, or khat (also qat and kat) are chewed by a large proportion of the adult population of the Yemen, and throughout Saharan and sub-Saharan Africa. The leaves are also chewed by members of the Yemeni and Somali community in the United Kingdom. The psychoactive constituents of khat are cathin (d-norcoephedrine), cathine, and cathinone (an alkaloid with structure resembling ephedrine and amphetamine) and users report a mild euphoria similar to that of amphetamine. Khat is acknowledged as a precipitant of psychosis and has also been reported to cause cognitive impairment. There are no previous reports of leukoencephalopathy in association with khat or amphetamine misuse; there was no evidence of acute inflammation, vasculitis, or infarction.

While undergoing rehabilitation there has been slow improvement in his cognitive and locomotor function. After 1 year he is able to open and close his eyes, occasionally verbalise, localise pain, and obey simple commands. His plantar are flexor but he has persistent grasp and palomental reflexes. His nutrition is maintained by gastrostomy and he has an indwelling catheter.

The clinical presentation, EEG, and MRI findings suggest a rapidly progressive leukoencephalopathy. There are no previous reports of leukoencephalopathy in association with khat or amphetamine misuse; it has, however, been reported in association with other recreational drugs taken by mouth or inhalation. An alternative for this man's presentation is a necrotising vasculitis, a well described complication of oral amphetamine misuse. The clinical features, MRI appearance, brain biopsy, absence of haemorrhage, and lack of response to steroids make this unlikely. The likely precipitant of this man's illness seems to be the use of khat. A drug screen on admission was negative, and his family denied misuse of other drugs. It remains possible that the sample of khat chewed by this man was contaminated. We are unaware of any previous reports of khat misuse with severe neurological deterioration; previous cases may not have been investigated or reported. In reporting this case our intention is to alert others to a possible complication of the misuse of this drug. Evidence of other cases would provide a powerful argument for the restriction of import and sale of khat.

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myelinated fibres were markedly decreased. The small vessels in the endoneurium (figure A). Some vessels had focal necrosis of the wall. The small vessels in the endoneurium. (bar=30 µm). (B) Most of myelinated fibres are undergoing axonal degeneration. Many macrophages containing myelin debris infiltrate the endoneurium. (bar=20 µm). (A) Sural nerve (toluidine blue staining) showing epineurial vessel surrounded by mononuclear cell infiltrates. Note fibrin deposition (arrow) and necrosis in media. (bar=20 µm). (D) Most of myelinated fibres are undergoing axonal degeneration. Many macrophages containing myelin debris infiltrate the endoneurium. (bar=80 µm).

The initial nerve conduction study showed severe diminution or absence of compound nerve action potentials (SNAPs) in median, ulnar, and sural nerves bilaterally. Electrophysiological studies of the affected muscles showed moderate neurogenic changes, but there were no fibrillation potentials except in the left anterior tibialis muscle. Sural nerve biopsy was performed. Epineurial vessels were surrounded by mononuclear cell infiltrates (figure A). Some vessels had focal necrosis of their wall. The small vessels in the endoneurium and epineurium showed sludging of red blood cells. The densities of large and myelinated fibres were markedly decreased (figure 1B). Total number of large myelinated fibres were markedly decreased (figure 1B). Total number of large and small myelinated fibres were markedly decreased (figure 1B). Total number of large and small myelinated fibres were markedly decreased (figure 1B). Total number of large and small myelinated fibres were markedly decreased (figure 1B). Total number of large and small myelinated fibres were markedly decreased (figure 1B). Total number of large and small myelinated fibres were markedly decreased (figure 1B). Total number of large and small myelinated fibres were markedly decreased (figure 1B).

Oral prednisolone (30–50 mg/day) for 4 weeks reduced the erythrocyte sedimentation rate and C reactive protein, but not the serum titre of cold agglutinins; neither was there any improvement of symptoms. He received massive dose intravenous corticosteroid therapy. This moderately improved the muscle strength and sensory disturbance. Follow up nerve conduction studies (71 days after the initial study) suggested conduction block of the right median nerve on the forearm (CMAP, duration at the wrist: 2.76 mV, 8.4 ms; CMAP, duration at the elbow: 1.87 mV, 8.8 ms), whereas CMAP could not be elicited in the initial study. We adopted the following criteria to define conduction block: <15% change in duration and >20% fall in negative peak amplitude between proximal and distal sites by percutaneous supramaximal stimulation of motor nerves. As the conduction block might delay smooth recovery of symptoms, Double filtration plasmapheresis was performed four times. After the second plasmapheresis, dysaesthesia and muscle strength improved remarkably. The titre of cold agglutinins was reduced to 1:64. The motor nerve conduction velocity (MCV) of the right median nerve likewise improved (pre-treatment: 40.0 m/s, post-treatment: 57.0 m/s). Double filtration plasmapheresis was followed by oral azathioprine (50 mg/day) with tapering of steroid. He was discharged on prednisolone (20 mg/day). In the subsequent 4 years, he had mild exacerbation of dysaesthesia that responded to intermittent steroid therapy.

Characteristic features of the present case are as follows: (1) subacute onset of mononeuropathy multiplex; (2) necrotising vasculitis with macrophage infiltration in the endoneurium; (3) probable conduction block in the median nerve; (4) increased concentrations of serum titres of cold agglutinin; and (5) marked response to plasmapheresis. Extensive investigations for other causes of cold neuropathy were negative except for an increased serum concentration of cold agglutinins, which strongly suggests that cold agglutinins may play an important part in the induction of neuropathy in this case.

Six patients with neuropathy associated with cold agglutinins have been reported including our patient. Cold agglutinins are cold reactive autoantibodies that react with the antigenic determinant termed Pr component. However, necrotising vasculitis has never been reported in neuropathy with cold agglutinins. This is the first demonstration of vasculitic neuropathy with cold agglutinins. Although the mechanism for neuropathy with cold agglutinins is unknown, mechanisms similar to those in cryoglobulinaemic neuropathy have been postulated. The hypotheses are (1) immunologically mediated demyelination; (2) ischaemic injury secondary to sludging or agglutination of red blood cells in the vasa nervorum; and (3) an associated vasculitis. The present case, we have confirmed the necrotising vasculitis and probable conduction block. Pathophysiological explanations for association of vasculitis and conduction block may be as follows. Firstly, conduction block may occur as a consequence of nerve ischaemia due to small vessel occlusion. There have been reports of conduction block occurring in vasculitic neuropathy which support this possibility. Secondly, humoral factors including cold agglutinins may induce immunologically mediated demyelination in the peripheral nervous system. Taken together, neuropathy with cold agglutinins may involve immunologically mediated demyelination, microcirculation occlusion, and vasa nervorum vasculitis. The diversity of pathomechanisms may come from the difference target antigens recognised by cold agglutinins. Plasmapheresis proved effective in all cases. These findings strongly suggest that humoral factors including cold agglutinins may play an important part in the induction of neuropathy with cold agglutinins. We recommend plasmapheresis as first choice treatment for neuropathy associated with cold agglutinins.

We thank Dr Gerard Salazar for critical reading of the manuscript, Ms M Teshima and N Hirata for their technical assistance, Dr S Kusunoki (Department of Neurology, Institute for Brain research, University ofTokyo) for analyses of antibodies to gangliosides, and Mr H Moru (Division of Blood Transfusion Medicine, University ofKagoshima) for characterization of cold agglutinin.
The cholinergic hypothesis of Alzheimer’s disease: a review of progress

I read with interest the review of Francis et al regarding the progress of the cholinergic hypothesis of Alzheimer’s disease. They mentioned that donepezil produced improvement or no deterioration in more than 80% of patients, and that such responses should be viewed positively considering the progressive, degenerative nature of the disease. Various donepezil manufacturer’s medical representatives presenting data from a clinical study also commonly use this statement. However, this only partially reveals the truth. In fact, the same study produced improvement or no deterioration in 59% patients on placebo. I think that the beneficial effect of donepezil in particular clinical trials should always be critically reviewed in comparison with placebo. In addition, as both 24 week placebo controlled donepezil trials performed so far excluded patients with behavioural disturbances, my impression is that the positive effect of donepezil on the symptoms of behavioural disturbances still remains controversial. In fact there are reports that donepezil might induce behavioural disturbances in patients with Alzheimer’s disease. The advice I would be extremely cautious about prescribing donepezil to patients with Alzheimer’s disease accompanied by behavioural disturbances. Finally, donepezil was never investigated in a 36 week randomised double blind study as was mentioned in the review. The authors are probably referring to the randomised 24 week double blind placebo controlled trial with an additional 6 week single blinded placebo phase.

The authors reply:
We thank Professor Babic for the letter, which raises several interesting points. We agree that it may be more helpful to put the results attributed to treatment with donepezil in the context of the placebo response. In general, looking at this as a class effect in relation to several compounds, the picture emerging is that about twice as many people obtain a response to active treatment as to that with placebo. The high placebo response is a common factor in most studies in this field and is worthy of some explanation in its own right. Although it seems that these studies compare drug treatment with that of a placebo (one treatment against no treatment), the reality is that it is a comparison of patients receiving two treatments against other patients who are receiving one form of treatment. The additional treatment regime is, of course, the care and attention that they receive by being part of the clinical study, which often seems to have an impact, not just on the patient but also on their main carer or carers.

As far as behavioural disturbances are concerned, however, our review was making the point that evidence from previous clinical trials to suggest that cholinomimetic drugs as a whole may have a beneficial effect on some non-cognitive behavioural symptoms. This has now been reported for at least two cholinesterase inhibitors, and two muscarinic agonists. In particular, a clear link is emerging between psychotic symptoms and cholinergic dysfunction. Thus, Boddick et al have shown that the M1/M4 agonist xanomeline causes a dose-dependent reduction in hallucinations, agitation, and delusions in a 6 month randomised double blind placebo controlled, parallel group trial. In addition, Cummings and Kaufer have shown that the cholinesterase inhibitor, metrifonate, was also shown to reduce the number of hallucinations in a 26 week randomised, double blind, placebo controlled safety and efficacy study in patients with Alzheimer’s disease. Further support for a link between acetylcholine and psychosis derives from postmortem data showing that the activity of choline acetyltransferase in the temporal cortex of patients with Lewy body dementia was lower in those patients with hallucinations than in patients without this feature. Finally, in animals the partial M1/M4 agonist (5SR,6R)-[3-propyloxy-1,2,5-thiadiazol-4-yl]-1-sazicyclo[3.2.1]octane produced a preclinical profile suggestive of antipsychotic efficacy and that the psychomimetic NMDA receptor antagonist ketamine (when administered at subanesthetic doses) reduced brain concentrations of acetylcholine. Thus, on the basis of both clinical and preclinical data, a clear rationale is emerging for prescribing cholinomimetic agents for treating the non-cognitive behavioural symptoms associated with dementia, particularly psychosis.

Professor Babic is also correct in identifying two of the studies referred to as the 30 week randomised multicentre placebo controlled parallel group studies, which included a 24 week double blind treatment phase. We are grateful for your correspondence to providing us with the opportunity to clarify these points.

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BOOK REVIEWS


The neuropathies of diabetes are common (as the chapters in this book repeatedly remind us) and can be very disagreeable. Symptomless neuropathy underlies foot ulceration and sepsis as the commonest clinical consequence of diabetic neuropathy but other extremely unpleasant disorders range from exceptionally severe pain to the whole range of problems resulting from autonomic failure. This book comprehensively covers every aspect of the subject, systematically (and at times exhaustively) from its epidemiology and pathogenesis (exhaustingly) to structural, functional, and clinical problems and their treatment. Most of the authors are well known in the field and their accounts are up to date and authoritative.

Unfortunately, struggle as they might, all authorities have difficulty in defining what they mean by diabetic neuropathy, in regard, understanding of this complication both in clinical and pathological terms, as well as with regard to treatment, lags far behind that of the other classic diabetic complications, nephropathy and retinopathy. Even its classification presents problems and attempts to do so are found in four different chapters, describing four classifications. Repetition is an unfortunate feature of this book and—quite apart from the confusion over classification—aspects of pathogenesis, structural changes, epidemiology, diagrams, and some reference to treatment (for example, that of pain) appear repeatedly in different chapters in greater or lesser detail.
This is certainly a book for the specialist and not at all (as the preface suggests) for the family practitioner. There are good reviews of nerve structure, causation, and treatment of painful neuropathies and focal neuropathies. The comprehensive survey of the Diabetes Control and Complications Trial (DCCT) shows in detail the only treatment which is truly effective (diabetic control); and the lengthy description of aldose reductase inhibitor trials establishes that, even after more than two decades of investigation, further trials are still needed.

Clinical evaluation of somatic and autonomic neuropathies are useful and also, to some extent, comprehensive but lack specificity—that is, normal values for simple tests are difficult to find. The huge subject of the diabetic foot is covered in these chapters and “the impact of micro and macrovascular disease” is compressed into the last nine pages of the book.

The bibliography is important and often very up to date with references ranging from 33 to 283 per chapter. If this book is at times confusing, this reflects the confusion regarding the nature and treatment of the diabetic neuropathies as much as the overlap and repetition found in its different chapters. It is a book of reference for the specialist who will be well served by the comprehensiveness of some of its reviews and their assembly of the appropriate literature.

PETER WATKINS


The quest for a means of accurate localisation of structures during neurosurgery has taxed the minds of clinicians from early in the history of the specialty, starting with Zerom’s encyclopaedia more than a century ago. Just as the solution to the mariners’ problem of determining longitude from which it partly takes its name, neuronavigation (“the surgeon’s sextant”) has relied on the advent of new technologies to provide solutions to an age old puzzle.

**Advances In Neuronavigation begins by tracing the history of stereotaxis from a Cartesian coordinate system devised by Clarke and Horsley at the beginning of this century, through ventriculography, stereotactic brain atlases, and CT/MR frame based stereotaxis. The final part of the first section discusses the roots of image guided frameless stereotaxis through the integration of high speed graphics computers, informatics, biotechnology, and robotics.**

The remainder of the text is divided into four sections. The first concerns the creation of maps from CT, MRI, MRA, PET, and various types of functional imaging. The following section discusses clinical applications of stereotaxis, beginning with different authors’ experiences of their own favoured frames, the biopsy of difficult lesions such as those in the brainstem or posterior fossa, and finally experience with different image guidance systems, and their integration with the operating microscope and endoscope. There then follows a series of chapters devoted to radiosurgery, and to image guidance in epilepsy and functional surgery. The final section is entitled *Frontiers In Neurosurgical Navigation* and considers, among other topics, intraoperative MRI, telesurgery in neurosurgery, and robotics.

The incorporation of new technology is likely to alter surgical practice radically over the coming decade and equipment that seemed at the cutting edge of technology only a few years ago, such as the mechanical arm, has already passed into near obsolescence at a bewildering rate. This volume provides an excellent account of the developments which have occurred in neuronavigation, and a thought provoking insight into the wider applications of equipment of which many of us use only a fraction of the potential capability. The title of the book should perhaps have included the word cranial, as there is almost no discussion of the impact that this technology has had in surgery of the spine. This aside it is an excellent book although, like the technology it chronicles, one which is likely to date quite rapidly.

ROBERT MACFARLANE


The title and back cover of the latest addition to *Neurology Lite* texts contains the usual proclamations. “Concise, key topics, revision aid, essential, review...” the well trailed soundbites demanded by the consumer in the increasingly competitive market “of wider - learn more” books. This book, however, is unusual and distinct. Unlike many rivals it is not an A5 facsimile of a superior parent A3 reference tome. Brevity, so essential to the success of an overview work, has sacrificed neither clarity nor clinical relevance. The strength of *Key Topics in Neurology* owes much to the author’s ability to negotiate skillfully the compromises necessary for a successful distillation of a large and complex field. He has not shied from wholesale culling of neurological ballast. The allied ability to distinguish and highlight the salient and relevant from the obscure and historical allows this small book to be surprisingly thorough in its coverage and topicality. There is sufficient up to date information on most areas of neurology such that this book would be useful for specialist registrars albeit without the detail or embellishment they seek. In terms of the aims of this book such observations must be regarded as complimentary.

My limited criticisms relate to details of layout and presentation. I found the exclusive alphabetical arrangement of chapters mildly disorientating in that, for example, *History taking in Neurology* is to be found at p 131. Similarly, the absence of diagrams and tables is an unexpected omission as I would imagine that this would have complemented the overall style of the book. These are minor gripes of what in print largely matches the sleeve hype and with a price tag of just £27-30 the book will be welcomed by undergraduates through to specialist registrars.

SIDDHARTHAN CHANDRAN

**Correlation**

K Sudo, N Fujiki, S Tsuji, M Ajiki, T Higashi, M Niino, S Kituchi, F Moriwaka, K Tashiro.

Focal (segmental) dyshidrosis in syringomyelia. *J Neurol Neurosurg Psychiatry* 1999;67:106-8. During the editorial process the footnote to table 1 (p 107) was wrongly transcribed. The last line—¶p value for each pair of items: hyperhidrosis v normohydrosis 0.0007; hypohydrosis v normohydrosis 0.7282; normohydrosis v hypohydrosis 0.0012 should read—¶p value for each pair of items: hyperhidrosis v hypohydrosis 0.0007; hypohydrosis v normohydrosis 0.7282; normohydrosis v hypohydrosis 0.0012.