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 temporal lobe epilepsy being considered for anterior temporal lobectomy. In these cases it is used to determine cerebral dominance for language,1 to assess the risk of severe postoperative amnesia,2 and to predict postoperative hemispheric specific memory changes.3 More recently, the use of the IAP has been extended to complimentary EEG localisation and radiological data by lateralisering temporal lobe dysfunction.

Recent reports have highlighted a hitherto unrecognized role in patients with refractory frontal lobe epilepsy being considered for frontal lobectomy. Specifically, observation of behavioural function during the period of the ablation may provide useful information about the integrity of the contralateral frontal lobe. This is particularly relevant in those candidates with a history of cerebral trauma in which damage to the bifrontal lobe is known or suspected. A review of the IAP studies performed on patients with temporal lobe epilepsy in our comprehensive epilepsy programme (1991–8) suggests that the emergence of frontal lobe behavioural features is common in patients in whom the astology leads to the suspicion of bifrontal compromise (for example, a history of traumatic head injury). By contrast, these features rarely appear in cases of non-traumatic astology, in which the integrity of frontal lobe systems is presumed. Although it remains an incidental finding in the context of determining the suitability of a candidate for anterior temporal lobectomy, this outcome may have potential implications for the selection of patients for frontal lobectomy.

We report a case of frontal lobe epilepsy secondary to a traumatic head injury. Out of concern for untoward postoperative behavioural change, we employed the IAP in an attempt to predict the risk of a frontal lobe syndrome.

A 39 year old man had a 23 year history of severe refractory epilepsy. The seizures postdated a road traffic accident at the age of 12 years when he sustained a head injury with an ill defined period of loss of consciousness. Seizures commenced within months of that injury and, although initially well controlled, became refractory within a few years. The seizures type included staring spells, violent tonic-clonic seizures, and atonic drop attacks. He had complications from his epilepsy including a fracture jaw, two episodes of severe burning due to seizures while showering, multiple episodes of postictal confusion and probable postictal psychomotor, an lung abscess secondary to aspiration, and episodes of status epilepticus. Interictal EEGs showed bilateral generalized spike and wave discharges at around 2 Hz-2.5 Hz with some mild increase in bilateral slow activity and no convincing evidence of electrophysiological focalisation. Video EEG monitoring showed apparent generalised seizures without any focal onset on scalp EEG. Brain MRI disclosed a well defined atrophic lesion involving the frontal lobes, which was considered likely to be post-traumatic in origin. Interictal FDG PET and HMlO SPECT disclosed hyperfusion in the left anterior frontal region commensurate with the abnormality shown on MRI. Although his electroclinical pattern was suggestive of symptomatic generalised epilepsy, because of the left frontal lesion, seizure onset from that region was considered likely.

Neuropsychological examination, his general cognitive level was normal. At a behavioural level, however, he presented as very puerile in manner with a very rigid, inflexible cognitive style. The neuropsychological opinion was of a mild frontal lobe syndrome consistent with the history of traumatic head injury. There was no current evidence of psychiatric disorder. Although having successfully passed his final year of secondary school (together with several courses of advanced education), he had remained unemployed due to his seizures. He was socially isolated and his interpersonal relationships were limited.

He had severe life threatening epilepsy with the surgical option the only remaining avenue of treatment. However, as surgical management would involve resection of the left frontal lobe against a background of traumatic head injury and the possibility of more generalised frontal lobe syndrome, a left hemispheric IAP was performed. Sodium amytal (125 mg) was administered via a slow hand injection. Of relevance, no crossflow into the contralateral anterior cerebral artery via the anterior communicating artery was present (as assessed by a separate injection of contrast medium). The injection was accompanied by a dense right hemiplegia and global aphasic arrest. Resolution of language was characterised by a dense perseveration of counting which could not be influenced by the examiner. Despite normal comprehension, he showed severely impaired capacity for motor regulation (apart from upper limb movements), together with marked behavioural disinhibition (agitation, swearing, verbosity, childishness). Although seemingly aware of some aspects of his behaviour (apologising for swearing), he seemed unable to control his responses. The overall impression was of a pronounced frontal lobe syndrome, suggesting that the right frontal lobe had incurred some damage secondary to the documented head trauma and that he must have been reliant on some left frontal contribution.

On the basis of the IAP findings, a selective cortical resection (as opposed to more extensive frontal lobe resection) to the region of damage was advised. Intraoperative electrocorticography showed active focal epileptiform discharges maximal in the inferior frontal lobe in the electrodes closest to the lesion. A cortical resection was performed with frameless stereotaxy guidance excision of the frontal lesion. Histopathology on the resected tissue showed an old post-traumatic cyst involving the cortex and white matter. His postoperative course was unremarkable. When reviewed 3 months after surgery he was seizure free. His performance on neuropsychological evaluation remained commensurate with presurgical status. There were no novel subjective complaints. Mood, behaviour, and temperament remained stable.

Despite its undoubted value in many individual cases of temporal lobe epilepsy, the IAP has remained a controversial assessment instrument.2 Amid this controversy its potential usefulness in other patient groups seems to have been overlooked. A primary criticism of its use in temporal lobe epilepsy has been the question of irrigation and whether the medial temporal lobe is adequately "disab"led during the procedure. This particular limitation is not applicable to the patient with frontal lobe epilepsy, as the region of interest is clearly ablated via supply from the carotid arterial system. Caution must, however, be exercised with respect to possible crossflow into the anterior cerebral artery via the anterior communicating artery. When such crossflow is present, the ability to assess validly the integrity of contralateral frontal lobe function will be compromised, as with the use in cases of temporal lobe epilepsy, only a restricted form of assessment is possible with the frontal lobe patient during the period of ablation. Allowing for the possibility of knowledge regarding 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 benzoquinolizine, was first introduced as a neuromuscular 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.1 We here report on the rapid reversal of depressive symptoms in a patient treated with TBZ for orofacial dystonia by administering the newly and highly selective noradrenaline (norepinephrine) reuptake inhibitor (SNRI) reboxetine.2

On admission, the 64 year old woman presented with perioral and lingual hyperkinesias as well as intermittent and involuntary movements of her lower jaw, which had lasted for about 2 years, causing her a considerable impairment in articulation. No history of neuropsychiatric 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 tetrabenazine medication (60 mg a day). This successful treatment response, however, was accompanied by a severe depressive syndrome, which was characterized by a mixed anxious-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 (SNRI) reboxetine,3 was first introduced as a neuroleptic (5-HT) performs a similar action into presynaptic secretory vesicles for release,4 when collaterals are insufficient.5 Therefore, the inhibition of vHMA T2 by compounds such as tetrabenazine thus results in consecutive noradrenaline depletion.6

Tetrabenazine (TBZ) is known to act as a monoamine depleting and dopamine receptor blocking drug.7 In more detail, TBZ binds to and inhibits specifically the human vesicular monoamine transporter isoform 2 (vHMA T2). Whereas the indolamine serotonin forms a similar affinity for both vHMA T1 and vHMA T2, catecholamines such as noradrenaline exhibit a threefold higher affinity for vHMA T2.8 As these specific transporters are responsible for packaging monoamine neurotransmitters into presynaptic secretory vesicles for release by exocytosis, the inhibition of vHMA T2 by compounds such as tetrabenazine thus results in consecutive noradrenaline depletion.8 Alterations of noradrenergic neurotransmission—that is, a neuronal noradrenaline depletion—can therefore be postulated to form one major origin of TBZ induced depressive syndrome. With this assumption, brain-specific catecholaminergic activity enhancers (CAEs) such as phenylethylamine have been shown to antagonise TBZ induced depression-like behaviour in rats.9 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.


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.1,2 A known mechanism is microtrauma due to abrupt head movements, for example, chiropractic manoeuvres. In addition a pathogenetic role of connective tissue diseases, cystic media necrosis, fibromuscular dysplasia, migraine, and inflammatory diseases has been postulated.3 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 compensation when collaterals are insufficient.4 Lesions of the cerebral spinal cord are rare because of its good collateral supply.5 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 hypalgiesia 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.

Tibial nerve somatosensory evoked potentials (SSEPs) had regular N22 and P40 latencies and amplitudes. Central motor conduction time (CMCT) values, 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 circumscription 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 threecervical trunk (cervical ascending artery) and the costocervical trunk also. The anterior spinal artery was inconspicuously 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 (CMCA) part of the vertebral arteries (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 in type III collagen, migraine, fibromuscular dysplasia, infections in the near past, and inflammatory vasculopathy.7 Magnetic resonance imaging with typical semilunar mural haematoma and in addition magnetic resonance angiography (MRA) with complementary documentation of an irregular lumen indicating occlusion have a high sensitivity and specificity in cases of internal carotid artery dissection.8 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.1

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-
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). Nine-teen 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

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### References


### 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.

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cerebral cavernous malformations, this haplotype is more likely to be predominant in Spain, and the strong founder effect seen in all published Hispanic-American families with cerebral cavernous malformations might be specific for this population.

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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 dis- ease to periventricular brain tissue can obstruct the flow of cerebrospinal fluid (CSF) produced in the ventricles to the subarach- noid space where it is normally absorbed by arachnoid granulations. This typically causes an obstructive or non-communication hydro- cephalus. A ventriculostomy can be customarily placed to drain CSF from a lateral ventricle through a pressure regulating valve and into the atrium or peritendineum or pleural cavity. Even though this technique has been successful in relieving the hydrocephalus, it has about a 50% chance of infection or failure from blockage.2

Another option for the treatment of obstructive hydrocephalus is third ventriculo- 

rostomy (figure A). Eight polyomorph microsatellite markers spanning the CCM1 interval were selected for linkage analysis. Four were chosen from the Génethon linkage map (D7S2410, D7S2409, D7S2407, and D7S562), 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 chromo- some (Genbank HSA000065; BAC RG085C05). The length of the genetic inter- val flanked by markers D7S2410 and D7S689 is 4 centimorgans (cM). Marker dis- tances between D7S2410/D7S2409, D7S1813/D7S1789, D7S562/D7S558, and D7S689 have been estimated to be 2.2 cM, and 1.8 cM, respectively.3 Oligonucleotide sequences are available through the Genome Data Bank (John Hopkins University, Balti- more). Genotyping and linkage analysis (LINKAGE package version 5.1) were per- formed as previously described.4 Lod scores were calculated in the five families having a sufficient number of poten- tial meioses—that is, CVE1 (eight), CVE4 (16), CVE7 (five), and CVE28 (seven). Lod scores higher than one were obtained for three families (CVE3, 4, and 28) for at least one marker. D7S689 had the highest score from the 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, D7S689). For family CVE25, two out of five patients had a lod score close to 0 to 1 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 maxi- mum combined lod score of 5.92 was ob- tained for marker D7S2410 at θ=0.

In seven families (CVE3, 4, 5, 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 haplo- type from their affected mother. Although the limited size of this family does not allow to formally conclude, this suggests genetic heterogeneity. In family CVE29, the two affected siblings inherited the same haplo- types from their mother and father whose status was unknown.

None of the families shared a common hap- lotype (figure B). In addition, the extended Hispano-American haplotype was not segre- gating 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 segregat- ing with the disease phenotype were identical to the ones observed in the Hispano-American haplotype. Consequently, we analysed the fre- quency of this combination of alleles within a panel of 80 haplotypes of 40 healthy white subjects. Frequency was 17% compared with 23% in our Spanish sample. Therefore, this finding might be attributed to a random distri- bution of these alleles.

In conclusion, linkage analysis of Spanish families with cerebral cavernous malforma- tions did not show any evidence for Hispanic- American haplotype sharing or a founder effect. Although our sample was limited in size and does not therefore formally exclude the presence of the Hispano-American haplo- type in additional Spanish families with
as 50%, with the highest failure rate in the first few months after shunt placement. The complication rates for both procedures are low. Third ventriculostomy and shunting can potentially cause a stroke, bleeding, ventriculitis, meningitis, a subdural haematoma, CSF leak, diabetes insipidus, and SIADH. However, shunting has additional risks of mechanical malfunction, complications associated with implanting a foreign body, and overdrainage syndrome.

Because third ventriculostomy restores near normal CSF dynamics, overdrainage is prevented. The procedure is also minimally invasive and safe. The procedure’s low morbidity, high efficacy, and potentially short hospital stay are well suited as a palliative treatment of hydrocephalus for patients with an expected shortened life span. We propose that third ventriculostomy should be offered as a first treatment to patients suffering from obstructive hydrocephalus from unresectable tumours.

**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 breast 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>Osteophagel carcinoma metastasis 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.

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 an increase in oxygenated haemoglobin (oxy-Hb) and total haemoglobin (total-Hb) with a decrease in deoxygenated haemoglobin (deoxy-Hb).

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 tasks.

**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.
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 measured 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, which entails reading a short descriptive passage aloud. The speech responses of the patient to the tasks were normal.

Figure B shows an example of changes in NIRS 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 gener-
ally 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 92.3% of young adult subjects (mean (SD) 28.8 (4.4) years) during the word fluency task (unpublished data). Therefore, although we could not measure the changes in rCBF in the left frontal lobe of the patient from our previous studies, strongly suggests that the tasks caused an increase in rCBF in the left frontal lobe of the patient.

A decrease in oxy-Hb and total-Hb recorded from the brain tumour indicates a decrease of local blood flow in the tumour because the NIRS measurement area was restricted to the brain tumour.3 Because the NIRS measurement area was limited to the brain tumour, decreases in oxy-Hb and total-Hb in the tumour imply a decrease of local blood flow in the tumour.4 This 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 hypothesise that a stealing of blood flow is one of the mechanisms.5 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.1 In one fourth of total migraineurs, aura symptoms are experienced by an aura.2 We describe a patient with recurrent episodes of migraine in whom headache was preceded by a constellation of visual symptoms, 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.3

A 29 year old female teacher presented with an 8 year history of paroxysmal alternating hemianopic 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 after the beginning 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 general physical and neurological examination in between the episodes was unremarkable. Neurologically, during the aura symptoms 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 and read each part 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 of 0.6 mm. 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 flunarazine 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. In this case it is suggested that the pathophysiological 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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Correspondence to: Dr Parvaiz A Shah, Firdousa-change in the basal ganglion and right cerebel-

6.01p, 0.064 Tesla) showed areas of high signal

stain. The CSF was sterile after 2 weeks of
toxoplasmosis, cryptococcus, and neurocyst-

lymphocyte/ml in the CSF. Screens for malaria
was 0.47 (63/140 mg%), the protein content
were all normal. The CSF: blood glucose ratio
both legs. Full blood count and results from
spastic weakness of his left face, left arm, and
his Glasgow coma score was 13. He had mild
examination 5 weeks after discharge showed
memory impairment. A follow up MRI

in July 1997. T2 weighted image shows

brain lesions and no new lesions (figure B).

further improvement, apart from minor
examination after admission he deteriorated with a
SMBV course was continued. On the 4th day
the second dose, he felt unusually lethargic although he
and started on an alternate day regi-

tatives and relatively easy to produce. In
India 3 million people receive postexposure
courses of STV (phenolised sheep brain) antrabries vaccine each year.1 These produce
neurological reactions, including postvacci-
nation encephalomyelitis, in up to 1 in 100 courses, with a 3% mortality.1 Clinical forms
include a reversible mononeuritis multiplex,
and meningoencephalitic and encephalomy-
eltic reactions. Myelin basic protein and
related neural proteins from the nervous

system 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-

dopment of the suckling mouse brain vaccine
(SMBV). The attenuated virus is cultured on
immature mouse brain tissue, which contains
little myelin, thus reducing the risk of compli-
cations. SMBV is inexpensive (US$1.5 per
treatment course) and easily manufactured
locally; it is the most widely used postexposure
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% mortality4 The
mortality was particularly high (60%) if there
was extensive CNS involvement. The third
type of vaccine available is the human diplo-
id cell culture vaccine (HDCV), which is
both safe and efficacious. However, the recom-

ed 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
comment 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 to STV,
this report confirms that it does still occur.
Both SMBV and STV are widely used 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 encephalitides and the urgent need for the development and
deployment of a safe, and critically, afford-
able postexposure exposure vaccine regimen.

The economic low dose multisite intradermal
regimen using the HDCV provides an exam-
ple 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 immu-

mediated encephalitides.”

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R KNEEN
J J FARRAR
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-noradrenephrine), 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. We report a case in which khat chewing has been associated with a severe and disabling neurological illness.

A 56 year old Somali living in the United Kingdom for the past 18 years was admitted to a psychiatric hospital with a 5 week history of progressive confusion and agitation. His family reported that he had been chewing khat, in their opinion to excess, every day during that time but had stopped 2 days before admission. There was one previous admission to hospital 9 months previously with khat induced psychosis, from which he recovered without complications within 24 hours. On this occasion, shortly after admission, his conscious level deteriorated abruptly and he was referred for neurological opinion. He was apyrexial and general medical examination was normal. He opened his eyes spontaneously but there was no verbal response and he did not obey commands. He withdrew all four limbs to pain. Upper and lower limbs were held in flexion with markedly increased tone. Reflexes were brisk but equal. The right plantar was extensor. There were bilateral palmar reflexes.

Full blood count, urea and electrolytes, glucose, liver function tests, thyroid function test, viral serology, and malaria screen all gave normal results. Tests for HIV antibody, serum angiotensin converting enzyme, white cell enzymes, and serum and urinary porphyrins were negative. Erythrocyte sedimentation rate on admission was 58 mm/h.

Examination of the CSF showed normal opening pressure; sugar 2.7 g/l, glucose 4.3 mmol/l (blood glucose 6.1 mmol/l), and no cells. His initial EEG was abnormal with diffuse slow waves indicative of widespread cerebral dysfunction. 

A chest radiograph and ultrasound examination of the abdomen were normal. Cranial MRI, although complicated by movement artefact, showed diffuse abnormality in the deep cerebral white matter of both cerebral hemispheres. Fourteen days after admission he was witnessed to have a single brief adverse seizure with eye and head deviation to the right.

The patient was admitted to a rehabilitation unit. His mini mental state examination score and Barthel scores were zero. Feeding by percutaneous gastrostomy was started. A trial of intravenous methylprednisolone (1 g on 3 consecutive days) gave no benefit. Repeated EEGs (on four occasions) showed diffuse slow waves only. A second MRI (figure) 3 months after onset of symptoms showed the presence of a continuing diffuse extensive abnormality in the deep white matter of both cerebral hemispheres with marked cortical atrophy. Brain biopsy (via right frontotemporal craniotomy) was performed 3 months after the onset of his illness. 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 extensor plantar muscles with severe dysaesthesia of both palms and plantaris. Pin prick and light touch were reduced as well as position and vibratory sensation in both hands and feet. Deep tendon reflexes were hypoactive. Babinski’s sign was negative.

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 injection. 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.
M-protein, direct and indirect Coombs tests, cryoglobulin, antibodies to mycoplasma, myelin associated glycoprotein, gangliosides (GM1, GD1b, asialo-GM1, GT1b, GQ1b, Gal-C), P-ANCA, and C-ANCA. The CSP was normal. Titre of cold agglutinins was detectable at 1:128 or 1:256 (normal:<1:256). The patient's serum agglutinated adult group O red blood cells, but not O red blood cells or human cord red blood cells, signifying cold agglutinins with 1 specificity. Immunelectrophoresis of the eluate confirmed IgM composition.

The initial nerve conduction study showed severe diminution or absence of compound motor action potentials (CMAPs) with mildly diminished conduction velocities. F wave latencies were mildly prolonged. There were no evoked sensory nerve action potentials (SNAPs) in median, ulnar, and sural nerves bilaterally. Electromyographic studies were no evoked sensory nerve action potentials except in the left anterior neurogenic changes, but there were no fibrillations or positive waves latencies were mildly prolonged.

M-erythrocyte associated glycoproteins and glycolipids in erythrocyte membranes. Arai et al reported a case of polyneuropathy and IgM M proteinemia with anti-Pr2 CA activity. IgM M protein cross reacted with sialosyl paragloboside, GT1b, GD1a, GD1b, GM3, and GD3 present in muscle and in endothelial cells of the peripheral nervous system. It has been speculated that anti-Pr2 IgM protein induced immune mediated damage to vascular endothelium and peripheral nervous system myelin. A similar pathomechanism has been postulated in the other cases. 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 may play an important part in the induction of neuropathy associated with cold agglutinins. 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 Hara for their technical assistance, Dr S Kusunoki (Department of Neurology, Institute for Brain research, University of Tokyo) for analyses of antibodies to gangliosides, and Mr H Moug (Division of Blood Transfusion Medicine, University of Kagoshima) for characterization of cold agglutinin.

Six patients with neuropathy associated with cold agglutinins have been reported including our patient. Cold agglutinins are cold reactive autoantibodies that react with the antigen determinant term I for the erythrocyte glycoproteins and glycolipids in erythrocyte membranes. Araki et al reported a case of polyneuropathy and IgM M proteinemia with anti-Pr2 CA activity. IgM M protein cross reacted with sialosyl paragloboside, GT1b, GD1a, GD1b, GM3, and GD3 present in muscle and in endothelial cells of the peripheral nervous system. It has been speculated that anti-Pr2 IgM protein induced immune mediated damage to vascular endothelium and peripheral nervous system myelin. A similar pathomechanism has been postulated in the other cases. 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 sluggish or agglutination of red blood cells in the vasa nervorum; and (3) associated vasculitis. In 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 immunemediated demyelination in the peripheral nervous system. Taken together, neuropathy with cold agglutinins may involve immunologically mediated demyelination, microcirculation obstruction, 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.
CORRESPONDENCE

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 present 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. Therefore, I wish to 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.

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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 exploration 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 studies coming from 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.4,5 In particular, a clear link is emerging between psychotic symptoms and cholinergic dysfunction. Thus, Bodick 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 inhibitors are effective in reducing psychotic features as cognitive disturbances; tacrine also reduces or abolishes hallucinations in Parkinson’s disease.6 Another 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/M6 agonist (3R,6R)-6-(3-propylthio-1,2,5-thiadiazol-4-yl)-1-azabicyclo[3.2.1]octane octanoate (V179–90) has shown 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 to your correspondent for 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. Symptoms of neuropathy underlie foot ulceration and sepsis as the commonest clinical consequence of diabetic neuropathy but this is but a tiny fraction of the 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 (exhaustively 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. Replication 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 served by the comprehensive nature 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 Zernor’s encephalometer 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, telepresence 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 MACPHERLANE


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 trained soundbites demanded by the consumer in the increasingly competitive market of “read less - 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 distill 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 grievances of what in print largely matches the sleeve hype and with a price tag of just £27-50 the book will be welcomed by undergraduates through to specialist registrars.

SIDDHARTHAN CHANDRAN

Readers may be interested in:


CORRECTION

K Sudo, N Fujiki, S Tsuji, M Aijiki, T Higashi, M Niino, S Kikuchi, 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 hypohydrosis 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.