LETTERS TO
THE EDITOR

Behavioural status during the intracarotid amobarbital procedure (Wada test): relevance for surgical management (J Neurol Neurosurg Psychiatry 1999;67:549–559)

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 postsurgical amnestic syndrome,2 to predict postsurgical material specific memory changes.3 More recently, the use of the IAP has been extended to complement EEG localisation and radiological data by lateralisising temporal lobe dysfunction.

The IAP represents the “worst case scenario” as the entire frontal lobe is included in the ablation. There are likely to be few surgical scenarios in which a comparable extensive resection of tissue is likely to be considered, and results must be interpreted in this context. This limitation not withstanding, the IAP does seem to have a role in separating out those patients in whom more extensive frontal lobe resections could be considered as opposed to those in whom a more conservative approach is warranted.

This case report forms only the basis for a novel hypothesis that clearly requires more rigorous scientific research before its clinical utility can be reliably established. Nonetheless, we think that it is worth drawing the attention of the epileptological community to the potential application of the IAP in the surgical management of extratemporal cases.

MARIE F O’SHEA
MICHAEL M SALING
Department of Neuropsychology
SAMUEL F BERKOVIC
Department of Neurology, Austin and Repatriation Medical Centre, Melbourne, Australia; and Department of Medicine, University of Melbourne, Grattan Street, Parkville 3052, Australia.

Correspondence to: Dr Marie F O’Shea, Department of Neuropsychology, Austin and Repatriation Medical Centre (Austin Campus), Studley Road, Heidelberg, Victoria 3084, Australia. Telephone 613 3 03 9496 5913; Fax 613 3 03 9457 2654.


He-2.5 Hz with some mild increase in bilateral slow activity and no convincing evidence of electrographic 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 right hemisphere, 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.

On neuropsychological examination, his general cognitive performance was normal. At a behavioural level, however, he presented as very peurile 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 elimination of his remaining seizure is unlikely. 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 dysfunction, 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 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 surgery) was performed and the period of ablation. An assessment focused on 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. An assessment focused on the positioning of treatments would seem most useful.

It should be borne in mind that the degree of frontal lobe dysfunction induced by the IAP represents the “worst case scenario” as the entire frontal lobe is included in the ablation. There are likely to be few surgical scenarios in which a comparable extensive resection of tissue is likely to be considered, and results must be interpreted in this context. This limitation not withstanding, the IAP does seem to have a role in separating out those patients in whom more extensive frontal lobe resections could be considered as opposed to those in whom a more conservative approach is warranted.

This case report forms only the basis for a novel hypothesis that clearly requires more rigorous scientific research before its clinical utility can be reliably established. Nonetheless, we think that it is worth drawing the attention of the epileptological community to the potential application of the IAP in the surgical management of extratemporal cases.
Reversal of tetrabenazine induced depression by selective noradrenaline (norepinephrine) reuptake inhibition

Tetrabenazine (TBZ), a synthetic benzoquinolizine, 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 characterised by the triad of drooling/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.1

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 of articulation. 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 tetrabenazine medication (60 mg a day). This successful treatment response, however, was accompanied by a severe depressive syndrome, which was characterised 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. Exposure to TBZ again ameliorated hyperkinesia, but provoked a depressive relapse. A comediaction 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 (hVMAT2). Whereas the indoleamine serotonin (5-HT) forms a similar affinity for both hVMAT1 and hVMAT2, catecholamines such as noradrenaline exhibit a threefold higher affinity for hVMAT2.2 As these specific transporters are responsible for packaging monoamine neurotransmitters into presynaptic secretory vesicles for release by exocytosis, the inhibition of hVMAT2 by compounds such as tetrabenazine thus results in consecutive noradrenaline depletion.3

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.4 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 dissec tion

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, during orthopaedic manoeuvres. In addition a pathogenic 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 decompensation when collaterals are insufficient.4 Lesions of the cervical 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 C3 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 neurologist had examined the patient using Duplex sonography which showed increased flow velocity on the level of the vertebral artery 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 dissec tions.

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 thyrocervical trunk (cervical ascending 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 dissec tion. The intradural origins of the anterior spinal artery (ACSA) were not visible. 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 thyrocervical trunk (cervical ascending 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 dissec tion. The intradural origins of the anterior spinal artery (ACSA) 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 demonstration of an intraluminal or tapering occlusion have a high sensitivity and specificity in cases of internal carotid artery dissec tion.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.9

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-
Correspondence to: Professor D Claus, Department of Neurology, Institute for Radiology, Klinikum Darmstadt, Teaching Hospital University Frankfurt, Germany.

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). Seventeen 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


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). Seventeen 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

cerebral cavernous malformations, this haplotype is much less common in Spain, and the strong founder effect seen in all published Hispano-American families with cerebral cavernous malformations might be specific for this population.

HJ is supported by the Schweizerische Stiftung für medizinisch-biologische Arbor Steiner, P.E., and the Fondo de Investigacion de la Seguridad Social (Fiss: 900407).

Correspondence to: E Tournier-Lasserve, INSERM U25, Faculté de Médecine Necker, Paris, France

E TOURNIER-LASSERVE
Hôpital Lariboisière, Paris, France


6 H Jung, P. Labaque, S. Laberge, E. Marechial, E. Tournier-Lasserve

7 J M Garcia-Moreno, M A Gamero, G Iquzmeno, Servicio de Neurologia, Hospital de Sanatorio Virgen Macarena, Avenida Dr Fedriani, 41071 Sevilla, Spain

8 E Tournier-Lasserve
Hôpital Lariboisière, Paris, France

Correspondence to: E Tournier-Lasserve, INSERM U25, Faculté de Médecine Necker, 156 Rue de Vaugirard, 75015 Paris, France. Telephone 0033 1 45 67 29 57; fax 0033 1 40 56 01 07; email: tournier@necker.fr

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 pterverricular brain tissue can obstruct the fourth ventricle or the aqueduct of Sylvius and cause communicating hydrocephalus. 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. 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 ventriculostomy, a minimal invasive endoscopic neurosurgical 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, it can be dangerous. In our experience, we have seen that patients with aqueductal stenosis and the pediatric population. To avoid placing shunts in patients with inoperable metastatic brain tumours who typically only have a few months to live, we have offered the patients third ventriculostomy as a palliative procedure.

We performed third ventriculostomy on seven 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 5 weeks after the operation. The remaining two patients had a hospital stay was prolonged due to 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 in 3 days, with a hospital stay of 48 hours from the procedure. There were no operative complications. All five patients had no evidence of redevelopment of hydrocephalus up to the last clinic visit.

Every patient except the person described in case 4 received brain radiation therapy after the palliative procedure. One of our patients (case 3) underwent a course of radiation treatment prior to the operation. Another patient (case 5) had radiation to her orbit in the distal 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 images, or during endoscopy. However, tumours in contact with CSF space can also cause a communicating 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 pterverricular metastatic disease is consistent with the results obtained with third ventriculostomy for adult patients with secondary hydrocephalus.3 This is comparable with the alternative shunting with an implanted catheter which has a first year revision rate as high as 70%.3

Letters, Correspondence, Book reviews, Correction

autosome with a dominant pattern of inheritance (Figure A).

Eight polymorphic microsatellite markers spanning the CCM1 interval were selected for linkage analysis. Four were chosen from the Génethon linkage map (D7S2410, D7S2409, D7S583, and D7S589), and three from the Cooperative Human Linkage Center (D7S1813, D7S1789, D7S558). The last one (M658) was identified by SL based on sequencing data of a bacterial artificial chromosome (BAC RG085C05). The length of the genetic interval flanked by markers D7S2410 and D7S689 is 4 centimorgans (cM). Marker distances between D7S2410/D7S2409, D7S689/D7S1789, and D7S689/D7S558 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.3 Lod scores were calculated in the five families having a sufficient number of potentially informative meioses—that is, CVE3 (eight), CVE4 (16), CVE5 (seven), CVE10 (seven), CVE25 (five), and CVE28 (seven). Lod scores higher than 1 were obtained for three families (CVE3, 4, and 28), and for at least one marker. D7S1813/3 and D7S689, respectively. For the remaining 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, patients had a lod score of 0 to 1.0 for all markers. In this family, two affected and one asymptomatic sibling with normal standard MFI 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 0.0.

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. Although the limited size of this family does not allow to formally estimate heterogeneity, this suggests a genetic heterogeneity. In family CVE29, the two affected siblings inherited the same haplotypes from their mother and father whose status was unknown.

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 Hispanic-American haplotype. Consequently, we analyzed the frequency of this combination of alleles within a panel of 80 haplotypes of 40 healthy white subjects. Frequency was 17% compared with 22% 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 Hispanic-American haplotype sharing or a founder effect. Although our sample was limited in size and does not therefore formally exclude the existence of a Hispanic-American haplotype 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 SDAH. 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 unrecteetable tumours.

As 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 deoxyhaemoglobin (deoxy-Hb)\(^{1,2}\), 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 (4×5 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 stimulations. 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>Oesophageal 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.


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.

![Figure A: CT angiography of the brain tumour. Note that the tumour was supplied by the branches of the left middle cerebral artery.](image)

(A) CT angiography of the brain tumour. Note that the tumour was supplied by the branches of the left middle cerebral artery. (B) Oxygenation changes in the brain tumour during the naming task measured by NIRS. The ordinates indicate concentration changes of oxy-Hb, deoxy-Hb, and total-Hb in arbitrary units (au). Horizontal thick bar indicates the period of the task.

![Figure B: Oxygenation changes in the brain tumour during the naming task measured by NIRS.](image)
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 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 Neurology 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) confrontational 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, 5 to 2, which entails reading a short descriptive passage aloud. The speech responses of the patient to the tasks were normal.

Figure 2 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 generally increased by all the tasks used in the present study.3,5 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 episode. 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 the younger sister were also having paroxysmal episodes of common migraine.

Her general physical and neurological examination in between the episodes was unremarkable. Neurological examination 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 the fragmentary aspects of a 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 and 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 white card placed at a prespecified location. 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 the pin 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.

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 is preceded by an aura.2 We describe a patient with recurrent episodes of migraine in whom headache was preceded by a constellation of visual symptomatology which constituted all 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.3

A 29 year old female teacher presented with an 8 year history of paroxysmal alternating hemicranial throbbing headache which was often associated with nausea and photophobia. Patients fulfilled the requisite criteria for establishing the diagnosis of migraine with aura as devised by the International Headache Society (1988).4 She used to have six to eight episodes of headache a month. There was no history of status migranus during these years. On several occasions, headache was preceded by a peculiar constellation of visual symptomatology comprising distortion of visual images followed by inability to perceive simultaneously objects in the visual field and touch an object under direct visual guidance. However, she could see the component parts of objects during the episode. These visual symptoms lasted for about 10–25 minutes and were followed by a hemispheric, 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 at 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 mother and the younger sister were also having paroxysmal episodes of common migraine.


Correspondence to: Dr Kaoru Sakatani, Department of Neurosurgery, National Friendship Hospital, Yinghua East Rd., Hepingli, Beijing 100029, People’s Republic of China. Telephone (fax) 0086 10 64201246; email sakatani@public.east.cn.net

Letters, Correspondence, Book reviews, Correction

Downloaded from http://jnnp.bmj.com/ on June 16, 2017 - Published by group.bmj.com
involving visual association areas and their associated pathways, optic ataxia, gaze apraxia, and simultagnosia seem to represent a dissociation of visual information from the frontal eye field and dorsal parietal regions.

PARVAIZ A SHAH
A NAPEEE
Division of Neurology, Department of Medicine, Government Medical College and Associated SMHS Hospital, Srinagar, Kashmir, J and K 190001, India
Correspondence to: Dr Parvaiz A Shah, Firdousa-

asymmetric, and showed no evidence of lesions were bilateral, widely distributed, and 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, eating, walking, and continent but with some persistent emotional liability and mild memory impairment. A follow up MRI examination 5 weeks after discharge showed further improvement, apart from minor abnormalities in the basal ganglion, and generalised increase in ventricular size, consistent with residual cerebral atrophy.

Rabies is caused by an RNA virus, a member of the Rhabdoviridae family, it infects mammals and can be transmitted to humans by contact, generally from an animal excreting the virus in the saliva. Rabies manifests as an acute encephalomyelitis, the development of which is almost invariably fatal. The distinction between rabies and postvaccination encephalitis is difficult and may be helped by antigen detection via a skin biopsy; however, this technique is not available in Vietnam. Paralytic rabies could not be excluded in this patient and hence steroids were not used initially. Steroids have been reported to increase mortality in experimental animals with rabies, and it has been suggested that they may abrogate the immune response to the postexposure vaccine, thus precipitating uncontrolled rabies.

There are three types of postexposure vaccine in use world wide. The Semple type (STV) is obtained from inactivated virus prepared on adult animal nerve tissue; it is inexpensive and relatively easy to produce. In India 3 million people receive postexposure courses of STV (phenolised sheep brain) antirabies vaccine each year. These produce neurological reactions, including postvaccination encephalomyelitis, in up to 1 in 200 courses, with a 3% mortality. Clinical forms include a reversible mononeuropathy multiplex, and meningoencephalitic and encephalomyelitic 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 development 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 complications. 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 reactions do occur with SMBV, Complications of the CNS have been reported to occur after vaccination with an incidence of 1:2700 treated people, with a 22% mortality. Mortality was particularly high (90%) if there was extensive CNS involvement. The third type of vaccine available is the human diploid cell tissue culture vaccine (HDCV), which is both safe and efficacious. However, the recommended regimen is not affordable in most developing countries.

When we approached the Rabies Laboratory, Ministry of Agriculture and Fisheries, United Kingdom for advice in this case their opinion 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 demyelinating 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 reactions to SMBV is very much lower than 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 steroids in postexposure vaccine encephalitis and the urgent need for the development and deployment of a safe, and critically, affordable postrabies exposure vaccine regimen.

The economic low dose multisite intradermal regimen using the HDCV provides an example 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 protection without the risks of postexposure immune mediated encephalitis.

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.

N V V CHAU
TT HIEU
Centre for Tropical Diseases, 190 Ben Ha Mau Bus, District 5, Ho Chi Minh City, Vietnam

R SELLAR
Department of Clinical Neurosciences, Western General Hospital, Edinburgh, UK

R KNEEN
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 community in the United Kingdom. The psychoactive constituents of khat are cathinone (a norpseudoephedrine), cathine, and cathinone (an alkaloid with a structure resembling amphetamine, with marked cortical atrophy. Brain biopsy (via right fronto craniootomy) 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 plantars are flexor but he has persistent plantar flexion. 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 appearances, 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 might have been 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.


Necrotising vasculitis with conduction block in mononeuropathy multiplex with cold agglutinins

Cold agglutinins are cold reactive autoantibodies that have haemolytic effects on red blood cells mediated via complement fixation. Leucoencephalopathy associated with khat misuse has been described, however details of its pathomechanism are unclear. Here, we report the clinical, electrophysiological, and pathological findings of a mononeuropathy multiplex in a patient with cold agglutinins, who responded very well to plasmapheresis.

A 72 year old man was admitted with a 1 month history of progressing dysaesthesia and weakness of the limbs. He had no anaemia, jaundice, hepatosplenomegaly, or other signs of leucoencephalopathy. Cranial nerves and the cerebellum were not involved. There was severe weakness and atrophy of bilateral thenar, interossei, and 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.

Laboratory investigation showed a raised erythrocyte sedimentation rate: 52 mm/hour (normal <10) and serum C reactive protein: 1.8 mg/dl (normal < 0.5). Blood cell counts were within normal limits. The following were normal or negative: IgG, IgA, IgE, IgM,
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 CSF was normal. Titre of cold agglutinins was detectable at 1:128 at 4°C (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 nerve action potentials (CNAPs) in the ulnar, median, and sural nerves bilaterally. Electromyographic studies (SNAPs) in median, ulnar, and sural nerves were mildly diminished conduction velocities. F wave latencies were mildly prolonged. There were no evoked sensory action potentials (SNAps) in median, ulnar, and sural nerves bilaterally. Electrophysiographic 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 showed sludging of red blood cells, which was more pronounced in the larger myelinated fibres (figure A). (bar=30 µm).

In figure B, most of myelinated fibres are undergoing axonal degeneration. Many macrophages containing myelin debris infiltrate the muscle (bar=20 µm). Some vessels had focal necrosis of their wall. The small vessels in the endoneurium showed sludging of red blood cells, which was more pronounced in the larger myelinated fibres (figure A). (bar=30 µm).

Characteristic features of the present case are as follows: (1) subacute onset of mononeuropathy multiplex; (2) necrotising vasculitis with macrophage infiltration of red blood cells; (3) probable conduction block in the median nerve; (4) increased concentrations of serum titres of cold agglutinin; and (5) marked response to plasmapheresis. Extensive investigation for other causes of neuropathy was 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 1 including our patient. Cold agglutinins are cold reactive autoantibodies that react with the antigen neuraminidase determinant of the outer leaflet of cell membranes. Arai et al 2 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 glycoproteins and glycolipids in erythrocyte membranes. Arai et al 2 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 glycoproteins and glycolipids in erythrocyte membranes. Arai et al 2 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 glycoproteins and glycolipids in erythrocyte membranes. Arai et al 2 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 glycoproteins and glycolipids in erythrocyte membranes. Arai et al 2 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 glycoproteins and glycolipids in erythrocyte membranes. Arai et al 2 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 glycoproteins and glycolipids in erythrocyte membranes. Arai et al 2 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 glycoproteins and glycolipids in erythrocyte membranes. Arai et al 2 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 glycoproteins and glycolipids in erythrocyte membranes. Arai et al 2 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 glycoproteins and glycolipids in erythrocyte membranes.
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 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 reason 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 26 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.

T BARIC
Department of Neurology, Medical School University of Zagreb, Kistiaecica 12, 10000 Zagreb, Croatia. Telephone 00385 1 217280, fax 00385 1 217280, email tomaslaz.babic@ugz.hr

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 other studies (see Table 2) suggest that cholinomimetics 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, Bodick et al have shown that the M1/M2 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 Kauffer have shown that the cholinesterase inhibitor tacrine also reduces or abolishes hallucinations in Parkinson's disease. Another cholinesterase inhibitor, metrifone, 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/M2 agonist (5R,6R)-(-3-propyloxy-1,2,5-thiadiazol-4-yl)-1-azabicyclo[3.2.1]octane (3.2.1)octane produced a preclinical profile suggestive of antipsychotic efficacy and that the psychomimetic NMDA receptor antagonist ketamine (when administered at subanaesthetic 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.

PAUL T FRANCIS
Neuroscience Research Centre, GKT School of Biomedical Science, King's College London, London SE1 9RT, UK

ALAN M PALMER
MICHAEL SNAPI
Cerebrus Pharmaceuticals Ltd, Womenham, Ribstonham, RG41 5UA, UK

GORDON K WILCOCK
Department of Care of the Elderly, Frongrith Hospital, Bristol, BS16 2EW, UK


The neuropathies of diabetes are common (as the chapters in this book repeatedly remind us) and can be very disagreeable. Symptoms less 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 general, 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 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 Zermor’s enccephalometer more than a century ago. Just as the solution to the mariners’ problem (the 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 obsolence 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 “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 skilfully 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 taking in Neurology and costs £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 Ajiki, 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—³p value for each pair of items: hypohydrosis v hyperhydrosis 0.0007; hypohydrosis v normohydrosis 0.7282; normohydrosis v hypohydrosis 0.0012 should read—³p value for each pair of items: hyperhydrosis v hyperhydrosis 0.0007; hyperhydrosis v normohydrosis 0.7282; normohydrosis v hypohydrosis 0.0012.
Reversal of tetrabenazine induced depression by selective noradrenaline (norepinephrine) reuptake inhibition

WOLFGANG SCHREIBER, JÜRGEN-CHRISTIAN KRIEG and TOBIAS EICHHORN

J Neurol Neurosurg Psychiatry 1999 67: 550
doi: 10.1136/jnnp.67.4.550

Updated information and services can be found at:
http://jnnp.bmj.com/content/67/4/550.1

These include:

References
This article cites 5 articles, 2 of which you can access for free at:
http://jnnp.bmj.com/content/67/4/550.1#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes