Anosognosia for hemiplegia after a brainstem haematoma: a pathological case

The pathogenesis of anosognosia for hemiplegia (AHP) remains unclear, but recent theories have involved global cognitive deterioration or more modular mechanisms.

Persistent AHP is usually found in left hemispheric or more modular mechanisms. Theories have involved global cognitive deterioration due to a high frontal periventricular damage and to a related simultaneous confusional state. We report a patient with severe and prolonged anosognosia for left hemiplegia occurring after a right pedunculopontine haematoma. A possible explanation for this AHP might be the association of a left complete somatosensory deficit secondary to brainstem lesion with a global cognitive impairment due to histologically established Alzheimer’s disease. This case, to our knowledge, is unique in the literature and it raises interesting questions on the origin of AHP.

An 83 year old right handed woman was admitted to hospital because she was found collapsed with a left hemiplegia. She had an history of hypertension treated with a diuretic. She had lived alone since the death of her husband, 15 years ago, and was taking good care of herself, despite a moderate impairment of memory for recent events noticed by her daughter since the past two years. On admission, she was lethargic with a blood pressure of 185/105 mm Hg, a heart rate of 110 beats/min. Her pupils were fixed and dilated, but reactive to light. She was able to follow verbal commands, and was able to point on command. We noticed that the patient acknowledged (but never reported spontaneously) mild memory disturbances and cognitive slowing. She twice received a psychiatric assessment that showed a slightly blunted affect, with no depression or anxiety. The patient died suddenly during the eighth week after onset. Ncropsy showed that death was due to bilateral pulmonary embolism. Her brain weighed 1210 g. The left temporal lobe showed a moderately atrophic aspect. There was no focal cortical or subcortical lesion in the cerebral hemispheres. A 1cm wide haematoma was found in the right rostral pons extending from the caudal midbrain to the middle pons (figure). We performed the usual histological staining (haematoxylin-eosin, Bodian silver, Luxol fast blue, and Congo red) and an immunohistochemical analysis of Aβ and tau proteins. Lesions of Alzheimer’s disease were found in all the cortical areas, characterised by numerous Aβ positive amyloid plaques. Neurofibrillary tangles were rare in the isocortices, but were numerous within hippocampal (mostly in CA2) and entorhinal cortices on both sides. Neuronal loss was more severe in the left CA1 subarea, but was symmetric elsewhere. We describe a patient with a mild Alzheimer’s disease who had a lateralised brainstem lesion and developed subsequently a severe and long lasting AHP, in all points similar to that described in right hemispheric damages. This AHP contrasted with a very mild anosognosia to cognitive deficits and normal concerns with other medical problems. We found no motor neglect (postulated as the main factor of AHP in this hypothesis), and because the AHP remained almost unchanged when the motor deficit started to improve. The patient’s death prevents us from knowing whether a greater recovery would have overcome the anosognosia. The patient showed no behavioural particularity that could contribute to the AHP; she presented no visuovernal confabulation nor delusion, and psychiatric examination disclosed no depression or specific attitude toward illness.

We think that this unusual AHP could result from the association in the same patient of a stroke and Alzheimer’s disease through a special pattern of cognitive deficit. Levine et al have reported several patients with pre-stroke dementia who sustained hemiplegia and had no AHP. These patients, however,
had no hemisensory loss. Starkstein et al. have shown that cognitive deficits are not necessarily to produce AHP but could constitute a contributing factor in some patients. In our patient, we are not clear whether the AHP was due to a global or to a specific cognitive impairment. We think that a global reduction of attentional resources cannot explain the AHP in this case, given the specificity of the anosognosia. We could not relate AHP to a degraded body scheme, a hemispatial neglect, or a hemiparesis. The memory deficit was mild, without confabulatory tendency, and it would not explain the AHP by a difficulty of remembering the newly acquired hemiplegia. Some theories of unawarness post that AHP could be, at least partly, related to some mental inflexibility or to deficits in self monitoring and internal representation. Such deficits are usually associated with damage to the frontal lobes or to fronto-subcortical circuits. In our patient, the analysis of the Mattis scale subscores showed a prominent frontal dysexecutive syndrome. This peculiar cognitive pattern may have been of some importance in the appearance of AHP in the patient. Starkstein et al. have proposed two domains of anosognosia in Alzheimer’s disease, cognitive and behavioural. Based on this very unusual case, we think that anosognosia to non-cognitive neuropsychological deficits might represent a third domain that should be assessed systematically in patients with mild Alzheimer’s disease and a stroke. Such studies might be very useful to the understanding of mechanisms of anosognosia.

Opsioclonus as a paraneoplastic manifestation of pancreatic carcinoma

Opsioclonus refers to involuntary, repetitive, and disorganised rapid conjugate eye movements in all directions of gaze. The diagnosis is usually a clinical one, as, strictly speaking, it requires the demonstration of no interaural acadic interval on oculography. It may be associated with myoclonus of the trunk and limbs and cerebellar dysfunction. Opsioclonus can occur with or without paralysis and has been associated with numerous neoplastic conditions, including neuroblastoma in children and breast, lung, uterine, ovarian, and thyroid carcinoma, and Hodgkin’s disease in adults. It has not previously been reported as a paraneoplastic phenomenon associated with carcinoma of the pancreas. A 70 year old man, with a past medical history of hypertension and osteoarthritis, presented with a 10 day history of intermittent vomiting and increasing gait unsteadiness. He complained of vertigo, which was worse on standing, and ataxia, falling to the right. There was no history of headache, neck stiffness, photophobia, blurred vision, deafness or tinnitus. Prior to his presentation to hospital, he had been commenced on promethazine by his local doctor, with no effect on his symptoms. Other medications at this stage included paracetamol, amitryptiline, and Paracetamol, amitryptiline, and there was a partial left lateral rectus palsy. His visual ahes were disturbed with left over right hypertropia. Opsioclonus was present with involuntary, rapid conjugate eye movements, including Opsoclonus in the right on horizontal gaze and an unsteady gait. Brain CT showed age related cerebral atrophy, with no infarction. A provisional diagnosis of vestibular neuritis was made, and he was started on 500 µg clonazepam twice a day.

Over the next four days, he remained nauseated and vertiginous. He then developed a left upper motor neuron facial weakness, left upper limb clumsiness, left ptosis, bilateral glossoptosis, dysarthria, and ataxia. A proximal diagnosis was abnormality of omnipause neurons, which are involved in the control of saccadic eye movements. The oculomotor examination was normal. The patient had a macroscopically normal brain, with no evidence of other abnormalities. The only neurological signs on examination were nystagmus to the right on horizontal gaze and an unsteady gait. Brain CT showed age related cerebral atrophy, with no infarction. A provisional diagnosis of vestibular neuritis was made, and he was started on 500 µg clonazepam twice a day.

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A postmortem disclosed an occult 3 cm multiloculated cyst in the tail of the pancreas. The morphological diagnosis was primary duct adenocarcinoma of the pancreas. There was also a 6 cm subcapsular hepatic nodule consistent with a metastasis from a pancreatic primary. There was no macroscopic evidence of cerebral haemorrhage, infection, or infarction. Microscopically, there was perivascular lymphocyte cuffing in the upper medulla, pons, midbrain, thalamus, and hippocampus, with some microglial proliferation and gliosis. The perivascular lymphocyte cuffing, microglial proliferation, and gliosis in the pons could explain the dysfunction of the omptic neurons in the PPRF. This abnormality may therefore provide a theoretical explanation for opsioclonus in this case.

An autoimmune basis to the syndrome has been suggested, but there seems to be insufficient evidence to support this. Paraneoplastic autoimmune syndromes, such as Eaton-Lambert syndrome, may present in many ways. Careful evaluation of the patient for the presence of an occult malignancy is important when there are other distinctive syndromes, such as Eaton-Lambert syndrome and subacute cerebellar degeneration. The index of suspicion of an occult malignancy should also be high in patients with present with opsioclonus.

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Female predominance in spasmodic dysphonia

We were interested to see the sex prevalence results in the recent review of focal dystonia by Soland et al. They found that of 956 patients with dystonia, 558 (58.4%) were female, for a ratio of 1.4:1. All but the cases of writer’s cramp had more females than males. In their spasmodic dysphonia group the ratio was 2:6:1, with adductors and 29 with abductor spasmodic dysphonia. The other ratio of females:males was 214:56 or 3.8:1. Thus females made up 79.3% of our population of patients with spasmodic dysphonia. Brokendown into subgroups, the female:male ratio was 4:1:1 for the adductors and 2:2:1 for the abductors. The mean age was 60 years for the men and 64.6 years for the women. Most (186) of these patients continue to be followed up for botulinum toxin injections.

Our results, in this much larger population of patients with spasmodic dysphonia, suggest a greater female predominance than most previous studies. The only other large magnitude study was by Blitzer and Brin who reported 260 patients with idiopathic dystonia, 558 (58.4%) were female, for a ratio of 1.4:1. They later separated out their patients with dystonia, 558 (58.4%) were female, for a ratio of 1.4:1. All but the cases of writer’s cramp had more females than males. In their spasmodic dysphonia group the ratio was 2:6:1, with adductors and 29 with abductor spasmodic dysphonia. The other ratio of females:males was 214:56 or 3.8:1. Thus females made up 79.3% of our population of patients with spasmodic dysphonia. Brokendown into subgroups, the female:male ratio was 4:1:1 for the adductors and 2:2:1 for the abductors. The mean age was 60 years for the men and 64.6 years for the women. Most (186) of these patients continue to be followed up for botulinum toxin injections.

In these studies did not disclose abnormalities. She had only leucocytes/mm^3 and platelets/mm^3. The white blood cell count was 11,000/mm^3 and the red blood cell count was 4.5 million/mm^3. The hemoglobin was 12.5 g/dl and the hematocrit was 36.5%. Serum electrolytes, glucose, protein, and amylase were within normal limits. Urinalysis was negative. There was no evidence of renal or hepatic dysfunction. Blood pressure was 120/80 mmHg. The patient was afebrile with a temperature of 37.2°C. The initial physical examination showed a right hemiparesis with weakness and atrophy in the right upper and lower extremities. Motor and sensory examinations showed severe weakness and atrophy in the right upper and lower extremities. Sensory examination showed a decreased vibratory sense in the right upper and lower extremities. Deep tendon reflexes were absent in all extremities. The plantar reflexes were plantar. The mouth was deviated to the left and there was a left facial weakness. The patient was unable to walk without assistance.

The patient was admitted to the hospital on April 11, 1997, and was discharged on April 21, 1997, without any further improvement. She has been followed up regularly since then and has shown no evidence of disease progression.

Recurrent Guillain-Barré syndrome and CNS demyelination

It is commonly assumed that multiple sclerosis exclusively affects the central nervous system but there is growing evidence that it is not so. There is evidence that dysfunction and tissue damage in Guillain-Barré syndrome, chronic idiopathic demyelinating polyneuropathy, and multiple sclerosis result from immunological mechanisms operating in the peripheral or central nervous system. Although it is commonly assumed that multiple sclerosis exclusively affects the central nervous system, central nervous system demyelination has been suggested, and only peripheral idiopathic demyelinating polyneuropathy. There are few reports of acute inflammatory demyelinating neuropathy associated with multiple sclerosis.

Here, we report a patient with a recurrent Guillain-Barré syndrome who developed a first episode of central nervous system demyelination several years later.

A 26 year old woman was admitted to our hospital because of an acute right hemiparesis. In 1977, at the age of seven, the patient gradually developed a tetraparesis with areflexia. The neurological deficit reached a peak two weeks after the onset of symptoms. Her CSF showed 217 mg/dl protein without cells. The motor and sensory nerve conduction studies included median, ulnar, peroneal, and sural nerves. The motor nerve conduction velocities were 25 ms in the median nerve, 30 ms in the ulnar nerve, and 40 ms in the peroneal nerve. Sensory nerve conduction and EMG studies did not show any abnormalities. She slowly improved and was discharged three weeks later without symptoms. The patient was asymptomatic until 1991, when she was readmitted because of an ascending weakness and distal paraesthesiae, two weeks after a flu syndrome with fever. Neurological examination disclosed paresis in all four limbs, more severe distally in the upper limbs and proximally in the lower limbs. She was areflexic. Sensory examination showed a mild deficit to pin prick, and vibration and reduced proprioception was found distally in her four limbs. Lasegue sign was positive in both legs. The CSF contained 148 mg/dl protein and 40 leucocytes/mm^3. Nerve conduction studies disclosed an absence of F responses and dispersion of motor nerve compound action potentials. Median, radial, ulnar, peroneal, and sural nerves were examined. Motor and sensory NCVs were normal except in the peroneal nerve (40 ms) and median nerve (48 ms). Distal motor latencies were 5 ms, 4 ms, and 8 ms in median, ulnar, and peroneal nerves respectively. The neurological deficit reached a peak three weeks after onset and she had recovered fully in two months and was therefor asymptomatic. A control electrophysiological study was performed several months later and no abnormalities were found.

In 1996, she was readmitted because of an acute right hemiparesis. Neurological examination showed a right hemiparesis, with right Babinski’s sign and without sensory impairment. The haematological and blood chemical values were normal. A CSF analysis showed 24 mg/dl protein with three leucocytes/mm^3 and no oligoclonal bands were detected. Brain MRI showed multiple T2 weighted hyperintense white matter lesions in both cerebral hemispheres, brain stem, and cerebellum. One of the lesions located in the left corona radiata disappeared completely after gadolinium administration. High dose intravenous steroids were started and there was a pronounced clinical improvement. When the patient was discharged 10 days later the neurological examination was normal. Motor NCVs were greater than 50 ms in the arms and 45 ms in the legs, and no prolonged motor distal motor latencies were found. Transcranial magnetic stimulation showed a delay in central motor conduction time in the right arm. An EMG examination did not show abnormalities. A new MRI performed two weeks later showed a decrease in inflammatory activity.

Our patient had a recurrent Guillain-Barré syndrome with subsequent development of a first attack of a central nervous system inflammatory demyelinating disease. Recurrent Guillain-Barré syndrome consists of multiple episodes of typical acute Guillain-Barré syndrome with CSF findings and EMG abnormalities during each individual episode similar to those described in the acute monophasic disease. Although our patient does not fulfill criteria of clinically definite multiple sclerosis, MRI and CSF findings make the diagnosis very probable. Cranial MRI lesions have been found in chronic inflammatory demyelinating polyneuropathy although without clinical symptoms suggestive of multiple sclerosis. Acute inflammatory demyelinating neuropathy associated with multiple sclerosis has been described in two other cases. As far as we know, this is the first case of recurrent Guillain-Barré syndrome associated with a central nervous system demyelinating disease. In our patient both peripheral and central nervous myelin involvement were clinically symptomatic.

It seems that dysfunction and tissue damage in Guillain-Barré syndrome and multiple sclerosis result from impairment of immune regulation within the peripheral or central nervous system. Peripheral and central nervous system myelins exhibit a similar macro-molecular organisation and some protein molecules are present in myelin from both systems; thus it is likely that under certain circumstances, immune processes may be directed selectively against either peripheral nerves or CNS white matter. In the animal model, experimental allergic encephalomyelitis, the induction of the disease is observed to be dependent on the interaction between peripheral and central nervous white matter. On the other hand, it has been suggested that activated T lymphocytes may function as effector cells that exert cytotoxic action towards Schwann cells or myelin.
Although caution is appropriate in interpreting the few reports in the literature supporting the idea that peripheral nerves are involved in multiple sclerosis, it seems likely that at least in some patients both peripheral and central nerve myelin may be involved in an acute demyelinating attack. Perhaps the peripheral and central nervous systems share antigenic properties.

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CORRESPONDENCE

Non- or pseudoepileptic seizures?

We agree with Scull that consensus is badly needed for the nomenclature of manifestations which mimic, but are not, epileptic seizures. His plea for using the term “non-epileptic seizure”, however, is unconvincing. Non-epileptic seizures cover a wide range of diagnoses, both organic and psychogenic. It is evident that, after it has been proved that seizures are not epileptic, another diagnosis should be sought. From the point of view of the epileptologist this diagnosis is, by definition, “non-epileptic”, just as epileptic seizures may be called “non-syncopal”, “non-narcoleptic” or “non-dissociative” by other specialists. We think that Scull does not have this wide range in mind when he proposes to use the term “non-epileptic seizure”.

From experience, we all know that there remains a group of patients, often with a diagnosis of epilepsy, who have non-epileptic seizures that closely mimic epileptic seizures and are referred to epileptologists. These seizures often turn out to be of psychogenic origin. Harm can be done when this is not recognised—for example, when treatment consists of increasing doses of antiepileptic drugs. Why not name these seizures what they are—namely, “pseudoepileptic”? The prefix pseudo indicates that things are not what they seem to be. It does not imply that the seizures themselves are not a real experience, or something to be ashamed of. It is our experience that this can be satisfactorily explained to patients. Therefore we prefer the use of “pseudoepileptic” instead of “non-epileptic seizures”.

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1 Scull DA. Pseudoseizures or non-epileptic seizures (NES); 15 synonyms. J Neurol Neurosurg Psychiatry 1997;62:200.

Scull replies:

I thank Kuyk and Leijten for their comments. In common English usage “pseudo” is a derogatory term and is taken by some patients to mean that the doctor thinks that their condition is fictitious. Dealing with the anger that patients feel when their diagnosis changes from “epilepsy” to a psychiatric label is always likely to be difficult. “Non-epileptic seizures” may not be an ideal label but aggravating patients with a term that can be misinterpreted is unhelpful.

DAVID A SCULL
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NEUROFILAMENT GENE MUTATIONS AND AMYOTROPHIC LATERAL SCLEROSIS
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Background and aims—Amyotrophic lateral sclerosis (ALS) is a progressive neurodegeneration of the motor system with death usually occurring from respiratory failure within 3-5 years of diagnosis. Pathologically neurofilament accumulations are seen in the proximal axon and cell body. Whereas superoxide dismutase (SOD1) mutations have been implicated in 1%-2% of cases to date, only five patients with neurofilament mutations have been described, all deletions in the heavy neurofilament subunit (NFH) tail. Therefore the NFH tail for mutations in the sporadic ALS population was analysed.

Methods—Clinical data and DNA were collected on patients attending a specialist clinic. Genotyping and mutation detection were performed by polymerase chain reaction (PCR) and single strand conformation polymorphism analysis (SSCP) followed by silver staining according to standard protocols. Samples showing band shifts on SSCP were subcloned and sequenced.

Results and discussion—Two novel mutations in a hypervariable region of the heavy neurofilament subunit gene (NFH) were found in two of 196 patients and none of 188 controls. The mutations are an 18 bp deletion and 24bp deletion from 1965-1988 and 1989-2006 respectively using the numbering of the published sequence. Each result in the loss of a single consensus phosphorylation motif, KSPXX. The clinical features of both patients were entirely typical of ALS. Both had El Escorial probable or definite ALS with onset in the limbs. The onset was at 66 and 73 years with survival of 19 and 33 months respectively.

Conclusion—Heavy neurofilament subunit gene mutations account for 1% of apparently sporadic ALS and are indistinguishable clinically from other forms.

INVESTIGATION OF THE POLYMORPHISMS IN THE ECNOS GENE IN PATIENTS WITH AND WITHOUT DIABETIC PERIPHERAL NEUROPATHY
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Nerve ischaemia plays a central part in the pathogenesis of diabetic neuropathy (DN). The constitutive isoform of nitric oxide synthase (ecNOS) generates nitric oxide (NO) which modulates basal vascular tone and regulates nerve blood flow and may be a potential contributor to the pathogenesis of DN. We studied the distribution of the polymorphisms at 5’ end of the ecNOS gene, the 27 bp repeat in intron 4 (ecNOS 4a/b) in 129 normal control subjects, 46 (21m) insulin dependent diabetic patients without complications, 37 (19m) DN patients and 33 (15m) IDDM patients with retinopathy nephropathy with a mean age of onset of diabetes of 16.9, 19.7, and 16 years (range 1-40) respectively and mean duration of diabetes of 24.7, 25.4, and 27.7 (range 11-47) years respectively.

There was an excess of ecNOS 4b/a heterozygotes among those patients with DN and other microvascular complications (C2=5.45, P=0.025, C2=4, P<0.05) respectively; also there was an excess of ecNOS 4b/a heterozygotes in DN patients with autonomic dysfunction in comparison to those without autonomic disturbances (C2=4.5, P=0.05). There were no significant differences in ecNOS genotypes between patients and controls.

In conclusion these data suggest that the ecNOS gene may be implicated in the pathogenesis of diabetic peripheral neuropathy.

LYME NEUROBORRELIOSES IN SOMERSET,
ENGLAND
N K Banerji, Musgrove Park Hospital, Somerset, England.

Few publications concerning Lyme neuroborreliosis have appeared from the United Kingdom. Six cases seen in Somerset, England are reported here.

Three men and three women between the ages of 29 and 65 who had neuroborreliosis were seen in Somerset over three years. Three had history of rash (erythema chronicum migrans) and two had symptoms of radiculitis. Among the five patients seen with cranial nerve lesions, facial palsy was the commonest. One had peripheral neuropathy only. Spontaneous resolution of initial symptoms and signs as the condition progressed was a feature of acute cases. Pleocytosis with raised protein in the CSF was seen in all patients except one who already had treatment with penicillin. Lyme serology was positive in CSF and blood in all cases.

It is suggested that fleeting symptoms and signs are good pointers to the diagnosis of Lyme neuroborreliosis. Abnormality of CSF in untreated cases, especially Lyme serology, is essential.

NEUROLOGICAL DEGENERATION IN THE WOLFRAM (DIDMOAD) SYNDROME
S Bundey, T G Barrett, University of Birmingham, Birmingham, UK.

Fifty four patients with this rare autosomal recessive syndrome were ascertained from multiple sources throughout the United Kingdom. The ascertainment criterion was childhood onset of diabetes mellitus and optic atrophy. The patients were aged 5-47 years with a mean of 29.5 years. Most patients also had diabetes insipidus and deafness, in accord with the recognised features of this syndrome. However, a new finding was the frequency of neurological complications which occurred in 20% of those under 20 and in 78% of those over 20. Ataxia was the most common symptom; others included startle myoclonus and central apnoea. Four of 12 deaths were due to central respiratory failure. MRI (n=7) disclosed cerebellar and brain stem atrophy, loss of pituitary bright signal and thinned optic nerves. Muscle biopsies (n=9) showed normal respiratory chain function and analysis of lymphocytic mitochondrial DNA showed no rearrangements (n=32). The clinical and neuroradiological findings indicate that cerebellar and brain stem degeneration are significant and common complications in older patients with the Wolfram syndrome.

VISUAL INVERSION OR ROTATION ASSOCIATED WITH DIFFERENT TYPES OF CEREBELLAR INFECTION
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Inversion, rotation, or “tilting” of vision is an unusual phenomenon. The pathophysiological mechanisms and anatomical structures involved are not well understood. Five patients are described in whom a history of acute visual inversion or rotation was elicited, associated with vertigo and in some with additional symptoms. In each case this was transient and in one there were a number of episodes. The visual disturbance was not always recorded in the initial history. Each patient underwent CT and/or MRI imaging of the brain. Four patients had unilateral infarction in the territory of the posterior inferior cerebellar artery (PICA). The fifth had bilateral infarctions in superior cerebellar artery (SCA) territories. Visual inversion has been reported hitherto as a rare symptom in association with verteobasilar ischaemia and Wallenberg’s syndrome. More recently there have been a few reports demonstrating cerebellar infarction, most involving the PICA territory, in particular that of its medial branch. Infarction of other areas of the cerebellum can be involved. Possible mechanisms for this phenomenon were discussed. On direct questioning this symptom was more common in cerebellar infarction than previously thought.

INTERNERS AND OLGODENDROCYTE DIFFERENTIATION
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Aims—Normal myelination of the CNS during development is obtained by the differentiation of migratory precursor cells into mature postmitotic oligodendrocytes. The aim of this study was to examine the role of...
the integrin family of cell surface receptors for extracellular matrix (ECM) in this differentiation process.

Methods—In vitro methods, involving purified rodent oligodendrocyte precursors, purified ECM ligands, and blocking antibodies and peptides were used. Repair in patients with RLS syndrome was investigated, in double-blind fashion. Further specific uses of apomorphine are being reviewed. In addition, door-to-door assessment for Parkinsonism was carried out in one electoral ward. The consecutive case files of 30 subjects referred for investigation of orthostatic hypotension due to Selegiline trial and longer follow up in the DATATOP study failed to show a neuroprotective effect. Selegiline combined with levodopa was associated with greater all cause mortality than levodopa alone in the UKPDRG trial, although no causal relationship with selegiline was proved. Mortality data from the UKPDRG trial is currently being analysed in a cause of death (CODE) study. Recently, it was found that levodopa induced psychosis caused selective and often severe orthostatic hypotension on head up tilt which was reversed by drug withdrawal. This finding was confirmed in a second study which examined the effects of head up tilt and standing on blood pressure, heart rate, and plasma catecholamines in 20 PD patients taking selegiline. Patients were examined on selegiline (10 mg/day) after 4 weeks on 3 mg/day, and at 4, 7, and 21 days after cessation. Selegiline was associated with systolic hypotension on head up tilt and standing as well as a supine pressor effect. The orthostatic hypotension reversed within several days of drug withdrawal. Treatment of orthostatic hypotension and a supine pressor effect is similar to the cardiovascular actions of selegiline's major metabolites, amphetamine and met-amphetamine, at doses which cause psychosis in normal humans, although non-selective blockade of monoamine oxidase was not excluded. Quantification, currently under way, of plasma amphetamine, metamphetamine, tyramine and p-hydroxyamphetamine concentrations may further define the mechanism of selegiline's cardiovascular actions.

ROLE OF PROLONGED HEAD UPTILT AND URINARY SODIUM EXCRETION IN NEUROLOGICAL AND PSYCHIATRIC DISORDERS

Aim—To evaluate the role of prolonged head up tilt (HUT) and 24 hour urinary sodium excretion (USE) as a first line investigation in recurrent syncope. Recurrent unexplained syncope occurs in up to 30-50% of cases and low sodium excretion or cardiac arrhythmias have been implicated. A further explanation is the occurrence of the paroxysmal orthostatic tachycardia syndrome (POTS).

Methods—30 subjects referred for investigation of blackouts (15 men, 15 women, mean age 46 years, range 20-60) and controls (10 men, five women, mean age 40 years, range 20-60) were studied using cardiovascular autonomic function tests, ECG, EEG, prolonged (30 min) HUT (60°), blood biochemistry, and 24 hour USE.

Results—22 out of 30 subjects (but not controls) had a positive tilt test defined by presyncope symptoms on HUT. Blood pressure and heart rate (BP, HR) fell in two subjects who had cardiac arrhythmias on subsequent 24 hour Holter monitoring. Mean BP fell with rise in HR >120 beats per minute in three subjects (POT type 2) whereas mean BP was unaffected in others despite symptomatic and rise in HR (>120 bpm, n = 13). Routine blood biochemistry and haemoglobin were normal in all and 24 hour USE was low normal (mean 137 mmol, range 100-160). Five subjects had low USE and salt supplementation (120 mmol/day) abolished syncope. EEG was abnormal in one who was negative to HUT.

Discussion—(1) Inexpensive prolonged (30 min) HUT and 24 hour USE could be incorporated as a first line test for investigation of
DISORDER OF A MITOCHONDRIAL RESPIRATORY CHAIN phenotype. are reflected by changes in T lymphocyte with beneficial clinical consequences, which inflammatory activity of multiple sclerosis beadorFACSseparation. in vitro lymphocyte depletion by magnetic clinical response with clinical disease sup-

comparison of the relative IFN stimulated with phytohaemoglutinin. Com-

peripheral blood mononuclear cells when were monitored over time by measuring the anti-CD4. Changes in immunological activity tients were treated with the humanised Cambridge, UK.

SHIFT FROM Th1 TO Th2 LYMPHOCYTE PHENOTYPE INDUCED BY MONOCLONAL ANTIBODY TREATMENT OF MULTIPLE SCLEROSIS PATIENTS A J Coles, M G Wing, D A S Compston, University of Cambridge Neurology Unit, Cambridge, UK.

It has been proposed that magnetisation transfer (MT) provides information about the integrity of myelin. Similarly, the measurement of N-acetyl aspartate (NAA) an amino acid localised to neurons and their processes—by magnetic resonance spectroscopy (MRS) has been used as index of axonal loss and/or dysfunction in multiple sclerosis (MS). MRI, MT imaging, and MRS were carried out on 18 patients with clinically definite MS. The group comprised patients with a wide range of disability (range 2-25 years, median 7 years). Single voxel MRS localised to a chronic area of high signal from hemispheric white matter which had been present for greater than 12 months was collected. MRS was then calculated from the corresponding volume. NAA was quantitated using the fully relaxed water signal as an internal standard of reference. There was a significant correlation between a reduction in the absolute concentration of NAA from a chronic MS lesion (range 3.5 mM-12.8 mM, median 9.25mM) visible on MRI and reduction in the MT value (range 14.6-28.6, median 25.3) from the same lesion (P<0.002, r=0.71).

These preliminary results support the hypothesis that demyelination and axonal loss occur together in destructive MS lesions and that there may be a common pathological mechanism producing both.

MELAS OR MNGIE?: AN UNUSUAL PRESENTATION OF A MITOCHONDRIAL RESPIRATORY CHAIN DISORDER R J Davenport, C J Mumford, L A Bindoff, S Jones, University of Edinburgh, Edinburgh, UK.

An 18 year old woman presented in 1996 with status epilepticus; two years previously she had undergone a partial gastrectomy and Roux-en-Y formation for repeated episodes of pseudo-obstruction for which no cause was identified. On admission, she had a lactic acidosis. Subsequent investigations showed 10% ragged red fibres on muscle biopsy, and a 3243 mutation on mitochondrial DNA analysis in blood and muscle. She has since had two further admissions with status, both preceded by a migraine headache, and has developed deafness. Her last admission was complicated by recurrent anoxia and vomiting which eventually settled. Although our patient had the 3243 mutation usually associated with MELAS, she is phenotypically quite unlike this syndrome; unusual presentations of 3243/MELAS are recognised, but gastrointestinal dysmotility has not been described. Gastrointestinal dysmotility does occur in mitochondrial respiratory chain disease as the MNGIE syndrome (mitochondrial neurogastrointestinal encephalomyopathy). However, these patients commonly have ophthalmoplegia and peripheral neuropathy which our patient does not, and epilepsy and migraine are not described, which are prominent features in this case.

This case emphasises two points; firstly, that patients with mitochondrial disease may initially present to specialists other than neurologists and the diagnosis may be delayed. Secondly, that whereas certain clearly identifiable phenotypic mitochondrial diseases exist, some patients do not fit easily into such categories.

DOES AXONAL LOSS AND DEMYELINATION OCCUR TOGETHER IN THE SAME LESIONS IN MULTIPLE SCLEROSIS? C A Davie, W I McDonald, A J Thompson, D H Miller, Institute of Neurology, Queen Square, London, UK.

It has been proposed that demyelination (MT) provides information about the integrity of myelin. Similarly, the measurement of N-acetyl aspartate (NAA) an amino acid localised to neurons and their processes—by magnetic resonance spectroscopy (MRS) has been used as index of axonal loss and/or dysfunction in multiple sclerosis (MS). MRI, MT imaging, and MRS were carried out on 18 patients with clinically definite MS. The group comprised patients with a wide range of disability (range 2-25 years, median 7 years). Single voxel MRS localised to a chronic area of high signal from hemispheric white matter which had been present for greater than 12 months was collected. MRS was then calculated from the corresponding volume. NAA was quantitated using the fully relaxed water signal as an internal standard of reference. There was a significant correlation between a reduction in the absolute concentration of NAA from a chronic MS lesion (range 3.5 mM-12.8 mM, median 9.25mM) visible on MRI and reduction in the MT value (range 14.6-28.6, median 25.3) from the same lesion (P<0.002, r=0.71).

These preliminary results support the hypothesis that demyelination and axonal loss occur together in destructive MS lesions and that there may be a common pathological mechanism producing both.

MOLECULAR GENETIC DIAGNOSIS OF FREIDREICH’S ATAXIA WITH APPARENT AUTOSOMAL DOMINANT SPINOCEREBELLAR DEGENERATION R de Silva, C Frew, A Cooke, R Davidson, Southern General Hospital, Glasgow and Yorkhill Hospital, Glasgow, UK.

Freidreich’s ataxia (FRDA) is an autosomal recessively inherited disorder in which spinocerebellar degeneration occurs, usually from the second decade of life. Recently, FRDA has been linked with mutations (GAA triplet repeats or point mutations) of the intronic X25 gene on 9q3. Genome analysis of affected members of a pedigree with presumed adult onset, autosomal dominant spinocerebellar degeneration has yielded an unexpected diagnosis of FRDA. A 26 year old man was seen with a seven year history of progressive dysarthria and limb ataxia. Examination also disclosed pes cavus, myasthenus, hyperactive lower limb reflexes and intact joint position sense. His 22 year old sister had had poor balance for seven years, and is now wheelchair bound and dysarthric. Their 46 year old father (who misuses alcohol) had had ataxia for at least two years. The daughter of the proband has presented with transient incoordination at the age of 18 months. PCR using primers for the GAA repeat at 9q3-3.1 on the proband and his siblings disclosed expanded allele smears of between 2000 and 3000 bp, making FRDA highly likely.

Symptoms and signs of ataxia in the proband’s father and daughter implied a dominant mode of inheritance. It is conceivable that FRDA heterozygotes can develop ataxia particularly in association with environmental insults.


Background—Some treatments for acute stroke—for example, thrombolysis, may increase the risk of death, but also reduce the proportion of dependent survivors. Therefore, groups of independent and dependent stroke survivors were compared as to how they rated their own quality of life.

Methods—The EuroQol is a generic instrument for the measurement of health related quality of life (HRQoL). It includes a visual analogue scale on which patients rate their own health between 0 (worst possible) and 100 (best possible), so providing an overall numerical estimate of their HRQoL. HRQoL was assessed by postal follow up with the EuroQol questionnaire in 1125 United Kingdom patients randomly selected from patients enrolled in the International Stroke Trial.

Results—903 patients responded (response rate 80%). Mean overall HRQoL among independent patients was 68 (95% CI 23 -100). This was significantly greater than in patients who were dependent at follow up (mean 44, 95% CI 1 - 87; P<0.01). However, 83% of dependent stroke survivors reported overall HRQoL within the range of the independent survivors (23 to 100) and 15% rated their overall HRQoL as greater than 68 (the mean of the independent survi-

Discussion—A high proportion of survivors of stroke who are dependent in ADL rate their HRQoL surprisingly highly, sometimes as high as independent survivors. Stroke free patients may prefer death to dependent survival, but patients who have survived a stroke in a dependent state seem to view things differently.

SUPRATENTORIAL WHITE MATTER VOLUMES ON MAGNETIC RESONANCE IMAGES CORRELATE WITH COGNITIVE PERFORMANCE IN MULTIPLE SCLEROSIS (MS) S G M Edwards, N Roberts, L D Blumhardt, University of Nottingham, Nottingham, UK.

Despite the high sensitivity of MRI and the high prevalence of cognitive deficits in MS, correlations between neuropsychological test performance and various MRI parameters have been weak and inconsistent. In the present study the aim was to correlate neuropsychological indices with the volumes of supratentorial structures and the area of the corpus callosum in 40 patients with clini-

supratentorial white matter (SWM), grey matter, and ventricles comprised 22.2
Background—There are about 20,000 subjects with the narcoleptic syndrome in the United Kingdom. Diagnosis depends on the definite presence of cataplexy defined as laughter triggered sudden loss of motor tone with mutism and dysthria accompanied by facial muscle flickering. Additional features are excessive daytime sleepiness, sleep precipitated, interrupted night sleep, and a high frequency of sleep paralysis and other motor parasomnias. Present treatment is unsatisfactory. The development of the sleep preventing drug modafinil may allow more effective treatment. The mode of action of this drug is not known.

Methods—Twelve subjects with the narcoleptic syndrome and 12 controls were studied using functional MRI of auditory and visual cortical areas, recording evoked responses to periodic auditory and visual stimuli. Echoplanar MR images were acquired using a 1.5 Tesla GE Signa Signal. The action of modafinil (400 mg) as a single oral dose (16 subjects) was compared with placebo (eight subjects).

Results—Modafinil caused an increase in self-rated levels of alertness in seven of eight narcoleptic subjects. Calcareous and auditory cortical activation, as determined by pixel count, was higher in normal than narcoleptic subjects and in males than females. There was no significant difference in pre and post-modafinil activation levels in either control or narcoleptic subjects. However, the response to modafinil, but not placebo, was correlated with pretreatment level of activation (auditory, $r=0.7$, $P<0.002$; visual, $r=-0.8$, $P=0.001$).

Conclusion—Functional MRI shows a slightly lower mean cortical activation in narcoleptic than control subjects. Low activation levels are increased by modafinil.

TREATMENT OF NEUROPSYCHOLOGICAL SYMPTOMS IN UNATTENDED AND LEVODOPA TREATED IDIOPATHIC PARKINSON'S DISEASE

C Ellis, G Lemmens, S C R Williams, J Dawson, A Simmons, P N Leigh, K R Chaudhuri, King's College Hospital and Institute of Psychiatry, London, UK.

Aim—To investigate long term memory and depression, in patients with neurological disability or handicap, without impairment or pathology (non-organic neurology).

Amnesia for childhood correlates with non-organic symptoms

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<th>Organic</th>
<th>Non-organic</th>
<th>Significance</th>
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<tr>
<td>n</td>
<td>55</td>
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<tr>
<td>1mem (y; median)</td>
<td>4</td>
<td>11</td>
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<td>Cmem (y; median)</td>
<td>6</td>
<td>18</td>
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<td>Memory blanks (n)</td>
<td>3</td>
<td>7.0</td>
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<td>RADSEC score (median)</td>
<td>4.0</td>
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Method—100 consecutive new neurological out patients were asked their age at first ever memory (Imem) and at onset of continuous memory (Cmem), and about memory blanks; evidence of depression was sought (brief assessment schedule depression cards: BASCDEC. Score >6.5 suggests depression).

Results—The table presents the results.

Conclusion—‘Non-organic’ neurological presentation is commonly associated with a delayed onset of continuous memory.

PERSISTENCE OF MONOSYNAPTIC GROUP IA PROJECTIONS BETWEEN ANTAGONIST MUSCLES IN STUDY normal restriction of reflexes to deltoid and showed persistence of monosynaptic heterotonal and longitudinal studies all subjects decreased in frequency by two years. A responses were frequent at birth and rapidly recorded in the surface EMG of 11 adults with spasticity after stroke. (2) syndrome,11tetraparetics,11hemiplegics), and di subjectswithspasticityofperinataloriginbut status declined (EDSS medians A=6.8, D=6.8, IY=8.0), whereas disability (FIM medians A=61.3, D=74, I Y=63.5), handi- (LHSS means A=60.3, D=64.4, I =61.6), and mood (GHQ medians A=9.5, D=1.5, I Y=4) maintained some improve- ment. Although a gradual reduction in disability, handi- was recorded, average scores remained above admission level. This suggests that the benefits gained from neurorehabilitation are sustained, at least in part, over a 12 month period, despite deteriorating neurological status.

CATEGORY SPECIFIC SEMANTIC LOSS IN DEMENTIA OF ALZHEIMER’S TYPE: INSIGHTS INTO THE ORGANISATION OF KNOWLEDGE IN THE BRAIN P Garrard, K Patterson, P Watson, J R Hodges, University of Cambridge Neurology Unit, Cambridge, UK.

In the context of focal brain injury, selective loss of semantic knowledge of natural kinds or artefacts is usually considered to reflect the differential importance of temporal and fron- todorical regions to the representations of perceptual and functional attributes, respec- tively. It is harder to account for as a feature of a more diffuse process, and previous cross sectional analyses of DAT patients have differed over whether category effects occur. In a series of 58 patients with probable DAT there was a significant group advantage for artefacts, possible reasons for the inconsist- ency of this finding in other studies was explored. A multiple single case strategy dis- closed patients with consistent advantages for both domains of knowledge. By ranking the group according to measures of naming perfor- mance and global intellectual ability, a strong double dissociation of semantic cate- gories was shown, dependent on the former but not the latter variable. The longitudinal profiles of individual patients were also examined. The findings were discussed in the context of two competing theories of semantics breakdown in DAT: an anatomically based model, and a distributed model. It is concluded that the findings are in keeping with the predictions of the former.

INTRA AND INTEROBSERVER VARIABILITY IN THE ASSESSMENT OF TEMPORAL LOBE ATROPHY P Garrard, N M Antoun, C E L Freer, J R Hodges, University of Cambridge Neurology Unit, Cambridge, UK.

Introduction: Quantification of the relative involvement of right and left temporal lobes in cases of semantic dementia is an essential first step in elucidating the contributions of these structures to the neural representation of semantic knowledge. Formal volumetric assessment is time consuming, and as yet neither a method nor a range of normality has been described. For within subject compar- isons a semiquantitative assessment of the degree of atrophy is an acceptable alternative approach. An attempt was therefore made to validate this method.

Methods—Two senior neuroradiologists gave independent assessments of the degree of atrophy of both temporal lobes on coronal MRI images of 14 patients with the clinical syndrome of semantic dementia. Anterior and posterior slices were graded on an integer scale from 0 (normal) to 3 (severe atrophy). The procedure was repeated after 24 hours.

Results—The strength of within observer agreement ranged from moderate to very good (K 0.41-1.00), with the strongest agreement on binary judgements (normal v abnormal – direction of asymmetry). Strength of between observer agreement was much weaker overall (K 0.16-0.62), with the strongest agreements again emerging for binary judgements.

Conclusion—Subjective assessment of tem- poral lobe atrophy is too variable a measure to justify its use in studies of functional- anatomical correlates of temporal lobe atro- phy.


Using coronary artery bypass (CPB) as a human model of cerebral ischaemia the hypothesis that the glutamate antagonist remacemide hydrochloride (RH) might re- duce both the incidence and severity of persistent cognitive deficits after coronary artery bypass surgery (CABS) was examined.

One hundred and seventy patients sched- uled to have elective, primary CABS were randomly allocated to receive RH (600 mg daily (n=87) or placebo (n=84) for five days before and after CABS. Cognitive function was measured one week before and six days and eight weeks after CABS using a battery of 10 neuropsychological (NP) tests. An NP deficit was defined as a score more than one SD from the preoperative mean test score in two or more tests. At six days 37% on placebo and 41% on treatment showed a deficit. By six weeks this had fallen to 12% on placebo and 9% on RH (Fisher’s exact P = 0.6). The study showed no evidence of neuroprotection by this gluta- mate antagonist but the paradigm seems use- ful for screening such compounds.


New disability measurement instruments must demonstrate advantages over existing measures to warrant adoption into routine clinical practice, particularly when they are resource consuming. The widely used Bar- thel Index (BI) is generally viewed as too simplistic, crude, and unresponsive (insensi- tive as a clinical change) to evaluate therapeutic effectiveness. The functional independence measure (FIM) was specifically developed to enable reliable, valid, and responsive disabil- ity measurement. Despite increasing world- wide use, and being widely regarded as a gold standard measure, evidence in support of the FIM’s superiority is limited.

This multicentre study compares the reli- ability, validity, and responsiveness of the FIM and BI in 209 patients undergoing inpa- tient neurorehabilitation.

Internal consistency reliability (Cronbach’s α) of both instruments was high; FIM=0.96; BI=0.91. Validity was assured by examining correlations between FIM and BI score.
with six other disability measures. Correlations were almost identical with all BI correlations (<0.07). Responsiveness was determined by calculating an effect size from admission and discharge ratings and was similar (0.85, 95% CI 0.65-0.95).

Whereas reliability, validity, and responsiveness of both instruments is demonstrated the complex and costly FIM offers little over the simple and cheap BI in terms of measurement properties in this population.

**FUNCTIONAL MAGNETIC RESONANCE IMAGING (fMRI) OF A SHORT TERM MEMORY TASK**

J Hykin, S Clare, R Bowtell, M Humberstone, P Morris, L D Blumhardt, University of Nottingham, Nottinghamshire, UK.

In this work fMRI is used to identify regions of the brain activated during separate parts of a short-term memory task.

Whole brain images were obtained on a 3.0 T MRI scanner at every two seconds. Four volunteers were studied. A four part short term memory task was used consisting of (1) Recognition; viewing three numbers over three seconds; (2) Retention; remembering the numbers for 11 seconds; (3) Recall and match; matching a number with the first 3; (4) 12 seconds rest. 32 tasks were performed. Images taken during rest were compared with images taken during the first three parts of the task. Significant changes in pixel intensities between rest and task were detected using a t test showing a threshold at P=0.01.

fMRI time courses from four regions were shown. The normal fMRI response is delayed and dispersed, however by deconvolving the response the true timing of brain activation can be resolved.

Significant regions seen are: fusiform gyrus (FG); reception, recall, and match. Medial temporal lobes (MTL); recall and match. Left supramarginal gyrus (LSMG); retention, recall, and match; medial frontal gyrus (MFG) all parts. Thus fMRI can be used for short cognitive events.

**HEREDITARY MOTOR AND SENSORY NEUROPATHY – LOM (HMSN)**

P K Thomas, L Kalaydjieva, R H M King, Edith Cowan University, Perth, WA, Australia and London University, London, UK.

An autosomal recessive peripheral neuropathy associated with deafness was initially identified in the Gypsy community in the town of Lom on the Danube in north west Bulgaria. Subsequently the disorder has been recognised in Gypsies in other Balkan countries. The onset is in the first decade and most affected people are severely disabled by the fifth decade. Deafness is invariably and usually present by the third decade. Examination shows sensorineural deafness, distally accentuated muscle wasting and weakness, tendon areflexia, distal sensory loss and foot and hand deformity. Motor nerve conduction velocity is severely reduced, in the demyelinating range, and sensory action potentials are depressed or absent. Brainstem auditory evoked potentials show increased interpeak latencies, suggesting demyelination. Sural nerve biopsies from early cases demonstrate a demyelinating neuropathy with poorly developed hypertrophic changes. The features in early cases have not yet been examined. Genetic studies have mapped the responsible gene to chromosome 8q24. Linkage age to approximately the same region has recently been reported in a black American family with autosomal dominant Dejerine-Sottas neuropathy, raising the possibility of allelic mutations in a novel myelin gene on chromosome 8q24. No myelin genes are currently known to be located at this site.

**CHILDREN WITH CEREBRAL PALSY HAVE NORMAL DEVELOPMENTAL RECIPROCAL INHIBITION**

S McDonough, S Miller, J A Byre, Newcastle upon Tyne University, Newcastle upon Tyne, UK.

**Introduction**—Contraction of antagonist limb muscles is prominent in infancy, persists in those with cerebral palsy, but is not characteristic of adult spasticity.

**Hypothesis**—Reciprocal inhibition is not mature at birth and fails to develop in those with perinatal brain damage.

**Subjects**—(1) Cross sectional study in 100 normal children (32 weeks gestation to 4 years) and 20 adults; (2) longitudinal study (12 months) of 30 normal neonates and 10 at high risk for spastic cerebral palsy. Ethical approval and written informed consent were obtained.

**Methods**—Reciprocal inhibition to contralateral biceps force was evoked by mechanical taps to the relaxed tendon of triceps brachii at intensities sufficient to activate L4/A afferents. The taps were delivered in pseudo-random binary sequences of 1.3 s duration, which were cross correlated with the surface EMG of biceps brachii.

**Results**—In both studies of normal subjects reciprocal inhibition was shown in 30% at birth and in all by 9 months. The 10 high risk babies (four with spastic tetraparesis at 12 months) demonstrated the same normal developmental pattern.

**Conclusion**—Contraction in cerebral palsy is not a consequence of failure of reciprocal inhibition.

**DISORDERED HETERO NYMOUS GROUP 1A MUSCLE REFLEXES IN SUBJECTS WITH BRAIN DAMAGE ACQUIRED PERINATALLY AND IN ADULTHOOD**

V M McLellan, J A Byre, S Miller, Newcastle upon Tyne University, Newcastle upon Tyne, UK.

**Introduction**—Persistence of aberrant reflex responses in subjects with perinatal brain damage suggests that not only the descending control of reflex activity, but also the development of appropriate spinal reflex connections are disrupted. This hypothesis was tested for heteronymous reflexes between antagonist muscle pairs at the elbow and shoulder.

**Adult subjects—**24 normal, 10 with cerebral palsy (six tetraparetic, four hemiparetic), 10 subjects with spastic hemiplegia after stroke.

**Methods**—Heteronymous reflex responses were recorded in the surface EMG of biceps and triceps brachii, posterior deltoid and clavicular pectoralis major. Heteronymous excitatory and inhibitory reflexes were recorded in turn from each muscle contracting to 10% MVC, while the tap was applied to the relaxed tendon of the other muscles. The taps were delivered in pseudorandom binary sequences of 1.3 s duration, which were cross correlated with the EMG, providing for each subject up to 36 trials for each muscle combination.

**Results**—The frequency of heteronymous excitatory and inhibitory responses was calculated for each muscle combination. In normal subjects inhibition was predominant between antagonist muscles, but an equal probability of excitation and inhibition between elbow and shoulder muscles was found. In cerebral palsy the frequency of heteronymous inhibitory responses was reduced and there was an abnormal increase in excitatory reflexes. In stroke there was a reduction of the frequency of both excitatory and inhibitory heteronymous reflexes.

**EPILEPSY SURGERY, VISUAL FIELDS, AND DRIVING**

H Manji, G T Plant, National Hospital for Neurology, London, UK.

**Aims**—The United Kingdom DVLA regulations stipulate “the minimal visual field for safe driving is a field of vision of at least 1200 on the horizontal using the Goldman perimeter 1114e setting (or equivalent). In addition, there should be no significant field deficit in the binocular field which encroaches within 200 of fixation above or below the horizontal meridian.” The aim of this study was to ascertain how many patients after temporal lobe resection fail the visual field criteria for driving.

**Methods**—23 patients (12 women, 11 men; mean age 33.4 years, range 21-47) who had undergone temporal lobe resection for epilepsy were randomly selected. The underlying diseases were: hippocampal sclerosis (HS) (17), non-specific gliosis (two), angioma (one), DNET (one), and low grade glioma (two). They underwent perimetry using the Goldman 1114e setting and the Esterman binocular field assessment.

**Results**—10/23 (43%) had normal fields. There were no significant differences in the presence of a field deficit between those with HS and those with other diseases (C2=0.11, P=0.9). 6/23 (26%) had field deficits but passed the driving criteria. 7/23 (30%) had deficits which failed the driving criteria. 3/23 (13%) of patients were fit free but failed the field criteria for driving.

**Discussion**—A significant number of patients who have undergone temporal lobe resection will not be eligible to drive in the United Kingdom because of significant field deficits even if they are rendered fit free.

**SAMPLE SIZE CALCULATIONS FOR MRI OUTCOME PILOT TRIALS IN MULTIPLE SCLEROSIS: RELAPSING-REMITTING VERSUS SECONDARY PROGRESSIVE SUBGROUPS**

D H Miller, N Turbridy, H Adier, F Barkhof, A J Thompson, Institute of Neurology, London, UK and Free University Hospital, Amsterdam, The Netherlands.

Serial brain MRI is widely used in pilot studies of new agents to monitor treatment efficacy in relapsing-remitting (RR) and secondary progressive (SP) multiple sclerosis (MS) subgroups. For pilot trials, separate sample size calculations for the SP subgroup are currently not available. The present study considers this issue.

The calculations are based on data from six months of monthly T2 weighted and gadolinium enhanced MRI in 31 RR and 28 SP untreated patients undergoing natural history studies. The calculations are for a placebo controlled, parallel groups design lasting six months. The sample sizes are based on boot strap analysis with an 80% likelihood of showing a given treatment effect.

With a single baseline scan, demonstration of a 50% reduction in newly active lesions requires 28 RR and 20 SP patients. With
an extra baseline scan one month before treatment, the samples sizes are 2×20 for RR and 2×30 for SP patients.

This study shows an important difference in the pattern of longitudinal MRI activity in RR and SP groups. The sample sizes required for RR patients are comparable with previous studies. Larger sample sizes are needed for the SP group, and an extra baseline scan results in a reduction in both groups. These data should be considered in planning pilot MRI outcome trials.

C REACTIVE PROTEIN AND OUTCOME AFTER ACUTE STROKE

K W Muir, C J Weir, W Alwan, C Povey, I B Squire, K R Lees, Acute Stroke Unit, Glasgow, Scotland.

Background—Raised C reactive protein (CRP) is a marker of risk in acute coronary syndromes and may represent an inflammatory element of atherosclerotic lesions. The effect of CRP on stroke outcome was studied.

Methods—Consecutive admissions to an acute stroke unit had blood analysed for CRP concentration within 72 hours of admission. Data on risk factors, stroke type, and severity were collected. Patient outcome was determined by record linkage to the Scottish Deaths Register. Survival and cause of death were analysed.

Results—263 of 283 patients had a stroke; 240 had ischaemic stroke, and 23 haemorrhage. Survival was significantly worse in those with CRP above the mean (P=0.0003, log rank test). In a Cox proportional hazards model, systolic pressure was related to survival independently of stroke severity, blood glucose, and age (P<0.05), a more definite relation being demonstrable for those with ischaemic stroke only (P=0.02). The cause of death certified was stroke or myocardial infarction in most patients.

Conclusions—Raised CRP within 72 hours of admission predicts survival after stroke. As deaths were predominantly due to atherosclerosis, this is consistent with a heightened role of inflammation in the pathogenesis of acute coronary and cerebrovascular syndromes and may be a useful clinical marker for aggressive intervention.

DYSARTHRIA CAN CONCEAL DYSPHASIA IN MOTOR NEURON DISEASE

W P Rakowicz, J R Hodges, Norfolk and Norwich Hospital, Norwich and Addenbrooke's Hospital, Cambridge, UK.

Cognitive impairment is not usually regarded as part of the core syndrome of motor neuron disease (MND). Nevertheless, a few patients have overt dementia, typically frontal type or progressive aphasia. Speech in MND is often reduced in loudness and volume. Bulbar symptoms. The question of whether dysphasia may also impair communication was considered.

16 consecutive patients presenting to a district neurology service over three years with a new diagnosis of MND fulfilling research criteria were assessed with a comprehensive battery of standardised neuropsychological tasks. Particular attention was paid to semantic and syntactic aspects of language production and comprehension.

Four of 16 patients (31%) became mute during the course of the study. Of these, three (19% of total, 75% of mute MND) had demonstrable language impairment. Only one reported seeking finding difficulties at the time of diagnosis. The other two denied language difficulties whereas their relatives ascribed all communication problems to deteriorating articulation. One non-mute patient (1/12) performed outside normal limits on language tests in the context of more generalised changes consistent with a frontotemporal dementia. The other 11/12 patients performed normally.

It is concluded that dysphasia is more common in MND than is generally appreciated, particularly in mute subjects, but can be missed because of prominent bulbar symptoms.

PROGNOSTIC IMPACT OF POST-ENCEPHALITIC DYSARTHRIA

N Robertson, J O’Riordan, J Chataway, D Kinsey, D Miller, A S Compston, University Department of Neurology, Cambridge, UK.

There has been no previous systematic study of conjugal MS. The study of conjugal pairs with complete clinical and radiological data and comprehensive information regarding disease transmissibility and the genetic contribution to disease frequency and clinical course.

Forty five conjugal pairs concordant for MS were studied; clinical features were compared in 33 where neither partner had symptoms before social introduction; 86 offspring were individually assessed for clinical evidence of neurological disease and those over the age of 16 underwent cranial MRI. There was no evidence for clinical concordance, clustering at year of onset, or distortion of the expected pattern of age at onset in the second affected spouse. Five of 86 offspring (5.8%) were concordant for MS; four of 86 (4.7%) reported isolated episodes of neurological dysfunction. Six of 39 (15.4%) offspring had MRI abnormalities which fulfilled criteria for the diagnosis of MS. Three others (7.7%) had lesions consistent with demyelination not meeting these criteria. In total 14% had some evidence of disease.

The recurrence risk in children of conjugal pairs is significantly higher than recurrence risks for offspring of single affected parents (1:200). The risk for developing MS is evidently inherited from both parents and this argues against genetic heterogeneity. There is no evidence for a transmissible agent or for a genetic effect on clinical course or severity.

AUDIT OF AN EMERGENCY CLINIC IN NEUROLOGY

N Robertson, S Shaunik, D A S Compston, Neurology Unit, University of Cambridge, Cambridge, UK.

Effective triage of primary care referrals is an essential part of neurology service management. In a retrospective analysis of selected patients referred for a rapid referral clinic the effectiveness of identifying patients with serious abnormalities requiring urgent assessment was analysed. Statistical correlation with symptom groups was presented and the effect of such a clinic on auxiliary services was evaluated.

Twenty five per cent of telephone referrals from primary care physicians led to identification of patients considered suitable for urgent evaluation; 323 patients were assessed over an 18 month period. After neurological review relevant abnormalities were identified in 73% and 33% were considered to have warranted urgent assessment. In addition 74% required radiological evaluation and 14% had a neurophysiological procedure; 17% of patients were admitted on the same day, 13% underwent CSF analysis, and 34% required some form of therapeutic intervention. In retrospect, patients with a clinical history of greater than 11 days rarely warranted urgent referral. Despite the number of patients reviewed, no effect was demonstrated on waiting times for standard outpatient review.

This work provides effective guidance to those clinicians involved in patient triage and assesses the burden of providing such a service.

IS RUPTURE OF CAROTID ATEROTHROMBOTIC PLAQUE DETERMINED BY LOCAL OR SYSTEMIC FACTORS?

P Rothwell, R Vilagra, R Donders, C P Warlow, Western General Hospital, Edinburgh, UK.

The risk of ischaemic stroke distal to an atherothrombotic carotid plaque is increased if the plaque surface is irregular. Likewise, acute cardiac ischaemia is almost invariably associated with an irregular or ruptured coronary artery plaque. The risk of major vascular events in the territory of a diseased artery seems to be determined as much by the stability of atherosclerosis as by its extent. Plaque stability is considered to be determined by local factors such as shear stress or intraplaque ischaemia, but may also be influenced by systemic factors. This paper tests the hypothesis that plaque stability is constitutionally, angiograms of 3007 patients with recently symptomatic carotid stenosis in the European Carotid Surgery Trial were studied. Plaque surface morphology in the symptomatic carotid artery was compared with that in the contralateral carotid artery, and related carotid plaque surface morphology to the risk of non-stroke vascular death during follow up. Plaque surface irregularity in the symptomatic carotid artery was highly predictive of irregularity in the contralateral carotid artery (risk ratio 2.57, 95% CI=2.12-3.12, P<0.0001), and was associated with an increased risk of non-stroke (mainly cardiac) death (log rank, P<0.0001). It is suggested that plaque instability is constitutionally. Further research is required to determine whether or not it is modifiable.

PATTERNS OF LONG ASCENDING PROPRIOSPINAL REFLEXS IN SHOULDER MUSCLES IN HUMAN SUBJECTS AFTER ELECTRICAL STIMULATION OF LOWER LIMB NERVES

M Sawers, J A Eyre, S Miller, Newcastle upon Tyne University, Newcastle upon Tyne, UK.

Introduction—In neonatal and adult subjects percutaneous magnetic stimulation of lumbo-sacral nerve roots evokes excitatory and inhibitory responses in surface EMGs of upper limb muscles at latencies sufficiently brief to be compatible with propriospinal transmission.

Aims—to determine if lower limb nerves contributed differentially and in a functional pattern to these long propriospinal reflexes.

Subjects—Eleven normal adults. Ethical permission and written, informed consent were obtained. Responses were recorded in the surface EMG of ipsilateral pectoralis
Epilepsy: Current Views

Results—Responses obtained in Pmaj and Pdelt had early (12-30 ms), intermediate (40-60 ms), and late (70-100 ms) excitatory and inhibitory components. In three subjects tested, the onset latencies of the early responses were 2.7-3.3 ms longer than estimates of minimum long propriospinal latencies, suggesting disynaptic or oligosynaptic linkage in a fast conducting propriospinal pathway. A pattern of responses emerged: (1) The diagnostic ratio of excitatory and inhibitory responses occurred more often evoked than intermediate and late responses with all three lower arm nerves (3) the common peroneal nerve is more likely to mediate responses than tibial or femoral nerves.

Linkage in Multiple Sclerosis


There is now overwhelming evidence that susceptibility to multiple sclerosis involves genetic factors. In the light of this we have screened the entire human genome for evidence of linkage and have identified several potentially linked regions. In the first stage of this screen 311 microsatellite markers were typed in 129 families. Twenty regions showing some evidence of linkage to disease were identified. In the second stage 69 markers from 16 of these regions were typed in a further 98 families. The evidence for linkage increased in four regions. The analysis was performed using the multipoint sib pair linkage program MAPMAKER/SIBS and the significance of the results was established using computer simulations. The strongest evidence for linkage was found on chromosomes 17q22-24 and 6p21 (the major histocompatibility complex). In addition, linkage disequilibrium at the TNFA marker from the 6p21 region was also detected. On the other hand, cytotoxic T cell assays, enzyme linked immunosorbent assay (ELISA), flow cytometry, and immunohistochemistry.

Results—Neurofilamentous accumulations and ubiquitin immunoreactive inclusions were found in both cases. In one these were found in both cases. In the other they were also present in pyramidal cells of the motor cortex. Electron microscopy disclosed bundles of neurofilaments I within anterior horn cells. There was no evidence of accumulation of SOD-1, SOD-2, or tau proteins.

Discussion—The cytoskeletal pathology of familial ALS with SOD-1 mutation falls within the range of all ALS pathology. The toxic accumulation of mutant SOD-1 is unlikely to be directly responsible for motor neuron injury.

Aim—To assess if specific immunity is required for inflammation induced by CNS viruses

Methods—C57BL/10 mice were inoculated with the non-neurovirulent influenza virus A/NT/60/68 either directly into the caudate nucleus or into the lateral cerebral ventricle. An assessment of local and systemic antiviral immunity was made using proliferative responses, cytotoxic T cell assays, enzyme linked immunosorbent assay (ELISA), flow cytometry, and immunohistochemistry.

Results and discussion—Virus inoculated into the brain parenchyma was immunologically silent in most mice 10 and 90 days after inoculation. By contrast, virus inoculated into the lateral ventricle was highly immunogenic. Although a lymphocytic inflammatory reaction was induced at both sites, only lymphocytes isolated from the brains of mice inoculated with ventricular virus were antigen specific. Activated antiviral CTL were purified from the brains of mice given a simultaneous parenchymal and intranasal challenge, indicating that the environment of the brain parenchyma was not inducing tolerance. Although most immune T cells were CD4+ and CD26+ and were thus activated or memory cells, a proportion were CD4+ and CD26+ and were therefore not activated.

These results indicate that inflammation can be induced by virus in the CNS even in the absence of specific antiviral immunity.

Regenerating Oligodendrocytes and Remyelination in Multiple Sclerosis

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Aims—To determine the possible contribution of mature oligodendrocytes to remyelination in multiple sclerosis (MS) lesions.

Methods—Adult rat glia were studied in vitro, in coculture with neurons, and after transplantation into demyelinated rat CNS lesions.

Results—Adult oligodendrocytes and their progenitors survive and proliferate under the influence of neurons in vitro, an effect enhanced by growth factors. When transplanting into denervated cells contribute to remyelination, and the non-dividing cells fail to survive. When lesions are irradiated after transplantation, to kill dividing cells, non-myelinating oligodendrocytes are able to survive in the lesions. The interactions of regenerating mature oligodendrocytes and neurons were therefore studied. Neurons inhibit mature oligodendrocyte processing, while permitting progenitor derived oligodendrocytes to extend complex processes. Dividing oligodendrocytes can be identified; however, they are derived from differentiating progenitors, rather than regenerating oligodendrocytes.

Discussion—Postmitotic mature oligodendrocytes do not have the attributes necessary for remyelination. It is hypoth-
oses that their absence from remyelinating lesions reflects limited access to survival factors through poor association with axons, as well as growth factor utilisation by dividing progenitors. Thus mature oligodendrocytes may play no part in remyelination in MS, and their presence in lesions may reflect the absence of the conditions required for remyelination.

A Clinical Role for 90Tc-HMPAO SPECT in the Differential Diagnosis of Dementia

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90Tc-HMPAO single photon emission computed tomography (SPECT) is increasingly used as a clinical tool in the diagnosis of dementia. However, its precise contribution in differentiating forms of dementia has not previously been quantified. Three hundred and sixty three dementia patients referred to the Cerebral Function Unit at Manchester Royal Infirmary were grouped on the basis of neuropsychological, neurological, and CT findings.

The diagnostic gain of 90Tc-HMPAO SPECT was documented.
encountered forms of dementia was determined by calculating the likelihood ratios of pairwise intergroup comparisons for different patterns of cerebral blood flow (CBF) abnormality. To quantify the clinical value of 99mTc-HMPAO SPECT; average likelihood ratios were calculated weighted according to the prevalence of CBF patterns. 99mTc-HMPAO SPECT was found to provide diagnostic gain for all intergroup comparisons. It was most useful in distinguishing Alzheimer’s disease and Lewy body dementia from frontotemporal dementia, and least useful in differentiating between Alzheimer’s disease and Lewy body dementia, and between vascular dementia and frontotemporal dementia. Study results provide a guide both to the optimal usage of 99mTc-HMPAO SPECT and the interpretation of individual test results.

**EFFECT OF LAMBERT-EATON MYASTHENIC SYNDROME (LEMS) ANTIBODIES ON TRANSMISSION FROM POSTGANGLIONIC PARASYMPATHETIC NEURONS IN THE MOUSE BLADDER**

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LEMS patients produce antibodies to P, Q, and sometimes N type voltage gated calcium channels (VGCCs) which have been implicated in the impaired skeletal neuromuscular transmission. The cause of the autonomic symptoms in LEMS has not been investigated. The aim of this study was to investigate a possible antibody mediated mechanism for the autonomic symptoms by studying transmission from parasympathetic neurons innervating the bladder of mice passively immunised with LEMS IgG. Mice were injected with IgGs (coded) from pooled controls (PC; n=10), a healthy subject (HC; n=10), a patient with myasthenia gravis (MG; n=8), and four LEMS patients: LE1-4 (n=8 of each). Strips of bladder dome were mounted in organ baths and electrically evoked contractions recorded in the absence and presence of conotoxin GVI, agatoxin IVA, and conotoxin MVIIC (N, P, and Q type VGCC blockers respectively). Contraction amplitudes were significantly less in LE3 and LE4 than in controls. Transmitter release coupled to P and Q type VGCCs was decreased in all mice treated with LEMS antibodies. This suggests that LEMS IgG reduces parasympathetic transmission through down regulation of VGCCs and this may underlie the autonomic symptoms of the disease.

**PERIPHERAL AND CENTRAL RESPONSES TO HIGH FREQUENCY NERVE STIMULATION USING A DECONVOLUTION TECHNIQUE**


Using standard averaging techniques, the maximum rates of stimulation at which sensory action potentials (SAPs) and cortical somatosensory evoked potentials (SSEPs) can be obtained are limited by the fact that successive responses overlap at rates of >1/t stimuli/s, where t is the total duration of the response in seconds. In practice, this limit may be up to 300 stimuli/s for SAPs and 20 stimuli/s for SSEPs. The investigation of rate dependent conduction block in peripheral and central lesions might be facilitated if this effect could be overcome. Faster stimulus rates would also allow SSEPs to be derived more rapidly, which may be of practical benefit in operative monitoring.

Various fast stimulation protocols for brainstem evoked potentials and SSEPs have been described. Median SAPs and SSEPs at stimulus rates of at least 1280 and 160 stimuli/s respectively in normal subjects have recently been obtained using quasirandom binary stimulus trains known as maximum length sequences. The overlapped records are deconvolved to obtain the response that would have been obtained using conventional slow averaging.

Patients with focal and generalised peripheral neuropathies and multiple sclerosis are currently being studied to determine whether this rapid simulation technique can detect conduction abnormalities covert to those methods currently employed.
BOOK REVIEWS


This book's reputation preceded its arrival on my desk with the news that Boston Spa already had a six month waiting list before it was on general release. What did one expect? My dictionary says a primer is an elementary reading book for children, a short introductory book. This hardly prepared one for the 6lb 2oz, 822 page encyclopaedia boasting 195 chapters written by 275 authors.

Its philosophy is admirable offering basic science for the clinician, and a clinical account for the basic scientist. The editorial guidelines should perhaps have been more rigorous, as some contributions have offered brief albeit expert overviews whilst others have produced a manuscript that would have grasped a plenary lecture at a specialist conference. Section editors should have offered brief orienting introductions. The same topic appears in more than one "chapter" that somehow does not illuminate the subject in the way that it does when a debate is formally set up. There are gems, however, and nowhere else can one read about blood flow, the blood brain barrier, acidosis, excitotoxins, calcium, free radicals, and nitric oxide, etc, alongside cardiac embolism, aneurysm surgery, thrombolysis, the dose of aspirin, and rehabilitation etc. The list of contributors is a who's who of mostly North American experts. Some will claim that there are better texts in which to consult for most neurologists and neurosurgeons beyond the current and future management of basal ganglia related disorders. However these points will be lost to most neurologists and neurosurgeons because the format of the book is rather daunting with every chapter detailing the experimental design and results with usually one concluding fact per chapter. Thus the book is inefficient in its presentation of data for those not directly working in the area in which it is important as most investigators who work in this field have contributed to this book and so are almost certainly in receipt of a complimentary copy. However collections of work such as are represented in this book are often herald changes in clinical practice, and so it is crucial that some of these points are brought out, perhaps by the use of introductory summary chapters at the start of each section.

The book opens with a reappraisal of the anatomical connections of the basal ganglia, and makes a number of important observations. Firstly it provides a framework for the modern management of basal ganglia disorders, by providing the anatomical, physiological and pharmacological organisation of these structures. After all it was only through experimental work that the scientific basis for modern management of basal ganglia disorders was established—indeed, for example, post-eroventral pallidotomy and subthalamic stimulators in Parkinson's disease. Of importance to these discussions are chapters which make the point that the segregated input from the cortex to the striatal complex, necessary for the parallel pathway hypothesis of basal ganglia function, is at best a gross simplification, not least because it reduces many basal ganglia structures to the level of simple relay systems. Furthermore current the model of basal ganglia dysfunction in movement disorders often omits a number of important connections including the input to the subthalamic nucleus (STN) from the primary and supplementary motor cortical areas; the amygdalostriatal projection; a possible thalamic projection to the STN and globus pallidum. This latter projection to the tegmentum, especially the pedunculopontine nucleus (PPN), is significant and consists of axon collaterals from the pallido (and nigro)-thalamic projection and may be as important as the cortical projection of the basal ganglia in the control of movement, especially locomotion.

Whilst this first section of the book provides much anatomical data on the
shortcomings of our current models of basal ganglia function in health and disease there is a useful discussion in the second section on the pharmacology of the pathways within the basal ganglia. Two major points come out of this section. Firstly the nigral dopaminergic projection activating the striatal dopamine receptors is important not only in synaptic transmission but the long term gene expression of other neurotransmitters. Furthermore the loss of this pathway as occurs in Parkinson’s disease may also lead to the loss of corticostriate and thalamostriate synapses which has implications in the therapy of this condition. Secondly a number of different neurotransmitter receptors have been isolated in the basal ganglia which may also be important in the future as targets for anti-Parkinson’s disease treatment, and includes the A2a adenosine receptor, the metabotropic glutamate receptor, and cannabinoid receptors.

The advent of surgical interventions clinically in Parkinson’s disease has led to some neurophysiological studies, which form the basis for the third section of the book. These studies connect to previous experimental observations have revealed that neurons in the striatum respond maximally to movements directed at targets of interest, or at the beginning of a complex movement. This implies that the basal ganglia are involved in the interface of sensory processing (including verbal commands), motor programming, and the desire to move, and in addition may be specifically involved in learning sequence motor tasks and attention. In contrast the PPN which has always been thought to be critical in locomotion has so far only shown changes in neuronal activity relating to voluntary arm movement, at least in nonhuman primates.

The fourth section of this book deals more with the clinical disorders of the basal ganglia, especially the anatomical and physiological substrates of the tremor, rigidity and akinesia which characterise Parkinson’s disease. No answers are apparent but PET data suggest the tremor is at least mediated by the pallido-thalamic (VIM nucleus) cortical pathways. Rats on the other hand associated with increased activity in the internal segment of the globus pallidus (GPi) and underactivity in cortical motor areas, and there is some correlation between the degree of clinical Akinesia and GPi hyperactivity. Furthermore the eye movement abnormalities of basal ganglia disease are coded for in the STN projection to the superior colliculus.

The last three sections of the book concentrate on models of basal ganglia disorders and raise a number of questions on the mode of cell death in Parkinson’s disease, including discussions on apoptosis; iron-ferritin accumulation (which may be secondary to nigral cell death) and new environmental toxins (for example, tetrahydro-B-carboline TâClo). In addition there is increasing interest in the cognitive aspects of Parkinson’s disease which may precede any motor manifestations, and thus be useful in studies designed to look at very early Parkinson’s disease.

Overall the book is interesting if somewhat repetitive with a large number of printing errors. The figures are adequate, but not of a very high quality. It is a tome for the student of neuroscience with an interest in basal ganglia related movement disorders, rather than the clinician wanting to catch up on some background neuroscience. This book is therefore more likely to find a home in libraries than the clinician’s bookshelf.

ROGER BARKER


The editor prefaccs this third edition with reference to the continued cost effectiveness of clinical evoked potential investigations and to the impact of structural and functional imaging. The latter has served to focus the clinical application of evoked potentials, which still provide a temporal resolution greater than modern imaging techniques. In combination with medicogical pressures in the United States, the use of intraoperative monitoring has also grown. These changes, in addition to paediatric applications and central motor conduction studies, are well described.

The book covers a broad range, with contributors from the United States and from Australia. The usual subjects are covered and each chapter is well referenced. Special attention is given to monitoring of the spinal cord and to cortid endarterectomies. There are also chapters on advanced techniques for analysis and on statistics.

I would recommend this book for its methodical approach to each subject, describing the practical background followed by the process of interpretation with respect to clinical questions. I only have one minor objection, that is the use of the term motor evoked potential to describe the compound muscle action potential produced by transcranial stimulation, which has never seemed right to me!

SIMON BONIFACE


This book is in the neurovascular topics series and perhaps represents the final recognition of the potential role of endovascular treatment in the management of vascular lesions of the nervous system. It is a multi-author work with a wide range of authorship of American neuroradiologists and neurosurgeons active in the field. Inevitable in work such as this, it represents differing views and approaches but provides a useful overview of the subject and the principles underlying the various management techniques.

The book highlights the rapid progress and change that has occurred in the subject, in particular the rapid development of devices which have enabled endovascular interventions to extend to almost all parts of the nervous system and the contribution of technical advances in angiographic equipment and the sort of requirements that are necessary to carry out these techniques safely. Throughout the chapters the emphasis on the cooperation of a neurovascular team comes through and in two final chapters John Pile-Spellman, William Young, and Lotti Hacein-Bey present excellent perspectives on the changes that have taken place and are likely to take place in the future in the management of intracranial vascular malformation. Robert Tarr’s final chapter provides some interesting personal reflections on possible innovative treatments that may be, in future, applied to the nervous system. The difficulties of the introduction of new technology in an intensely regulated environment, the move from the laboratory, and the experimental animal into clinical work, will increasingly present organisational challenges, particularly regulatory issues and training.

This book provides a useful overview for clinicians in the neurosciences who wish to update themselves on the current and future prospects of neurological endovascular intervention.

ANDREW MOLYNEUX

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