Tetraparesis after posterior fossa surgery

We are interested in reaching surgeons who have witnessed patients exhibiting any degree of tetraparesis in the sitting, sitting-squatting, or horizontal position after posterior fossa surgery. We have been collecting such patients for nearly 15 years and are interested in evaluating further case histories, surgical and anaesthetic records, postmortem data, and radiological studies when possible. Complete patient and surgeon anonymity will be maintained. We plan on testing our hypothesis for the cause of this devastating complication by compiling case data and identifying similarities. Please forward appropriate case information to us.

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HIV related vasculitic mononeuropathy multiplex: A role for IVlg?

Necrotising vasculitis is one of the pathological findings of mononeuropathy multiplex in patients infected with HIV. It is an infrequent complication that can occur at different stages of immunosuppression and with a prognosis correlating with the degree of immunocompetence. We report a patient with AIDS affected by necrotising vasculitis, who was successfully treated and followed up for 19 months.

A 35 year old woman with AIDS presented in February 1995 with a two week history of progressive weakness and pain of her right hand and a left foot drop. The patient had been followed up neurologically since March 1994 for a distal sensory neuropathy, confirmed by electrophysiological studies. Her distal sensory neuropathy involved the lower limbs and was thought to be a result of HIV infection but exacerbated by zalcitabine and didanosine.

Her medical history included recurrent pneumonia, syphilis, gonorrhoea, oral candidiasis, and Clostridium difficile colitis. Severe headaches had been evaluated in May 1994 with a normal MRI and lumbar puncture (venderal disease research laboratory test negative). Her CD4 count had dropped significantly from 392 to 94/mm³ between February and December 1994.

In February 1995, her neurological examination showed normal cognition, language, and intact cranial nerves. Motor examination disclosed normal tone, intrinsic muscle weakness of the right hand involving muscles supplied by both median and ulnar nerve, and trace movement with attempted dorsiflexion of the left foot. Muscle stretch reflexes were symmetrically brisk but ankle jerks were absent. Plantar responses were flexor bilaterally. Skin evaluation indicated the presence of livedo reticularis. Electrophysiological studies showed a generalised axonal sensorimotor polyneuropathy with a superimposed mononeuropathy of the right median nerve.

Her packed cell volume was 29%, white cell count 2400/mm³, normal platelet count, CD4 cell count 10³/mm³, CD4 count 100 per mm³, cerebrospinal fluid cell count 5 celluloid, normal cerebrospinal fluid total protein, 1.2 mg/dl, negative antigp120, p24, CD4, CD8, and T cell receptor PCR. Her virus load was undetectable by in situ hybridisation and 10³ per ml. Her virus load was undetectable by PCR. Laboratory test revealed normal liver function and renal function tests were normal. Cytomegalovirus antibodies were present in the serum, but a polymerase chain reaction in blood was negative.

A combined biopsy of the left superficial peroneal nerve and posterior tibialis muscle was performed. The peroneal muscle showed evidence of moderate acute and chronic degeneration. Intramuscular as well as perivascular mononuclear cell infiltrates and fibrous necrosis with histologically similar perimyovascular blood vessels were noted. The superficial peroneal nerve showed severe reduction in the number of large myelinated fibres with evidence of frank fibre degeneration on teased nerve preparation. Several epineurial blood vessels were thrombosed and recanalised. No cytomegalovirus inclusions were noted and cytomegalovirus immunostaining was negative.

After her biopsy results, 1g prednisolone was given intravenously for three days, followed by oral prednisone at 60 mg/day. The pain improved significantly after the second day of intravenous steroids without any change in her strength. Two months after initial treatment, her strength was improved; however, she had developed a cushingoid appearance and hypertension. Prednisone was slowly tapered to 20 mg/day but more symptoms developed in her right hand. In June 1995, the patient presented with pneumococcal pneumonia and pneumococcal meningitis. High dose steroids were restarted and 2 g/kg intravenous immunoglobulin (IVlg) monthly, was added. The patient's strength improved further, and IVlg infusions were stopped after four consecutive months, while steroids were tapered slowly.

In October 1995, she was diagnosed with cytomegalovirus retinitis in the left eye and was treated with intravenous ganciclovir. Despite this intercurrent illness, the patient's strength continued to improve, and she regained full abduction of her right fingers and left foot dorsiflexion. In May 1996, a protease inhibitor was added to her double protease inhibitor regimen, and the dosage of steroids and thereby the reduction of the dosage of steroids and thereby reducing the risk of bacterial infections, therefore allowing a safer administration of immunosuppressive treatment.

The patient we describe improved and has remained stable 19 months since the onset of necrotising vasculitis, after treatment with a combination of steroids and IVlg. We can only speculate on the contribution of IVlg in the successful treatment of this one patient. We suggest that steroids remain the drug of choice in patients with AIDS and necrotising vasculitis. Nevertheless, IVlg may be a useful adjunctive therapy allowing the reduction of the dosage of steroids and thereby reducing the risk of bacterial or other opportunistic infections.

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Eyebrow lifting test: a novel bedside test for narrowing of the palpebral fissure associated with peripheral facial nerve palsy

A widened palpebral fissure has been regarded as one of the hallmarks of peripheral facial nerve palsy. It is very helpful in differentiating two types of palpebral narrowing—that is, one caused by weakness of the frontal muscle and the other by weakness of the levator palpebrae superioris. Proptosis—palpebral narrowing—in the acute stage all were alert and cooperative. All showed drooping of the upper eyelid. No patient showed excessive contraction of the orbicularis oculi muscles as occurs in blepharospasm. All of the peripheral facial nerve palsy group were unable to close their eyes. In the remaining patients with unilateral oculomotor nerve palsy, it was much higher. In the remaining three patients with unilateral peripheral facial nerve palsy or oculomotor nerve palsy and two with bilateral palsy, there was no remarkable laterality of the position of the eyebrows. However, on closer inspection the eyebrow on the narrower side of the palpebral fissure in two patients with peripheral facial nerve palsy (one unilateral and one bilateral) was definitely lower although the degree was slight.

In all of the peripheral facial nerve palsy group palpebral narrowing disappeared when the eyebrow on the affected side was lifted slightly, whereas in all of the oculomotor nerve palsy group palpebral narrowing remained unchanged, even when the eyebrow was lifted to its maximal extent (figure). In two of the patients with unilateral or bilateral peripheral facial nerve palsy, and in two of the patients with unilateral oculomotor nerve palsy, lifting of the eyebrow on the affected side led to drooping of the contralateral eyelid, although this phenomenon was not found in the others (figure).

Elevation of the upper eyelid is served chiefly by the levator palpebrae superioris, innervated by the oculomotor nerve, and accessory to Müller's muscle via the oculomotor nerve. The frontal muscle participates in eyelid elevation indirectly through the attachments into the eyebrow. Therefore, the palpebral narrowing due to frontal muscle weakness occurs as a result of drooping of the eyebrow, and is essentially different from palpebral narrowing caused by weakness of the eyelid muscles.

We applied this principle to an "eyebrow lifting test". As we described, the result of this test was clear cut. All the palpebral narrowing due to peripheral facial nerve palsy disappeared, and all the narrowing caused by oculomotor nerve palsy remained unchanged. This implied that the peripheral facial nerve palsy related narrowing was attributable to weakness of the frontal muscle but not of the levator palpebrae superioris.

In patients with drooping of the contralateral eyelids elicited by lifting of the eyebrow, their attempts to overcome palpebral narrowing may have induced an increase in innervation to both levator palpebrae superioris muscles resulting in elevation of the contralateral eyelid, because Hering's law of equal innervation to agonist muscles applies to the levator palpebrae superioris as well as to the extraocular muscles. Therefore, it is plausible that in the two patients with peripheral facial nerve palsy resol

(A) Bilateral peripheral facial nerve palsy. Top: primary position. Narrowing of the palpebral fissure is severe on the right side, and moderate on the left side. There is no remarkable laterality of the position of the eyebrows. Bottom: during eyebrow lifting test. The narrowing of the palpebral fissure is abolished on the right side, but is worsened on the left side. (B) Left oculomotor nerve palsy. Top: primary position. The narrowing of the palpebral fissure on the left side is severe, and the position of the eyebrow is much higher on that side. Bottom: during the eyebrow lifting test. The size of the palpebral fissure remains unchanged on the left side, but is narrowed on the right side.

Covered more than one half of the cornea, and (3) severe ptosis if the palpebral fissure was nearly closed.

The subjects were six patients with peripheral facial nerve palsy with palpebral narrowing with but no abnormality of the pupils and eye movements (five men, one woman; age range, 33 to 72 years; mean age 60.3 years) and five patients with oculomotor nerve palsy having ptosis but without facial palsy (two men, three women; age range, 45 to 64 years; mean age 59.5 years). In all subjects peripheral facial nerve palsy or oculomotor nerve palsy developed acutely or suddenly. The palpebral narrowing was confirmed by the patient or family by comparison with the previous state. The aetiologies of peripheral facial nerve palsy consisted of peripheral facial nerve injury at craniotomy (one patient), sarcoidosis (one patient), and Bell's palsy (four patients), and those of oculomotor nerve palsy consisted of oculomotor nerve injury due to aneurysmal surgery at the top of the basilar artery (two patients), cavernous sinus syndrome (one patient), IC-PC aneurysm (one patient), and midbrain infarction (one patient). The patient with peripheral facial nerve palsy and sarcoidosis and the patient with oculomotor nerve palsy and midbrain infarction had bilateral palsy. On neurological examination at their acute stage all were alert and cooperative. All showed drooping of the upper eyelid. No patient showed excessive contraction of the orbicularis oculi muscles as occurs in blepharospasm. All of the peripheral facial nerve palsy group were unable to close their eyes tightly. All of the oculomotor nerve palsy group had either a dilated or normal sized pupil, but no weakness of the upper face on the affected side. With the patient looking straight ahead, the following items were evaluated: (1) severity of palpebral narrowing (ptosis), (2) position of the eyebrow on the affected side, and (3) change of palpebral narrowing when the eyebrow on the affected side was lifted manually by the examiner ("eyebrow lifting test").

Of the patients with unilateral peripheral facial nerve palsy, two showed severe, two moderate, and one mild palpebral narrowing. One patient with bilateral peripheral facial nerve palsy showed severe palpebral narrowing on one side and moderate narrowing on the other side. Of the patients with unilateral oculomotor nerve palsy, three showed severe and one mild palpebral narrowing. One patient with bilateral oculomotor nerve palsy showed severe narrowing on both sides.
Palpebral narrowing associated with peripheral nerve palsy showed a varying degree of drooping of the eyebrow. There were patients with a severe degree of narrowing. This indicates that the frontal muscle which has been considered as an accessory muscle, occasionally plays a very important part in eyelid elevation. We suspect that this is closely related to the skin condition of the upper face. Some Japanese people, especially elderly ones, have excessively loose skin of the upper eyelid or forehead, resulting in "masked" palpebral narrowing. In such a situation, occurrence of frontal muscle weakness can produce severe palpebral narrowing. In conclusion, the "eyebrow lifting test" is simple but very helpful in differentiating between two types of palpebral narrowing due to weakness of the frontal muscle and levator palpebrae superioris.

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Generalised motor neuron disease as an unusual manifestation of Borrelia burgdorferi infection

Lyne borreliosis is a well known multisystem disease caused by the spirochete Borrelia burgdorferi and can produce a wide array of neurological abnormalities in humans. The most frequent are meningitis, cranial neuritis, and painful radiculoneuritis. Other clinical manifestations include chronic encephalomyelitis, spastic paraplegia, and axonal polynuropathy. Our report concerns what we think to be the first case of a patient with upper and lower motor neuron disease and Borrelia burgdorferi infection of the CNS. A causal relation is strongly supported by an evaluation of the Borrelia burgdorferi specific antibody index and the patient’s favourable response to medical treatment. Fifteen months before admission a 33 year old patient noticed weakness in his right hand followed by weakness of the left hand and a progressive gait disturbance. Although he had no pain or sensory disturbance and no history of a tick bite, an erythema migrans, or arthralgias, his physician tested him for Borrelia burgdorferi specific antibodies in the serum because he lived in an endemic region. The test disclosed high concentrations of specific IgG antibodies (1:1200, cut off <1:200). The patient was treated with doxycyclin for two weeks. A control examination performed in a different laboratory still disclosed high concentrations of specific IgG antibodies (1:160, cut off 1:40). Treatment was started again with cefotaxim (2g intravenously for five days). Six months later he was admitted to our hospital because of persisting paresis and muscle atrophy.

On admission, clinical examination disclosed hyperactive deep tendon reflexes with a clonus in both ankles. The muscles of both hands and forearms showed atrophy and severe paresis (figure). His gait was clumsy and stiff, and there was mild spastic paraparesis. There was no sensory loss, and cerebellar function was normal.

Needle EMG disclosed severe active denervation in the small hand muscles bilaterally. Mild to moderate signs of axonal damage were seen in the right anterior tibial muscle and in the left masseter muscle. Motor and sensory nerve conduction velocities were normal. No conduction block could be detected. F waves were abolished. Visual and sensory evoked potentials were normal. Motor evoked potentials disclosed prolonged central conduction times to both anterior tibial muscles and to the left abductor digiti minimi muscle.

Summary of antibody tests

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<th>Follow up *</th>
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*Five months after treatment.

Severe atrophy of hand muscles.

Routine blood chemistry was normal. Serum Treponema pallidum and GM1-specific antibodies were not detected. Borrelia serology tests showed slightly raised concentrations of Borrelia burgdorferi specific IgG antibodies in serum and clearly raised concentrations in the CSF. At the time of the first lumbar puncture (after antibiotic treatment), CSF contained five white blood cells/µl and a total protein concentration of 410 mg/l. Reiber-formula analysis indicated an intrathecal synthesis of IgG and IgA. Employing a sensitive affinity blotting technique most of the oligoclonal IgG bands in the CSF were shown to be specific for Borrelia burgdorferi. This finding was confirmed by western blotting using identical concentrations of IgG in the CSF and serum. A higher number of Borrelia burgdorferi specific antibody bands were found in the CSF than in serum. The calculation of the Borrelia burgdorferi specific antibody index from enzyme linked immunosorbent assay (ELISA) studies disclosed raised values for IgG and IgA. Specificity of intrathecally produced IgG antibodies for Borrelia burgdorferi was confirmed by employing a highly specific 14 kDa fragment of the flagellin as antigen in enzyme linked immunosorbent assay (ELISA). The table shows the detailed data of the antibody tests on admission and on follow up examination five months later. MRI of the cervical spinal cord and the brain disclosed no abnormalities.

The patient was treated with ceftriaxone intravenously for two weeks, followed by oral
predications for 10 weeks. After this treatment the patient’s condition improved slowly but continuously. At the time of the last clinical control examination 18 months after hospital discharge the patient was able to work without physical impairment.

Clinical and all electrophysiological findings met all the criteria for the diagnosis of motor neuron disease. Clinical signs of lower motor neuron involvement were present in both arms. Electromyographic studies disclosed axonal loss at three different levels—suprascapular (anterior tibial muscle), cervical (hand muscles), and supraspinal (masseter muscle). Clear signs of damage to the upper motor neuron were also present. Although the symptoms of the patient could be explained by cervical myelitis the EMG findings with evidence of axonal damage in the anterior tibial and masseter muscle as well as the lack of any sensory abnormalities argue strongly against this possibility.

In addition, signs of inflammation in the CSF were not consistent with a diagnosis of amyotrophic lateral sclerosis. We identified a Borrelia burgdorferi infection of the CNS as the cause of the inflammation. Evidence included a raised specific IgG and IgA antibody index, the demonstration of Borrelia burgdorferi specific oligoclonal IgG bands in the CSF and the predominance of individual Borrelia burgdorferi specific antibody bands in CSF (as indicated by western blotting). The absence of a high white cell count and protein in the CSF could be attributed to prior antibiotic treatment. Clinical and duration, antibiotic treatment was renewed and combined with a long term steroid therapy. Four months later a CSF examination showed a considerable decrease of antibody concentrations, and the patient’s condition continued to improve.

In the light of the evidence, it seems safe to conclude that the patient’s symptoms were due to a CNS Borrelia burgdorferi infection which merely mimicked amyotrophic lateral sclerosis. Several reports have been published on spirochetal diseases leading to isolated damage to the motor system. Spinal meningitis has been reported to cause a clinical syndrome mimicking motor neuron disease.1 Fredrikson and Link published a case report of a patient with isolated upper motor neuron disease.2 Reiber H, Felgenhauer K. Protein transfer at the blood brain barrier and the quantitation of the humoral immune response within the central nervous system. Clin Clin Acta 1987; 163:319–26. 3 Kaiser R, Rasch C, Gassmann G, Vogt A, Lücking C. Intrathecal antibody synthesis in Lyme neuroborreliosis: use of recombinant p41 and a 14-kDa flagellin fragment in ELISA. J Med Microbiol 1993;39:280–7.

Severe but transient parkinsonism after tetanus vaccination

A 38 year old metal worker with a history of hypertension and hyperthyroidism presented with fluctuating fever and sweating, palpitations, tremor of the upper parts of both legs, and diplopia. These symptoms had been present for five days and had started within hours after he had received the last of three vaccinations for tetanus (TE antoexam berna, contents: 20 LF tetanus toxoid, 2 mg aluminium phosphate, and 0.1 mg thimerosal, Primmed BV, Almere, The Netherlands). These vaccinations were given because of an injury to his right index finger one month before. There was no family history of movement disorders. Physical examination showed profuse sweating, normal consciousness, a temperature of 37 °C, systolic rigidity of all four limbs, and a painful tremor in the upper parts of his legs. Muscle strength, tendon reflexes, and sensation were normal.

Within a few days the patient reported to severe hypokinetic dystarhria, a mask-like face, and a resting tremor of both hands, and he had bradykinesia and generalised rigidity, together with a cogwheel phenomenon in the arms.

Laboratory examination showed a creatine phosphokinase activity of 2682 U/l (normal <190 U/l) and normal blood concentrations of manganese, copper, ceruloplasmin, and carbon monoxide. His CSF showed 50 lymphocytes (normal range 0–3), slightly raised total protein (0.54 g/l; normal range 0.15–0.45 g/l), normal IgG index (0.43; normal <0.66), and negative serological tests on Epstein-Barr virus, cytomegalovirus, human herpes virus, simian virus, syphilis, Borrelia burgdorferi, and Mycoplasma pneumoniae. Brain MRI was normal. Single photon emission computed tomography (SPECT) with T-1-iodobenzamide (IBZM), specifically binding to the cerebral dopamine receptor (D2), showed a decreased ganglia: cortex ratio, indicating a postsynaptic disorder. Nevertheless, biperiden, levodopa and carbidopa, and pergolide were prescribed, resulting in gradual but impressive clinical improvement within several weeks.

The clinical syndrome was unclear during the first few days after admission, but gradually developed into a hypokinetic rigid syndrome with resting tremor, generalised bradykinesia, and rigidity. This responded well to treatment with levodopa/carbidopa and a dopamine agonist.

Possible causes of a rapidly progressive form of parkinsonism are encephalitis, intoxication, head trauma, tumour, ischaemia, or hydrocephalus.1 Imaging studies showed no abnormalities, thereby excluding the last three possible causes. Repeated history taking failed to disclose head trauma. The profession of the patient might suggest poisoning, but blood concentrations of manganese and copper were normal. The CSF showed mild pleocytosis, but serological testing for various specific microorganisms did not show any recent infection. Radionuclide imaging showed a pattern similar to that seen in progressive supranuclear palsy or multiple system atrophy.3

The sequence of events strongly suggests a relation between the vaccination and the neurological syndrome, although the causal nature is difficult to prove.4 To our knowledge, there are no reports of parkinsonism after tetanus immunisation in adults,2,5 and also an immunological cross reaction of antibodies with neuronal tissue directly after the last injection. This might also explain the pleocytosis and raised protein and IgG content in the CSF. The alternative explanation was that one of the substances in the vaccine vehicle, thiomersal or aluminium phosphate, that one of the substances in the vaccine vehicle, thiomersal or aluminium phosphate, that is tetanus toxoid, caused an immune mediated reaction of the CNS. In addition, the tetanus vaccine contains thimerosal, an antibiotic that has been shown to be effective in the treatment of tetanus, although we are aware that a causal relation between the vaccine and the hypokinetic rigid syndrome is far from established, we have no better explanation. We wish to record the patient history as a reference, in case analogous patients might be seen in the future.

We thank Dr J W van Isel, University Department of Nuclear Medicine, Utrecht, for kindly providing the SPECT.

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Cardiogenic syncope in temporal lobe epileptic seizures

Cardiac arrhythmias may cause syncopal attacks masquerading as epilepsy. Conversely, epileptic seizures can induce tachyarhythmias or bradycardias (and rarely, as a result of tonic clonic seizures). Distinguishing between these two possibilities may prove difficult without concomitant ECG and EEG recording.

A 39 year old male lorry driver, without cardiac and neurological disorders and not taking medication, was admitted to a coronary care unit after a cluster of episodes of loss of consciousness preceded by epigastic warm sensation and a bitter taste in the mouth, and followed by pallor, sweating, muscle jerking, and rigidity with arrest of the pulse. The episodes occurred both in orthostatism and clinostatism. Clinical investigation, laboratory tests, clinostatic and orthostatic blood pressures, echocardiography, and ECG at rest, during exercise, and during carotid sinus massage were normal.

He experienced another attack while on continuous ECG monitoring. A nurse stated that the patient complained, while standing, of epigastric discomfort, followed by a fleeting phase of unresponsiveness and purposeless arm and mouth movements. A few seconds later he fell and showed a generalised tonic convulsion. The pulse, apparently normal during the initial phase of the episode, abruptly ceased when the patient collapsed. The ECG recording (fig 1) showed a progressive decrease of heart rate, culminating in a sinus arrest of 9.5 seconds, preceding the fall. Another four episodes of sinus arrest of 4–5 seconds, without tonic convulsions, were recorded on the next day.

A permanent demand ventricular pacemaker programmed to trigger at 40 beats per minute (bpm) was applied, but episodes of epigastric discomfort with lack of responsiveness and automatisms, not followed by syncope or convulsions, recurred on the next day and prompted his transfer to a neurological unit. A standard ECG showed focal spike and wave with delta slowing on the right centrotemporal region (C4-T4). A Medilog 9000 ambulatory ECG recording captured a seizure (fig 2) beginning with right centrotemporal recruiting sharp waves, followed by a progressive sinus bradycardia and culminating in a junctional escape rhythm at 47 bpm. The sinus rhythm was recaptured by a transient sinus tachycardia. Other episodes of psychomotor type occurred in subsequent days, but there were no falls or tonic convulsions. The epileptic seizures were secondary to a right anterior temporal low grade astrocytoma, and subsided after treatment with carbamazepine and removal of the tumour. The pacemaker was left in place, and the patient has been free of seizures, without anticonvulsants, for three years.

Epileptic seizures often cause disturbances in cardiac rhythm, generally consisting of mild changes in heart rate such as sinus tachycardia. The possibility of life threatening cardiac arrhythmias has been suggested by the higher incidence of sudden unexpected deaths among patients with epilepsy than in the normal population.

Males, young adults with anatomical causes of seizure disorder, patients not receiving or receiving subtherapeutic levels of antiepileptic medication, with concomitant heart disease, and with alcohol misuse present the major risks. Generalised tonic-clonic seizures, alone or in combination with partial complex seizures, are usually involved, and among proposed mechanisms is an intense sympathetic discharge to the heart, possibly time locked with vagal impulses and resulting in disordered cardiac rate, rhythm, or output. There are only a few proved observations of epileptic bradycardia and asystole, and only in isolated cases has the cardioinhibitory effect of a seizure been documented by simultaneous EEG and ECG. In animals, neurenomeciated bradycardia has been elicited by electrical stimulation of various regions of the limbic system. In humans, repeated observations pioneered by Van Buren have shown that seizure related bradycardias accompany electrical discharges originating from the temporal lobe, strengthening the hypothesis that neural structures within or adjacent to this lobe mediate cardioinhibition. A right-left hemispheric asymmetry for heart innervation has been suggested, but in the reported cases of ictal cardiac arrest right sided, left sided, and bilateral epileptic foci can be found.

Our case resembles that described by Smaje et al, in which temporal lobe seizures secondary to a right hemispheric intracranial tumour induced recurrent episodes of sinus arrhythmias, followed by syncope and muscle jerking; in this patient as well, surgical removal of the tumour reversed the epileptic seizures and the secondary cardiac involvement. Patients 1 and 2 of Constantin et al are similar. In these patients, monitoring led to the false diagnosis of primary cardiac arrest and to the implantation of a permanent pacemaker.

In our patient, the presence of epigastric sensations and purposeless arm and mouth movements preceding the fall should have suggested the diagnosis of partial complex seizures, but clinical clues were disregarded in the face of a repeated documentation of sinus arrest. Actually, only simultaneous EEG and ECG recording makes it possible to recognise the concurrence and the timing of cerebral and cardiac disturbances, and this examination should be recommended in patients with episodes of loss of consciousness of an unclear nature. Finally, it is likely that falling and tonic convulsions after sinus arrest were anoxic rather than epileptic in origin, as they did not show when sinus arrest was shorter than nine seconds, nor after
pacemaker implantation. Besides, in the episode shown in fig 1 the fall and tonic spell occurred at the end of the period of asystole, whereas in the episode reported in fig 2 there was no EEG generalisation of the paroxysmal activity. However, simultaneous ECG-EEG recording of a tonic seizure could not be obtained.

Figure 2  Simultaneous 15 lead EEG and one lead ECG recording of a partial complex seizure. A paroxysmal right temporal discharge (horizontal arrow), preceded by interictal spikes and sharp waves, is followed five seconds later by progressive bradycardia (vertical arrow). Thirteen seconds afterwards a junctional escape rhythm occurs (trace between stars, enlarged in the bottom tracing) at a mean rate of 47 bpm. Recapturing by the sinus rhythm (first beat after right star) takes place 34 seconds from the onset of the EEC discharge, and culminates in a sinus tachycardia at 120 bpm, which rapidly subsides after the cessation of the EEC paroxysm. The entire seizure lasted 54 seconds.

Letters


Recurrent coital amnesia

Transient global amnesia (TGA) is a well defined and not uncommon clinical entity, comprising the sudden development of a dense anterograde amnesia, usually accompanied by repetitive questioning, without alteration in consciousness or other epileptic phenomena, or the development of focal neurological features. Behaviour during the episode may otherwise appear normal and recovery is complete within 24 hours, except for an amnestic gap for the duration of the attack together with a short and variable period of retrograde amnesia. The cause of TGA is not known, but it seems to be strongly associated with migraine, although other causes, including transient cerebral ischaemic attacks and epilepsy, have been reported. Attacks of TGA have apparently been precipitated by various physical and emotional stresses, including sexual intercourse. The wife of a 64 year old man complained that on five separate occasions between March 1977 and October 1995, her husband had exhibited stereotyped attacks of amnesia after intercourse. During these events he would repeatedly ask questions such as “What are we doing?” , “What time of year is it?” , and “What time of day is it?” , but readily recognised his wife and subsequently other people during the amnestic period. He seemed aware that he was experiencing difficulties but there was no alteration in conscious level, and his activities during intercourse and afterwards were otherwise unremarkable. The amnestic state lasted about 30–60 minutes on each occasion and he then recovered completely, except that he had no memory for the period of intercourse and only a very hazy recollection of foreplay. He had no associated headache with these episodes, but gave a 20 year history of migraine without aura, and he had also experienced previous episodes of coital cephalalgia, with severe ocipitonoocal headache at climax lasting some 20 minutes. He had never experienced TGA attacks under other circumstances, and had had intercourse without developing neurological symptoms on many other occasions.

His cardiovascular and neurological examinations were normal, and brain CT and extracranial ultrasound studies were normal. His EEG showed some sharply contoured theta activity in the right frontotemporal area.

The history of recurrent TGA attacks, together with the EEG abnormalities, raises the possibility of an epileptic aetiology in this patient, but this seems unlikely. Patients with epileptic TGA nearly always develop typical complex partial seizures within a year of the first TGA attack. Pure amnestic seizures are characterised by similar selective memory impairment with preservation of other cognitive abilities, but are much briefer, not accompanied by retrograde amnesia, and patients are unaware that there is anything wrong during attacks. Also, such attacks almost invariably occur in patients who have other, more typical complex partial seizures. TGA in this patient therefore seems likely to be a manifestation of migraine.

The fact that a person can repeatedly experience selective amnesia for sexual intercourse, but otherwise function normally during the amnestic period, raises interesting social and medicolegal considerations!

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Severe sensorimotor polyradiculoneuropathy after ingestion of ethylene glycol

Ethylene glycol is the principal constituent in most motor vehicle “antifreeze” solutions. Reports of its potentially lethal effects if ingested first appeared soon after its widespread introduction in the 1930s. The principal toxic effect of ethylene glycol is renal failure due to deposition of oxalate crystals within tubules. It is thought that together with metabolic acidosis and cardiopulmonary collapse, accounts for the high mortality. The lethal dose is estimated to be 100 ml. Although rare, neurological complications are well recognised. Cranial nerve palsies and optic atrophy are the most often reported. The mechanism of neuronal damage is unknown. Deposition of oxalate crystals in cranial nerves has been reported at necropsy and in animal studies. We describe a case in which the ingestion of ethylene glycol led to a severe sensorimotor polyradiculoneuropathy.

A 43 year old man was transferred to the regional renal unit after presenting to a local casualty department in acute renal failure. Six days before admission he had deliberately ingested 250 ml antifreeze. There was a history of hypertension, acute myocardial infarction, atrial fibrillation, and a stroke, resulting in a left hemiparesis two years previously. He was taking digoxin, warfarin, and an ACE inhibitor. On admission the pulse was 80 beats/min and blood pressure 150/60 mm Hg with a respiratory rate of 18/min. Examination of the limbs except for some abduction of the distal flexors of the right upper limb. He was arreflexic and the plantars were unreactive. There was complete internal and external ocular motility, light sensation in each eye, and normal F wave latencies described in that condition. The patient had no obvious evidence of denervation with reduced amplitude of compound muscle action potentials due to deposition of oxalate crystals on acetylcholinesterase positive neurons.1 We describe a case in which the ingestion of ethylene glycol led to a severe sensorimotor polyradiculoneuropathy.

At necropsy and in animal studies. We describe a case in which the ingestion of ethylene glycol led to a severe sensorimotor polyradiculoneuropathy.

The possibility of this having been a critical illness neuropathy has been considered. However, the typical features of multisystem failure, sepsis, and normal F wave latencies described in that condition were not evident here. It is possible that some instances of respiratory collapse and subsequent failure to wean off ventilation previously described after ethylene glycol poisoning may be attributable to unrecognised polyradiculoneuropathy. We would conclude that there is a case for monitoring all patients admitted with ethylene glycol poisoning with respect to their neurological status and respiratory function, including measurement of forced vital capacity and electrophysiological studies.

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ABN medal

Peter Kynaston Thomas CBE

Professor PK Thomas, a past President of the Association of British Neurologists, has made outstanding contributions to neurology as investigator, clinician, author, educator, and editor.

“PK”, as he is universally and affectionately known, trained with JZ Young in the Anatomy Department at University College. After working at the Middlesex, the National, and Montreal General hospitals, he was appointed consultant at the Royal Free Hospital in 1962, and soon afterwards at the National and Royal National Orthopaedic Hospitals. In 1974 he became Professor of Neurology at the Royal Free Hospital School of Medicine and the Institute of Neurology. His research output has continued unchecked after the conferment of his emeritus title in 1991. His formidable publication record includes, so far, 211 original articles, 13 review articles, 100 book chapters, and 13 books. He pioneered the study of cutaneous nerve biopsy and illuminated many aspects of peripheral nerve structure and function. His research has improved our understanding and management of nerve injury and inherited, metabolic, and inflammatory neuropathies. His publications are models of scholarship, written with the meticulous care which he generously shares with authors who submit articles to the books and journals which he edits.

“PK” has already earned the respect of the international neurological community and been honoured by his country as Commander of the British Empire. Last year the Association of British Neurologists took solace from awarding one of its first medals to “PK’s” greatly loved wife, Anita Harding. This year the Association is proud to award its medal to “PK” himself, in admiration of his science, his scholarship, his unflagging energy, and his unfailing fortitude.

Platform presentations

PREGNANCY AND MULTIPLE SCLEROSIS (PRIMS): A EUROPEAN MULTICENTRE STUDY, PRELIMINARY RESULTS

M Hutchinson, C Confavreux, M Hours, T Moreau, P Cortinovis-Tournaire, A Biron, and PRIMS participants, Hospital de l’Antiquaille, Lyon, France and St Vincent’s Hospital, Dublin, Eire

The aim of the PRIMS study was to ascertain in a prospective manner the effect of pregnancy and the postpartum period on the course of multiple sclerosis by the measurement of relapses and progression of the residual disability. From 12 European countries 232 pregnancies resulted in the delivery of a live infant and after excluding 12 second pregnancies, 220 pregnancies were analysed. Relapse rates (RRs) were assessed for each quarter of the year before the pregnancy, each trimester of pregnancy, and for the six months postpartum; annualised RRs per person were calculated. The RR remained constant in the year before pregnancy but fell in the first two trimesters of pregnancy (P<0.05) with a further fall in the third trimester (P<0.001). There was an increase in the RR in the first three months postpartum (P=0.05) in comparison with the prepregnancy rate. The RR for the second postpartum period was non-significantly higher (P=0.13). The RR for the nine months of pregnancy was significantly reduced (P=0.05) but when the pregnancy year (pregnancy and three months postpartum) is considered the RR was not significantly different from that of the prepregnancy year.

A LINKAGE GENOME SCREEN IN MULTIPLE SCLEROSIS


There is now overwhelming evidence that susceptibility to multiple sclerosis involves genetic factors. In the light of this the entire human genome has been screened for evidence of linkage and several potentially linked regions have been identified. 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 X chromosome evidence for linkage in male-male pairs suggests a possible X linked dominant component to the disease.

This is the first genome screen to be completed in any neurological polygenic disease.

A LONGITUDINAL STUDY OF COGNITIVE, NEUROLOGICAL, AND MAGNETIC RESONANCE IMAGING CHANGES IN EARLY MULTIPLE SCLEROSIS

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Thirty six patients with recently diagnosed, clinically definite multiple sclerosis (MS) were included in a neuropsychological and MRI follow up study. The test/retest interval was two years. Patients were individually matched, on a range of demographic variables, with healthy controls who completed the psychometric battery at the same time intervals.

With the exception of verbal intelligence, the MS group was impaired on all areas of cognition assessed at baseline testing. Stepwise multiple regression analyses indicated that total lesion area (TLA) and physical disability (by self report), but not other clinical variables, were robust predictors of cognitive dysfunction.

At follow up, 10 patients had entered the secondary progressive phase of the disease and 18 had deteriorated by EDSS. Changes in disease status were mirrored by parallel changes in self reported disability but were relatively independent of increased lesion load. For the MS group as a whole, there was no evidence of significant change in cognitive ability over time. However, further analysis of the cognitive data showed changes dependent on the change in MRI lesion load. Patients in the MRI unchanged group maintained stable scores or improved slightly whereas those in the MRI changed group failed to show improvement or deteriorated slightly.

A SYSTEMATIC REVIEW OF BRAIN MRI IN THE DIAGNOSIS OF MULTIPLE SCLEROSIS

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Although there are many published studies of the use of brain MRI in the diagnosis of multiple sclerosis (MS), most report data on a very few cases, many of which were highly selected. As a consequence, there is considerable variation in the reported sensitivity of MRI. Moreover, it is unclear to what extent sensitivity is determined by factors such as field strength, the clinical presentation of the patient, and the clinical diagnostic criteria. The largest study to date of the sensitivity of brain MRI at clinical presentation is reported (309 patients with possible, probable, or definite MS in Edinburgh between 1990 and 1995). In addition, using Medline (1980-96) and reference lists, a further 80 published studies from 32 journals were identified. Of these, 36 studies failed to meet

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This study underlines the uniqueness of this patient group, highlighting the differences between primary progressive MS and the more extensively studied secondary progressive group. The large cohort studied gives the potential to gain further insights into the pathogenesis of progressive disability in multiple sclerosis.

IDENTIFICATION AND SIZING OF THE GAA TRINUCLEOTIDE REPEAT EXPANSION OF FRIEDRICH'S ATAXIA IN 56 PATIENTS: CLINICAL AND GENETIC CORRELATES

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Fifty six patients with a clinical diagnosis of Friedreich's ataxia (FA) were investigated for the trinucleotide (GAA) repeat expansion recently found within the gene X25 on chromosome 9. All 56 were found to be homozygous for the expansion, with all but two patients having alleles of differing sizes. The expansion size varied from 2 to 5 kb, with normal alleles around 1.5 kb. Sizing of the single copy of the expansion in eight sets of parents disclosed pronounced instability in the transmission of the expansion, with both increases and decreases in allele size. In patients with FA there was a significant inverse correlation between the average of the two expansion sizes and age of onset of symptoms. The GAA repeat expansion was found in the homozygous state in atypical cases of FA, such as older age of onset, preservation of lower limb reflexes, and cardiac presentations. In three families the father had the onset of a spinocerebellar ataxia as an adult, and in two the possibility of partial heterozygote carrier fathers has been raised. More importantly, the history of an ataxic syndrome in a parent does not exclude the diagnosis of FA in the offspring.

THE TRINUCLEOTIDE REPEAT EXPANSION ON CHROMOSOME 12 (SCA2) IN AUTOSOMAL DOMINANT CEREBELLAR ATAXIAS

P Giunti, M G Sweeney, M B Davis, N Wood. Institute of Neurology, London, UK

Affected members of 59 families with various autosomal dominant late onset cerebellar ataxias (ADCA) and 40 patients with a similar phenotype but no family history, were investigated for the trinucleotide (CAG) repeat expansion which has been found in pedigrees showing linkage to SCA2 locus on chromosome 12. The SCA2 mutation was found in 10 of 13 families with ADCA.

Type I. Five of the 10 were British: the others originated from Italy, Denmark, West Indies, and India. The SCA2 trinucleotide expansion was not found in 11 families with ADCA and seven females (ADCA II) or in 35 with the pure type of ADCA (ADCA III). It was also not found in the 40 patients with idiopathic ADCA. DNA analysis for the SCA2 mutation is useful for diagnosis in single patients or small families with an ataxic syndrome and can be used for presymptomatic testing.

A GENETIC STUDY OF PAROXYSMAL DYSTONIC CHOREOATHETOSIS IN A BRITISH FAMILY


Paroxysmal dystonic choreoathetosis (PDC) is an unusual dominantly inherited disorder characterised by attacks of involuntary dystonic and choreoathetoid movements. Typical attacks start as hemidystonia and progress to become generalised affecting all limbs, trunk, and neck muscles as well as speech. Attacks last several hours and can be precipitated by stress, excitement, alcohol, or caffeine. Clear consciousness is preserved throughout and patients are normal between attacks. The gene for PDC has recently been mapped to the long arm of chromosome 2. A six generation British family with PDC is described with the results of fine genetic mapping and candidate gene linkage analysis.

Positive lod scores were obtained for six genetic markers on 2q including a lod score of 5.08 at a recombination fraction of 0.0 for the marker D2S163. Construction of haplotypes allowed definition of a multipoint interval of 4 centimorgans (cM) of genetic distance between flanking markers.

The findings confirm the assignment of the gene for PDC to a locus on the long arm of chromosome 2 and provide evidence for the locus homogeneity in PDC. The disease interval has been narrowed to 4cM and the findings provide support for the involvement of the gene for a chloride/bicarbonate exchanger as a candidate gene for PDC.

GENETIC COUNSELLING FOR MITOCHONDRIAL DNA DEFECTS

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In the absence of an effective treatment for mitochondrial DNA (mtDNA) disease, genetic counselling is of the utmost importance. However, extreme genetic and phenotypic diversity has prevented the identification of maternal risk factors for having an affected offspring. As a consequence genetic counselling has been limited to a discussion of maternal inheritance for most mtDNA mutations, and advice about the male predominance of Leber's hereditary optic neuropathy (LHON).

264 mother/child pairs were studied involving the transmission of the more common heteroplasmic mtDNA point mutations (A3243G MELAS, A8344G MERRF, and G3460A, G1778A, and T8993C LHON) in the hope of improving the counselling to patients with mitochondrial disease.

The results show:

(1) The risk of having an affected offspring is different for mothers carrying the A3243G and A8344G mutations.

(2) Higher levels of the A3243G and A8334G mutations were associated with an increased frequency of affected offspring.

(3) For LHON, mutation of a mother had >20% mutant mtDNA in her blood, higher levels of mutation were not associated with a greater chance of having an affected son.

It is concluded that the analysis of mutant mtDNA can be used to predict the risk that a mother will have an affected child.
PHENOTYPIC MANIFESTATIONS OF CHROMOSOME 17P11.2 DUPPLICATION

P K Thomas, W Marques Jr, M B Davis, M G Sweeney, R H M King, J Tyson, S Malcolm. Institute of Neurology, and Royal Free Free School of Medicine, London, UK

Findings on 61 patients with a chromosome 17p11.2 duplication (HMSN 1a) showed a Charcot-Marie-Tooth (CMT) phenotype in 50 and a Roussy-Lévy phenotype in eight. Of the patients with a CMT phenotype, three had associated pyramidal signs, one of whom also had cerebellar and bulbar involvement. Diaphragnatic weakness was present in three severely affected cases. One case presented in middle life with incapacitating muscle cramps associated with calf hypertrophy and only mild signs of neuropathy. Prominent sensory loss was a consistent feature in one family, resulting in acrodystrophic changes. Concurrent focal peripheral nerve lesions were also present in seven patients, both with the CMT and Roussy-Lévy phenotypes. By contrast with the findings in younger patients, in this series of older patients with more advanced disease, biopsy myelin thickness tended to be relatively reduced for axon size, indicating remyelination and/or hypomyelination, and there was regression of the onion bulbs. The possession of two copies of the PMP22 gene within the duplicated region on chromosome 17p therefore gives rise to a range of phenotypes and not solely to a CMT syndrome, and the pattern of histological change in the peripheral nerves alters with advance of the disease.


Trends suggesting that endarterectomy reduces stroke risk in asymptomatic carotid stenosis have led to calls for ultrasound screening. A simple model was used to determine who might benefit or be harmed by three screening strategies: carotid ultrasound followed by catheter angiography, or by magnetic resonance angiography (MRA), or ultrasound alone. Estimates from the literature were used for sensitivity and specificity of ultrasound and MRA, risks of angiography and endarterectomy, and risk reduction after surgery for severe stenosis. Overall risks and benefits of screening were calculated for different levels of prevalence of severe asymptomatic stenosis in the screened population. In the general population (<1% prevalence) screening would lead to more strokes than it prevents. Even using the most optimistic published figures, significant benefits are not seen until prevalences of around 20% are reached. With more realistic assumptions the prevalence would have to be even higher. The public health impact of screening such high prevalence groups would be very limited, and they cannot be reliably identified at ultrasound. A person presenting with a positive ultrasound test should only be considered for surgery if their risk of truly having severe asymptomatic stenosis is high, and then the safest referral route is via MRA.

VERTEBROBASILAR INSUFFICIENCY: IS IT DIAGNOSABLE BY TRANSCRANIAL DOPPLER?

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The term “vertebrobasilar insufficiency” is often used inappropriately, but a group of patients in whom recurrent hindbrain dysfunction is due to ischaemia, possibly related to local hypoperfusion, exist, and recognition can be difficult. Hypoperfusion is often on the background of exhaustion of the cerebrovascular reserve, which can be measured using the transcranial Doppler to assess the response of cerebrobasilar arteries to changes in carbon dioxide (CO₂ reactivity). This technique was applied to the basilar artery to assess its diagnostic utility.

Eighty-nine patients with hindbrain ischaemia, 28 healthy controls, 23 with labyrinthine disorders, and 28 with amusia, conducted a flow velocity testing. Changes in blood flow velocity to hypercapnia (vasodilatory reserve) and hyperventila tion (vasonstrictive reserve) were measured.

Testing was well tolerated. There was a significant reduction in mean baseline reactive flow in patients with hindbrain ischaemia compared with each separate control group (P<0.02). The difference was entirely due to loss of vasostrictive reserve.

It is concluded that hypoperfusion on the background of exhausted basilar reserve may be important in hindbrain ischaemia and can be practically measured by CO₂ reactivity. This may be useful to distinguish those patients with an ischaemic basis for recurrent hindbrain dysfunction from those with symptoms of other causes.

VESTERBROANGIOGRAPHY TO INVESTIGATE POSTERIOR CIRCULATION ISCHAEMIA: IS IT WORTHWHILE?

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Angiography after a posterior circulation ischaemic event is often not considered because of the perception that the findings do not alter patient management. However, percutaneous transluminal angioplasty (PTA) is now available for the treatment of vertebral stenosis and anticoagulation may be indicated for dissection and occlusion.

All summaries of patients discharged from consultant neurologists at Atkinson Morley's Hospital between 1991 and 1996 were reviewed. Fifty three patients with posterior circulation ischaemia studied by vertebro angiography were identified and all angiograms were reviewed. Vertebral angiography was significantly abnormal in 32 patients (60%). Five (9%) had vertebral dissections, nine (17%) had unilateral occlusion of one artery, one had a basilar artery aneurysm with thrombus in the wall, and one had basilar artery stenosis. Sixteen (30%) had vertebral artery stenosis. The severity of the stenoses was 50%-99% in five patients (9%) and 70% or greater in 11 patients (21%). Twelve stenoses were considered suitable for PTA (23%). Eleven patients were anticoagulated (21%). The presence of carotid atheroma did not predict significant findings in the posterior circulation.

The natural history of vertebral artery disease is unknown but the results indicate that angiography after posterior circulation ischaemia will identify a significant number of potentially treatable lesions.

DISAPPEARING CEREBRAL INFARCTS ON MRI

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Brain MRI will become increasingly important in the diagnosis and follow up of stroke patients. However, the time course of changes...
that occur in maturing cerebral infarcts is not well documented. The surprising finding is reported that on T2 weighted images, the infarct "disappears" at 12 days.

Cerebral infarcts in three patients were studied on several occasions, from within 72 hours of the onset of symptoms up to three months. T2 and proton density (PD) weighted images were obtained with a 1.5T whole body system (Signa, GE) and routine clinical imaging sequence. Imaging parameters were TR=17-19 ms and 95-102 ms, TE=3500 ms. The apparent T2 and a PD ratio (infarct/contralateral) was calculated for each examination.

In each patient, the infarct was clearly visible as an area of high signal intensity on the admission scan. On day 12, large regions of the infarct became almost invisible. After day 12, the infarct became clearly visible again. These image changes corresponded to variations in the apparent T2 of the infarct. The PD ratio of the infarct, although raised, remained fairly constant throughout.

This report shows that the visibility of an infarct varies with time. Large cerebral infarcts may be missed if the MRI is performed around 12 days.

**SERONEGATIVE MYASTHENIA GRAVIS PLASMAS TRANSMISSION INHIBIT ACETYLCOLINE RECEPTOR FUNCTION**

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Antibodies to the muscle acetylcholine receptor (AChR) are detected by immunoprecipitation of 125I-o-bungarotoxin labelled AChR in myasthenia gravis (MG), but about 15% of patients are AChR negative (SNMG). However, it has been previously shown that plasma fractions from SNMG patients show inhibition of the function of the AChR in a muscle cell line TB671 that expresses the fetal form of the AChR.

A subclone of TB671, TB671-1, that expresses the adult human AChR rather than the fetal form has now been used, and the plasma effects confirmed. Interestingly, the inhibition found (five of seven SNMG plasmas) was greatest (>60%) within 15 minutes of application of the plasma, but partially reversed in the continued presence of the plasma. Acetylcholine receptor (up to 40% inhibition) were also seen on miniature end-plate potentials at the mouse neuromuscular junction with four of five SNMG plasmas. Control plasmas showed <10% inhibition.

These results suggest that SNMG plasmas contain a factor that can interfere with the function of adult human AChR, and that is active at the neuromuscular junction. As we suggested previously, the effect may be due to modulation of AChR function via second messengers rather than to direct binding to the AChR.

**IS A RANDOMISED, PLACEBO CONTROLLED TRIAL OF LOCAL THROMBOLYSIS IN CEREBRAL VENOUS SINUS THROMBOSIS FEASIBLE?**

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Cerebral venous sinus thrombosis (CVST) is an uncommon disorder with variable outcome. Treatment remains controversial, and the results of a double blinded, placebo controlled trial of low molecular weight heparin are awaiting publication. We report two patients with deteriorating Glasgow coma score in whom local thrombolysis was delivered during transfemoral venous angiography. Both made excellent recoveries, as assessed by the Glasgow outcome scale (GOS). These two patients are contrasted with 15 patients admitted over a four year period with a similar diagnosis in whom the management has been variable. Their clinical presentation, neuroimaging, management, and GOS are reviewed. Seven patients had papilloedema at presentation, and would not have been eligible for inclusion in the aforementioned trial.

There is uncontrolled data to support the agressive management of CVST with thrombolysis. There is, however, no randomised clinical trial to support such an approach. The current CVST trial addresses a heterogeneous group of patients in whom, in our experience, good outcome has occurred, in most irrespective of therapeutic approach. Whether trials of thrombolysis in life threatening CVST can be conducted, what methodology should be adopted, and whether such trials should be placebo controlled is discussed. This presentation might lead to a United Kingdom wide, multicentre trial of local thrombolysis in CVST.

**PROGNOSTIC FACTORS IN GUILLAIN-BARRÉ SYNDROME**

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To determine prognostic factors in Guillain-Barré syndrome, data were analysed from 376 patients randomised in a controlled trial of plasma exchange, intravenous immunoglobulin, or both treatments. The patients were divided into five groups according to motor nerve conduction studies: demyelinating, axonal, internal, normal, or equivocal. Significantly more patients whose nerves were initially inexible (six of 12 (50%; 95% confidence interval (95% CI) 21-79%)) were unable to walk unaided 48 weeks after disease onset, compared with the demyelinating (44 of 258 (17%; 95% CI 13-22%)), axonal (10 of 10 (10%; 95% CI 0-44%)), normal (1 of 9 (11%; 95% CI 0-48%)), and equivocal (of 87 (7%; 95% CI 3.1-14%)) groups. Median number of days until ability to walk again was longer for the inexible group (>336 days; 95% CI 65->336 days) than for the normal (17 days; 95% CI 8-65 days), equivocal (23 days; 95% CI 19-31 days), demyelinating (51 days; 95% CI 41-63 days), and axonal (41 days; 95% CI 21-234 days) groups. Regression analysis was used to derive an equation predicting disability grade on a seven point scale at 48 weeks after onset. Disability was worse with older age, weaker arms at onset, recent gastrointestinal infection, and smaller motor action potential amplitudes. There was no significant predictive effect from sex, absence of sensory symptoms and signs, or delay until randomisation.

**TRANSVERSE MYELITIS AS THE FIRST PRESENTATION OF CONNECTIVE TISSUE DISEASE AND GOOD OUTCOME AFTER EARLY IMMunosUPPRESSION WITH CYCLOPHOSPHAMIDE AND AZATHIOPRINE**


Transverse myelitis is a well described but rare complication of systemic lupus erythematosus (SLE) and has occasionally been seen in association with other connective tissue diseases. It can occur as the first manifestation of SLE although it is more often the first presentation of a demyelinating disorder. Establishing the cause in patients without any preceding infective illness or relevant history remains challenging, making the early introduction of potentially therapeutic but toxic treatments difficult. However, reports of early use of high dose steroids in SLE associated transverse myelitis suggest that early intervention is beneficial although not curative. And, most recently, case reports have described a great improvement after cyclophosphamide in patients with established SLE who subsequently develop transverse myelitis.

Five female patients (ages 26-68, mean 38.8 years) presented with transverse myelitis and histories, clinical signs, laboratory tests, and MRI were suggestive of underlying connective tissue disease. Two patients, who had a poor or unsustained response to high dose methyl prednisolone, showed a dramatic improvement after pulsed cyclophosphamide at low doses without complication. A third responded quickly to azathioprine and oral prednisolone. All remain well with minimal residual deficit (follow up five months to three years). It is suggested that an underlying connective tissue disease should be sought in female patients with transverse myelitis.

**ATTEMPTED INDUCTION OF EXPERIMENTAL AUTOIMMUNE NEURITIS WITH PMP22**

C M Gabriel, F Walsh, K J Smith, R A C Hughes. Guy’s Hospital, London, UK

Experimental autoimmune neuritis (EAN) is an accurate animal model of the commonest form of Guillain-Barré syndrome—acute inflammatory demyelinating polyradiculoneuropathy. It has previously been shown that two myelin proteins, P2 basic protein and P glycoprotein are capable of inducing EAN. It was investigated whether the 22 kDa peripheral nerve myelin protein PMP22, the product of the CMT1a (Charcot-Marie- Tooth disease type 1a) gene, will induce EAN. PMP22 cDNA produced by the reverse transcriptase polymerase chain reaction was expressed in E coli as a fusion protein with glutathione-S-transferase. Lewis rats were immunised with 50 μg purified PMP22 fusion protein and controls were immunised with the same amount of glutathione-S-transferase. Lewis rats were immunised with 50 μg purified PMP22 fusion protein and controls did not. The mean (SD) distally innervated sciatic nerve CMAPs after 20 days were 4 (1.6) mV in the PMP22 group and 7.3 (2.8) mV in the control group (P<0.05). There was sparse infiltration, oedema, and...
The annual incidence of myelopathies was 1.1% of the HIV seropositives. Various non-vaccular myelopathies were as frequent as VM in HIV infection. The pathogenesis of VM may involve a combination of immune mediated myelin and oligodendrocyte injury, impairment of repair mechanisms due to depletion of S-adenosyl methionine, and HIV augmentation of macrophage activation.

**Does serotonin have a CNS action in migraine?**

P J Goadsby, K L Hoskin. Institute of Neurology, London, UK

The development of serotonin (5HT₅)₂-like agonists as treatments for the acute attack of migraine has led to considerable interest in their mechanism of action and, to some extent, renewed interest in the role of 5HT in the disorder. The initial synthesis of this class of compounds was predicated on the clinical finding that intravenous 5HT terminated acute attacks of migraine. In this study electrophysiological methods have been used to characterise possible CNS actions of serotonin in migraine. The superior sagittal sinus was isolated in the u-cholesterol (60 mg/kg, intraperitoneally) and 20 mg/kg intravenous supplement two hourly) anaesthetised cat. The stimulus was stimulated electrically (100 V, 250 μs duration, 0.3 Hz) and neurons in the dorsal C2 spinal cord were monitored by electrophysiological methods. After baseline recordings in each animal 5HT (15 μg/kg/min) was infused for five minutes in the presence of either vehicle (group A) or the 5HT₁B/D antagonist GR127935 (100 μg/kg, intravenously; group B). The baseline probability of cell firing after sagittal sinus stimulation was 0.61 (0.1) at a latency to the fastest peak of 11.1 (0.4) ms. In group A 5HT infusion alone had a small effect of increasing mean blood pressure (12 (3) mm Hg) which in itself did not alter cell firing. In group A 5HT alone had an inhibitory effect on evoked trigeminal activity which developed 15-20 minutes after commencement of the infusion. The inhibition of cell firing lasting for 20 minutes after which the activity returned to baseline. In group B the combination of 5HT and GR127935 had no effect on trigeminal cell firing although the small hypertensive effect was still present. These data indicate that 5HT inhibits evoked trigeminal nucleus firing via a receptor at which GR127935 is an antagonist, such as 5HT₁B. It is likely that some part of the effect of 5HT in migraine relates to inhibition of the trigeminal nucleus activity although these data do not absolutely exclude non-neuronal actions.

**How long is the interval needed to detect atrophy due to Alzheimer’s disease from MRI?**

N C Fox, P A Freeborough, K M Kakouzi, M N Rossor. The National Hospital for Neurology and Neurosurgery, London, UK

The measurement of brain atrophy by positional matching (registration) and subtraction of serial MRI has been shown to distinguish Alzheimer’s disease (AD) from normal aging when the atrophy is measured over a year. The utility of such assessments would be greatly increased if it was possible to identify atrophy due to AD from scans performed...
Over a shorter interval. Twenty four normal controls had two MR scans separated by intervals of six to 30 months (mean 15 months). Six patients with probable AD had scans with intervals of three to seven months (mean five months). Atrophy calculated from the registered pair was expressed as a percentage of brain volume lost.

For the control group the mean (SD) brain loss was 0.14% (0.4%); only one control had a loss greater than 0.7%—this patient had been started on diuretics in the interval. For the AD group the mean (SD) loss was 1.4% (0.6%)—10 times the control loss despite the shorter intervals. Only one patient in the AD group had brain atrophy of less than 1% (with a loss of only three months).

These results suggest that an interval of four months may be enough to identify atrophy due to AD from registered MRI.

**IDIOPATHIC ATAXIA OF LATE ONSET: GLUTEN SENSITIVITY IS PART OF THE ANSWER**

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More than 85% of patients with coeliac disease (CD) have no gastrointestinal symptoms. Definition of CD based solely on small bowel morphology has been replaced by the more inclusive term “gluten sensitivity”, a state of heightened immunological responsiveness (reflected by circulating antigliadin antibodies) to ingested gluten in genetically susceptible subjects. Ataxia is the commonest neurological complication of CD. Among Harding’s exclusion criteria for diagnosis of idiopathic ataxia, cerebellar ataxia is the presence of chronic diarrhoea, acknowledging that CD is associated with cerebellar ataxia.

Using antigliadin antibodies we have identified 22 patients with idiopathic ataxia and gluten sensitivity (mean age (range) 59 years (20-85), 17 male, 5 female). 85% of them have HLA genotype of CD (A1, B8, DR3, DR7, DR4, DQ2, DQ8). The commonest presenting symptom was gait ataxia. Three patients had extrapyramidal signs. Neurophysiological examination in 19 patients showed sensory axonal neuropathy in 15 (sensory-motor axonal neuropathy in eight, motor axonal neuropathy in five, mixed demyelinating/axonal in one, mononeuropathy multiplex in one). Necropsy in one patient showed Parkin-like cell loss and lymphocytic infiltration of the cerebellum and posterior columns.

Gluten sensitivity may be present in many patients with idiopathic cerebellar ataxia. This has important aetiological and therapeutic implications.

**CNS TISSUE SOD1 MUTATIONS IN MOTOR NEURON DISEASE: CORRELATIONS WITH CLINICAL AND MOLECULAR PATHOLOGICAL FEATURES**

P J Shaw, J Tomkins, P G Ince, K Bushby, K Mantle. University of Newcastle upon Tyne, Newcastle, UK

Point mutations in the gene encoding Cu/Zn superoxide dismutase (SOD1) underlie 20% of familial motor neuron disease (F-MND) cases. It is unknown whether somatic SOD1 mutations in CNS tissue could underlie some cases of sporadic MND. There are few published reports of the pathology of MND in cases with defined SOD1 mutations and it is unknown whether specific mutations are associated with particular molecular pathological findings.

The aims of this study were to: (1) determine whether somatic mutations of the SOD1 gene are associated with sporadic MND; (2) correlate the genetic mutations identified with clinical and molecular pathological features.

Eighty cases of MND from the Newcastle Brain Tissue Bank have been screened for SOD1 mutations using simultaneous SSCP (single strand conformation polymorphism) and heteroduplex analysis of genomic DNA (extracted from cerebral cortex, as well as an alternative source), followed by direct sequencing of PCR products. Molecular pathology of the neuronal lesions was examined using antibodies to ubiquitin and neurofilament proteins.

Abnormalities in the SOD1 gene were found in six of 80 cases. These comprised point mutations in exon 4 (E100G, one case; I113T, two cases). Two cases had previously undescribed deletions in the 3 untranslated region of the gene, which were not found in 200 control samples. In one case there was a point mutation in the intronic sequence preceding exon 2.

There was no evidence that somatic mutations of the SOD1 gene are a common cause of sporadic MND. The molecular pathology associated with different SOD1 mutations showed distinct patterns: in particular, the I113T cases showed dramatic ubiquitin positive neurofilamentous inclusion bodies within motor neurons.

**A UNITED KINGDOM GENETIC STUDY OF PARKINSON’S DISEASE**

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The recent finding of linkage to markers on chromosome 4q 21-23 in one multicase family suggests that some cases of Parkinson’s disease (PD) have a genetic aetiology. Family studies provide conflicting evidence regarding frequency of familial PD but have not included physical examination of relatives.

Ninety four probands (mean age 63.0) with clinically typical idiopathic PD were recruited from 93 families. We have examined as many living first and second degree relatives as possible. Four relatives were found to be mildly affected when the family history had suggested that they would be normal. A sibling of one proband was said to be affected but was found to be normal on examination.

Twenty five of 94 probands had affected first or second degree relatives. The segregation ratio (SR) in sibs was 0.05 in all families and 0.21 in 25 familial cases. In parents the SR was 0.04 in all families and 0.16 in familial cases. The age at onset in probands was significantly less than in ancestors (mean difference 17.9 years, 95% CI 9.7 to 26.1) suggesting anticipation. There was no difference in paternal age compared with population in familial (mean difference 0.53, 95% CI -2.46 to 3.53) or sporadic cases (mean difference 0.69, 95% CI -0.87 to 2.25).

The study is continuing but it has been shown that failing to examine available relatives will miss some secondary cases. Similar SR in sibs and parents, and anticipation suggest that autosomal dominant inheritance with reduced penetrance could be responsible for a proportion of cases. The absence of paternal age effects suggests that sporadic cases are not due to new dominant mutations.

**A CONTROLLED COMPARISON OF THE EFFECT OF PERGOLIDE AND BROMOCRIPTINE ON MOTOR CONTROL IN PARKINSON’S DISEASE**

A S El-Baghdady, R A Grünewald, H J Sagar. Royal Hallamshire Hospital, Sheffield, UK

Pergolide and bromocriptine are both effective dopamine agonists used in Parkinson’s disease (PD). Pergolide has theoretical advantages in motor control because of a dual action on D1 and D2 receptors compared with bromocriptine, which acts as an agonist on D2 only. The dose equivalence of the two drugs is important in clinical practice but has not been formally evaluated.

Twenty two patients with Parkinson’s disease whose symptoms were inadequately controlled on combination therapy with levo- dopa and either bromocriptine (n=9) or pergolide (n=13) were recruited. After crossover, the dosage was adjusted at weekly intervals to achieve the same degree of motor disability as at trial entry. The dose was then adjusted further to optimise motor response.

The dose equivalence of pergolide and bromocriptine after crossover was 16:1 whereas after optimisation it was 27:1. Both drugs significantly improved the overall unified Parkinson’s disease rating scale (UPDRS) score (P<0.0001) especially sub- scores of orientation (P<0.0001), daily living activity (P<0.0002), motor examination (P<0.0001), and dyskinesia (P<0.004).

This study shows that careful dose adjustment improves apparent refractory motor disability in PD, but pergolide has no superiority over bromocriptine.

**Poster presentations**

**RECURRENT SACRAL RADICULOMYELOPATHY CAUSED BY HERPES SIMPLEX TYPE II: A CASE REPORT**

J Allanson, C Aitken, N Duncan, M K Sharief, M Swash. The Royal London Hospital, London, UK

The most common neurological causes of acute urinary retention in young adults are lumbosacral disc herniation, spinal cord compression, spinal demyelination, or myelitis. However, para or postinfectious sacral radiculopathy is well recognised and the specific association of urinary retention with genital herpes simplex virus (HSV) infection is referred to as Elsberg syndrome. Whereas many women being treated for genital herpes simplex infections experience some minor urinary symptoms, rarely a more severe necrotising myelitis may occur. Recurrent neurological problems with recurrent episodes of genital herpes can occur and the use of prophylactic acyclovir to avoid these has been suggested.
**FRIEDREICH'S ATAXIA PRESENTING WITH Chorea**


Friedreich's ataxia (FA) is an autosomal recessive disorder characterised by progressive limb and gait ataxia. Recently, a trinucleotide repeat expansion in intron I of the FXS gene on chromosome 9 has been shown to be the genetic defect in FA. Direct mutation analysis is now possible allowing delineation of the range of phenotypes associated with this genotype. This 21 year old man was previously well other than surgery for thoracic scoliosis at the age of 14. He presented with a two year history of involuntary movements of all four limbs, an inability to sit still, and difficulty running. There was no family history. Examination showed generalised chorea. There were no cerebellar signs. He was areflexic with no other sensory abnormalities. Plantar responses were flexor. His gait was abnormal because of choreiform intrusion and was not broad based. Neurophysiology showed a mild axonal neuropathy. Genetic analysis confirmed that he was homozygous for the FA intron 1 expansion.

Chorea is a rare manifestation of FA which has previously been controversial. This is the first report of chorea in a patient confirmed to have the FA genetic abnormality. It is suggested that molecular genetic testing for the FA expansion should be considered in cases of chorea of unknown cause. (A video of this case was presented.)

**T CELL RESPONSES TO THE ε-SUBUNIT OF THE ACETYLCHOLINE RECEPTOR (AChR) IN MYASTHENIA GRAVIS**


The generation of pathogenic anti-AChR antibodies in myasthenia gravis (MG) is thought to be a T cell dependent process. Such T cells recognise a small fragment (epitope) of the protein presented by an HLA class II molecule. The AChR is composed of the subunits α, β, δ and ε which are all denervated muscles; in adult endplates ε replaces the ε-subunit. Identification and characterisation of autoreactive T cells in MG is vital if specific immunotherapy is to be developed. Despite intensive efforts by several groups very few clones have been isolated, and these are specific for natural AChR a subunit epitopes. Recently three CD3+CD4+ T cell clones recognising an epitope on the human recombinant ε-polypeptide were expanded with the cytoxine interleukin-2, and then cloned by limiting dilution. In each case the epitope is mapped to an extracellular domain, ε residues 190-229, but the clones will also respond to whole AChR delivered to antigen presenting cells by adsorption on to immunomagnetic beads. These findings implicate for the first time the ε-subunit as a potentially important autoantigen in MG.

**RELAPSING POLYNEUROPATHY AND BRAINSTEM ENCEPHALITIS: A CLINICAL AND PATHOLOGICAL CASE REPORT**

S Hutchinson, J O’Riordan, M Farrell, M Hutchinson. St Vincent's Hospital and Beaumont Hospital, Dublin, Eire.

Coexistent brainstem encephalitis and peripheral neuropathy have previously been described. This is the first pathological report of such a case. A 75 year old man is reported who had a subacute onset of bilateral ophthalmoplegia, facial palsy, bulbar palsy, limb ataxia, extensor plantar responses and an areflexic tetraparesis. There were no cerebellar signs. He was areflexic with no other sensory abnormalities. Plantar responses were flexor. His gait was abnormal because of choreiform intrusion and was not broad based. Neurophysiology showed a mild axonal neuropathy. Genetic analysis confirmed that he was homozygous for the FA intron 1 expansion.

Chorea is a rare manifestation of FA which has previously been controversial. This is the first report of chorea in a patient confirmed to have the FA genetic abnormality. It is suggested that molecular genetic testing for the FA expansion should be considered in cases of chorea of unknown cause. (A video of this case was presented.)

**5-HT₄c RECEPTOR STIMULATION IN THE TREATMENT OF LEVODOPA INDUCED DYSKINASIAS**

S H Fox, A Plowright, B Henry, A R Crossman, J M Brothie. University of Manchester, Manchester, UK

Dyskinesias are among the most debilitating side effects encountered after long term levodopa treatment of Parkinson's disease (PD). The neural mechanisms underlying PD involve overactivity of the output regions of the basal ganglia—that is, substantia nigra pars reticulata (SNR) and medial segment of the globus pallidus (GPM). By contrast, levodopa induced dyskinesia is characterised by underactivity of the SNR and excitation of the GPM. The selective 5-HT₄c receptor antagonist, SB 206553 (20 mg/kg) caused a pronounced increase in this hyperkinesia to 267% compared with vehicle. The serotonin selective reuptake inhibitor clomipramine significantly reduced levodopa induced hyperkinesia by 68% (10 mg/kg, 1.5 mg/kg) compared with vehicle. The effect of clomipramine was completely blocked by SB 206553 suggesting an involvement of 5-HT₄c receptors. Thus 5-HT₄c receptor agonists may be useful adjuncts to levodopa in the treatment of PD. Indeed, such effects may underlie the finding that fluoxetine has some benefit in reducing apomorphine induced chorea.

**TUMOUR NECROSIS FACTOR MICROSATELLITES SHOW SIMILAR ASSOCIATIONS IN PRIMARY PROGRESSIVE AND RELAPSING-REMITTING/SECONDARY PROGRESSIVE MULTIPLE SCLEROSIS**

G V McDonnell, C W Kirk, C Graham, A Droogan, S A Hawkins. Royal Victoria Hospital, and Belfast City Hospital, Belfast, UK

Previous allelic association studies with microsatellite markers within a 20 kb region around the tumour necrosis factor (TNF) genes showed significantly different allele distributions for TNF-α and β markers in relapsing-remitting/secondary progressive MS (RR/SPMS) vs normal controls. Considering the suspected immunogenetic heterogeneity in MS, these associations have been tested in primary progressive MS. Association studies were performed on 206 normal controls, 178 RR/SPMS patients, and 100 PPMS patients (all Northern Irish origin) using polymorphic dinucleotide repeat markers TNF-α, TNF-β, and TNF-δ. Forward primers were *A*2 and *A*3, reverse primers were *G*6 and *G*8, and 6-Fam, polymerase chain reaction products were analysed on an Applied Biosystems 373A fluorescent fragment analyser, and Genescan 672 software was used for allele sizing. Statistical analysis involved a χ² test for multiple independent variables. TNF-α marker allele distributions differed significantly between PPMS patients and controls (P=0.025, df=6) but were similar in PPMS and RR/SPMS patients (P=0.002, df=8). For the TNF-δ marker, alleles 127...
and 128 showed association with both patient categories (PPMS v controls, P=0.03, df=2; RR/SPMS v controls, P=0.005, df=2). No association occurred with the TNF-α marker in either patient group (PPMS v controls, P=0.92, df=4; RR/SPMS v controls, P=0.76, df=4). These data indicate that the TNF contribution to MS genetic susceptibility is similar across its full clinical range.

TOXIC EFFECTS OF FREE RADICALS IN AN IN VITRO MODEL OF MOTOR NEURON CELL DEATH

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There is evidence that free radicals contribute to cellular damage in motor neuron disease (MND). Free-radical mediated cell damage has been examined in a hybrid neuroblastoma-motor neuron cell line, NSC34. The aims were to produce a model of motor neuron toxicity which replicates the biochemistry of MND, to look at the mechanisms of cell death, and to investigate different ways of preventing cell death. 

Millimolar concentrations of ascorbate in the presence of Fe²⁺ can generate free radicals. Addition of 5 mM ascorbate to the culture medium caused a significant reduction in heavy metalloproteinic membrane protein and to investigate different effects on heavy metalloproteinic membrane protein and cell death. Cytotoxicity was shown to be present in the presence of DNA-histone complexes in the cytoplasm of treated cells, which inhibits RNA synthesis, or with benzamide, which was shown by the presence of DNA-histone complexes in the cytoplasm of treated cells, and inhibit tubulin were unaffected. The distribution of phosphorylated neurofilament and aromatic compounds, with benzamide, which inhibits poly(ADP-ribose) polymerase. This suggests that the induced cell death is apoptotic.

In conclusion, this work represents the initial characterisation of a cell culture model which is relevant to MND. Some morphological and biochemical features of cell death have been described and some potential inhibitory compounds identified. These cells are currently being transfected with plasmids expressing mutant Cu/Zn superoxide dismutase found in familial MND to determine the effect on cell sensitivity to free radical damage.

REGIONAL BRAIN ATROPHY, CAG REPEAT NUMBER, AND CLINICAL PHENOTYPE IN HUNTINGTON’S DISEASE

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CAG repeat numbers in the Huntington gene were correlated with the regional brain atrophy and clinical phenotype in 23 adult onset (range 17-63; mean 44.6 (SD 15.2) years), 10 early onset cases of Huntington’s disease. All had chorea and dementia during life.

The frontal cortical, but not striatal, atrophy was related to age of onset of chorea (r=0.48; P=0.03) and dementia (r=0.50; P=0.03). The second also correlated with the temporal cortex atrophy (r=-0.48; P=0.04), but not with age at death. This may suggest greater cortical involvement in younger cases.

Thus tissue atrophy in advanced Huntington’s disease seems unrelated to the underlying genetic defect, and may be, at this stage, affected by other (secondary?) pathogenetic factors. However, a correlation between earlier clinical onset and CAG expansion suggests a proportionately accelerated neurodegeneration in preclinical Huntington’s disease.

ABNORMALITY IN VISUOSPATIAL FUNCTION OF PATIENTS WITH PARKINSON’S DISEASE

G L Ong, W K M Poorn, L G Ripley, J E Rees. Sussex Eye Hospital and the University of Sussex, Brighton, UK

The purpose was to evaluate the pathophysiology of visuospatial impairment in Parkinson’s disease (PD) and its progression as a function of disease duration.

Using an automated CRT based test, the achromatic contrast sensitivity, orientational contrast sensitivity, and chromatic discrimination thresholds of 31 patients with PD and 29 age matched controls were assessed. The achromatic and orientational contrast sensitivity (vertical and horizontal gratings) were measured using sinusoidal gratings of various spatial frequencies. Chromatic-discrimination thresholds were measured along the red/green and tritan con fusion axes. Patients with PD were categorised using Hoehn and Yahr stages of stability. Data were analysed using a paired Student’s t test and Scheffe’s multiple comparison test.

The achromatic contrast sensitivity of patients with PD was significantly lower at all spatial frequencies compared with controls (P<0.0001). On an individual basis, 14 of the 31 patients with PD had significant horizontal contrast sensitivity deficit. Chromatic discrimination thresholds (tritan; P=0.001, Red/green; P<0.05) were significantly raised in patients with PD.

The findings are consistent with the theory that visuospatial impairment in PD could be due to changes not only in the retina but also in the visual cortex.

DO T2 AND GADOLINIUM ENHANCING T1 LESIONS REFLECT SEPARATE UNDERLYING PATHOLOGICAL PROCESSES IN MULTIPLE SCLEROSIS?


Not all hyperintense T2 signal may arise from previous gadolinium enhancing T1 lesion. Thus under some conditions, changes in T2 weighted lesion volume and gadolinium enhancing T1 lesion frequency may reflect fundamentally different pathological processes. To test this lesion frequency maps in a population of 20 patients with multiple sclerosis were compared.

The MRI images were registered in standard stereotaxic space and lesions segmented out. The data for all patients were then averaged to yield separate lesion frequency distribution maps for the T2 or the gadolinium enhancing T1 lesions. These maps suggest significant discrepancies between gadolinium enhancing T1 and T2 lesion distribution.

The brain was then divided into periventricular and peripheral regions. For the periventricular region the ratio of T2 lesion inside to outside was 1.7:1 whereas for T1 enhancing lesions the ratio was 0.7:1. The differences between the distribution ratios were highly significant (P = 0.0009).

These results raise three possibilities: (1) T2 lesion is not critically dependent on previous T1 enhancement. (2) The periven tricular white matter may be more susceptible to developing T2 weighted signal change. (3) There is selective burnout of the periventricular region with disease progression.

These findings suggest that T2 hyperintensive and gadolinium enhancing T1 lesions may provide quantitatively different information concerning disease progression.

TRANSCRIPTIONAL CONTROL OF THE HUMAN MUSCLE ACETYLCOLINE RECEPTOR GENES


A critical step in neuromuscular junction development is the switch of acetylcholine receptor (AChR) expression from fetal subtype (α,b6γ7) to adult subtype (α,b6c). Animal studies show that the mechanism of regulation involves the binding of trans activating factors to AChR gene promoter regions. Two important elements identified are E and N boxes, implicated in tissue specific and synapse specific expression respectively. This study investigates the human γ and ε promoter regions, searching for homology with animal models.

The promoter regions of human genomic γ and ε subunit genes were subcloned, sequenced to nucleotides -943 and -1574, and compared with transcriptional control elements of other species. E boxes and conserved regions present in the γ subunit promoter show over 80% sequence identity between human and rat mouse consistent with their role in tissue specific transcriptional regulation. By contrast, E boxes sequences in ε promoters are not highly conserved between species, suggesting a
lesser role in transcriptional control of the $e$ subunit. A highly conserved $N$ box region is located in the $e$ promoter between nucleotides -92 and -97, but not in the $g$. This further implicates the $N$ box in the regulation of synapse specific expression and is supporting evidence for a differential mechanism of synaptic versus extrasynaptic AChR expression.

MANAGEMENT OF PATIENTS WITH SINGLE SEIZURES

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This prospective study was designed to analyse the local management of single seizures. The protocol involved referral by accident and emergency physicians to an epilepsy nurse specialist, a neurologist, and a neuroradiologist.

The first 100 referrals were received within a 28 month period. The male to female ratio was 1.4:1.4 and 80% of referrals were between the ages of 16 and 50. Over 80% of all single seizure referrals were seen by the epilepsy nurse specialist and neurologist in less than four and 28 weeks respectively. Brain CT was abnormal in 21% of cases. Abnormalities included seven malignancies, eight patients with cerebrovascular disease, and two patients with previous brain surgery.

Of 100 cases, 56 had a seizure disorder of which 14 were classified as provoked seizures, 13 unprovoked, and 29 were recurrent unprovoked. The recurrence rate in this group was 52%. Of the 14 provoked seizures fully 70% were related, seven were considered reflex awoke seizures, one patient had herpes encephalitis, and one patient had a significant head injury.

Only 75% of referrals had clear documentation of driving advice from accident and emergency. One patient had been initiated on antiepileptic drugs, which was contrary to the agreed protocol.

ABDOMINAL MYOCLONUS AND MYORHYTHMIA IN NEOPLASIA

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Paraneoplastic syndromes with abnormal movement are rare. Two cases are described in which movement disorder was a major feature.

A 70 year old man developed intractable hicups and non-obstructive sleep apnoea in May 1996. Four months later he gradually developed paraesthesia with a sensory level at T8 and abdominal myoclonus. These were continual rhythmic myoclonic jerks of anterior abdominal muscles at about 60/minute, not interfering with breathing and present during sleep. There was no paraspinal rigidity. Lumbar puncture showed raised protein (1.43 g/l) with normal cell morphology. MRI of the spine and brain stem was repeatedly normal and so was a radioisotope bone scan. Electromyography showed pronounced denervation in lower limbs, absent F responses, but normal nerve conduction. Prostatic biopsy confirmed adenocarcinoma. Prostatic cells were negative for $e$.

The diagnosis was paraneoplastic encephalomyelitis secondary to prostatic adenocarcinoma.

A 61 year old woman developed progressive cerebellar ataxia in 1989. One year later she developed non-Hodgkin's lymphoma treated by chemotherapy. In 1995 she was bedbound because of severe ataxia and had developed a 2 Hz tremor of the mouth, neck, and limbs both at rest and on movement (myorhythmia). Jerky eye movements were noted, suggestive of opsoclonus. Lumbar puncture disclosed raised protein (3.7 g/l). MRI showed advanced cerebellar, brain stem, and central cerebral atrophy but no lymphoma. Purkinje cell antibodies were not detected.

The diagnosis was paraneoplastic myorhythmia and opsoclonus secondary to non-Hodgkin lymphoma. A videotape of the involuntary movements was shown.

UNUSUAL PRESENTATION OF ALCAPTONURIA WITH NEUROPATHY AND MYELOPATHY: A CASE REPORT

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Alcaptonuria is a rare autosomal recessive disorder characterised by complete deficiency of homogentisic acid oxidase and inability to metabolise homogentisic acid. Affected persons excrete homogentisic acid in the urine which becomes dark when alkalinised or oxidised. Older alcaptonuric patients have intensely pigmented connective tissues—ochronosis—particularly involving cartilaginous joint surfaces of the large weight bearing joints.

A 55 year old Egyptian patient presented with neuropathy and myelopathy after injury to the right leg. There was no history of any disease. Radiological changes in the spine, hips, and knees suggested the diagnosis of alcaptonuria, which was confirmed by clinical and laboratory data. MRI detected cervical cord compression at the C3/C4 level by alcaptonuric affection of the spine. He also had axonal neuropathy evidenced by electrophysiological studies and nerve biopsy. Myelopathy secondary to alcaptonuria has been reported in a few patients, but there seems to be no report of an association between alcaptonuria and peripheral neuropathy.

A STUDY OF THE GLUTATHIONE S-TRANSFERASE M1 GENE IN PARKINSON’S DISEASE

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There has been considerable interest in the role of oxidative stress and free radicals in the pathogenesis of Parkinson's disease (PD). Glutathionisation serves as a major antioxidant defence against reactive species derived from hydrogen peroxide. The glutathione S-transferases (GST) is a family of enzymes that catalyse glutathione conjugation with electrophilic compounds. Thus the GST enzyme family serve as an intracellular defence mechanism via detoxification of potential mutagens, carcinogens, and xenobiotic compounds. Of the GST enzymes, much work has already been published concerning the association of null homoyzogotes of the GSTM1 gene and susceptibility to several forms of malignancy. More recently, a single report has suggested a significantly increased frequency of the GSTM1 gene deletion in PD compared with controls (67% v 51%). As part of a study of several candidate xenobiogenic genes, this hypothesis was explored further by studying a larger group of patients with PD.

Genomic DNA was analysed by the polymerase chain reaction (PCR) in 187 patients with PD and 392 controls, and the PCR products were studied after gel electrophoresis for the presence or absence of the GSTM1 gene. All subjects were white and unrelated. The diagnosis PD was made using the United Kingdom PDS Brain Bank criteria.

The frequency of the GSTM1 deletion was not different in the patients with PD (97/187; 52%) compared with controls (203/392) (52%).

In conclusion, the study looked at a larger group of patients with PD and controls than the initial report. Therefore, it seems that deletions of the GSTM1 gene do not play a significant part in the aetiology of PD, and further work should be directed towards the study of other genes.

INCREASED PROTEIN DEGRADATION IN A MITOCHONDRIAL DISEASE AND ITS MODULATION BY DICHLOROACETATE

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Pyruvate dehydrogenase deficiency is one of the best characterised childhood inherited metabolic disorders associated with early neurodegeneration and developmental brain abnormalities. Most cases are genetic defects to the critical X linked pyruvate dehydrogenase (PDH)-ketoacid decarboxylase polypeptide (E1). A patient cell line with an E1u missense mutation (R302C) which results in reduced immunoreactive protein concentrations (~20% of normal) was utilised. E1u and E1a levels seem normal but the mutant polypeptide is degraded abnormally rapidly (wild type $K_{d}$=0.027, mutant $K_{d}$=0.06). The working hypothesis is that alterations in the conformation or phosphorylation state of the mutant E1u protein may modulate the stability and catalytic capacity of the pyruvate dehydrogenase complex.

Dichloroacetate (DCA) is a simple organic compound utilised clinically in the treatment of a variety of mitochondrial disorders. It acts primarily by modulating the activity regulating phosphorylation of the E1u subunit through the inhibition of the E1u-specific kinase. However, chronic DCA treatment of cell lines causes a 2 to 2.5 fold reduction of the rate of E1u degradation. This effect is fully reversible. Rates of cytoplasmic and mitochondrial protein turnover were increased during DCA treatment, suggesting that it is having a specific effect on the E1u subunit turnover.

HUMAN EMBRYO KINASE 2 (HERK2) IN A GLIOMA SUBGROUP: THE O-2A LINEAGE AND NERVOUS SYSTEM DEVELOPMENT

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A cell line of the human oligodendrocyte-type 2 astrocyte (O-2A) lineage has been grown from a human glioblastoma multiforme (the Hu-O-2A/Gb1 cell line). Hu-O-2A/Gb1 cells...
have a similar antigenic phenotype, growth factor response profile, and proton nuclear magnetic resonance spectra to that of rodent O-2A progenitor cells. As part of this characterisation Hy-O-2A/Gb1 ribonucleic acid yielded HEK2 receptor tyrosine kinase fragments. Of 19 low passage malignant human glioma cell populations examined, high HEK2 messenger ribonucleic acid expression was limited to those having strong glial characteris-tics. In situ hybridisation confirmed high HEK2 expression in the three original glioma cell lines and tumour samples from which the strongly positive HEK2 cell populations were derived. Therefore a distinct subset of gliomas show high HEK2 expression. Differential in vitro HEK2 expression was found in both the Hy-O-2A/Gb1 cell line and the rodent O-2A lineage depending on cell phenotype. During human nervous system development in situ hybridisation showed HEK2 expression in the ventricular and subventricular layers of the rhombencephalon, cerebellum, and spinal cord where developing glial lineage cells might be found, but also in areas where neurons predomi-nate.

HEREDITARY SPASTIC PARAPLEGIA WITH LATE ONSET DEMENTIA: LINKAGE TO CHROMOSOME 2 (SPG4 LOCUS)

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Hereditary spastic paraplegia (HSP) may have autosomal dominant (AD), autosomal recessive, or X linked inheritance in pure or complicated forms. Pure AD-HSP has been linked to loci on chromosomes 2, 14, and 15. The locus at chromosome 2p21-24 (SPG4) accounts for 45% of pure AD-HSP. 43 members of an Irish family with AD HSP and dementia had neurological and neuropsychologi-cal examinations. Genetic linkage was carried out using microsatellite markers spanning the candidate regions for pure HSP on chromosomes 2, 14, and 15. Twelve members were considered definite, nine probable, and two possible AD-HSP. Five affected mem-bers over the age of 50 years and one of 12 sibling controls showed a similar pattern of cognitive impairment on assessment, which was unlike that seen in Alzheimer's disease. Genetic linkage was established to the candidacy region for pure HSP on chromosome 2 (SPG4) by linkage to the marker D2S2374 (two point lod score=3.34, theta=0.05, assuming 90% penetrance).

This is the first report of linkage of AD-HSP with late onset dementia to the SPG-4 locus for pure AD-HSP and suggests either close proximity of two genes for HSP, allelic heterogeneity, or variable phenotypic expression.

OPTIMISATION OF CONTRAST ENHANCED MRI AS A MEASURE OF MULTIPLE SCLEROSIS DISEASE ACTIVITY


Gadolinium (Gd-DTPA) increases the sensi-tivity and reliability of MRI for detection of active multiple sclerosis (MS) lesions. Three potential methods were studied for further improving sensitivity: 0.3 mmol/kg (triple dose) Gd-DTPA, magnetisation transfer (MT) contrast imaging, and the introduction of a delay between contrast injection and imaging. Fifty patients were studied on two occasions, 24-72 hours apart, with triple and single dose Gd-DTPA. Pairs of postcontrast T1 weighted images with and without MT were obtained for three time periods (early: 0-20 minutes, early delay: 20-40 minutes, and late delay: 40-60 minutes). Overall, triple dose Gd-DTPA resulted in the detection of 75% more enhancing lesions than single dose (P<0.002). In isolation, MT or delay alone failed to significantly increase sensitivity whereas a combination of MT and early delayed imaging significantly increased sensitivity (single dose: 47% increase, P<0.05; triple dose: 27% increase, P<0.001). The most sensitive imaging modality (MT, late delay, and triple dose Gd-DTPA) re-sulted in 126% more enhancing lesions than standard single dose imaging (P<0.005). In primary progressive MS, no approach improved sensitivity over standard single dose imaging, supporting previous evidence that progression to disability may be related to other factors besides inflammation. In conclu-sion, a combination of MT, delay, and tri-ple dose Gd-DTPA may prove beneficial in treatment trials for relapsing-remitting and secondary progressive MS.

T1 HYPOINTENSITY, DISABILITY, AND ATROPHY OF THE SPINAL CORD IN MULTIPLE SCLEROSIS

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There is a strong relation between atrophy of the spinal cord assessed with MRI and disability in multiple sclerosis (MS). A similar relation has been shown in the cerebrum where atrophy evolves independently of blood-brain barrier breakdown, as assessed with gadolinium enhanced MRI. This may suggest a distinct pathogenesis for the develop-ment of disability in progressive MS. The pathological process that underpins atrophy is unclear but the question has been addressed by studying the relation between atrophy, disability, and intrinsic change in the cord. Sixty patients with MS and 30 normal controls underwent spinal cord imaging using a T1 sequence to acquire axial sections of the cord at the C2 level. These sections were histogram matched to allow comparison of image intensity and a manual outlining technique was applied from which mean cord image intensity over 10 axial slices was calculated. Within the patient group there was a significant relation between atrophy and T1 hypointensity (r=0.36, P<0.005). T1 hypointensity also correlated with disability as measured with the EDSS (r=-0.39, P<0.005). This study shows that atrophy is associated with a generalised reduction in signal on T1 weighted images. It is possible that this change may represent diffuse gliosis.

CORRELATION OF CLINICAL SUBTYPES OF MULTIPLE SCLEROSIS WITH CRANIAL AND CERVICAL PLAQUE DISTRIBUTION IN MRI

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The purpose was to compare lesion site and extent on cranio-ocular MRI with clinical subtypes in multiple sclerosis (MS).

One hundred and twenty nine patients with clinically definite MS underwent cranio-ocular MRI. Number, clinical site of attacks, and neurological dysfunction were documented. Plaque number, size, and position were measured from cranial MRI. Cervi-cal cord lesions were documented and cord diameter at C5 measured.

One hundred and twenty nine patients (relapsing-remitting (RR) 70; secondary progres-sive (SP) 31; benign MS (BMS) 20, and primary progressive (PP) 8) were studied. 64.5% had cervical cord plaques (PP 100%, SP 65%; RR 64.2%; BMS 50%). Of these, motor sensory attacks were the significant initial presentation (PP 100%, RR 78%, SP 60%, BMS 60%) and neurological (PP and SP 100%; RR and BMS 60%). In patients without cervical cord lesions polysymptomatic brainstem and cerebellar attac-kts were significant at initial presentation and pyramidal signs without weakness were common (BMS 50%; RR 47%); 30% of SP and 25% of PP had plaques involving >50% cross sectional area of the cord compared with RR (4.5%) and BMS (1%). Cervical lesion load was highest in BMS (BMS 43.1 (1.8); SP 37.08 (2.4); PP 29 (2.4); RR 21.96 (1.0)). Patients without cord lesions had higher mean cranial lesion load, particularly the SP group (40.21 (2.1) v 33.93 (1.4)). Infratentorial lesions were high in SP (SP 13.4%; PP 6.8%; RR 6.5%; BMS 6.1%). In conclusion, differences in lesion site and extent correlated with different MS subtypes.

THE DIAGNOSIS OF MARFAN’S SYNDROME

D Harriman. Wetherby, Yorkshire, UK

One hundred years ago Marfan presented a five year old girl whose limbs were unduly long and slender and the muscles thin; the fingers and toes showed pronounced arachnodactyly. Knee joint movement was impeded by tendon shortening. Long term follow up disclosed an improvement in physical status.

Subsequent reports of the syndrome added other sites of connective tissue disorder, cardiovascular and ocular; autosomal domi-nant inheritance was established. Tissue cul-ture showed that the collagen produced in the syndrome was abnormally soluble. More recently, muscle biopsies on affected patients have shown one or other form of congenital myopathy, body, concentric laminated body, undifferentiated muscle tissue.

The patient reported here was an 8 year old boy with long, thin limbs, hypertensisible joints, and arachnodactyly. A motor point muscle biopsy displayed large numbers of small mitochondria in both main fibre types (pleoconial myopathy); in places muscle tissue was malformed and contained remnants of adipose tissue. A peripheral neu-romuscular junction was demonstrated in which neu-romuscular junctions showed impaired...
axonic flow. It seems that the concept of Marfan's syndrome should now be extended to include genetic association with other congenital disorders; the possible deleterious effect of abnormal collagen on adjacent tissues should also be borne in mind.

IS THE DIAGNOSIS OF THE HYPERVENTILATION SYNDROME USEFUL?

G N Fuller, S Lhatoo. Gloucester Royal Hospital, Gloucester, UK

The hyperventilation syndrome is a diagnosis which provokes much controversy. There is disagreement over whether the patients are hyperventilating, and if they are, whether this is causative or an epiphenomenon.

A total of 105 patients with the hyperventilation syndrome seen during a 23 month period, out of 2597 new outpatients (4% of new patients) were reviewed. Patients were noted to either have hyperventilation syndrome alone (54), or associated with another diagnosis (23), or after another diagnosis (28). Treatment involved a detailed description of the hyperventilation syndrome and referral to physiotherapy for breathing retraining.

Follow up in 101 patients (median 4.5 months) found a good or excellent response in 79 of the 91 who attended physiotherapy, with a resolution of symptoms in a further eight who did not attend physiotherapy. The remainder had little or no response, none deteriorated.

Whereas the diagnosis of hyperventilation may not reflect the correct pathophysiological causation for the symptoms in these patients, this study suggests that using the diagnosis, which allows the patient to understand their symptoms on the basis of a simple physical model and leads to a logical course of breathing control therapy, results in a high rate of recovery. This suggests that the diagnosis is useful in clinical practice.
Eccentric seizures induced by television

As Cabrera-Valdivia et al suggest, eccentric experiences during spontaneous epileptic seizures are exceedingly rare. Intensely pleasurable experiences are, however, common in self induced seizures, as in the patient whom they describe. Of the 5% of people with epilepsy who are photosensitive some 30% can be shown by prolonged EEG telemetry in a well lit environment to induce epileptiform discharges by various means, either shaking or outstretched fingers of one hand in front of the eyes or carrying out a manoeuvre involving upward deviation of the eyes with the fluttering of the eyelids.1,2 Patients are usually able to discuss their habit but some 50% can be persuaded to do so and commonly describe pleasurable sensations ranging from release of stress to ecstasy. Some may induce orgasm.3 Patients who described similar experiences self induced by approaching closely to a television set have been reported previously.4

4 Cabrera-Valdivia et al reply: We appreciate the interest of Binnie and Wilkins and Kastelein-Nolst Trenité regarding our report on Dostoevsky’s epilepsy.1 We agree in part with their comments. However, the cases that they quote as having similar experiences self induced are not described under the term “ecstatic” or “Dostoevsky’s” epilepsy. The patient reported by Andermann1 had typical absence attacks with jerking of the whole body, and the children who were described also had similar attacks with 3-5 Hz during hyperventilation, and elicited by intermittent photic stimulation; the patient described this as a “trance-like” or “hypnotic” feeling without any reference to the affective state.

Francisco Cabrera-Valdivia
Felix Javier Jiménez-Jiménez
Jose Tejeiro
Lucía Ayuso-Peralta
Manuel Prieto
Esteban García-Albea

Dostoevsky’s epilepsy induced by television

I refer to the letter written by Cabrera-Valdivia et al in which they describe a 25 year old woman with “ecstatic epilepsy” evoked by sitting next to a television. This compelling pleasing behaviour, which is called self induced epilepsy, is often described in patients who are photosensitive and television sensitive.

The first cases of self induced television epilepsy were described by Andermann1 in 1971 and by Jeavons and Harding2 in 1975. Some 150 self inducing patients have been described in the literature between 1932 and 1995. Two thirds of these patients are females, which is according to the sex distribution in photosensitive patients in general. The onset of the self inducing behaviour is at a mean of 6 years of age (range 1-15). Treatment is difficult as many do not want to get rid of this phenomenon.1 Over the past 15 years some 50 self inducing patients have been investigated in the Epilepsy Centre, Meer and Bosch, Heemstede, The Netherlands.

One of these patients, who had a history similar to the 25 year old woman was described in 1989.1 This female was compulsively attracted to the television and to a fluorescent lamp, sunlight, and venetian blinds since childhood. She was often found with her nose pressed up against the television set. Sometimes her head was nodding and she seemed to be in a trance. At the age of 17 she now admits to self induction only if she is upset. In normal circumstances she feels too ashamed to use this manner of self induction.

It is very likely that the Spanish woman, as described in this letter, is photosensitive. There is no mention of a negative response to photic stimulation. Furthermore, it can well be that a false negative response is found as it is of the utmost importance to perform photic stimulation with an appropriate stimulus and to stimulate at different eye conditions. No television sensitive patients have been seen or described who are not photosensitive or pattern sensitive as well.

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Correspondence: Dr C Ballard, The Neurochemical Pathology Unit, Newcastle General Hospital, Westgate Road, Newcastle-upon-Tyne NE4 6BE, UK.


Holmes et al reply:
In reply to the comments by Ballard et al we have extended our original study by ApoE genotyping an additional 68 Alzheimer's disease cases from the Camberwell Dementia Case Register bringing the total to 232 cases fulfilling NINCDS-ADRDA criteria (154 probable and 78 possible, mean age 82.4 (SEM 0.4) years, 178 (77%) women). In all other respects the patient selection and assessment were identical to that previously reported and gave rise to frequencies of 0.03, 0.66, and 0.30 for the ApoE 2, 3, and 4 alleles respectively. In this extended study in accord with our previous findings the only significant association was between the presence of the ApoE e2 allele and the Cornell score (Mann-Whitney U test, P = 0.03) and with the presence of depressive symptomatology (Mann-Whitney U test, P = 0.01) after Bonferroni correction. However, we welcome the opportunity to present the full data set before Bonferroni correction (table) as it concurs with the findings of Ballard et al and other studies' which suggest an association of the ApoE e4 allele with psychotic phenomena as well as suggesting a possible association with wandering behaviours and eating disturbance. Unlike Ballard et al we did not, however, find a negative (or positive) association between depressive symptomatology and the presence of the ApoE e4 allele suggesting that it is the presence of the ApoE e2 allele rather than the absence of the ApoE e4 allele that is associated with depressive symptomatology in Alzheimer's disease.

Clive Holmes
Declan McLoughlin
John Powell
Simon Lovestone


**TABLE 1**

<table>
<thead>
<tr>
<th>Symptom group</th>
<th>Subjects with one or more symptoms (n (%))</th>
<th>Association with presence of ApoE e2 allele (P values)</th>
<th>Association with presence of ApoE e4 allele (P values)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persecutory delusions</td>
<td>105 (50)</td>
<td>0.45</td>
<td>0.02*</td>
</tr>
<tr>
<td>Other delusions</td>
<td>31 (13)</td>
<td>0.37</td>
<td>0.05*</td>
</tr>
<tr>
<td>Auditory hallucinations</td>
<td>30 (13)</td>
<td>0.11</td>
<td>0.83</td>
</tr>
<tr>
<td>Visual hallucinations</td>
<td>53 (23)</td>
<td>0.25</td>
<td>0.98</td>
</tr>
<tr>
<td>Other hallucinations</td>
<td>18 (8)</td>
<td>0.09</td>
<td>0.15</td>
</tr>
<tr>
<td>Misidentifications</td>
<td>42 (21)</td>
<td>0.12</td>
<td>0.20</td>
</tr>
<tr>
<td>Depression</td>
<td>115 (50)</td>
<td>0.0005**</td>
<td>0.11</td>
</tr>
<tr>
<td>Aggression</td>
<td>121 (52)</td>
<td>0.38</td>
<td>0.18</td>
</tr>
<tr>
<td>Wandering</td>
<td>131 (56)</td>
<td>0.98</td>
<td>0.04*</td>
</tr>
<tr>
<td>Stereotypes</td>
<td>182 (78)</td>
<td>0.09</td>
<td>0.23</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>166 (91)</td>
<td>0.73</td>
<td>0.58</td>
</tr>
<tr>
<td>Eating disturbance</td>
<td>88 (38)</td>
<td>0.35</td>
<td>0.04*</td>
</tr>
</tbody>
</table>

*P<0.05; **P<0.001.

BOOK REVIEWS


What is the point of these pocket companions in neurology? There are certainly plenty of them: either distillations of authoritative textbooks (such as this and the companion to Victor's department) or culled from residency teaching programmes (for example, The Little Black Book of Neurology produced from Robert Daroff's department). The "salient points of clinical diagnosis and management—those most useful at the bedside" have been extracted from Bradley, Daroff, Fenichel, and Marsden's two volume textbook. Does this mean we can get early advice from grizzled neurological veterans? Well, not really. Emergency treatments are reasonably covered. But this book will not transform your difficult clinics. If you wondered about treating insomnia, all you will learn is that management should be "individually designed dependent on the causative factors". As much space is devoted to the treatment of the Lambert-Eaton myasthenic syndrome as to the symptomatic management of multiple sclerosis; more to Lesch-Nyhan disease than to tension headache. Here is a clue to the real purpose of these little books. They are to be pulled out in those quiet moments to indulge in that most neurological of activities, the pursuit of the arcane. There are excellent chapters on the neurocutaneous disorders and inborn errors of metabolism. There are three good pages on the mucopotosaccharidoses and a cracking appendix on neurogenetics. What does it matter that not one clinical trial in the management of stroke, carotid stenosis, Guillain-Barre syndrome, or CIDP is mentioned?

ALASDAIR COLES


It is not uncommon to find neuroanatomy books that bewilder the uninitiated undergraduate, or clinician for that matter. It is therefore refreshing to find that this book by Garoute confronts this issue and makes it an understandable text. The key to all learning lies in starting from the basics and dealing with concepts, which makes hanging details on a lot easier. This book assumes a negligible background in neuroscience and starts from the fundamentals of descriptive neuroanatomy of the human nervous system through to its embryology and some aspects of its pathology. Importantly, it does not deal with the anatomy in isolation and makes enough reference to physiology to put the topic into perspective making it more functionally relevant than most of its contemporaries.

The use of enormous numbers of diagrams has meant that the text is a bare minimum with most of the information in illustrated form making it easier to assimilate. In using this idea it seems that one or two diagrams have become rather too complicated and they are very difficult to interpret. The clinical cases are a little uninspiring and could have been used to create a lot more enthusiasm. However, the questions at the end of the topics are a useful adjunct to test ones understanding of the subject and could be exploited usefully by those teaching neuroanatomy.

Overall the beauty of this book is to make it simple enough for the most ignorant of students but yet enough detail is present in it for it to be an ideal crammer for undergraduates coming up to examinations. The price makes it very affordable and I recommend it highly.

OMAR MALIK
Tetraparesis after posterior fossa surgery

T KURZE and J D GROSS

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