ABN abstracts

Proceedings of the Association of British Neurologists, Cardiff City Hall, Cathays Park, 2 April–4 April 2003

01 EARLY RISK OF RECURRENT STROKE BY AETIOLOGICAL SUBTYPE: IMPLICATIONS FOR STROKE PREVENTION

J.K. Lovett, A. Caull, P.M. Rothwell, on behalf of the Oxford Vascular Study Stroke Prevention Research Unit. Radcliffe Infirmary, Oxford, UK

The early risk of stroke after a TIA or minor stroke has recently been shown to be higher than was previously supposed. However, stroke is a heterogeneous syndrome and recurrence risk may differ between aetiological subtypes. Data on the risk of early recurrence by subtype are important for the organisation of stroke prevention services and triage.

Methods: We determined the early recurrent stroke risk by aetiological subtype in the Oxford Vascular Study (OXVASC), and performed a meta-analysis with unpublished data from the Oxfordshire Community Stroke Project (OCSP) and published studies reporting equivalent data.

Results: Data on 1670 patients were available from OXVASC, OCSP, and two published studies. Recurrent stroke risk varied significantly between subtypes (p < 0.001). Patients with stroke due to large artery disease (LAD) had the highest odds of recurrence at both seven days (OR = 3.1, 95% CI = 1.4–6.9) and 30 days (OR = 3.1, 95% CI = 1.9–5.2) days. Odds of recurrence at 30 days for other subtypes were: cardioembolic (OR = 0.9, 95% CI = 0.5–1.6); undetermined (OR = 1.0, 95% CI = 0.6–1.6); and small vessel (OR = 0.2, 95% CI = 0.1–0.6).

Conclusions: The highest risk of early recurrent stroke is in patients with LAD, emphasising the need for carotid endarterectomy and other preventive treatments to be instigated urgently.

02 INTERICTAL CELLULAR ENERGY RESERVES IN MIGRAINEURS WITH PROLONGED AURA OR COMA AND MIGRAINOUS STROKE: A BRAIN 31P-MR- SPECTROSCOPY STUDY


Introduction: The pathophysiology of migraine neuronal deficits is poorly understood. A previous 31P-MR-spectroscopy study identified possibly reduced interictal cerebral energy reserves in migraineurs. We hypothesised that low cellular energy reserves are pathogenic if they should be most marked in patients with a history of very prolonged deficits or migrainous coma.

Methods: We performed interictal brain 31P-MR-spectroscopy in normal controls, and in migraineurs with a history of short deficits (maximum −24 hours), prolonged deficits (≥7 days), migrainous coma, and migrainous stroke (persisting deficit, infarct on imaging). We measured phosphocreatine/inorganic phosphate (PCr/PI), phosphocreatine/ATP (PCr/ATP), and Pi/ATP.

Results: Compared with controls (n = 16), the PCr/PI ratio (reflecting cellular energy reserves) was not reduced in migraineurs with short aura (n = 5), or in patients with migrainous stroke (n = 4). However, the ratio was significantly reduced in migraineurs with prolonged deficit or coma (n = 10), and there was an inverse relationship with the duration of the neurological deficit (p = 0.004). There were no significant differences in PCr/ATP and Pi/ATP values.

Conclusion: Reduced interictal cellular energy reserves in some migraineurs may predispose them to to prolonged neurological deficits or coma. However, interictal cellular energy reserves are normal in migrainous stroke, suggesting that the pathological mechanisms of reversible cerebral dysfunction and infarction differ.

03 CHANGING PRACTICE IN ACUTE STROKE MANAGEMENT IN ACCIDENT AND EMERGENCY (A AND E) DEPARTMENT: THE UTILITY OF STROKE RECOGNITION INSTRUMENT FOR A AND E PHYSICIANS

A. Mohal Nor, J. Davis, P. Darman, A.G. Dyker, S. Louw, M. Davis, B. Sen, G.A. Ford. The Freeman Hospital; Newcastle University; Royal Victoria Hospital; Newcastle General Hospital, Newcastle upon Tyne, UK

Introduction: Acute stroke “brain attack” is an acute medical emergency requiring urgent assessment. Despite this management of stroke in the A and E setting is generally given a low priority and diagnostic accuracy is poor. We determined the clinical characteristics of suspected stroke patients referred to A and E department to develop a stroke recognition tool for A and E physicians.

Methods: Information on all suspected stroke/TIA referrals and diagnoses from A and E department were prospectively recorded over a 1 year period. Patients were also examined by a research fellow. A stroke recognition instrument was developed based on the prevalence of signs in strokes and non-stroke patients.

Results: 398 patients were referred (159 strokes; 178 non-strokes; 61 TIA’s). A seven item scoring system (score between −2 and 5) stroke recognition instrument was designed based on history (loss of consciousness and convulsive fits) and neurological signs (face, arm, leg weakness, dysphasia/dysarthria, and visual field defect). When internally validated at a cut off score of >0 it showed a diagnostic sensitivity = 92%, specificity = 86%, positive predictive value = 85% and negative predictive value = 93%. The external validation process is ongoing.

Conclusions: These data suggest that a relatively simple A and E stroke recognition instrument could be utilised by A and E physicians to improve acute stroke diagnosis.

04 DIFFUSION WEIGHTED MAGNETIC RESONANCE IMAGING IN ACUTE ISCHAEMIC STROKE: PATHOPHYSIOLOGICAL INSIGHTS WITH QUANTITATIVE POSITRON EMISSION TOMOGRAPHY (PET)


The core of the irreversibly damaged brain tissue increases in volume over hours following occlusion of the middle cerebral artery. Hyperintense lesions on acute magnetic resonance (MR) diffusion weighted imaging (DWI) have been taken to represent this core and in conjunction with perfusion MRI used to identify MR thresholds for penumbra. Evidence now suggests this DWI lesion is in whole or part reversible, thus contributing to the discrepancies in the results. Clarification of the pathophysiological tissue compartments comprising this lesion is required. A 53 year old patient was imaged 7–9 hours following stroke onset with back to back DWI and quantitative PET mapping of cerebral blood flow (CBF) and cerebral metabolic rate of oxygen (CMRO2). Voxels within the DWI lesion were thresholded out visually and transferred to the coregistered PET maps. Histograms of the values of these voxels for each PET parameter were constructed and CBF and CMRO2 thresholds for penumbra and core from previously documented research applied. The diffusion lesion consisted of core as well as a substantial proportion of penumbra, which varied with different lesion definition. This study for the first time documents that the DWI lesion can contain still viable tissue and therefore may not represent only irreversible core.

05 CELLULAR INFLAMMATION IN ACUTE ISCHAEMIC STROKE: AN IMAGING BASED STUDY


Background: Animal studies have shown that neutrophils are recruited early in cerebral ischaemia and may be responsible for the “no reflow” phenomenon. Human studies have contributed less direct evidence from a number of “in vivo” imaging studies.

Hypothesis: That selectively labelled neutrophils may be mapped to areas of cerebral infarction in acute ischaemic stroke (IS) patients and
that such a response may be correlated with neurological status and outcome.

Methods: Following informed consent, patients with CT (computed tomography) confirmed IS were recruited. Autologous neutrophils were separated, labelled with 111 indium tropaneolamine, and injected within 24 hours of ictus. Single photon emission computed tomography (SPECT) studies were performed at set times in conjunction with CT. Regions of interest (ROI) were defined and asymmetry indices (AIs) calculated. Outcome was measured using the validated National Institute of Health Stroke Scale (NIHSS).

Results and Conclusion: Fourteen confirmed IS patients entered the study, six of whom died prior to 3 month follow up. Within 24 hours of IS ictus, labelled autologous neutrophils were mapped to regions of cerebral ischaemia as defined structurally by co-registration, and may be present from as early as 19 hours following clinical onset. Such accumulation may correlate with early neurological status.

**06 CEREBRAL VENOUS SINUS THROMBOSIS: TREATMENT WITH ENDOVASCULAR THROMBOLYSIS**

A.F.A. Merrison, S. Renowden, I.E.C. Ormerod. Frenchay Hospital, Bristol, UK

Cerebral venous sinus thrombosis (CVST) may account for up to 2% of strokes in young adults. Conventional treatment consists of anti-coagulation with heparin and/or warfarin. Where this fails, and in severe cases, endovascular approaches, involving direct infusion of thrombolytic agents, have been used.

We present 11 patients (13 procedures), including two children, who received thrombolysis with recombiant tissue-type plasminogen activator (r-tPA) for CVST. Six patients had received treatment with heparin, five patients with extensive CVST had not. All were deteriorating clinically prior to thrombolysis.

Nine patients had post-thrombolysis imaging. Partial recanalisation was achieved in six and complete recanalisation in one. None of the patients experienced significant haemorrhage post-thrombolysis, including two patients with haemorrhagic infarction and one with subarachnoid haemorrhage.

Three patients died. All had three or more venous sinuses involved and had features suggesting severely raised intracranial pressure. Their lowest Glasgow Coma Score pre-thrombolysis was lower than that of survivors. Two of those who died presented with seizures.

Eight patients survived. Seven of these, for whom follow up details were available, were fully independent at 6 to 12 months.

Endovascular thrombolysis for CVST can result in sinus and venous recanalisation and lead to an excellent outcome for most patients.

**07 THE CLINICAL APPLICATION OF NEUROIMAGING IN EPILEPSY**

U.C. Wiesmann. The Walton Centre for Neurology and Neurosurgery, Liverpool, UK

Objective: To evaluate the clinical use of neuroimaging in epilepsy.

Methods: The scan reports of 919 outpatients were reviewed.

Results: 391 patients had no scan (idiopathic generalised epilepsy n=53, localisation related or symptomatic generalised epilepsy n=183, single epileptic attack n=18, remission n=21, non-epileptic attack n=16).

529 patients had a scan (result not available n=33, CT only n=163, standard MRI n=178, high resolution MRI (images with 1.5 mm slice thickness) n=154).

252 of 495 scans (51%) were abnormal (hippocampal sclerosis n=128, atrophy or white matter lesions n=35, vascular abnormalities n=27, tumours n=25, brain damage n=24, malformations of cortical development n=13).

The prevalence of detected abnormalities was 54% in localisation related epilepsy, 18% in single seizure patients, 16% in epilepsy in remission and 0% in IGE and non-epileptic attacks (excluding atrophy and white matter lesions).

Conclusions: Abnormalities were detected in more than half of all patients with localisation related epilepsy, and in approximately one in five patients with single seizures or epilepsy in remission. Many patients had no scan or only CT or standard MRI. The true prevalence of structural abnormalities may have been higher. Scanning did not add any information in patients with idiopathic generalised epilepsy or non-epileptic attacks.

**08 RETENTION TIME AND RATES FOR EPILEPSY PATIENTS TREATED WITH ADJUNCTIVE TOPIRAMATE, LAMOTRIGINE, AND GABAPENTIN**


Objective: To compare long term retention times (as a global measure of efficacy and tolerability) of patients treated with topiramate (TPM), lamotrigine (LTG), gabapentin (GBP) as adjunctive epilepsy treatment.

Methods: A retrospective single centre study was carried out in 250 randomly selected patients. Retention time was statistically compared using Kaplan-Meier (KM) and Cox regression analysis. Retention rates at various time points were derived.

Results: Retention times were collected for 339 treatment episodes between January 1996 and December 2000. Retention time of TPM was significantly better than GBP (Cox: p = 0.014) and similar to LTG (Cox: p = 0.416; KM: p = 0.958). Cox retention rates of TPM reached 43% at 4 years + 37% for LTG and 10% for GBP. The estimated Cox hazard ratio of stopping treatment was 1.69 (95% CI: 1.11–2.66) for GBP and 1.16 (95% CI: 0.81–1.59) for LTG, both compared to TPM. The risk of stopping treatment increased with a history of depression (2.0 times) and learning disability (1.7 times), was lower in males (0.7 times) and increased as the number of concomitant anti-epileptic drugs decreased (2.4 and 2.0 times for one or two, compared to 3 or more).

Conclusions: Retention time and rates of epilepsy patients treated with add on TPM and LTG is higher than with GBP.

**09 USE OF ECG IN THE EVALUATION OF SYNCOPE: A RETROSPECTIVE AUDIT**

M.J. Ansari, S. Hadjikoutsis, P.E. Smith. University Hospital of Wales, Cardiff, UK

The diagnosis of syncope rests principally upon the history, but investigations may be required to support the clinical diagnosis. ECG is recommended in all patients with syncope. We carried out a retrospective audit of patients, with final diagnosis of syncope, seen in the epilepsy unit, University Hospital of Wales, in 2001–2002. The primary objective was to find out whether an ECG was done or not, and if done whether it was normal or abnormal.

Seventy patients (44 (63%) female, mean age 32 years (range 15–75)) were identified. The duration of syncope varied between 1 and 30 minutes. The average number of episodes was 3 (range 1–10). Symptoms occurred over 1 to 5 years. The final syncope diagnosis was: vasovagal 59% (n = 41), unclassified 21% (n = 13), psychogenic 10% (n = 7), cardiogenic 4% (n = 3), convulsive 3% (n = 2). ECG was performed in 93% (n = 65) of cases. Eight of these (12%) were abnormal. The ECG was abnormal and diagnostically useful in all three cases of cardiogenic syncope (two prolonged PR interval, one sinus bradycardia). The ECG was normal or showed non-specific abnormalities in all other cases.

In conclusion, ECG is recommended but is commonly normal in patients with syncope. However, an abnormality of the baseline ECG is a useful predictor of cardiogenic syncope, suggesting the need to pursue evaluation for cardiac causes in these patients. Equally important, a normal ECG is associated with a low risk of cardiac syncope as the cause.

**10 MEMORY PERFORMANCE AND MAGNETIC RESONANCE SPECTROSCOPY OF THE TEMPORAL LOBES IN IDIOPATHIC GENERALISED EPILEPSY**

J.M. Dickson, S.J. Howell, P. Griffiths, I. Wilkinson, R.A. Grunewald. University of Sheffield, Sheffield; Royal Hallamshire Hospital; Sheffield, UK

To investigate the relationship between neuronal dysfunction and memory performance in patients with idiopathic generalised epilepsy (IGE) using magnetic resonance spectroscopy (MRS) of the temporal lobes of the brain.

Methods: Seventeen patients with IGE and 12 healthy control subjects underwent neuropsychological testing of verbal and visual recall and recognition. Single voxel MRS spectra were obtained in each subject from the white matter of both temporal lobes and the areas were calculated under the three prominent resonances: N-acetyl aspartate (NAA), creatine (Cr), and choline (Cho). Results are expressed in terms of the ratios of: NAA/choline, NAA/creatine and NAA/creatine/choline.

Results: The patients performed worse than the controls on four of the neuropsychological measures: visual recall, face recognition, visual recognition and speed of processing (Student’s t test p < 0.05). Visual
The relevance of antibodies that neutralise the in vitro effect of IFN-γ (IFN-γ) in viral cytotoxic assays to multiple sclerosis outcomes is unresolved. Evidence: 48 week results show a 30% relative reduction in accumulative rate of relapse with Rebif® versus Avonex® despite NAb development in 25% of Rebif® patients versus 2% on Avonex®. Indeed, 64% of NAb+ve Rebif® patients remained relapse free versus 52% of all Avonex® patients and 51% of NAb-ve Avonex® patients. A 36% relative reduction in mean 12 active lesion count occurred with Rebif® versus Avonex® (median 0.0 v. 0.5, adjusted mean difference 1.4; p < 0.01). NAb+ve Rebif® patients had significantly fewer active lesions than Avonex® patients (mean 0.7 v. 1.9; median 0.0 v. 0.5; p < 0.01). With Rebif®, NAb-ve patients had significantly more active lesions than NAb-ve patients (mean 1.6 v. 0.6; median 0.0 v. 0.0; p = 0.008). However, NAb+ve Rebif® values were similar to Avonex® (mean 1.4, median 0.5). Over 48 weeks, fewer NAb+ve Rebif® patients had relapses than all patients on Avonex®, with comparable MRI outcomes. Rebif® treatment in patients remaining NAb-ve (75%) had a highly significant benefit on relapse and MRI outcomes versus Avonex®, showing the benefit of high and frequent IFN-γ 1a dosing.

14) EVIDENCE FOR PROGRESSIVE NORMAL APPEARING GREY AND WHITE MATTER MTR ABNOMALITY IN EARLY RELAPSING-REMITTING MULTIPLE SCLEROSIS: A 2 YEAR FOLLOW UP STUDY


In multiple sclerosis (MS), early change in the normal appearing grey and white matter may play a role in the development of cumulative disability. The aim of this study was to ascertain whether early, progressive change is detectable with magnetisation transfer imaging (MTI) in a cohort of minimally disabled early relapsing-remitting MS (RRMS) subjects.

Twenty three subjects with early RRMS (disease duration 1.9 years) and 17 healthy controls were imaged at baseline. Of these, 22 MS subjects and 13 controls were also imaged at 1 year and 17 MS subjects and 10 controls were imaged at 2 years. An MTI sequence was acquired in all subjects at all time points permitting the calculation of a magnetisation transfer ratio (MTR) map. Normal appearing grey (NAGM) and normal appearing white matter (NAWM) segments of this map were generated and histograms of these segments were derived.

Baseline NAWM and NAGM MTR were significantly reduced in MS subjects when compared with controls. In the subjects with MS, at 1 and 2 year follow up, NAWM and NAGM MTR were significantly reduced when compared with baseline. This study suggests the MTR may have a role in monitoring normal appearing tissue change in early MS.

15) QUANTIFICATION OF WALKING MOBILITY IN MULTIPLE SCLEROSIS (MS) USING AN AMBULATORY ACTIVITY MONITOR: A PILOT STUDY

O.R. Pearson, M.E. Busse, R. van Deursen, C.M. Wiles. University of Wales College of Medicine, Cardiff, UK

Introduction: Walking mobility in MS is assessed using subject or observer rated tools but it is uncertain how these relate to real life mobility. Ambulatory monitoring (SAM) allows unobtrusive counting of every step over many days.

Methods: MS patients and healthy volunteers underwent two monitoring periods of one week, 3 x 10 metre observed walks at “preferred” speed and were evaluated using disability and quality of life (QOL) scales.

Results: 12 MS patients (11 female, mean age 36.7 years, height 1.65 m, Expanded Disability Status Scale (EDSS) 2.0–6.5) and 14 volunteers (11 F, 35.4 years, 1.7 m) completed monitoring. The 7 day average stride count (range, SD) in 24 hours in patients was 3015 (285–5450, 1631) and in volunteers 5431 (2810–7932, 1388). Reliability (intraclass correlation) in volunteers was r = 0.82 (p = 0.0001) and in patients r = 0.93 (p = 0.0000). Average stride count did not correlate with gait speed in volunteers ( Spearman r = −0.25) but did in patients (r = −0.76, p < 0.002). Correlation (Spearman r) with EDSS was 0.79 (p < 0.01) and with Rivermead Mobility Index 0.75 (p < 0.01). Correlation with Multiple Sclerosis Impact Score (physical component) was 0.72 (p < 0.01), with SF-36 (physical component) 0.66 (p < 0.05) and with UK Neurological Disability Scale (mobility) −0.57 (p < 0.05).

www.jnnp.com
Conclusion: Ambulatory monitoring is feasible in MS and likely to be reliable and valid. The face validity of counting every step over many days in the patient’s own environment underlies a view that such methodology may become the gold standard for measurement of actual (rather than claimed or derived) walking mobility.

A FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY OF THE LONGITUDINAL RESPONSE TO PHOTIC STIMULATION FOLLOWING ACUTE OPTIC NEURITIS


Introduction: Previous work using functional magnetic resonance imaging (fMRI) has identified increased activity in extraoccipital regions in patients who had recovered from optic neuritis, which may contribute to recovery. To investigate the spatial and temporal evolution of these regions, a longitudinal study was conducted over 1 year in patients with acute optic neuritis.

Methods: 21 patients were recruited. MRI and clinical examination were performed at baseline, 2 weeks, 1, 2, 3, and 6 months, and 1 year. A longitudinal regression analysis was performed to describe trends in the fMRI response over the first 6 months. A cross sectional study was performed to investigate dynamic differences between patients and controls.

Results: The regression analysis showed recovery of visual cortex function over the first 6 months. The cross sectional analysis demonstrated fMRI activity in the insula, corpus striatum, lateral temporal, orbitofrontal and posterior parietal cortices with a dynamic involvement over time. The peak differences between patients and controls occurred at 1–2 months and subsided after 3–6 months. The extraoccipital responses for affected and fellow eye stimulation showed similar activation patterns.

Conclusions: This work demonstrates strikingly dynamic changes in brain activity outside the visual cortex in patients, compared with controls, during recovery from acute optic neuritis.

A 5 YEAR LONGITUDINAL MRI STUDY OF PRIMARY PROGRESSIVE MULTIPLE SCLEROSIS


Background: There has been little meaningful correlation between clinical and MR changes in primary progressive multiple sclerosis (PPMS), although all studies have been of short duration (2 years or less). In this longitudinal study lesion loads, cord and brain volumes are measured in a PPMS cohort over 5 years and compared to two clinical measures.

Methods: 41 PPMS patients representing a wide range of ages and disease duration attended for MRI and clinical examination on four occasions over 5 years. T2 lesion load, T1 hypointensity load, brain and cord volume were measured at each point by a single observer.

Results: Significant changes were seen in all MR measures over 5 years (p<0.001) with time plots revealing a wide variety of change between individuals. Modest associations were found between increase in disability and decrease in cord area and increase in T2 load (r=0.31, p<0.05 both). Deterioration in cognition was associated with greater rates of brain atrophy (r=0.31, p<0.05 also). Changes in cord volume were found to be independent of changes in other MR measures.

Discussion: While longer periods of follow up associations can be found between MR and clinical measures providing some support for their use as surrogates in therapeutic trials in PPMS. Patients with PPMS display a surprisingly wide range of MR and clinical behaviours.

THE PREVALENCE OF MULTIPLE SCLEROSIS IN IRELAND: EVIDENCE FOR A NORTH-SOUTH GRADIENT

C. McGuigan, A. McCarthy, C. Quigley, L. Bannon, S.A. Hawkins, M. Hutchinson. St Vincent’s University Hospital, Dublin, Ireland; Royal Victoria Hospital, Belfast, UK

Objectives: To compare the prevalence of MS in two Irish counties: Donegal in the north west of the island and Wexford in the south east.

Methods: Patients with clinically definite or probable MS (Poser criteria) who were resident within the county borders on 1 January 2001 were considered prevalent cases for the study. Sources of ascertainment included a postal survey of general practitioners, county physicians, consultant neurologists, respite facilities and local MS charities. Hospital coding lists and intercessor prescription lists were also reviewed. Review of clinical case records and/or patient examination confirmed the diagnosis of MS.

Results: In County Donegal, 229 prevalent cases were identified giving a prevalence rate of 176.1 per 100 000 (95% CI: 154.2–200.1). In Wexford there were 126 prevalent cases resulting in a prevalence rate of 120.7 per 100 000 (95% CI: 100.5–143.7).

Conclusions: The south east of Ireland has a higher prevalence rate of MS than previously reported; however, the rate still remains significantly lower than that in the north. This north-south gradient is possibly due to genetic variations in the background populations; HLA typing in both Donegal and Wexford is ongoing to test this hypothesis.

A POPULATION BASED STUDY INTO LATE ONSET CEREBELLAR ATAXIA (LOCA) IN SOUTH EAST WALES


Background: Most late onset cerebellar ataxia (LOCA) cases are sporadic; a proportion has an established acquired or genetic aetiology, whereas the remainder are idiopathic (ILOCA). We have conducted a population based study into prevalence and causation of LOCA in SE Wales.

Methods and materials: Multicentre ascertainment sources were used to identify all cases prevalent on 1 January 2001 with a predominantly progressive cerebellar ataxia with age at onset over 18 years, in a region with 742 400 inhabitants. Those with acquired aetiologies were excluded and a prevalent register constructed from ILOCA and known genetic LOCA cases.

Results: We identified 76 cases; 70 (92.1%) with apparently idiopathic LOCA, and six (7.9%) with established genetic basis. For ILOCA, the crude prevalence rate was 9.4 per 100 000 (95% CI: 7.2–11.6) while for known inherited LOCA, it was 0.81 per 100 000 (95% CI: 0.2–1.4). Mean age at onset of ILOCA was 53.2±13.6 years, of whom 58.6% were male. Cases with extracerebellar features (67.3%) exceeded those with a relatively pure cerebellar syndrome (32.7%). Mean disease duration was 9.2±7.4 years and 92% remained ambulant.

Discussion: This population based study is the first in the UK and provides an insight into prevalence and aetiology of LOCA within a defined region, and will provide a basis for the use of expanding genetic tests in LOCA cases.

TIME TO MOVE FROM GUT TO BRAIN: GLUTEN ATAXIA RESPONDS TO GLUTEN-FREE DIET EVEN IN THE ABSENCE OF AN ENTEROPATHY

M. Hadjivassiliou, G.A.B. Davies-Jones, D.S. Sanders, R.A. Grünwald. The Royal Hallamshire Hospital, Sheffield, UK

The effect of a gluten free diet was studied in 40 patients with gluten ataxia. Twenty four adhered to the diet with elimination of antigliadin antibodies (treatment group (TG)). Thirteen refused or abandoned the diet (control group (CG)). At six months, 10 of 13 (76.9%) of TG had clinical (32.7%) and 5 of 11 (45.5%) of CG had clinical (36.4%) improvement. Results were similar at 12 months. Coeliac disease was diagnosed in 9/13 (69.2%) of TG and 0/11 (0%) of CG (p=0.005). Coeliac disease was confirmed in 2/9 (22.2%) of TG and none of 0/0 (0%) of CG (p=0.01). The effect of a gluten free diet was studied in 40 patients with gluten ataxia. Twenty four adhered to the diet with elimination of antigliadin antibodies (treatment group (TG)). Thirteen refused or abandoned the diet (control group (CG)). At six months, 10 of 13 (76.9%) of TG had clinical (32.7%) and 5 of 11 (45.5%) of CG had clinical (36.4%) improvement. Results were similar at 12 months. Coeliac disease was diagnosed in 9/13 (69.2%) of TG and 0/11 (0%) of CG (p=0.005). Coeliac disease was confirmed in 2/9 (22.2%) of TG and none of 0/0 (0%) of CG (p=0.01).

AGE OF ONSET IS A SIGNIFICANT FACTOR IN DETERMINING THE PHENOTYPE OF PRIMARY TORSION DYSTONIA

S. O’Riordan, T. Lynch, M. Hutchinson. St Vincent’s University Hospital; Mater Hospital, Dublin, Ireland
Objective: Primary torsion dystonia (PTD) is clinically and genetically heterogeneous. The study aim is to test the hypothesis that while different gene mutations are responsible for PTD, clinical phenotype is determined by age of onset.

Methods: (1) Fifteen multiplex families with PTD were ascertained and videotaped examinations of all consenting individuals were rated for affected status and distribution by three neurologists. (2) A systematic review was performed of series of patients with sporadic PTD published on MEDLINE between 1970 and 2000. The analysis of 33 published series of sporadic PTD a similar significant distal to proximal trend was observed (p<0.0001; upper limb 38 years, cervical 41.1, laryngeal 46.2 and cranial 55.8).

Conclusion: Both the family study and published series of sporadic PTD confirm a significant effect of age at onset on phenotypic presentation of dystonia with a distal to proximal anatomical gradient in the mode of presentation with increasing age.

22 ESSENTIAL TREMOR AND DYSTONIA: EVIDENCE FOR SIMILAR PATHOPHYSIOLOGY?

N. Frima, R.A. Grunevald. University of Sheffield, Sheffield, UK

Biceps tendon vibration of an immobilized arm produces an illusion of arm extension, the vibration-induced illusion of movement (VIIM). This is abnormal in patients with dystonia and essential tremor. In dystonia the abnormality is corrected by volitional fatigue. To investigate whether the two disorders share other pathophysiological features, the change in VIIM with volitional fatigue was measured in patients with essential tremor.

The VIIM in 18 patients with essential tremor (mean age SE: 62.2 ± 2.5 years) was compared with 18 healthy control subjects (58.9 ± 3.0 years) before and after fatigue. Blindfolded subjects were asked to track the perceived movement of the vibrated arm with the opposite arm. Extension of the tracking arm was measured after 45 seconds. The task was repeated following fatigue of the vibrated arm. Vibration of the immobilized biceps produced a subnormal VIIM in patients with essential tremor (12.8 ± 2.2), compared to control subjects (28.6 ± 1.7, p=0.003 unpaired t test). The VIIM increased following volitional fatigue of the arm (patients: 16.2 ± 2.1, control subjects: 26.9 ± 2.0, F(1,34)=21,554, p<0.01, repeated measures ANOVA).

Abnormal VIIM is a feature of both idiopathic focal dystonia and essential tremor, and in both disorders corrects after fatigue of the vibrated arm. This implies that both disorders share common pathophysiological features, perhaps based on abnormal elasticity of muscle spindles.

23 ASSOCIATION STUDIES OF GENETIC VARIANTS IN THE VASCULAR ENDOThelial GROWTH FACTOR (VEGF) GENE AND PROMOTER REGION IN AMYOTROPHIC LATERAL SCROSIS PATIENTS AND CONTROLS

I. Van Marion, R.H. Musson, H.S. Pall, K.E. Morrison. University of Birmingham, Birmingham, UK

VEGF is a major angiogenic factor and potent mediator of vascular permeability. In 2001 a transgenic mouse with a deletion in the hypoxia response element of the promoter of the VEGF gene was described, showing the unexpected phenotype of weakness and wasting and pathological features similar to those of human ALS. Previous studies have shown an influence of certain single nucleotide polymorphisms (SNPs) within the VEGF gene on VEGF levels. We have therefore undertaken genetic association studies of VEGF polymorphisms in ALS patients and age matched controls to determine whether any of these are susceptibility factors for ALS.

Segments of VEGF and its promoter were sequenced in over 100 ALS cases and controls. Polymorphisms, some of them novel, were detected at regions of the analysis of these polymorphisms has identified differences in allele frequencies between patients and controls. Two SNPs were identified as independent risk factors for ALS and a specific extended haplotype showed a 3.5-fold increased risk for ALS. Additional studies by collaborators have shown these polymorphisms to correlate with levels of VEGF, expression and functional proteins. It is known that hypoxyca induced VEGF has a protective role against ischemic motor neuron loss. These findings suggest that VEGF is a candidate modifier of motor neuron degeneration in ALS and open novel therapeutic strategies.

24 GASTROSTOMY TUBES FOR MND IN SCOTLAND: FREQUENCY, TIMING AND SURVIVAL

R.J. Swingler, S. Calville, R.B. Forbes. Ninewells Hospital, Dundee; Royal Victoria Hospital, Belfast, UK

Aims: To describe the frequency, timing and outcome from gastrostomy in ALS/MND.

Methods: We used Scottish Morbidity returns (SMR1) to identify patients placed on the Scottish MND Register between 1989 and 1998 who were discharged with a diagnostic code for an endoscopic gastrostomy procedure (OPCS4 G44.8). A survival analysis was performed using Kaplan-Meier and Cox proportional hazards methods.

Results: 142 PEG episodes were identified in 1226 patients, 130 of which occurred before censoring date of 31 December 1999. The rate of gastrostomy has increased between 1989–1998 and the cumulative incidence was 11%. Mean age of PEG tube was 66.8 years, with a mean disease duration of 24 months. Median survival from PEG insertion was 146 days. The 1 month mortality postgastrostomy was 25%. Gastrostomy did not confer a survival advantage.

Conclusions: We found that gastrostomy feeding tubes are being inserted more frequently in people with ALS/MND. An unexpectedly high early mortality was detected. This may reflect a lack of selection bias compared to previously published series. However, we are reviewing the medical records of MND patients to look for other factors that may have influenced survival after PEG.

25 A RANDOMISED CONTROLLED TRIAL OF MODAFINIL FOR TREATMENT OF DAYTIME SOMNOLENCE IN MYOTONIC DYSTROPHY


Patients with myotonic dystrophy (MyD) frequently suffer from excess daytime sleepiness (EDS). We have investigated the use of modafinil in myotonic dystrophy patients with EDS recruited from a clinic population screened with the Epworth Sleepiness Scale (ESS). Patients scoring 10 and above were invited to participate in a randomised double blind crossover trial of modafinil versus placebo, with 4 weeks in each arm of the study separated by a 2 week washout period. The primary outcome measures were change in both the ESS and the Maintenance of Wakefulness Test (MWT). In agreement with previous studies, sleepiness is not correlated with CTG expansion size. Treatment with modafinil showed a non-significant reduction in median ESS. However, the median MWT score was prolonged by treatment (31.7 to 40 minutes, p=0.006). There were no significant adverse cardiac effects of the drug in this group of patients (resting 12 lead and 24 hour ECG monitoring). We conclude that selected patients with myotonic dystrophy and EDS may benefit from modafinil. In this patient group the ESS may not be the most reliable measure of sleepiness. Despite the potential for cardiac disease in these patients, the drug was well tolerated with no adverse effects.

26 A NEW PERRIAINXID Mutation in CMT4F

A.C. Williams, I. Baris, E. Battaglou, P.J. Braphy. University of Edinburgh, Edinburgh, Scotland, UK; University of Istanbul, Turkey

Charcot-Marie-Tooth disease has an incidence of 1 in 2500. The molecular basis of many forms of the disease is now known, with 12 genes and more than 22 loci identified linked to the disease. We previously described that autosomal recessive Charcot-Marie-Tooth (CMT) type 4F is caused by mutations in the PERIAINXID gene. To date, seven PERIAINXID mutations have been identified. We now describe a homozygous point mutation in the PERIAINXID gene in a Turkish patient with autosomal recessive demyelinating CMT disease that introduces an early stop codon into the Periaxin protein (R1070X). We performed immunohistochemistry on a sural nerve biopsy from this patient and showed the presence of a truncated L-periaxin protein, lacking the C-terminal part. This was confirmed by western blot analysis.

L-periaxin homodimerises and underpins the DRP2-dystroglycan interaction that may have influenced survival after PEG.
Fib6, which directs peroxin for ubiquitination and degradation by the proteasome. The disruption of Peroxin degradation and hence regulation in Schwann cells may lead to demyelination.

### 27 GUILLAIN-BARRE SYNDROME REMAINS A HIGH MORBIDITY ILLNESS: REPORT OF A SWANSEA 10 YEAR COHORT

T.P. Pickersgill, C. Rickards. Morriston Hospital, Swansea, UK

**Introduction and Methods:** Morriston Hospital neurology department is a tertiary referral centre for seven general hospitals in south west Wales with a population base of approximately 800 000. Cases of Guillain-Barré syndrome (GBS) between 1989 and 1998 were identified by searches of coding records, admission books, discharge summaries, neurophysiology records, and ITU databases.

**Results:** 60 patients were identified (33 male (55.0%)). Mean (range, SD) age was 50.3 years (14.4–82.3, 19.0) giving a crude incidence of 0.75/105/year. Median admission duration was 29 days (2–278, 55.6). 23 (38.3%) were admitted to ITU of which 16 (26.6%) were ventilated for a mean of 30 days. Median length of ITU stay was 14.5 days (1–94, 23.8). Five patients (8.3%) had the Miller Fisher variant. Mortality was 3.3%.

**CSF analysis** was available on 40 patients: five (12.5%) had pleocytosis (<5 wbc/mm3, maximum 28) and 28/38 (73.7%) had raised protein (median 0.79 g/dl). 39 patients had neurophysiological studies.

**Treatment:** 14 patients required only supportive care or physiotherapy. 16 underwent plasma exchange (PE), 17 received intravenous immunoglobulin (IVIG), two had steroids, and 11 had combination treatment with PE, IVIG or both, immunosuppressants.

**Outcomes:** 49% were bedbound at the illness nadir; only 24.6% remained mobile throughout. 39/53 (73.6%) were discharged with a degree of disability, judged to be significant in 17.

**Conclusion:** This cohort has similar age, sex, mortality, admission duration and ITU admission rates to other series reported. Despite advances in treatment, GBS morbidity remains high.

### 28 PROTEOMIC ANALYSIS OF MITOCHONDRIAL PROTEIN EXPRESSION IN A CELL CULTURE MODEL OF SOD1-RELATED FAMILIAL AMYOTROPHIC LATERAL SCLEROSIS

C.A. Wood-Allum, S. Allen, P.J. Shaw. Sheffield University, Sheffield, UK

**Introduction:** Amyotrophic lateral sclerosis (ALS) is an incurable, adult onset neurodegenerative disease causing progressive muscle weakness. Some 10% of ALS is familial, of which 20% is the result of mutations to CuZn superoxide dismutase (SOD1). Recently, mitochondrial dysfunction has been implicated in ALS pathogenesis.

**Aims:** This study examines changes in mitochondrial protein expression due to expression of mutant SOD1 in a cell culture model of SOD1 familial ALS and aims to clarify the molecular basis of the observed mitochondrial dysfunction.

**Methods:** Two dimensional gel electrophoresis of mitochondrially enriched preparations of NSC34 cells stably transfected with empty vector, normal human SOD1 or G93A mutant human SOD1 was used to identify SOD1 mutation specific changes in protein expression. Phoretix two dimensional gel analysis software was then used to identify differentially expressed protein spots of statistical significance (non-parametric, paired Wilcoxon test) and MALDI-TOF mass spectroscopy performed on the spots of interest. Database searching was then used to generate candidate protein identities.

**Results:** Three proteins are up regulated in cells expressing G93A mutant human SOD1 compared to those expressing normal SOD1 and two are down regulated. To date, three of these have been identified. One down regulated protein forms part of the mitochondrial antioxidant defence system. The functional significance of these changes is under investigation.

### 29 MEETING THE ASSOCIATION OF BRITISH NEUROLOGISTS GUIDELINES: PROVISION OF 24 HOUR ACUTE NEUROLOGY CARE BY NEUROLOGISTS

C.B. Carroll, J.Z. Zajicek. Derriford Hospital, Plymouth, UK

The ABN has published standards of care for patients with acute neurological disease. Derriford Hospital provides a 24 hour neurology on call service to a population of 500 000 with the equivalent of four consultants, three SpRs and four SHOs with a 37 bed ward. All admissions to the neurology department were analysed prospectively for a 3 month period (March to May 2002).

There were 692 admissions (equating to 2500 per year); forms were completed for 93%. 78% of admissions were emergency. 16% were routine. The main diagnostic categories were stroke (29%), headache syndrome (13%), and epilepsy or seizures (12%). With regard to emergency admissions, 94% were seen by a neurology SHO within 6 hours and 81% by an SpR or consultant within 24 hours. 55% of patients were commented on for non-neurological wards for their entire admission. Median length of stay for stroke patients was 9.5 days, compared with 4 days for other patients. 37% of patients received a neurology follow up appointment.

Currently each SpR spends 18 hour per week involved in the care of acute neurological admissions. Meeting the ABN guidelines will require an increase in neurology bed provision to at least 15.2 per 100 000 population, with the equivalent of three consultant sessions (11 hours/week).

### 30 HEREDITARY SPASTIC PARAPARESIS ASSOCIATED WITH MUTATION IN SPASTIN (SPG4): A DISORDER OF AXONAL TRANSPORT

C.J. McDermott, A. Griersson, J. Wood, P.J. Shaw. University of Sheffield, Sheffield, UK

**Introduction:** The most common cause of HSP is mutation in the spastin gene. Both the normal function of spastin in the CNS and the mechanism by which mutation in spastin causes axonal degeneration are unknown.

**Aim:** To investigate the cellular mechanisms of disease in spastin HSP.

**Methods:** Wild type and mutant spastin expression constructs were delivered along with antibodies to the spastin protein. Neuronal and non-neuronal cells were transiently transfected with either wild type or mutant spastin and the effects on various cellular functions investigated.

**Results:** Wild type spastin when overexpressed in cultured cells had a punctate, perinuclear cytosolic pattern of staining. This was in marked contrast to mutant spastin which had a filamentous staining pattern which extended into the axonal process of neurons. Over expression of wild type spastin but not mutant spastin was associated with a dramatic reduction in microtubule staining. Mutant spastin overexpression was associated with an abnormal perinuclear clustering of mitochondria, suggestive of an impairment of axonal transport.

**Conclusion:** Spastin is a microtubule severing protein. Mutant spastin loses the ability to sever microtubules and has an abnormal interaction with microtubules. This abnormal interaction causes a disturbance of intracellular transport which is likely to have a deleterious effect on long axons.

### 31 CLINICAL UTILITY OF 18F FLUORO-2-DEOXYGLUCOSE (FDG) PET SCANNING IN UNDIAGNOSED PROGRESSIVE NEUROLOGICAL SYNDROMES

S.J. Allider, M. Hadjivassiliou, B. Sharrack, W.B. Tindale, M.B. Hanney, P. Hiller, E.J.R. Van Beck. Royal Hallamshire Hospital, Sheffield, UK

Patients with neurological syndromes secondary to paraneoplastic disease are often difficult to diagnose using conventional investigations. FDG-PET can improve detection of occult malignancy. We have assessed the sensitivity and specificity of FDG-PET in patients with undiagnosed rapidly progressive neurological syndromes.

**Methods:** From February 2001, 22 patients underwent PET imaging. All investigations were reviewed. PET scans were reported as either highly suspicious (HS), low suspicion of pathological uptake (LS) or no abnormal uptake (NAU). Patients were prospectively followed up.

**Results:** 10 men, 12 women with a mean age of 65 were studied. Presenting syndromes were ataxia (4), neuropathy (12), myeloradiculopathy (1), LEMS (1), and miscellaneous (3). Mean follow up was 15 months (2–28). 1/22 patients had positive anti-neuronal antibodies. 10/22 patients scans were HS, five LS, and six NAU. In patients with HS, PET identified a lesion from which a diagnosis was obtained in 8/10 (seven malignancy, one infection). One patient died shortly after PET scanning with presumed lung cancer. In the final patient no evidence of malignancy has been found to date. In the 12 patients with LS or NAU, an alternative diagnosis was made in five at follow up. In the remaining seven patients no malignancy has been found. The estimates for sensitivity and specificity are 100% and 96% respectively.

**Conclusion:** FDG-PET scanning in our population of patients has a high sensitivity and specificity for detection of relevant lesions, with a high yield of occult malignancy. FDG-PET scanning therefore appears a useful tool when applied to patients with undiagnosed rapidly progressive neurological syndromes.
SHOULD INTENSIVE PREVENTIVE TREATMENT BE CONTINUED INDEFINITELY AFTER A TRANSIENT ISCHAEMIC ATTACK?

E. Flassmann, T.G. Clark, M.F.G. Murphy, P.M. Rothwell. Radcliffe Infirmary, Oxford; University of Oxford, Oxford; Institute of Health Sciences, Oxford, UK

Background: Several different medical treatments have now been shown in trials to reduce the risk of vascular events during the first few years after a TIA. However, the risk of stroke falls with time, and it is uncertain whether intensive medical treatment should be continued indefinitely, particularly in elderly patients who have remained free of recurrent events for several years.

Results: We identified 290 patients with a previous TIA who were alive and stroke-free at a median of 3.8 years (interquartile range: 2.2–5.8) after their last TIA, and followed them up for a further 10 years. We determined the risks of stroke, myocardial infarction and vascular death, and also calculated standardised mortality ratios (SMRs).

Conclusions: The 10 year risk of stroke was 18.8% (95% CI = 13.6–23.7, 45 patients). The 10 year risk of stroke, myocardial infarction or vascular death was 42.8% (95% CI = 36.4–48.5, 114 patients), and did not diminish with time. Death due to stroke was no more common than expected (SMR = 1.23, 95% CI = 0.75–1.91, p = 0.4), but there was an excess of coronary deaths (SMR = 1.47, 95% CI = 1.10–1.93, p = 0.009).

CEREBROVASCULAR DISEASE AND THE FAILURE OF ELIMINATION OF AMYLOID-β FROM THE AGING AND ALZHEIMER BRAIN: IMPLICATIONS FOR THERAPY

R.O. Weller, H.-Y. Yow, I. Mazzanti, Z. Walsh, J.A.R. Nicoll. University of Southampton School of Medicine, Southampton; Newcastle upon Tyne, UK

Alzheimer’s disease (AD) is characterised by the accumulation of ubiquitinated tau within neurons and the extracellular deposition of amyloid-β (Aβ) in plaques and in vessel walls as cerebral amyloid angiopathy (CAA). Therapies aimed at removing Aβ from the aging brain and the failure of clearance of Aβ from the aging and Alzheimer brain and that this should be considered in the planning of therapeutic strategies that seek to encourage the elimination of Aβ.

RABIES REVISITED

P. Shah, G. Stewart, D. Nathwani, P. McIntyre, A. Shearer, G. Orange, A. Foaks, K. White. Ninewells Hospital, Dundee; Veterinary Laboratories Agency, Weybridge, Surrey, UK

In the developing world rabies is suspected in any patient with progressive paralytic illness with history of contact with wild animals. Although this case will not affect the United Kingdom’s rabies free zone status, this reminds us that in certain occupational groups, this condition can present as an unusual acute neurological illness.

For the last century Great Britain has been an acknowledged rabies free zone. In 1996 a daubenton bat from Surrey was found at a free zone. In 1996 a daubenton bat from Surrey was found at a free zone. In 1996 a daubenton bat from Surrey was found at a free zone. In 1996 a daubenton bat from Surrey was found at a free zone. In 1996 a daubenton bat from Surrey was found at a free zone.

We present the findings of a recent case of human rabies from Scotland.

A 55 year old conservationist and bat handler presented with haematemesis, pyrexia and progressive encephalitic and paralytic illness. Prior to presentation he had developed painful paraphrenia in the left arm, which had been bitten by a daubenton bat 6 months previously. He had not had rabies vaccination. Respiratory failure preceded areflexic paralysis initially of arms then legs, leading to death. The CSF analysis, biopsy from the previous bite site, biopsy of skin of

TRANSCATHETER CLOSURE OF PATENT FORAMEN OVALE IN PATIENTS WITH RECURRENT CRYPTOGENIC POSTERIOR CIRCULATION ISCHAEMIC EVENTS

A.R. Saha, S.J. Brecker, A.Y. Al-Menar. Atkinson Morley’s Hospital, London; St George’s Hospital, London, UK

Secondary prevention for stroke patients with patent foramen ovaole (PFO) is a subject of considerable debate. We report our single centre experience of transcatheter closure of PFO using Amplatz PFO occluder device in 10 patients. All patients were under the age of 55 years and had a preceding history of recurrent posterior circulation ischaemic events. Standard diagnostic investigation, including thrombophilia screening and angiography, did not reveal any identifiable risk factor for stroke and thus the ischaemic events were considered cryptogenic. Transoesophageal echocardiography confirmed PFO with a mean size of 25 mm (range 10–35 mm). All patients underwent transcatheter closure with an average procedure time of 45 minutes. There were no immediate or late complications from this procedure. None of the patients had further ischaemic cerebrovascular events during a mean follow up of 20 months. Thus in high risk patients with recurrent cryptogenic strokes, PFO closure appears to be a simple, quick and effective procedure with a low overall complication rate. However to identify patients most likely to benefit from this intervention, further randomised controlled studies are warranted.

THE DIFFERENTIAL DIAGNOSIS OF CREUTZFELDT-JAKOB DISEASE: DATA FROM THE NATIONAL CJD SURVEILLANCE UNIT

S.A. Cooper, C.A. Heath, R.S. Knight. University of Edinburgh, Edinburgh, UK

Introduction: The importance of accurate premortem diagnosis of CJD is enhanced by current low postmortem rates. Here we discuss referrals to the UK surveillance system (NCJDSU) of suspected CJD in which an alternative diagnosis has been proven.

Methods and Results: Since 1990 the National Creutzfeldt Jakob Disease Surveillance Unit (NCJDSU) has had 1620 referrals of suspected CJD. 50 cases have been visited by an NCJDSU registrar and subsequently had alternative diagnoses proven at postmortem.

The commonest final diagnoses were primary neurodegenerative disorders (29) (Alzheimer’s disease (191) and cerebrovascular disease (5). Other diagnoses included neoplasia and paraneoplastic disorders (6), inflammatory brain disorders (4) and leucencephalopathy (2). In four cases CJD was excluded with no proven alternative diagnosis. Reasons for initial suspicion of CJD included myoclonus and suggestive EEG changes. On review however, only one EEG was sufficiently
characteristic. A false positive CSF 14-3-3 was seen most commonly in paraneoplastic syndromes.

Conclusion: As atypical cases of CJD exist it is necessary not to set too rigid case definitions that may discourage referrals of unusual cases. However, understanding the most common distinguishing features between CJD and other diseases is likely to increase diagnostic accuracy.

38 THE PREVALENCE OF OLIGOCOCLANAL BANDS IN THE CEREBROSPINAL FLUID OF PATIENTS WITH PRIMARY NEURODENERATIVE DEMENTIA


Recent European and American guidelines on the diagnosis and management of dementia include advice that younger patients with dementia should undergo cerebrospinal fluid (CSF) examination. Interpretation of the findings can be challenging. The presence of central nervous system (CNS) specific oligoclonal bands (OCB) is considered suggestive of an inflammatory aetiology and their occurrence in degenerative disease is not well established. We reviewed retrospectively the prevalence of OCB, determined using agarose isoelectric focusing, in a series of 131 patients with a clinical diagnosis of a degenerative dementia who had undergone CSF examination. Seventy-five (55%) patients had Alzheimer’s disease (AD), forty-seven (36%) had frontotemporal lobar degeneration (FTLD), seven (5%) had dementia with Lewy bodies and the remaining seven (5%) patients had other rarer neurodegenerative dementia. Neuropathological examination had been performed in 15 (11%) patients. CNS specific OCB were present in nine (7%) patients in this cohort: four with FTLD, four with AD and one with Creutzfeldt-Jakob disease. All had normal CSF white cell counts. Investigation of these patients, including two with neuropathologically verified AD and one with postmortem confirmed CJD, did not reveal an alternative aetiology for their dementia. Thus a central immune response can occur in primary neurodegenerative dementias albeit uncommonly.

39 ADULT ONSET DEMENTIA WITH PROMINENT FRONTAL FEATURES IN X-LINKED ADRENOLEUKODYSTROPHY WITH R152C MUTATION IN ABCC1 GENE

A.J. Larner. Walton Centre for Neurology and Neurosurgery, Liverpool, UK

Objectives and Methods: Clinical, neuropsychological and neuroimaging findings in a patient with biochemically and genetically confirmed X-linked adrenoleukodystrophy (X-ALD), who developed dementia with prominent frontal features in the fourth decade of life, are presented.

Results: Aged 4, the patient was diagnosed with adrenocortical insufficiency after two brothers died from adrenocortical failure; elevated plasma levels of very long chain fatty acids were subsequently demonstrated. Aged 38, behavioural changes developed: verbal aggression, neglect of personal hygiene, predilection for sweet foods. Clinical, neuropsychological and neuroimaging (CT: brain imaging showed extensive confluent white matter change (CT: low density; T2 weighted MRI: high signal intensity). Analysis of the X-ALD (ABCC1) gene showed a missense mutation (codon 454C>T) predicting the R152C substitution in the transmembrane domain of ALD protein.

Discussion: The commonest adult presentation of X-ALD is adrenomyeloneuropathy; rapidly progressive cerebral disease, typical in childhood, is rare in adults. In the few previous reports of adult onset dementia without prior neurological features, frontal type pattern of deficits is prominent.

Conclusion: X-ALD may manifest with frontal-type dementia in the fourth decade of life without prior neurological features.

40 CEREBRAL ATROPHY VARIATION OVER SHORT TIME INTERVALS IN TRANSIENT ISCHAEMIC ATTACK (TIA) PATIENTS


Introduction: Annual cerebral atrophy rates have been found to be significantly higher in TIA patients compared with age matched controls. A subgroup of 16 cognitively normal TIA patients had serial imaging at 6 month intervals over 2 years to examine how rates of atrophy varied.

Method: Consecutively acquired cerebral volumetric magnetic resonance images (MRI’s) were registered and atrophy quantified using a validated technique (boundary shift integral). The 16 patients had at least four MRIs separated by 6 months intervals. No patient suffered a further TIA or stroke; vascular risk factors were characterised.

Results: Atrophy rate was not uniform; nine had highest atrophy rates immediately following TIA (average 25.5 ml scan 1–2; 6 ml scan 2–3, 3–4 10 ml), two showed increasing rates throughout the study (4 ml scan 1–2; 15 ml scan 2–3, 27 ml scan 3–4). Five had rates that fluctuated. Individuals’ vascular characteristics changed little with no influence on changes in atrophy rate.

Conclusion: An individual’s atrophy rate varied markedly, perhaps reflecting “activation” periods of cerebrovascular disease. The role of vascular disease in cerebral atrophy has ramifications for quantifying neurodegenerative disease progression, since it is a common comorbidity. Future studies, using surrogates of vascular disease activation, are required.

41 EPILEPSY IN PRIMARY CARE: CHARACTERISTICS OF MONOTHERAPY RESPONDERS VERSUS NON-RESPONDERS

C. Lawthom, J. Beavis, A. Thapar, S.A. Mensah, P.E.M. Smith, M.P. Kerr. University Hospital of Wales, Cardiff, UK

We present data from a large primary care based cohort of adults with epilepsy comparing characteristics of responders (those achieving seizure freedom) and non-responders treated with monotherapy. Information is derived from patient questionnaires and GP records. The database comprises 514 patients in 42 practices, of whom 72% are managed on monotherapy. Seizure freedom has been achieved in 56% of the monotherapy group compared with a seizure freedom rate of 51% overall.

Gender and living alone did not affect the rates of response to monotherapy. Regular access to specialist services was negatively associated with seizure freedom, possibly reflecting referral patterns to epileptologists. However, information regarding initial or isolated referrals at the time of diagnosis is not available and the data may reflect discharge of well controlled patients from epilepsy services.

As a group, monotherapy patients not attaining seizure freedom experienced higher rates of depression and were more bothered by seizures. They were more likely to receive disability living allowance and have regular access to specialist services. These data serve to highlight the cost of ongoing seizures to the patient and to society. Further study may elucidate patient factors amenable to treatment. The primary aim of epilepsy treatment must be the attainment of seizure freedom.

Abstract 41

<table>
<thead>
<tr>
<th>Responders (seizure freedom)</th>
<th>Yes %</th>
<th>No %</th>
<th>Yes %</th>
<th>No %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular access to specialist services</td>
<td>15</td>
<td>11.86</td>
<td>18.3</td>
<td>81.6</td>
</tr>
<tr>
<td>Current depression</td>
<td>5.2</td>
<td>94</td>
<td>9.7</td>
<td>90.3</td>
</tr>
<tr>
<td>Seizures extremely bothersome</td>
<td>20</td>
<td>80</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td>Receiving disability living allowance</td>
<td>6.7</td>
<td>93.4</td>
<td>21</td>
<td>79</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Missing data %</th>
<th>Yes %</th>
<th>No %</th>
<th>Yes %</th>
<th>No %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular access to specialist services</td>
<td>15</td>
<td>18.3</td>
<td>81.6</td>
<td>34</td>
</tr>
<tr>
<td>Current depression</td>
<td>5.2</td>
<td>94</td>
<td>9.7</td>
<td>90.3</td>
</tr>
<tr>
<td>Seizures extremely bothersome</td>
<td>20</td>
<td>80</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td>Receiving disability living allowance</td>
<td>6.7</td>
<td>93.4</td>
<td>21</td>
<td>79</td>
</tr>
</tbody>
</table>

www.jnnp.com
**ESTIMATED IMPACT OF SEIZURE FREQUENCY ON SURVIVAL IN EPILEPSY**

E. Remak, J. Hutton, K. Peeters, M. Price. MEDTAP International Inc, London, UK; Janssen Pharmaceutica, Beerse, Belgium; Janssen-Cilag, UK

**Background:** Mortality in epilepsy is significantly greater than in the age matched general population, and seizure frequency is the factor most strongly associated with an increased risk of sudden unexpected death in epilepsy (SUDEP).

**Objective:** To estimate life expectancy of epilepsy patients according to seizure frequency.

**Methods:** Age-specific mortality ratios were calculated for hypothetical patient cohorts by combining estimates of general population death rates, standardised mortality ratios of epilepsy, and relative risk of SUDEP according to seizure frequency. Four cohorts aged 15 were simulated: epilepsy patients with 0–2, 3–12, or >12 seizures during last year, and a general population control cohort.

**Results:** Residual life expectancy of epilepsy patients aged 15 was more than 14 years shorter than that of the general population. According to this extrapolation, approximately 40% of patients with recurrent seizures would have died by age 55, whilst around 90% of the general population cohort would still be alive.

**Conclusions:** Seizure frequency is strongly associated with survival. All epilepsy patients have an excess mortality compared to the general population, and large gains in life expectancy may be achieved by eliminating seizures even compared with those having relatively few (0–2 annually) seizures.

**SPINAL CORD ATROPHY IN MULTIPLE SCLEROSIS**

N. Evangelou, G. DeLuca, T. Owens, M.M. Esiri. Queen’s Medical Centre, Nottingham; Radcliffe Infirmary, Oxford; University of Oxford, Oxford, UK

**Objective:** To determine the cause of spinal cord atrophy in multiple sclerosis, a major determinant of disability.

**Methods:** Five different sections of the spinal cord were examined histopathologically in 33 controls and 55 MS cases. Multiple regression models were used taking into account sex, age, duration of the disease, and location of the cord sections.

**Results:** The MS cords were smaller than the controls taking into account the location of the sections examined (p<0.001). The duration of the disease seems to play the most important part in determining cord atrophy (p<0.001). Individual lesions have a lesser role, although interestingly, whether lesions caused shrinkage or swelling of the cord locally depends on the location of the lesion. Lesions in the cervical and lumbar cord were associated with significant local atrophy, whereas throracic lesions were associated with swelling of the cord.

**Conclusions:** The duration of the illness seems to have a greater role in determining the size of the spinal cord rather than individual lesions. This could either be due to warlerrer degeneration from the cumulative number of lesions in the brain and cord or due to an alternative atrophic process.

**IS INPATIENT REHABILITATION USEFUL IN RELAPSING-REMITTING MULTIPLE SCLEROSIS?**


**Background:** Patients with relapsing-remitting multiple sclerosis (RRMS) often make incomplete recovery from disabling exacerbations, despite corticosteroid therapy. Inpatient rehabilitation has been shown to be valuable in progressive MS, but its role in RRMS is less apparent.

**Methods:** We assessed the effect of rehabilitation in consecutive patients with RRMS admitted to a neurorehabilitation unit. Outcome measures employed comprised the Expanded Disability Status Scale (EDSS), the Barthel Index (BI), and the Functional Independence Measure (FIM) on admission and discharge, as well as a visual analogue scale (VAS) of the patients’ perception of rehabilitation benefit. Confounding factors including the timing of steroid therapy and readmissions were also evaluated.

**Results:** RR patients improved considerably following rehabilitation, with mean changes of −0.8 EDSS, 4.5 BI and +15.6 FIM points (effect sizes of −1.01, 0.97 and 0.86, respectively), which were significantly greater than other MS subtypes. RR patients rated their admissions highly (mean VAS 8.5, SD 1.5), and the VAS scores correlated modestly with disability measures (Spearman’s r = −0.42, 0.31 and 0.24 versus EDSS, BI and FIM, respectively; p = 0.007–0.040). Repeat admissions and the timing of steroid administration did not affect outcome significantly.

**Conclusions:** Inpatient rehabilitation can be a valuable adjunct to standard treatments in RRMS, and should be considered in patients with incomplete recovery from relapses who have accrued moderate to severe disability.

**DISEASE MODIFYING THERAPY FOR MULTIPLE SCLEROSIS: INCREASING AVAILABILITY IN THE UK**

M.A. Noori, M.K. Sharief. Guy’s, King’s and St Thomas School of Medicine, London, UK

Disparities in the availability of disease modifying drugs (DMDs) for the treatment of multiple sclerosis (MS) are apparent throughout the world. We present data gathered from national health statistics to show that the UK, where 6% of all patients with MS receive DMDs, compares badly with other countries in Europe (eg 36% in Portugal, 34% in Germany, 31% in France, and 25% in Spain) and worldwide (eg 45% in the USA and 38% in Australia). A new funding initiative was introduced in the UK in 2002, in which the costs of therapy are shared between the NHS and the drug manufacturer according to a sliding scale of effectiveness. This extremely welcome initiative promises to double the proportion of UK patients who receive DMDs.

However, the full benefits of the risk sharing scheme remain to be achieved; our results show that in 2002 the proportion of patients receiving DMDs in the UK increased by 1% from 2001.
These data help evaluate the rate of progress in increasing availability of DMDs in the UK, and the overall population benefits entailed therein. The success of this positive and cost effective initiative will become apparent as the rate of DMD use approaches parity with other European countries.

48 BRAIN TISSUE DIFFUSION ABNORMALITIES MAY OCCUR EARLY IN RELAPSING-REMITTING MULTIPLE SCLEROSIS


Introduction: Diffusion tensor MR imaging (DTI) has revealed changes in multiple sclerosis (MS) brain tissues which are most evident in subjects with relatively long disease durations. However, it remains unclear when these changes begin. This work aimed to explore this in a cohort of subjects with early relapsing-remitting (RR) MS (within 3 years of first symptom onset).

Methods: Sixteen RR MS patients (mean age 32.7 years, median disease duration 1.6 years, median EDSS 1.25) and 17 normal control subjects (mean age 39.1 years) were studied. Fractional anisotropy (FA) and mean diffusivity (MD) histograms were estimated from the normal appearing brain tissue defined as grey and white matter excluding lesions and cerebrospinal fluid. Statistical analysis allowed for age and potential partial volume effects.

Results: A significant decrease in mean FA (p = 0.014) and increase in FA peak histogram height (p = 0.002) was observed in the MS cohort, while the MD analysis showed no significant difference between the cohorts.

Discussion: This suggests that subtle abnormalities occur early in MS that affect the directional preponderance (FA) but not mean amount of FA peak histogram height (p = 0.002) was observed in the MS cohort, p

49 DOUBLE BLIND, RANDOMISED PLACEBO CONTROLLED, CROSSOVER TRIAL OF TOPIRAMATE IN CENTRAL NEUROPATHIC PAIN DUE TO MULTIPLE SCLEROSIS

D.J. Rog, C.A. Young. Walton Centre for Neurology and Neurosurgery, Liverpool; University of Liverpool, Liverpool, UK

Central pain, caused by a lesion or dysfunction of the central nervous system, occurs in between 17% and 52% of people with multiple sclerosis (MS). Randomised controlled trials are needed in this area to inform evidence based prescribing. We conducted a randomised, double blind, placebo controlled crossover trial in 32 patients with MS and dysaesthetic central pain states, of topiramate in doses of up to 200 mg per day, at a maximum titration of 25 mg per week. Six patients were male, mean age 47 years (range 23–71, SD 11), mean EDSS 5.3 (2.9–8.5, 1), mean duration of MS since diagnosis 11 years (2–22, 7) and mean duration of pain was at least 9.9 years (1.5–30, SD 7.6). Three patients had primary progressive, 11 secondary progressive, and 18 relapsing-remitting MS.

In a double blind fashion, 12 patients preferred treatment with topiramate, two placebo, four neither treatment and 14 patients withdrew, mostly when taking topiramate. Intention to treat analysis demonstrated no significant differences in average weekly pain levels measured using the Neuropathic Pain Scale 10 item score, or mood or quality of life between each treatment. However in those favouring topiramate a significant reduction in pain was found (11 = –4.216, p < 0.001).

50 INFLAMMATION IN EARLY PRIMARY PROGRESSIVE MULTIPLE SCLEROSIS


Background: Established PPMS appears to have less inflammation than other forms of MS. However, it is unclear if this holds true for the rarely studied early PPMS. We looked for evidence of inflammation in early PPMS in a comprehensive clinical and MRI study.

Methods: 34 patients with PPMS with disease duration of less than 5 years attended for clinical and MRI examination, including administration of triple dose gadolinium DTPA (Gd).

Results: Mean disease duration was 3.4 years. Thirty five per cent of patients showed some enhancement at baseline. Gd enhancement in early PPMS was greater in female subjects (p = 0.004), and associations were found with younger age (r = 0.40, p = 0.022) and greater disability (r = 0.63, p < 0.001). Enhancement was also associated with increased lesion volume and reduced white matter fraction.

Discussion: Inflammation is seen more frequently in early PPMS but is still not seen in the majority of subjects. A better understanding of disease heterogeneity in PPMS may be important for the development of effective therapeutic interventions.

51 A STUDY OF CLINICALLY UNAFFECTED MUSCLES IN PATIENTS WITH A DIAGNOSIS OF PREVIOUS PARALYTIC POLIOMYELITIS: CLINICAL, ELECTROPHYSIOLOGICAL AND METABOLIC EVALUATION

G.S. Gorman, O. Hardiman, S. Connolly. St Vincent’s University Hospital, Dublin; Beaumont Hospital, Dublin, Ireland

Introduction: The late effects of paralytic poliomyelitis can include progressive weakness. Macro electromyography (Macro-EMG) studies provide information about the size of motor units and can indicate the degree of initial motor neuron loss and subsequent reinnervation in muscles of patients with a history of paralytic poliomyelitis.

A cohort of 22 patients, fulfilling the criteria of ‘post-polio syndrome’, underwent clinical, electrophysiological, and metabolic analysis.

Method: Macro-EMG analysis of a muscle from a clinically unaffected limb was compared to published normal data. Fasting serum samples were analysed for insulin-like growth factors (Igf’s) and their binding proteins.

Results: The median macro motor unit potential (macro-MUP) amplitude was increased in 17 of the 22 subjects (mean = 3 times normal; range = 1.2 to 18 times normal). The mean circulating concentration of Igf-II was 36% higher than that of an age and sex matched control population (p < 0.001).

Conclusion: There is evidence from Macro-EMG that significant reinnervation can occur in muscles from clinically unaffected limbs in patients with “post-polio syndrome”. This may be useful as a prognostic indicator in the evolution of the condition. Changes in circulating Igf-II were also evident, suggestive of altered Gh/Igf regulation in this population.

52 THE ‘JUMPING STUMP’ SYNDROME: IS IT A PERIPHERAL, CENTRAL OR PSYCHOGENIC PROBLEM? A REPORT OF THREE CASES

S.H. Alusi, J. Thomas, C.G. Inman. University Hospital of Wales, Cardiff, UK

Abnormal movements of amputation stumps are reported to occur in 1:1000 amputee patients. Upper and lower limb stump involvement has been reported and various terms, such as spasms, jumps, myoclonus and chorea, have been used to describe the movements. Symptoms onset varies from 2 weeks to 2 years postamputation. Antispasticity drugs, anticonvulsants, and psychological factors have been used with variable success. The pathophysiology remains unclear.

We present three patients (with video illustration) who experienced abnormal “clonic” movements in their lower limb stumps within 2 months of amputation. The severity of the movement disorder rendered the use of limb prosthesis and hence walking difficult. Peripheral triggers were present in all three of these patients, as were the phantom limb sensations and or pain. Psychogenic factors related to the preamputation illness seemed to have some role. A trial of intrathecal baclofen was useful in one patient. Clonazepam and oral baclofen were less effective.

A hypothesis of a peripherally triggered but centrally mediated mechanism is suggested and the role of deafferentation at the spinal level is discussed.

53 PD LIFE: A PROSPECTIVE MULTICENTRE LONGITUDINAL AUDIT OF QUALITY OF LIFE IN PARKINSON’S DISEASE ACROSS THE UK

K.R. Chaudhuri, L.S. Taurah, D.G. MacMahon, L. Findley, L. Kelly, D. Burn, O.J. Foster, and members of the UK P.D.L.I.F.E. committee. UK Parkinson’s Disease Society; University Hospital of Lewisham London; King’s College Hospital London; Camborne and Redruth Community Hospital; Cornwall; Atkinson Morley Hospital; London; St Georges Hospital; London; Harold Wood Hospital; Romford; Newcastle General Hospital, Newcastle, UK

Background: PD LIFE is a collaborative academic led prospective national audit that aims to review Parkinson’s disease (PD) patients on a yearly basis for 5 years monitoring (a) baseline and general changes in quality of Life (QoL), (b) indirect estimation of the cost effectiveness of
available treatment, (c) prescribing trends across the United Kingdom (UK), (d) and QoL changes which may trigger changes or initiation of treatment.

Methods: Administration of the PDQ-39 scale and audit form monitoring changes in treatment, and comorbidity. Inclusion/exclusion criteria include PD patients at an early (diagnostic and maintenance) stage, drug naive or receiving monotherapy.

Results: In the pilot phase eight core UK centres have started recruiting patients (n = 202). 50/202 patients have completed an initial follow up assessment at a mean duration follow up period of 144 days. By 2003 we hope to collect baseline data on a total of 500 patients and follow up data on 200 patients.

Conclusions: Preliminary data from the pilot phase of this study suggests that administration of the PDQ-39 should be determined by changes or initiation of treatment rather than having fixed measurement points. Initial pilot results indicate levodopa to be the most commonly prescribed drug used for the treatment of early PD within the UK.

54 DIAGNOSTIC ACCURACY IN EARLY PARKINSON’S DISEASE: A CLINICAL AND IMAGING FOLLOW UP STUDY

V.L. Marshall, W.H.I. Oerte, J. Patterson, D.M. Hadley, O. Pogorel, H. Höflken, A. Gerstner, D.G. Grosset. Institute of Neuropsychological Sciences, Glasgow, UK; Philips University, Marburg, Germany

Objective: Parkinson’s disease (PD) and essential tremor (ET) share certain clinical features, making diagnosis difficult in some cases. Striatal uptake of the dopamine transporter radioligand [123I]FP-CIT reflects nigrostriatal integrity and is reduced in PD but normal in ET. We report an 18 month interim analysis of FP-CIT SPECT.

Methods: 34 subjects with a Unified Parkinson’s Disease Rating Scale motor score of 16 or less were enrolled because of clinical uncertainty between PD/ET/tremor disorders. At T = 0 and 18 months clinical confirmation of parkinsonism was sought with visual assessment of FP-CIT uptake.

Results: FP-CIT imaging at T = 0 using 18 month clinical and imaging diagnoses as a comparator has sensitivity of 91% and specificity of 92% for PD. At T = 0, there were 21 abnormal scans (baseline diagnosis 20 PD, 1 ET) and 13 normal scans (baseline diagnosis seven PD, six ET/ataxic tremor). At T = 18 scan groupings remained unchanged (normal or abnormal). In the abnormal scan group one diagnosis of ET changed to PD, and in the normal group five diagnoses of PD changed to ET/ataxic tremor.

Conclusion: In this select group a clinical baseline diagnosis of PD was incorrect for 5/34 (15%) patients reinforcing usefulness of FP-CIT imaging.

55 ASSESSMENT OF ATAXIA SEVERITY USING THE ATAXIA RATING SCALE (ARS) IN LATE ONSET CEREBELLAR ATAXIA (LOCA) PATIENTS

M.B. Muzaimi, A.E. Stroud, H. Wynne, I. Sutherland, C.M. Wiles, P. Enderby, N.P. Robertson. University of Wales College of Medicine, Cardiff; Prince Charles Hospital, Merthyr Tydfil; University Hospital of Wales, Cardiff; University of Sheffield, Sheffield, UK

Background: Currently there is lack of clinically practical and/or validated scales for ataxia. The semi-quantitative Ataxia Rating Scale (ARS) is devised and tested for reliability and validity, compared with Barthel, in a cohort of patients with late onset cerebellar ataxia (LOCA).

Methods and materials: Nineteen tasks in four subgroups give a maximum 100 point score: posture and gait = 34, limb = 32, speech = 8 (modified from Frenchay Dysarthria Assessment) and oculomotor = 6. Activities of daily living (ADL) were evaluated using Barthel and ARS in 50 LOCA patients.

Results: ARS scores (mean ± standard deviation; range) were: total (37.82 ± 15; 12 to 75); posture/gait (14.56 ± 6.19; 4 to 29); limbs (19.54 ± 8.37; 4 to 39); speech (1.5 ± 1; 0 to 4); oculomotor (2.3 ± 1.81; 0 to 6). Barthel scores: two patients severe disability (ADL: 5 to 9); five = moderate disability (ADL: 10 to 14); 38 = mild disability (ADL: 15 to 19); five = independent (ADL: 20). A significant inverse association (Spearman’s r = -0.729, p < 0.01) was shown between total ARS score and ADL index. The 19 tasks in ARS were internally consistent (Cronbach’s α = 0.884).

Conclusions: This study yields a scale with indicative scores for the ataxia components, their impairment and disability in patients with LOCA.

56 ROLE OF ANTINEURONAL AUTOANTIBODIES IN POPULATION BASED SAMPLES OF APPARENTLY IDIOPATHIC LATE ONSET CEREBELLAR ATAXIA (ILOCA)

M.B. Muzaimi, L. Clover, B. Lang, K. McKeith, A. Vincent, N.P. Robertson. University of Wales College of Medicine, Cardiff, UK; John Radcliffe Hospital, Oxford, UK

Background: Antineuronal autoantibodies (Abs) in late onset cerebellar ataxia (LOCA) are associated with paraneoplastic manifestations of certain cancers, as well as increasing in non-paraneoplastic cases. We have explored their significance in a prevalent, population based sample of patients with apparently idiopathic LOCA (ILOCA) in South Wales.

Methods and materials: Sera of 54/70 (77.1%) patients (mean disease duration: 9.1 years; range: 1 to 30) were analysed using indirect immunohistochemistry and/or western blot (IHC/WB) for anti-Hu, Ma1, Ri, tr, and Yo Abs, and using immunoprecipitation (IP) for P/Q-type voltage gated calcium channel (VGCC) and glutamic acid decarboxylase (GAD) Abs. Results of each assay were compared with known negative, normal, and positive controls.

Results: On IHC/WB, 6/54 sera showed staining patterns suggestive of anti-Hu (n = 3), Yo (n = 2) and tr (n = 1), but were excluded on WB. 1/54 revealed an “atypical” staining, with identification of an approximately 30 kDa protein of unknown significance at present. On IP, none were positive for anti-VGCC Abs, and 2/54, who were negative for Abs on IHC/WB, were found to have abnormally high titres for anti-GAD Abs.

Discussion: Our data have revealed 3/54 (5%) amongst ILOCA cases with positive Abs and highlights the role of these Abs as diagnostic tools in the investigation of ILOCA. To date, studies on further patients are underway.

57 PIRIBEDIL IN ESSENTIAL TREMOR AND PARKINSON’S DISEASE

R.P. Sheridan, T.J.L. Malone, G.M. Fenwick, V.R. Pearce. Royal Devon and Exeter Hospital, Exeter, UK

Introduction: Piribedil is a non-ergoline dopamine agonist widely used outside the UK. Tremor in Parkinson’s and essential tremor may be unresponsive to treatment and older patients are prone to side effects of anticholinergics and other drugs. We report our experience with piribedil in patients intolerant or unresponsive to other agents.

Methods: Prospective recording of 81 patients treated with piribedil between 1994 and 2002.

Results: Data available in 77 patients with Parkinson’s (86%), essential tremor (8%) or other (6%). Mean age commencing piribedil 70.8 years (range 45–86). Primary indication for piribedil was tremor (83%), improved motor control (12%), and other (5%). Mean treatment duration 112 months (9–688). Mean daily dose achieved 121 mg (20–200). After 3 month trial symptomatic benefit in 69% (n = 53). Piribedil discontinued in 55% (n = 42), either no benefit 13% (n = 10) or side effects 42% (n = 32). Side effects included confusion (n = 8), hallucinations (n = 5), worsening tremor (n = 4), and dyskinesia (n = 3).

In 16 patients aged 80 years (80–91) or over, 14 found symptomatic benefit. Three discontinued because of side effects (nausea, dyskinesia, hypotension). Hallucinations in one disappeared on reduced dose.

Conclusions: Piribedil appears effective at treating tremor in those unresponsive or intolerant of other agents, and is relatively well tolerated in older patients.

58 MELANOMA, LEVODOPA, AND PARKINSON’S DISEASE (PD)

N. Turner, Z. Coven, P.K. Newman. Middlesbrough General Hospital, Middlesbrough, UK

Cases first reported in the 1970s linked melanoma and levodopa therapy in PD. This unsubstantiated myth persists in cautions contained in the British National Formulary and as a contraindication in product literature and the Physicians’ Desk Reference.

Cases re-examining a PD database of 680 and a melanoma database of 353 cases, revealed five patients with melanoma and PD of whom four had been treated with levodopa for variable periods before
the onset of melanoma. Although greater than the number expected by chance, this and previous anecdotal data do not support an association.

Levodopa is an intermediate in the formation of melanin after hydroxylation to dopaquinone and subsequent steps. However there is no evidence that possible exogenous priming of melanin synthesis has any influence on growth or recurrence of melanoma tumour cells. By contrast, experiments in vitro suggest that levodopa has a toxic effect on melanoma and it has been tested inconclusively as a treatment.

PD patients who develop or have had melanoma should not be restricted if levodopa therapy is otherwise indicated.

61 LITHIUM RESPONSIVE HYPNIC HEADACHE IN A PATIENT WITH MULTIPLE SCLEROSIS
P.T. Brooks, S. Hadijikoutsis, T.P. Pickersgill. University Hospital of Wales, Cardiff, UK

Hypnic headache is a rare primary headache disorder, characterised by recurrent, severe, nocturnal headache without autonomic symptoms; predominantly affecting elderly women. The condition is characteristically responsive to lithium. Bilateral headache is typical but, increasingly, cases of unilateral headache are recognised.

We present the case of a 67 year old woman with a 3 year history of exclusively nocturnal headache, occurring once or twice every night, waking her from sleep after several hours. The pain was severe, lasted on average 1 hour, was situated in the left frontal region and was not associated with autonomic, visual or other symptoms. She rarely had daytime headache. A previous diagnosis of multiple sclerosis (MS) was made at the age of 38 on clinical grounds, later confirmed by abnormal visual evoked potentials and a typical MR scan appearance. Her headache disorder had been treated unsuccessfully with simple and compound analgesics, tricyclic and SSRI antidepressants, indomethacin and antiepileptic drugs. Treatment with lithium carbonate 300 mg at night resulted in a rapid and significant improvement in her symptoms.

We think that this is the first description of hypnic headache in a patient with MS and postulate that structural/inflammatory mechanisms may be relevant in the aetiology of what is generally considered a primary headache disorder.

62 BRAIN SCARRING: EFFECTS OF EXTRACELLULAR MATRIX ON ASTROCYTE PHENOTYPE
N.J. Gutowski, J.E. Holley, J.L. Whatmore. Royal Devon and Exeter Hospital, Exeter, UK; Peninsula Medical School, Exeter, UK; Peninsula Medical School, Plymouth, UK

Astrocytes are the main supporting cells of the brain and are normally in a quiescent state. Following various brain injuries, astrocytes can form a glial scar which inhibits brain repair. The scar consists of postreactive astrocytes (SAs). In vivo we have found that human cerebral white matter SAs express the proteins embryonic neural cell adhesion molecule, epidermal growth factor receptor, and basic fibroblast growth factor. We wish to identify factors that produce a human SA phenotype thereby finding ways of inhibiting scarring and aiding repair. It would be advantageous to have an in vitro model to identify these factors, but this requires a baseline quiescent astrocyte phenotype. Human cerebral white matter astrocytes cultured in serum have a non-quiescent phenotype. In serum free chemically defined medium astrocytes on the extracellular matrix poly-L-lysine have only a partially quiescent phenotype. By changing the extracellular matrix on which astrocytes are cultured, striking differences in phenotype expression were found. Extracellular matrices (fibronectin, tenascin C, laminin, vitronectin and collagen IV) which are found in the human brain were used. This has allowed us to closely mimic the phenotype of normal quiescent astrocytes in vivo, therefore establishing a viable model for normal human quiescent astrocytes in vitro.
increase at 40%. By contrast controls showed a stepwise increase in MEP
to 40% with no further increase at 60%.

Conclusion: COPD patients have a reduced cortical reserve perhaps
because they are already facilitated at rest by an increased work of
breathing.

64 FEATURES OF PATIENTS WITH COELIAC DISEASE AND
COEXISTENT NEUROLOGICAL ILLNESS: A
RETROSPECTIVE STUDY

D.S.N.A. Pengiran Tengah, A.J. Wills. Queen’s Medical Centre,
Nottingham, UK

Objective: Detailed case report analysis of patients with coeliac disease
(CD) and coexistent neurological dysfunction.

Methods: Patients recruited via voluntary reporting scheme coordi-
nated by the British Neurological Surveillance Unit (BNSU). Patients’
contact details were obtained from referring consultant. Patients were
contacted for signed consent allowing access to their casenotes.

Results: In the first 12 months of reporting, there were 17 positive
returns (for comparison paraneoplastic syndromes had 47 positive
returns). Nine sets of notes (53%) were reviewed (6 male, 3 female).
Eight patients gave their signed consent (47%). Three were unable to
give signed consent although we have the anonymised notes of one of
these patients. One patient declined to participate. One patient did not
return consent. We have not received patient contact details of the
remaining four neurological diagnoses included epilepsy, learning
difficulties, myelopathy, axonal neuropathy and migraine.

Conclusions: We found little evidence supporting a hypothesis of a
neurological syndrome as a result of CD (CD and coexistent neurological
dysfunction is only rarely reported in a neurological setting even
compared to other rare conditions). These patients form a heterogeneous

65 "MALIGNANT" VENOUS CONGESTION

K.M. Gormley, M.A. James, D.A. Hilton, N.J. Gutowski. Royal Devon and
Exeter Hospital, Exeter; Peninsula Medical School

A 59 year old man went to his optician asking for new glasses. There
was no significant history. He had papilloedema. On the basis of normal
imaging and a normal cerebrospinal fluid (CSF), except for a raised
pressure of 38 cm of water, benign intracranial hypertension was
diagnosed. Three months later he developed partial seizures with
secondary generalisation. A magnetic resonance venogram (MRV)
showed superior sagittal sinus and right lateral sinus filling defects and
he was warfarinised. By the following month he had developed
extrapyramidal features and cognitive impairment. Further magnetic
resonance imaging (MRI) showed extensive bilateral cerebral white
matter changes, the MRV revealed occluded transverse sinuses and a
discontinuous sagittal sinus. CSF pressure was elevated with a
lymphocytosis. Subsequent extensive investigations were normal. His
condition was steroid-responsive. Off steroids he declined again and a
right frontal brain biopsy including leptomeninges was non-specific. He
continued to have more seizures requiring sedation on intensive care.
Further MRIs showed new areas of non-enhancing focal signal
abnormality in the temporal and cerebellar regions. He continued to
deteriorate and died. Postmortem revealed extensive white matter
degeneration with focal infarction secondary to acute-on-chronic venous
congestion. This is an unusual presentation of "malignant" venous
congestion.