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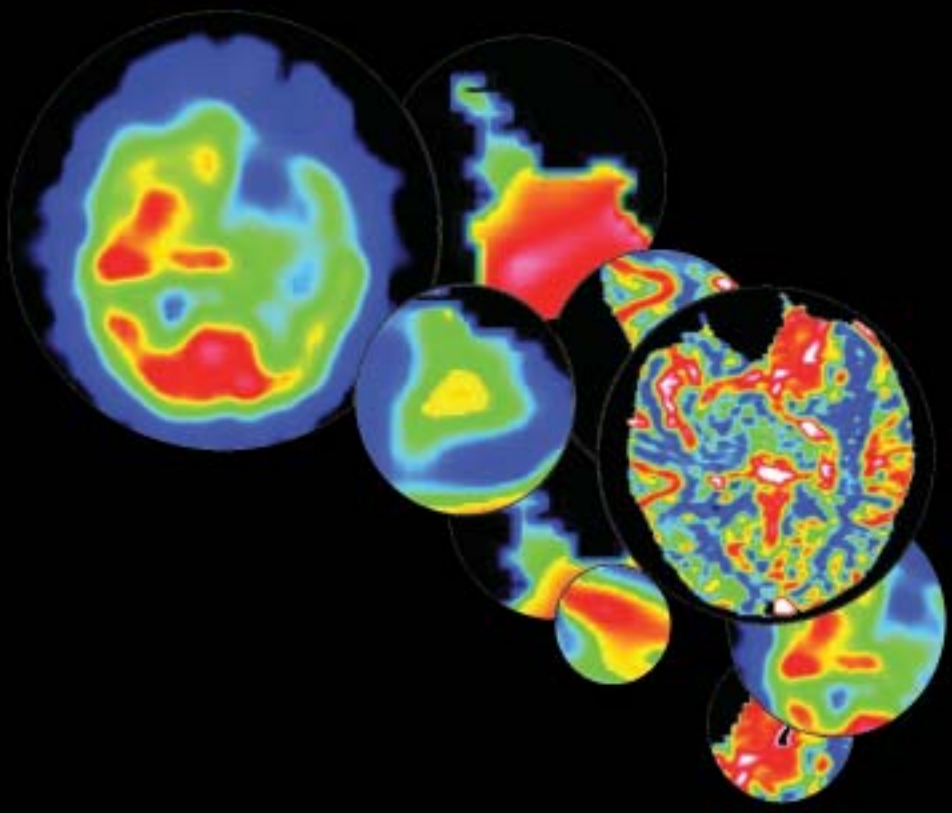

journal reviews • events • management topic • industry news • rehabilitation topic

Review Article:

Neurological associations of coeliac disease

Interview:

Dr Oliver Sacks & Dr Paul Cox - The Parkinsonism dementia complex of Guam and flying foxes

Rehabilitation Article:

Mood and affective problems after traumatic brain injury


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*Crawford P *et al*. Seizure 1999; **8**: 201-217.
LAM/FPA/02/692 - MWL February 2002

contents

july/august 2002

Welcome to another edition of ACNR which we hope continues to combine a range of interesting and readable articles and items.

This issue begins with an excellent topical review on the neurological complications of coeliac disease by Adrian Wills and Pengiran Tengah. This comes at a time when the relevance and extent of gluten enteropathy to a range of neurological conditions, especially cerebellar ataxia is being re-defined, especially by the Sheffield group. Whatever one thinks about the true incidence of these associations, it is important to remember coeliac disease in a range of neurological conditions, although the response to treatment is often disappointing.

Following on from this controversial issue comes another on the cause of the ALS-parkinsonian-dementia complex found in the Guam peninsula. The development of this isolated cluster of neurological disease has generated much interest from epidemiologists and neurologists alike and with it a range of aetiological theories, of which the latest developed by Cox and Sacks has recently been published in Neurology and involves the eating of flying foxes. Huw Morris provides an interesting commentary on this article, in particular to a series of questions and answers that we posed and obtained from the principal authors. Huw spent some time in Guam and is able to rely on his own experiences and local knowledge and contacts to provide the interesting counterpoint that forms his commentary.

We also have a useful update on the surgical treatment of dystonia using stereotactic surgery, an area that is looking exciting and may be of great therapeutic potential, especially given the paucity of effective medical therapies. Obviously proper trials need to be done to verify the approach (such as the randomised study already started by Professor Aziz), to prevent the adoption of a therapeutic strategy based on anecdote. We also have an excellent review from Fergus Gracey on the affective problems of traumatic brain injury, a topic that is often neglected, and an excellent historical account of Phineas Gage by Larner and Leach.

There is our usual collection of anatomy primer, journal reviews, conference and book reviews. Our regular Management feature is unfortunately delayed this issue – as we go to press, Gillian Hall is imminently expecting her second child. However, it will be back in September. Talking of babies, we'd like to congratulate our Rehabilitation Editor, Stephen Kirker, on the birth of baby Tom. Finally, we welcome Patrick Chinnery to the journal review team. So there it is, another action packed issue which you can read at leisure, now that those tense sporting moments which dominated last month have finally passed!

Roger Barker
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Features

Regulars

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Neurological associations of coeliac disease

Authors

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Dr Adrian Wills is a Consultant Neurologist at Queen's Medical Centre, Nottingham, The Derbyshire Royal Infirmary and an Honorary Consultant Neurologist at the National Hospital, Queen Square. He has a particular interest in nerve and muscle disease and the neurological complications of enteric disease.

Introduction

Coeliac disease (CD) has attracted much interest in recent years because of a putative association with neurological disorders. Classically, CD is known to be an inflammatory disease of the small bowel mucosa as a result of sensitivity to gluten, a component of wheat, barley and rye. The treatment consists of a strict gluten-free diet (GFD) which results not only in symptomatic improvement but also restoration of the normal mucosal architecture. However it is increasingly recognised that CD can have atypical presentations. Cooke and Smith[1] first described the neurological associations of CD in 1966. Since then numerous neurological disorders have been described in association with CD predominantly epilepsy, ataxia and neuropathy. The nature and mechanism of these associations remain unclear. This review will attempt to describe some of the more commonly described neurological disorders seen with CD and the basis of an association, if indeed there is one.

Coeliac disease

The concept of incidence and prevalence of CD has changed greatly over the years. What was once thought to be a childhood illness typically presenting with malnutrition and abdominal symptoms is now acknowledged to be a condition of all ages that may also present with atypical and often subtle symptoms. The notion of an 'iceberg' of CD has been used to describe the majority of patients with CD who remain undiagnosed because of asymptomatic, occult or latent disease[2]. Furthermore, population screening studies have revealed that CD is a common condition with a prevalence of at least 1:82 in certain populations[3].

Patients with a genetic susceptibility to gluten may have no intestinal abnormalities on small bowel biopsy. The precise mechanism for the activation of gut inflammation by gluten is not known although it is presumed to be immunological. Immune mechanisms such as the deposition of circulating immune complexes in other organs are also thought to cause the extra-intestinal manifestations of gluten sensitivity. Dermatitis herpetiformis (DH), characterised by IgA deposition in the papillary dermis, is a blistering skin condition (See Figure 1) that exemplifies an extra-intestinal manifestation of gluten sensitivity. There is robust immuno-pathological and genetic data that DH and CD are closely related conditions. Although less than 10% of DH patients have gastrointestinal symptoms, they are all said to have gluten-sensitive enteropathy[4].

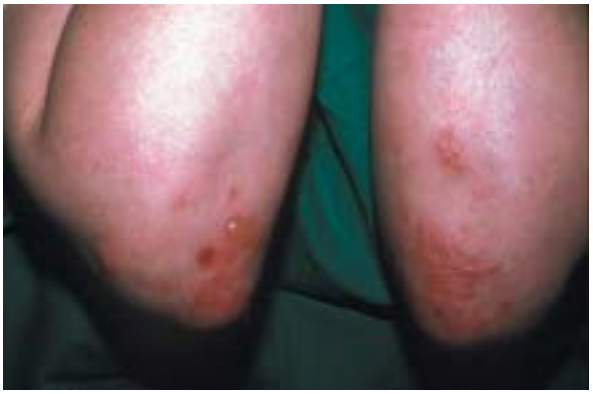

Figure 1 - Blisters on the elbow of a patient with dermatitis herpetiformis.
Reproduced courtesy of Professor Lionel Fry, Imperial College, London.

Serological testing

Serological testing for CD has been greatly refined in recent years. Immunological approaches now available include screening for antireticulin antibodies (ARA), IgA and IgG antigliadin antibodies (AGA), endomysial antibodies (EMA) and tissue transglutaminase antibodies (tTG). EMA has been shown to be better than AGA in terms of both sensitivity and specificity[5,6]. In one study the positive predictive value of EMA was 100% compared to only 28% for IgA AGA[6]. Further studies have shown that IgG AGA is even less reliable than IgA AGA in identifying CD[7,9] with one study showing the positive predictive value of the former to be 0%[10]. The presence of positive coeliac antibodies with normal small bowel architecture remains problematic. Follow-up of patients with normal small bowel architecture and positive coeliac antibodies has shown that positive ARA is a good predictor for later development of the disease when compared to AGA, particularly the IgG subclass[10].

Epilepsy

The association of epilepsy and CD has been demonstrated in a number of studies[11,14]. The nature of this association remains unclear. Interestingly, a number of studies, mainly in Italy, have described a further association between CD, epilepsy and cerebral calcifications[13, 15-17] (See Figure 2). There is no clear explanation for this finding although folic acid deficiency has been proposed[16,15]. Studies in Ireland[11] and Finland[14] have not shown these calcifications suggesting that this may be a geographically or ethnically restricted finding.

Ataxia

The patients originally described by Cooke and Smith[1] in 1966 had a variety of diagnoses. Of the 16 patients described, the majority were found to have a predominantly sensory ataxia although three were also said to have a cerebellar ataxia. Since then there have been varying reports in the literature regarding the association of cerebellar (rather than sensory) ataxia and CD. Vitamin E deficiency and cerebellar ataxia has been described in CD with an improvement following vitamin E therapy[18-20].

Three groups have shown an increased incidence of CD in series of patients with idiopathic cerebellar ataxia[21-23]. Hadjivassiliou *et al* proposed the term 'gluten ataxia' to describe a group of their patients with idiopathic ataxia, positive AGA antibodies and a HLA genotype (DQw2) appropriate for coeliac disease[21]. They further proposed a mechanism of immune-mediated neuronal damage triggered by gluten. In the light of their reliance on IgG AGA as a screening tool these concepts need to be interpreted with caution. The common HLA haplotype (also seen by Burk and co-workers[23]) is a noteworthy finding that merits further attention. Interestingly a recent study by Bushara and co-workers showed raised AGA in patients with both hereditary ataxia (9 of 24) and sporadic ataxia (7 of 26). A study by Combarros *et al* of 32 patients with idiopathic cerebellar ataxia showed no coeliac antibody positivity[24].

Myoclonic ataxia (Ramsay-Hunt Syndrome) has also been described in association with coeliac disease[25-28]. Tijssen and co-workers[29] described in detail 3 patients with cortical myoclonus. Two of these had myoclonic ataxic syndrome associated with proven coeliac disease whilst the third may have had coeliac disease on the basis of a reduced vitamin B12 antemortem. They speculated Purkinje cell damage through toxins or autoantibodies in the CSF. CSF AGA was measured in 1 patient and this was negative.

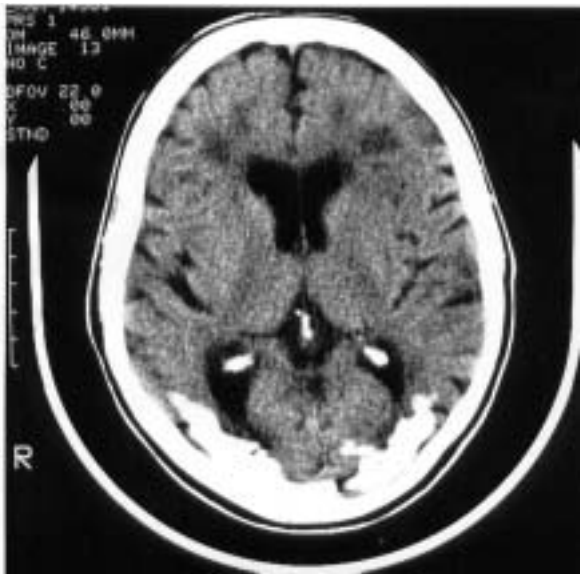

Figure 2 - CT scan of the brain showing bilateral occipital calcifications in a patient with epilepsy and coeliac disease.

Reproduced courtesy of Dr. Gordon Plant, The National Hospital for Neurology and Neurosurgery, Queen Square, London

Other neurological associations

There have been a few descriptions of patients with CD and peripheral neuropathy, both axonal and demyelinating, but no clear effect of gluten on the neuropathy has been established[30-32]. Other case reports in the medical literature have included such diverse conditions as CNS vasculitis[33], brainstem encephalitis[34], dementia[35] and chronic progressive leukoencephalopathy[36]. Some studies have suggested an association with migraine[37] whereas others have not[38].

Conclusions

There appears to be some evidence of an association between CD and certain forms of epilepsy but the basis of association with other neurological syndromes is less certain. At present, the scanty available data on neurological associations of CD is extremely heterogeneous with no universally acceptable scientific explanation for a causative effect. Given that CD is common, one possibility is that certain neurological "associations" are purely coincidental. Alternatively, similar HLA haplotypes may confer an increased likelihood of autoimmune disease as exemplified by the increased incidence of hypothyroidism[39] and Type 1 diabetes mellitus[40] in CD.

Another possible explanation is malabsorption causing vitamin and trace element deficiency as there are descriptions of patients whose neurological illnesses have improved with treatment of their CD. Besides vitamin E and folic acid deficiency as mentioned previously, tetany[41] and myopathy[42] caused by calcium deficiency have also been described. Although this does not satisfactorily explain patients in whom no vitamin deficiency is found[25, 31, 43] or in whom vitamin replacement has no effect[26,30], this possibility should still be carefully considered in CD patients who develop neurological illness. As yet, no studies have effectively addressed the role of trace vitamin deficiency (e.g. niacin, riboflavin and thiamine) in the development of neurological complications.

Gluten neurotoxicity, as suggested by Hadjivassiliou and co-workers[21], has been postulated as a mechanism to explain the apparent association of gluten sensitivity with various neurological disorders. In DH, gluten exposure is potentially greater than in CD as patients whose dermatological symptoms are controlled on dapsone may continue to consume gluten. Recent work by Wills *et al*[44] failed to demonstrate an increased prevalence of neurological complications of DH.

Clearly, further more detailed investigation is required into this disease. We propose large studies looking for the prevalence of neurological conditions in CD and DH, and further investigation of the role of auto-immunity, particularly susceptible HLA groups, in neurological diseases seen with CD. However we would recommend more stringent antibody testing in neurological patients given the poor predictive value of some coeliac antibodies particularly IgG AGA.

Acknowledgements

We are grateful to Professor Lionel Fry, Imperial College, London for providing the photograph shown in Figure 1 and Dr. Gordon Plant, The National Hospital for Neurology and Neurosurgery, Queen Square, London for providing the CT brain scan shown in Figure 2.

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Flying bats in Guam - the cause of the complex

In this issue we are pleased to publish an interview with Drs Oliver Sacks and Paul Cox, following their recent research which suggested that eating flying foxes was responsible for an isolated cluster of ALS-parkinsonian-dementia complex found in the Guam peninsula.

As an interesting counterpoint to this article, we are also publishing a commentary by Dr Huw Morris. Dr Morris, who spent some time in Guam, is able to rely on his own experiences and local knowledge and contacts to provide a cautionary note.

1. What are characteristic clinical features of ALS-Parkinson dementia complex?

There can be separate presentations of a motor neurone disorder (with wasting and spasticity, ultimately death from bulbar palsy), parkinsonism (usually with marked rigidity and akinesia, less tremor, than in ordinary PD), and a dementia (often presenting as an amnesic syndrome) – or these can co-exist in a single individual. ALS-like presentations were much commoner in the earlier days, whereas parkinsonism-dementia ones predominate now - **OS**

2. What has happened to the disease since the second world war?

The disease has become much rarer, altered its presentation (as noted above) and its age of onset: back in the early 1950s there were people in their twenties affected, now they are mostly late middle-aged or elderly people. No-one (or very few people) born after 1960 seems to have contracted the disease – though there may be, apparently, an 'incubation period' of decades between the initial 'event' (infectious, toxic, whatever) and the appearance of the complex - **OS**

A flying fox eating the fruits of a cycad in Guam. One of the main food sources of the flying fox are the fruits of the native cycad trees which contain potent neurotoxins, chemicals that can damage nerve cells.

Photo Credit: Dr. Merlin Tuttle, Bat Conservation International

A flying fox is prepared for consumption at a Chamorro feast. The Chamorro, who are the native peoples of the Pacific island of Guam, boil the animal in coconut milk and consume it in its entirety. Research published in the March issue of Neurology conducted by a National Tropical Botanical Garden investigator suggests a possible link between plant toxins ingested through consumption of flying foxes and a high incidence of central nervous system disease in Guam.

Photo Credit: Dr. Merlin Tuttle, Bat Conservation International

3. How common is the condition in people migrating to and from Guam?

The 100,000-odd Chamorros in California (many of whom left Guam forty years ago) have the same incidence of diseases as those in Guam. The disease is almost or virtually unknown except in the native Chamorro population of Guam (and the native populations of the Kii peninsula and two villages in Irian Jaya, where a similar disease occurs). Migrants to Guam do not, apparently, get affected - **OS**

ALS-PDC is a disease primarily of the Chamorro people, but did not characterise non-Chamorro residents on Guam unless they adopted a traditional Chamorro lifestyle - **PC**

4. What is the evidence for a genetic as opposed to an environmental cause for this condition?

The evidence against a genetic causation is the absence of clear 'Mendelian' patterns of inheritance. The epidemiological evidence (or hint) of environmental determinants comes from the confinement of the disease to Guam (and two other places), and its much higher incidence, in Guam, in certain villages. Again it is known

that cycads are full of neurotoxins – neurocycadism has long been recognised among cattle in Australia who browse on the Macrozamia there – and careful washing etc is required. But there could also have been an infectious cause of lyticobodig (ALS-PD), an inapparent infection (as often happened with those who subsequently developed postencaphalitic parkinsonism and other postencephalitic parkinsonism syndromes - OS

5. Why flying foxes as causative animal?

Because flying foxes native to Guam feed on the native cycads there, and may bioconcentrate some of their (lipophilic) toxins.

Support for an environmental cause is suggested by the coincidence between the decline of lyticobodig after 1960 with the decline in eating of cycad flour (long-noted) and the virtual extinction of the native cycad-eating bat around the same time (which we are now noting) - **OS**

The Chamorro diet and indeed the Chamorro cultural character were uniquely characterised during the twentieth century by mass consumption of flying foxes which led to the extinction of one flying fox species on Guam and the near-extinction of the other species. This in turn led to the importation of other flying fox species from other island nations where cycads do not play a prominent role in the vegetation. As a result of the change in sources of flying foxes, the putative ingestion of biomagnified cycad neurotoxins began to decrease in the 1960s and reached negligible levels in the 1970s when the entire genus Pteropus in Guam teetered on the edge of extirpation. The rise and fall of consumption of Guam flying foxes was shadowed by a rise and fall of the incidence of ALS-PDC in Guam - **PC**

6. Do other communities eat flying foxes and if so do they have a similar condition?

In parts of Polynesia, flying foxes were eaten, but never with the same relish or in their entirety as they are in Guam. And, in those islands of Polynesia where they are eaten, cycads do not play an important role in the vegetation. These islanders do not show higher levels of ALS-PDC - **PC**

7. Is there evidence for a similar aetiology in the recently described PD-like illness endemic in Guadaloupe?

At present different phytotoxins are under suspicion in Guadaloupe, namely those present in soursops and other Annoneaceae – very potent infusions of these are widely used in folk medicine there. There has been no suggestion of an animal vector - **OS**

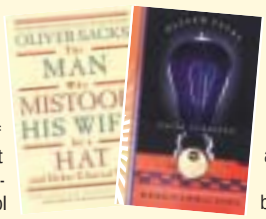
8. How can the theory be proven?

- By chemical analysis of carcasses of (preserved) Guamanian bats.
- By seeing if they have any neurological lesions similar to those of ALS-PD.
- By feeding other bats on cycads and seeing if they in fact accumulate and concentrate on the toxins - **OS**

Authors

Dr. Oliver Sacks is concerned with the link between body and mind, and the ways the whole person adapts to different neurological conditions.

He was born in London and obtained his medical degree at Oxford. In the early 1960s he moved to the United States, where he completed an internship at UCSF and a residency in neurology at UCLA. Since 1965 he has lived in New York, where he is clinical professor of neurology at the Albert Einstein College of Medicine, adjunct professor of neurology at the NYU School of Medicine and consultant neurologist to the Little Sisters of the Poor and at Beth Abraham Hospital.



In 1966 Dr Sacks was a consulting neurologist for Beth Abraham, where he encountered an extraordinary group of patients, many of whom had spent decades in strange, frozen states, like human statues, unable to initiate movement. These patients were survivors of the great epidemic of sleepy sickness that had swept the world from 1916 – 1927. They became the subjects of his book, Awakenings (1973), which later inspired a play by Harold Pinter, "A Kind of Alaska" and the Oscar-nominated Hollywood movie, "Awakenings," starring Robert De Niro and Robin Williams. Dr. Sacks is perhaps best known for his best-selling 1985 collection of case histories from the far borderlands of neurological experience, The Man Who Mistook His Wife for a Hat. In 1989, he received a Guggenheim Fellowship for his work on what he calls the "neuroanthropology" of Tourette's syndrome, a condition marked by involuntary tics and utterances. His seven books have received numerous awards and been translated into 22 languages.

Dr. Paul Alan Cox is Director of the Congressionally chartered National Tropical Botanical Garden in Hawaii and Florida. He also serves as the King Carl XVI Gustaf Professor of Environmental Science at the Swedish Biodiversity Center.

TIME magazine in 1997 honoured him as one of 11 "Heroes of Medicine" for his ongoing search for new medicines from plants. For his efforts in saving tropical rainforests, in 1997 he shared the $75,000 Goldman Prize, known as the "Nobel Prize" of the environment. A former Brigham Young University Dean, Cox was named in 1998 by CHOICE magazine as one of the top university leaders in America.

Cox received his Ph.D. in Biology from Harvard University, his master's degree in ecology from the University of Wales, and his bachelor's degree in botany and philosophy from Brigham Young University. He has authored three books and over 120 scientific papers. Married to the former Barbara Wilson, he lives with his family on the island of Kauai.

The parkinsonism dementia complex of Guam and flying foxes

Author

Dr Huw Morris is a Specialist Registrar in Neurology at the National Hospital for Neurology and Neurosurgery, London. His research interest focuses on tau related neurodegeneration including progressive supranuclear palsy, fronto-temporal dementia and the parkinsonism dementia complex of Guam.

The identification of the high prevalence of parkinsonism dementia complex (PDC) and amyotrophic lateral sclerosis (ALS) on the Western Pacific island of Guam in the 1950s and 1960s raised hopes that the cause of these diseases could be identified on these island(s), and that this discovery would help to explain neurodegenerative diseases such as Parkinson's disease (PD), Alzheimer's disease (AD) and ALS in other parts of the world.[1] While the cause of ALS and PDC on Guam remains elusive, genes responsible for autosomal dominant forms of PD, ALS and AD have been discovered. Contrary to widespread neurological belief, PDC and ALS on Guam are unlikely to be due to cycad ingestion in tortilla flour. The excitatory amino acid beta-methylamino L-alanine (BMAA) is present in cycads, and experimentally does lead to an acute neurological syndrome in exposed animals.[2] Similarly, the motor neuron disease lathyrism relates to beta-N-oxalylamino-L-alanine (BOAA) exposure in humans following ingestion of chickling peas. Unlike lathyrism, PDC does not have a clear temporal relationship to cycad ingestion and it has been estimated that one would have to eat several kg of cycad every day to lead to a comparable exposure to that used in the animal models.[3]

> "Exotic geographical locations require exotic medical hypotheses, and Cox and Sacks propose..... that ingestion of a type of Guamanian bat known as flying foxes leads to ALS and PDC by the process of 'biomagnification'"

Exotic geographical locations require exotic medical hypotheses, and Cox and Sacks propose, in the March 26 issue of Neurology and in this issue of Advances in Clinical Neuroscience and Rehabilitation, that ingestion of a type of Guamanian bat known as flying foxes leads to ALS and PDC by the process of "biomagnification".[4] These bats were apparently frequently eaten on Guam at social and ceremonial gatherings and some species were hunted to extinction by the mid 1970s. The decline of flying foxes in Guam closely parallels the decline in the incidence of ALS, and the villages that had the highest incidence of PDC and ALS, Umatac and Inarajan, are reported to have had the highest consumption of bat meat. This theory invokes substantial BMAA accumulation in bat tissue, which would result in a sufficient excitatory amino acid load to cause chronic neurotoxicity in humans. It is interesting to speculate how another mammalian species could be resistant to a toxin that is lethal in humans. This could relate to the relative lifespans of bats and humans, and cumulative toxicity in human consumers of bat meat. Alternatively, there are known to be species differences in the propensity to develop tau containing neurofibrillary tangles – humans and ungulates such as sheep develop neurofibrillary tangles whereas monkeys do not, and this may relate to species differences in alternative splicing of the tau gene.[5] A neuropathological examination of wild pigs on Guam, which avidly eat cycads in the wild, has not revealed neurofibrillary tangle formation (Dr. J. Steele, personal communication).

Some type of traditional Chamorro custom may account for PDC and ALS and explain the declining prevalence of these diseases, and the intriguing hypothesis put forward by Cox and Sacks adds to a number of proposed explanations. However, up to this point detailed anthropological enquiry in areas of Guam affected by these diseases has not identified any differences in lifestyle between areas of high and low prevalence (Dr. V. Keck and Dr. J. Steele, personal communication).[6] The decline in the prevalence of these diseases could also be interpreted in genetic terms with increased social mobility and out breeding leading to a decline in recessive or co-dependant genetic factors. The clustering of these diseases in some families in Southern Guam has been confirmed in a recent long term follow up case control study confirming the excess of cases in first degree relatives of affected individuals as compared with spouses and Chamorro controls.[7] In the meantime, an analysis of excitatory amino acids in bat meat on Guam will be shortly underway. Whether an environmental cause, genetic factor or combination of these was primarily responsible for these mysterious diseases, it seems likely that the further away the epidemic becomes, the harder it will be to come to any firm conclusions.

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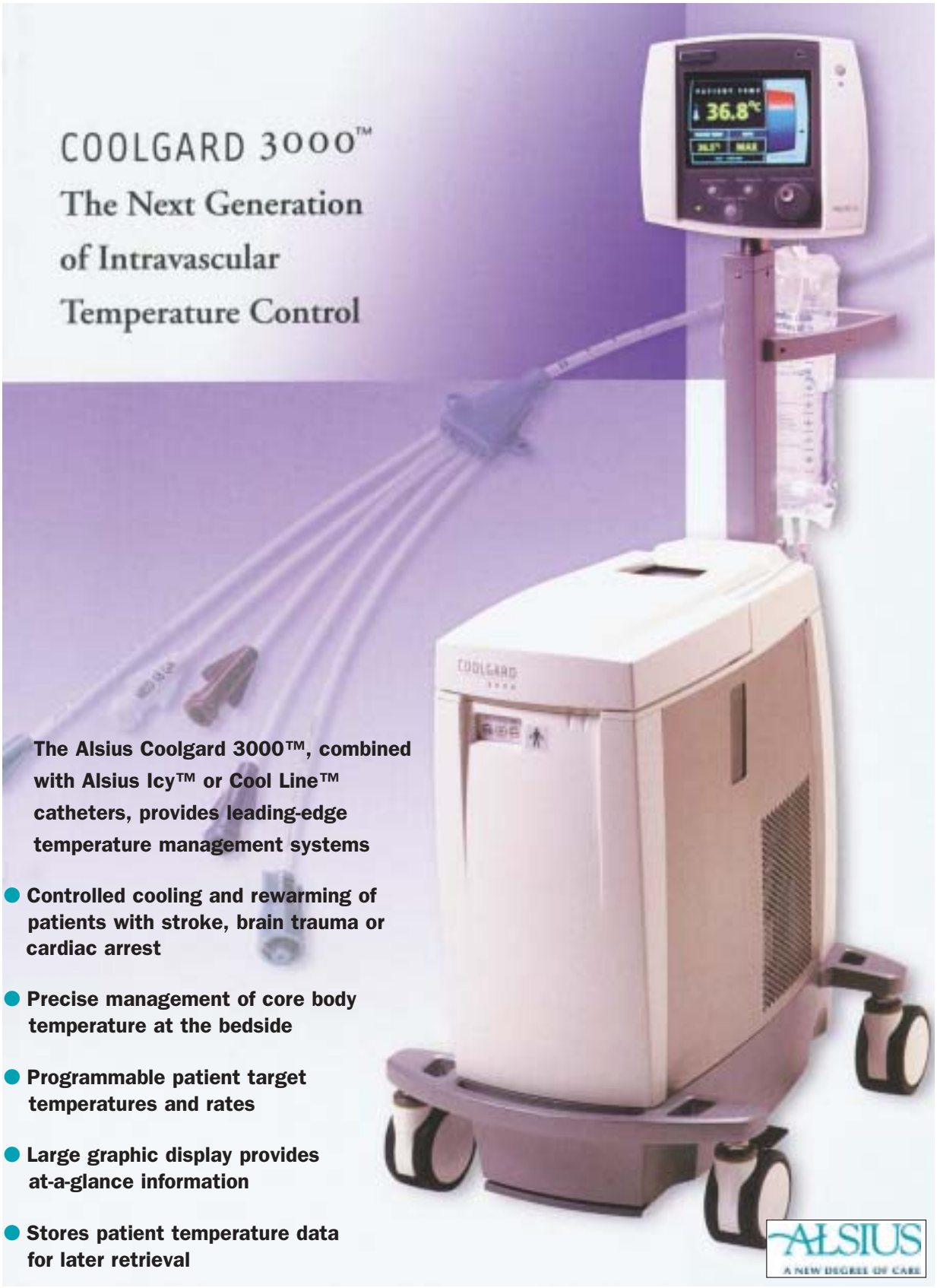

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Recent advances in the surgical treatment of dystonia

Dystonia is an interesting neurological disorder that continues to cause the clinician difficulties in formulating appropriate management strategies. Therapy is linked closely to the classification of dystonia and so the characterisation into aetiological sub-type and distribution of the condition should be established prior to devising any treatment plan. In a small minority of patients (eg. Wilson's disease, dopa-responsive dystonia (DRD)), specific treatment can be instituted but in the majority of cases therapy is symptomatic, directed at decreasing the intensity of the dystonic contractions. However a lack of knowledge relating to the underlying pathophysiology has hindered the discovery of effective pharmacological treatments for most forms of dystonia. Nevertheless because of the reversibility and responsiveness of DRD to L-dopa therapy, all patients with childhood onset dystonia should therefore be given an adequate trial of this drug. Unfortunately, treatment of dystonia with oral agents is otherwise generally unsatisfactory. For those with symptoms and signs unresponsive to levodopa, other oral medications, including anticholinergics, tetrabenazine, baclofen and benzodiazepines, may provide mild to moderate relief. More effective treatment exists for the focal dystonia in particular the use of botulinum toxin, although injections of toxin into the affected muscle groups tends only to produce transient relief and generally need to be repeated every 3-6 months. For patients with more widespread dystonia, or those with disease refractory to medical therapy or botulinum toxin injection, there appears now an increasing role for functional neurosurgical intervention.

Case Report: Idiopathic Torsion Dystonia

This 7 year old girl first began to exhibit features of dystonia at the age of 3 years. Her condition was progressive in nature to the point where at presentation, she was anarthric, fully dependent on her parents for care and in constant pain due to generalised dystonic spasms. Genetic analyses revealed that she was negative for the DYT1 gene. Medical therapy including L-dopa, benzhexol, clonazepam and botulinum toxin had not provided any long-lasting benefit. Her Fahn and Marsden dystonia rating scale scores were 109/120 for movement and 29/30 for disability. No changes were observed until stimulation was initiated one month after implantation of bilateral electrodes into the posteroventral internal globus pallidus (GPi). She subsequently experienced gradual improvement in most aspects of dystonia. At 3 months her Fahn and Marsden rating scores had improved to 47/120 for movement and 14/29 for disability. She continued to improve and was able to communicate, attend school, walk unaided and remain continent.

The first recorded case of surgery for dystonia dates back to 1641 when the German physician Minnius treated torticollis by sectioning the sternocleidomastoid muscle. The Russian surgeon Buyalsky (1850) appears to have performed the first spinal accessory nerve section for spasmodic torticollis followed by Morgan in 1867 and Collier in 1890. Spinal cord root section to treat spasmodic torticollis, involving unilateral section of the first three anterior cervical roots, was first proposed over a century ago by Keen (1891). This procedure of cervical rhizotomy was refined over the years by surgeons including Dandy in 1928 who combined intradural section of the cervical sensory and motor roots with accessory nerve section. By 1979 variations of this procedure were still considered the operation of choice for cervical dystonia refractory to medical therapy. However, long-term follow up has disputed the effectiveness of these techniques. The issue of long term efficacy, together with the high incidence of denervation related complications, has now led to the virtual abandonment of these procedures. Extensive muscle resections, microvascular decompression of the accessory nerve, peripheral facial neurectomy and cervical cord stimulation are further examples of procedures that have been used to treat dystonia but that have also fallen out of favour. Apart from intrathecal baclofen infusions, practically all the surgical methods for treating generalised dystonia, preceding the stereotactic era, have either been ineffective or of poor comparable benefit. This has consequently given rise to the replacement of these operations by functional stereotactic procedures for patients with dystonia.

The introduction of stereotactic surgery allowed Bertrand (1978) to combine thalamotomy and peripheral denervation with improved outcomes. Further development of stereotactic techniques coupled with satisfactory results encouraged its use by functional neurosurgeons who have attempted to treat dystonia by lesioning a variety of different deep brain

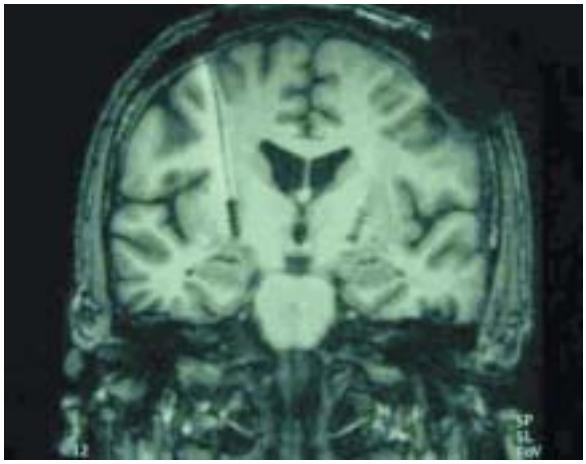
Authors

Professor Aziz studied physiology at University College London graduating in 1978. During this time he developed his keen interest in the role of the basal ganglia in movement disorders. He studied medicine at King's College London (1978-1983) and obtained his surgical fellowship in 1987 following which he has pursued a career in neurosurgery. He is currently a consultant neurosurgeon at the Radcliffe Infirmary, Oxford and Charing Cross Hospital, London. He is an expert in functional neurosurgery and has a special interest in the surgical treatment of movement disorders including dystonia.

Mr. John Yianni trained at University College London, qualifying in 1996. He completed his basic surgical training in Oxford, obtaining his surgical membership in 1999. Subsequently he joined the Oxford Movement Disorder Group based at The Radcliffe Infirmary Oxford, where he is currently clinical research fellow working towards an MD. His field of interest includes stereotactic functional neurosurgery for movement disorders, in particular dystonia.

Pre-op: Severe generalised dystonia with bulbar features. At the time of surgery she was bed-bound, doubly incontinent, anarthric and dysphagic.

Post-op: Some dystonic posturing of left foot and right hand remains. Speech improving and swallow normal. Mobilising independently and attending school.



Post-operative MRI of a patient following implantation of bilateral DBS electrodes.

structures including the internal capsule, cerebral peduncles, dentate nucleus, various basal ganglia and thalamic targets. As in other hyperkinesias, medial pallidotomy was the first stereotactic operation to be performed, initially for spasmodic torticollis in 1953 by Riechert followed by its use for generalised dystonia in 1957 by Cooper. Unfortunately in comparison with thalamic surgery only a few small series of pallidotomy for dystonia were published at that time. Hence by the 1960's, thalamotomy was emerging as the stereotactic procedure of choice. In 1976 Cooper published the results of thalamotomies that he had performed on over two hundred patients, reporting good or moderate improvement in 70% of his patients series. There was also some evidence that lesioning this target benefited patients with secondary dystonia, hemidystonia and tardive dystonia. However, in contrast to pallidotomy, the high incidence of postoperative dysarthria and dysphagia usually prevented surgeons from performing simultaneous bilateral thalamic surgery. Also, compared to Cooper's original series, subsequent studies from other centres have produced more variable and generally less impressive results. Consequently the ideal subcortical target for lesional surgery has remained the subject of much discussion although more recent evidence favours the medial pallidum.

The success of Deep Brain Stimulation (DBS), within the last few years, as treatment for a number of different movement disorders could soon see it as the first-line treatment for dystonia refractory to medical intervention. It has the advantages over lesional surgery of being reversible, adaptable and avoids concern about the effects of lesioning the developing brain in the case of children. DBS also allows bilateral surgery to be undertaken because of the reduced level of morbidity involved. As dystonic posturing may be very severe, DBS is usually performed under general anaesthesia for dystonia, unlike functional surgery for tremulous disorders, which usually occurs with the patient fully awake.

A new method for successfully treating spasmodic torticollis by implantation of stimulators into the thalamus was described by Mundinger in 1977. Since then, it has been demonstrated that targeting thalamic nuclei can produce favourable results in a number of different forms of dystonia. For example, Vercueil (2001) employed this technique in twelve patients with generalised dystonia resulting in a satisfactory outcome in five of the patients.

Because of the success of thalamotomy and neurophysiological evidence implicating the thalamus in the pathogenesis of dystonia, the pallidum was not initially the favoured target for DBS. There are only a few reports of the effects of pallidal stimulation in dystonia and these are mainly case reports or small case series. Although to date there do not appear to be any formal comparative studies of thalamic versus pallidal stimulation, there are several instances where patients with stimulators in both deep brain structures appear to have benefited more from pallidal rather than thalamic stimulation.

Present evidence favours the view that GPi is superior to thalamic stimulation for primary and secondary dystonia and it would appear that DBS is one of the most effective means of alleviating dystonia. Generalised dystonia, particularly in those patients who are positive for the DYT1 gene, is the best indication followed by spasmodic torticollis, where respectively mean 70% and 40% improvements have been reported. Post-traumatic dystonias with visible brain lesions on imaging do not appear to respond well to DBS. Furthermore, it is also important to note that a feature of these dystonic conditions is that the response is gradual, manifesting as a progressive improvement in the condition over months to years. Experience gained from the patients treated by our group suggests that maximal or near maximal improvement occurs at about one year in patients with generalised dystonia. Those with spasmodic torticollis improved at a slower rate, gaining most benefit approximately two years post-surgery. Longer-term follow-up will be needed to confirm that these benefits are maintained and also to help ascertain what the optimal parameter settings are.

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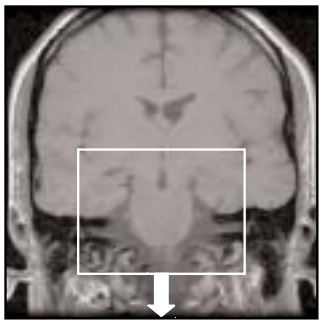
The cerebello-pontine angle

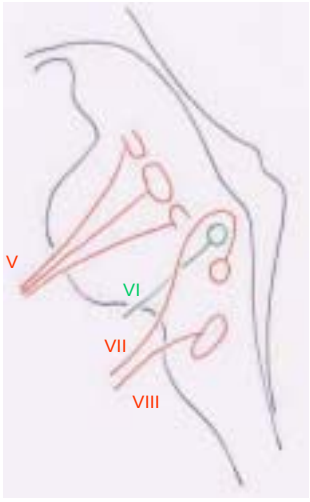
The basics. The cerebello-pontine angle is the space bound by the cerebellum, pons and temporal bone and contains the short intracranial courses of the fifth, seventh and eighth cranial nerves. By far the most common pathology in this area is the acoustic neuroma (or, more correctly, schwannoma) which classically gives rise to sensorineural deafness, ipsilateral facial palsy, ipsilateral cerebellar signs and trigeminal sensory loss.

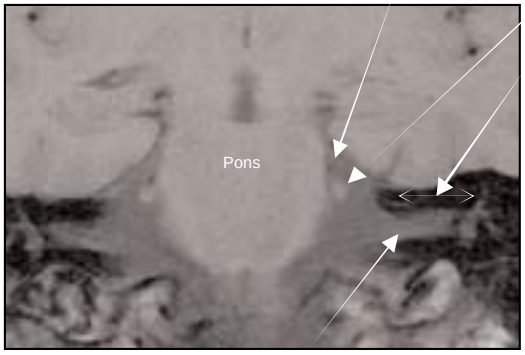


Coronal MRI of the pons

Five nerves enter the internal auditory canal:

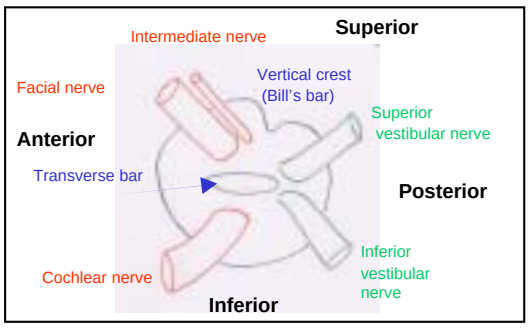
- Facial
- Intermediate (usually enters with the facial nerve, but sometimes travels with the superior vestibular nerve)
- Cochlear
- Superior & inferior vestibular nerves





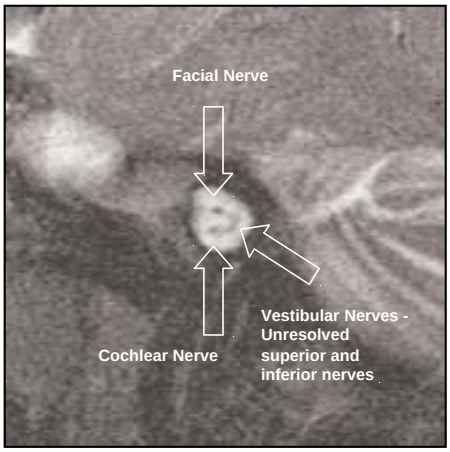
Nerves VII and VIII

This image demonstrates the relationship between the nerves running in the internal auditory canal and the trigeminal nerve.

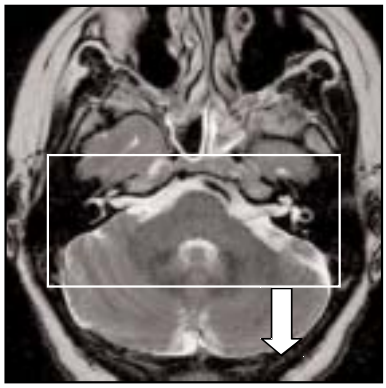


Acoustic neuromas usually (85%) arise from the inferior vestibular nerve, less often (10%) the superior vestibular nerve and never the cochlear nerve. The facial and cochlear nerves are pushed forward by a tumour of the inferior vestibular nerve.

Sagittal MRI of the internal auditory meatus

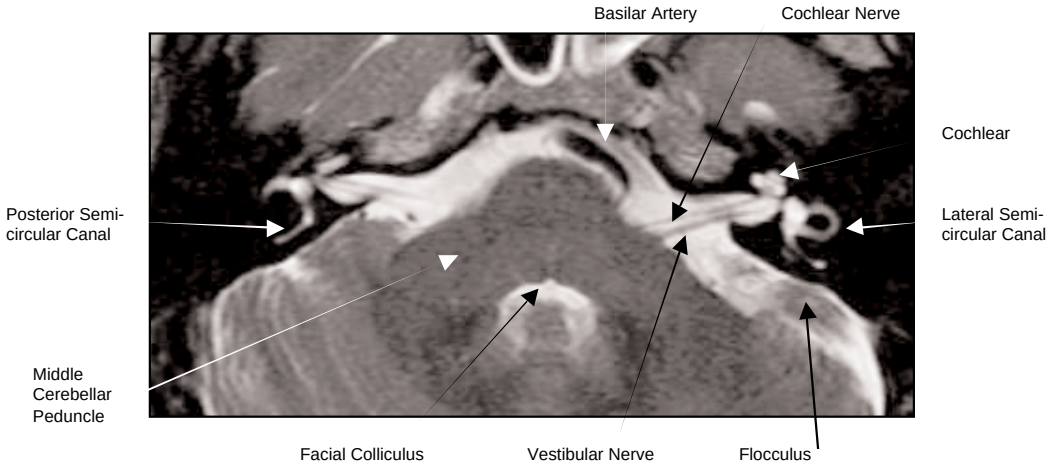


Justin Cross and Alasdair Coles



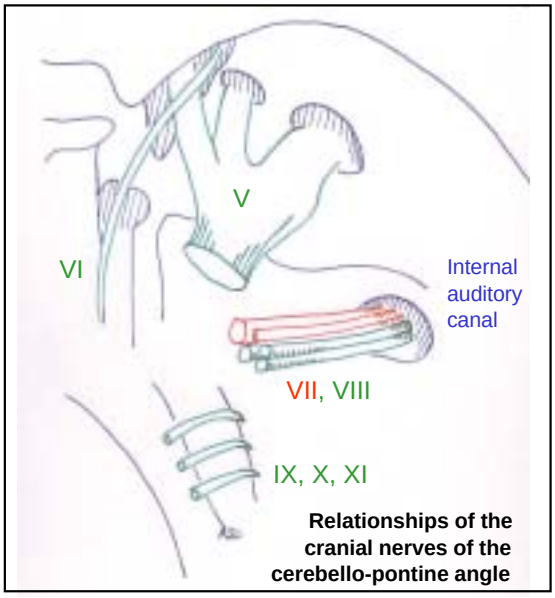
Large cerebello-pontine angle lesions may compress the pons, the ipsilateral cerebellar hemisphere, the trigeminal nerve anteriorly and superiorly, and the IX, X and XI nerves posteriorly. Although the sixth cranial nerve emerges from the anterior pons between the fifth and seventh nerves, it immediately runs upwards into the subarachnoid space around the basilar and so usually avoids compression from cerebello-pontine angle lesions.

Axial section of the pons



Cerebello-pontine angle lesions

- **75% acoustic schwannoma**
- **10% meningioma**
- **5% epidermoid**
- **Rare:**
  - Metastases
  - Paraganglioma (glomus jugulare tumours)
  - Other schwannomas (facial and trigeminal)
  - Vascular lesions



Relationships of the cranial nerves of the cerebello-pontine angle

References

University of California Acoustic Neuroma team
http://itsa.ucsf.edu/~rkj/IndexAN.html
Johns Hopkins Acoustic Neuroma Textbook
http://www.med. jhu.edu/radiosurgery /braintumors /acoustic/textbook/

Mood and affective problems after traumatic brain injury

Author

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Introduction

Survivors of traumatic brain injury (TBI) are vulnerable to a range of psychosocial difficulties. The impact of unrecognised and untreated emotional sequelae of TBI upon psychosocial outcome has been highlighted. Psychosocial problems present the greatest challenge to rehabilitation services[1]. Despite some shifts towards recognition of such problems[2], increased understanding of the emotional and psychosocial aspects of brain injury and the provision of services for treatment is required to meet the high level of unmet need within this client group.

What are the common difficulties?

High rates of psychiatric disorder have been identified amongst survivors of traumatic brain injury using established diagnostic criteria[3,4]. Depression, anxiety disorders (such as Post Traumatic Stress Disorder, Obsessive Compulsive Disorder and Panic Disorder), and irritability or anger problems would appear to be the most common diagnoses, and premorbid psychopathology may predict substance abuse disorders post-trauma. Typically, studies show that about a third of TBI survivors experience emotional problems between 6 months and a year post injury[5,6], others place levels even higher[7]. The presence of emotional or behavioural problems post injury which impact on the individual's family have been reported at 84% [8]. Clinically significant levels of hopelessness (35%) suicidal ideation (23%), and suicide attempts (18%) post-injury have been identified[9].

Approximately 50-80% of TBI survivors admitted to hospital following closed head injury report symptoms of post concussive syndrome (PCS)[10]. PCS symptoms include headache, fatigue, sensory sensitivity (to noise or light), memory and attentional problems, low mood, anxiety and irritability. Whilst symptoms generally improve within 3-6 months, for about 15% of survivors such symptoms may persist beyond three years[11].

Disorders of motivation are another commonly occurring neurobehavioural consequence, characertised by apathy, indifference or lack of concern, and lowered initiation, verbal output and libido[12].

Identification of disorders

Clarity of diagnosis and aetiology may be compromised by complexity of the problem[13], the limitations of measures which may reflect a different set of aetiological assumptions to those used within a purely psychiatric setting[14], and the use of terminology for experienced and expressed emotional states which poorly represents the subjective experiences of clients[15].

Neurologically based apathy has been shown to share negative, but not somatic or affective, symptom features of depression[12]. The affective and cognitive symptoms of post concussive syndrome, depression, anxiety, irritability[6], and post traumatic stress disorder[16] share features, but may have differing aetiology. Symptoms consistent with dysexecutive syndrome such as perseveration, impulsivity, and irritability can be mistaken for behavioural indicators of OCD, although affective and cognitive indicators (in terms of beliefs about obsessive-compulsive thoughts and behaviours) differ.

How can mood and affective problems be understood?

Biopsychosocial frameworks

Frameworks for considering sources of emotional sequelae[14] and for identifying areas for assessment and intervention in neuropsychological rehabilitation[17,18] have been proposed. These 'biopsychosocial'[19] models argue for parallel consideration and application of a range of factors and models.

Gainotti[14] proposed three categories of factors in considering emotional consequences of brain injury: neurological, psychological, and psychosocial.

Neurological factors

Neurological factors are fundamental to the experience and processing of emotions. Fronto-temporal-limbic circuitry appears to be particularly implicated in a range of emotional disturbances. Ventro-medial frontal areas are thought to play an important role in motivation and anticipation[20]. Right hemisphere and subcortical lesions have been associated with disorders of motivation[21]. Impairments of emotion recognition create difficulties responding appropriately in interpersonal situations. Sensory changes such as intolerance of light or noise, in addition to the secondary psychological impact of other physical and cognitive impairments are also relevant. Distinctions between neurological impairment of self-awareness, and psychological denial of disability have been made[22].

Psychological factors

Gainotti draws on psychodynamic theories of denial in issues of emotional adjustment following brain injury. Other papers have highlighted the important roles of pre and post-morbid coping style[21,23], personality[13], client's own causal explanations for their difficulties[24], and pre-injury psychopathology as factors influencing emotional outcome.

Work focusing on the TBI survivor's adjustment to their injury in terms of their subjective experience of themselves[2,7,25] has demonstrated how survivors may experience distressing threats to their sense of identity. These are summarised below.

repeated failure and associated frustration
others not believing reports of cognitive difficulties
loss of memories
comparison of self pre and post injury
loss of identity through labelling and fear of stigma
discrepant information from medical services (i.e. being told that there's nothing wrong, or being given a very poor prognosis)
discrepancy between being 'normal' (but not receiving services) and being diagnosed (but being labelled or stigmatised by society)

Table 1: subjective complaints of survivors of TBI.

The important aspect of the individual's readiness or motivation to change socially problematic behaviour[26], and the application of behavioural models focusing on environmental contingencies influencing behaviour have been discussed[26,27].

Psychosocial Factors

Gainotti recognises the twofold impact of the consequences of the brain injury upon both the individual's system of social activities and relationships, and upon others within their social system. Reduction in size of social system, nature of relationships (e.g. changes in intimacy and sexual relationships), changes in roles, and increased financial burden are highlighted as imposing a significant burden on both the individual and their family. Gainotti notes that family members cope with the physical consequences better than the emotional or behavioural difficulties. Caregivers do not shift towards more adaptive, problem-focused styles of coping over time post injury, and use of an emotion focused (rather than

Locus of damage, system damaged	Cognitive impairment	Environmental Trigger	Hypothesised subjective experience or thoughts	Behavioural expression of emotion	Outcome
Fronto-temporo-limbic circuitry	Problems with emotional and behavioural control	Relatively minor interpersonal stressor	Having a 'short fuse', 'exploding' "I can't bear this"	Verbal aggression	Guilt, sadness. Anger at self: "why am I like this?"
Diffuse axonal damage	Slowed speed of processing	Conversation with group of friends in the pub	Frustration, feeling left out, feeling inferior "I'm useless now - no-one wants to know me"	Social withdrawal	Friends stop contact - Increased depression and further social withdrawal "what's the point in carrying on"
Frontal damage	Memory problems secondary to attentional impairment, and impulsivity	Leaving the house to attend rehabilitation	Doubt and anxiety "I've forgotten something" "If I forget it the others will think I'm stupid"	Checking and re-checking before leaving	Late arriving for rehabilitation, anxious, ashamed, withdraws socially
None identified	Sensitivity to noise or light	Noisy and bright work environment	'overload', irritation, distractability, distress	Irritability or verbal aggression to others present, poor productivity	Loss of job - anger at others "they don't understand my problems" further withdrawal and depression

Table 2: Hypothetical scenarios demonstrating links between neurological, cognitive, environmental, behavioural and interpersonal factors.

problem focused) style of coping is related to degree of caregiver emotional distress[28].

Environment

Features of the environment also influence the expression or maintenance of affective problems through the interaction of demands, vulnerabilities, and reinforcement. In this sense the literature presents mood and affective problems not only within a biopsychosocial framework, but also in terms of a stress-vulnerability model. Table 2 above demonstrates some hypothetical affective scenarios, based on a selection of potential factors within a cognitive-behavioural framework.

How should mood and affective problems be approached?

Gainotti refers to Prigatano's arguments for the principles of holistic rehabilitation, targeting affective problems, self-awareness and acceptance, and return to a productive lifestyle through integrated group based rehabilitation. However, such services are not widely available, so what can be done within existing services?

The framework for cognitive rehabilitation proposed by Wilson[18] highlights the need for integrating a range of models. The starting point for this framework is the individual and their family. Given the interdependence and overlap between vulnerability factors, treatment of mood and affective problems should not be viewed as separate from other rehabilitative efforts. The utility of an intervention is not necessarily dependent on the causal factor so much as the nature of the problem being faced by the individual. For example, if an individual is frustrated by their failure to arrive at appointments on time due to a memory impairment, then this 'mood issue' can be treated through compensatory memory strategies. Nevertheless, appropriate prescription of medication for disorders with a significant treatable neurological component should of course be considered.

Focusing specifically on the treatment of mood and affective problems, cognitive-behavioural therapy (CBT)[29] is being increasingly applied. Recent articles describe some of the alterations to traditional cognitive therapy techniques when working with those who have cognitive impairments[6,24,30]. Adaptation of CBT can be considered on the basis of increased understanding of relationships between cognition and emotion [31,32,33,34]. Approaches which target adjustment[36] or development of new beliefs and assumptions, rather than changing pathologically 'irrational' beliefs[35], could also be of benefit.

Some of the core aspects of CBT (see Table 3) offer great potential for addressing cognitive impairments within therapy. Findings from case studies describing the treatment of irritability[6] and PTSD[24], are promising, although important caveats for certain techniques have been identified. For example, 'perseveration of emotional response' during exposure work (an evidence based CBT intervention for PTSD) has been noted as a consequence of emotional activation in the context of executive functioning problems[37].

Core feature of CBT	Area of cognitive impairment or difficulty which may be compensated for
collaboration	Confidence, acceptance, stigma
emphasis on monitoring problems and successes	Awareness, confidence, improved encoding and specificity of autobiographical recall
emphasis on 'stop, think, reflect' approaches and development of 'internal dialogue'	Awareness, impulsivity
provision of written information to client and family (as appropriate)	Memory, understanding
use of practical tasks as points of learning (behavioural experiments)	Abstract thinking, comprehension, new learning
use of audiotapes of sessions or techniques for the client to refer to between sessions	Memory
ongoing summarising by the therapist	Memory, attention
the development of a visual conceptualisation or formulation with the client	Attention, abstract thinking, comprehension
development of an independent problem solving approach to everyday difficulties as experienced by the client	Executive impairments of problem solving

Table 3: Features of CBT in relation to areas of difficulty post brain injury.

Conclusion

The importance of careful psychological and neuropsychiatric assessment for identifying causal, contributory, or maintaining factors of affective problems following TBI has been highlighted. The need to consider the subjective understanding and experience of the TBI survivor and their family or caregiver has also been emphasised. Increasingly, the need for a biopsychosocial approach to understanding the consequences of brain injury, and in particular emotional consequences, is being highlighted. The amelioration of mood and affective problems may require reference to a broad range of models. These should consider physical and cognitive impairments, functional difficulties, and social and cultural factors. Sharing of the clinical conceptualisation, in an appropriate form, with the client and their family is advised to maximise collaboration and engagement. Functional rehabilitative efforts are likely to have a positive impact on emotional well being through improved quality of life. Modified cognitive behavioural therapy may provide both a system and a set of interventions that are particularly appropriate for mood and affective problems.

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2002

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E. abn@abnoffice.demon.co.uk

EPTA Summer Scientific Meeting
6 July, 2002; Liverpool, UK
E. nigel.hudson@phnt.swest.nhs.uk

10th International Congress of Neuromuscular Diseases
7-12 July, 2002; Vancouver, Canada
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E. Congress@venuewest.com

7th European Congress of Neuropathology
14-17 July, 2002; Helsinki, Finland
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6th Conference on Parkinson's Disease & Parkinsonism
17 July, 2002; London, UK
Medical Education Partnership, Tel. 020 7072 4191, Fax. 020 7072 4392,
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8th International Conference on Alzheimer's Disease and Related Disorders
20-25 July, 2002; Stockholm, Sweden
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International Symposium on Neurobiology and Neuroendocrinology of Aging
21-26 July, 2002; Bregenz, Austria
Dr Bartke, Tel. 618 453 1512, Fax. 618 453 1517, E. abartke@siumed.edu

Bridging Basic & Clinical Epileptology
21 July - 4 August, 2002; San Servolo, Italy
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August

Recent Advances in Neurotraumatology (ICRAN)
1-4 August, 2002; Bali, Indonesia
Dr Beny A Wirjomartani, Fax. 62 222 035 836/62 222 041 694,
E. ns-mspu@indo.net.id or lcran2002@yahoo.com

Neuropathic Pain Satellite Symposium
14 August, 2002; Tijuana, Mexico
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29th Scandinavian Congress of Rheumatology
15-18 August, 202; Tromso, Norway
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Clinical Information Systems & Electronic Records
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WFNRS Symposium Neuroradiologicum XVII
18-24 August, 2002; Paris, France
Tel. 0033 3 83851456,
Fax. 0033 3 838 51391

Multiple Sclerosis: Genetics, Pathogenesis & Therapy
18-22 August, 2002; Copenhagen, Denmark
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Cognitive Behavioural Therapy & Neuropsychological Rehabilitation
22 August, 2002; Ely, UK
Alison Gamble, Tel. 01353 652173,
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11th European Congress of Clinical Neurophysiology-ECCN
24-28 August, 2002; Barcelona, Spain
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34th International Danube Symposium
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Healthcare for Older People
31 August-13 September, 2002; Edinburgh, UK
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September

Better Care for Children & Adults with Epilepsy - A Consensus Conference
4-5 September, 2002; Edinburgh, Scotland
Margaret Farquhar, Tel. 0131 247 3636, Fax. 0131 220 4393, E. m.farquhar@rcpe.ac.uk

5th Congress of the European Association for Neuro-Oncology
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5th International Congress International Society for Neuroimmunomodulation
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Effectiveness of Rehabilitation for Cognitive Deficits
17-19 September, 2002; Cardiff, UK
Tel. Kath Giblin, 029 2087 5356,
Fax. 029 2087 4858

British Sleep Society Annual Scientific Meeting
18-20 September, 2002; Cambridge, UK
E. bssoffice@huntingdon52.freeserve.co.uk

SMART Introductory & Assessors Course
18-20 September, 2002, London, UK
Conference administrator, Royal Hospital for Neurodisability, Tel. 020 8780 4500 ext 5236, E. conferences@rhn.org.uk

Neurobiological Background to Rehabilitation
19-21 September, Goteborg, Sweden
Tel. +46 31 81 82 20, Fax. +46 31 81 82 25, E. rehab2002@gbg.congrex.se

Nordic Movement Disorder Symposium
20-21 September, 2002; Oslo, Norway
Tel. 47 22 561 930, Fax. 47 22 560 541,
E. congrex@congrex.no

9th International Child Neurology Congress & 7th Asian and Oceanian Congress of Child Neurology
20-25 September; Beijing, China
Fax. 0086 10 66176450,
E. icnc@public3.bta.net.cn

30th Annual Scientific Annual Congress of Neurological Surgeons
22-25 September, 2002; Philadelphia, US
Tel. 847 692 9500, Fax. 847 692 2589

British Human Genetics Conference
22-25 September, York, UK
Tel. 01216 272 634, Fax. 01216 272 634,
E. york2002@bshg.org.uk

Meeting of British Psychophysiology Society
23-25 September, 2002; Glasgow, UK
Hartmut Leuthold, Tel. 0141 330 6847,
Fax. 0141 330 4606,
E. h.leuthold@psy.gla.ac.uk

Management of Advanced Disease
24 September, 2002; London, UK
RSM, Fleur Raggatt, Tel. 020 7290 2984,
E. geriatrics@rsm.ac.uk

2nd International Conference on Metals and the Brain
25-28 September, 2002; Fez, Morocco
Tel. 00 21 255 930 499,
E. kingcongres2002@iam.net.ma

October

Violence & Agression Awareness for Public Sector Employees
1 October, 2002; London, UK
Conference administrator, Royal Hospital for Neurodisability, Tel. 020 8780 4500 ext 5236, E. conferences@rhn.org.uk

Epilepsy: The Issues for Women & Girls
2 October, 2002; Truro, UK
www.epilepsy.org.uk/bea/seminarfrm.html

Facial Oral Tract Therapy
2-3 October, 2002; London, UK
Conference administrator, Royal Hospital for Neurodisability, Tel. 020 8780 4500 ext 5236, E. conferences@rhn.org.uk

ABN Autumn meeting/British Neuropsychiatry Association
2-4 October; London, UK
Susan Tann, ABN, Tel. 020 7405 4060, Fax. 020 7405 4070,
E. abn@abnoffice.demon.co.uk

Prevention in Physical Medicine & Rehabilitation: Innovation in Ergotherapy
2-5 October, 2002; Hannover, Germany
Fax. +49 511 532-8124, E. kongress2002.dgpmr-dve@mh-hannover.de

7th International Congress of the World Muscle Society
2-5 October, 2002
Mr Jacob Muller, Tel. 0031 71 527 52 97,
Fax. 0031 71 527 52 62,
E. j.j.l.muller@lumc.nl

BAS-BNS Autumn Meeting 2002
3-4 October, 2002; York, UK
Audrey Bowen, Tel. 0161 275 3401.
EPTA Autumn Scientific Meeting
5 October, 2002; York, UK
E. nigel.hudson@phnt.swest.nhs.uk

15th Congress of the European College of Neuropsychopharmacology
5-9 October, 2002; Barcelona, Spain
Tel. +31 205 040 207, E. ecnp@congrex.nl

5th European Congress on Epileptology
6-10 October, 2002; Madrid, Spain
E.epicongress@eircom.net
Neurology - European Cruise
7-19 October, 2002; Istanbul, Turkey
Tel. 800 422 0711, Fax. 727 527 3228,
E. kciotti@continuingeducation.net

Approaches to the Cervical Spine
7-9 October, 2002; London, UK
Neurosurgery Courses Assistant, RCSE,
Tel. 0207 869 6335, Fax. 0207 869 6329,
E. neurosurgery@rcseng.ac.uk

15th Meeting of the European Society for Stereotactic and Functional Neurosurgery
9-12 October, 2002; Toulouse, France
Tel. +33 5 61 32 26 16, E. ylazorth@cict.fr

Annual Conference on Alzheimer's
9-15 October, 2002; Barcelona, Spain
Tel. +49 0 605 097 220,
E. ps@profi-sales.com

2nd Latin America Committee for Treatment & Research in MS (LACTRIMS)
9-12 October, 2002; Monterrey, Mexico
www.lactrims2002.com.mx,
E. lactrims@hsj.com.mx

British Society of Neuroradiologists Annual Meeting
10-11 October, 2002; Winchester, UK
Drs Millar or Barker, Wessex Neurological Centre, Tremona Road, Southampton, SO16 6YD

Annual Meeting of the American Neurological Association
13-16 October, 2002; New York, US
Tel. 952 545 6284, Fax. 952 545 6073,
E. lorijanderson@msn.com

Practical Management of Memory Problems following Acquired Brain Injury
17-18 October, 2002; Ely, UK
Alison Gamble, Tel. 01353 652173,
Fax. 01353 652164, E-Mail.
alison.gamble@pow.lifespan-tr.anglox.nhs.uk

British Geriatrics Society Autumn Meeting
17-18 October, 2002
Tel. 020 8977 0011, Fax. 020 8977 0055,
E. hmc@hamptonmedical.com

ECNR - European Course in Neuroradiology
19-24 October, 2002; Crieff, Scotland
Dr Wendy Taylor,
E. w.taylor@ion.ucl.ac.uk

Alzheimer's Disease International's 18th Annual Conference
23-26 October, 2002; Barcelona, Spain
Tel. 0034 93 201 7571, Fax. 0034 93 201 9789, E. suport@suportserveis.com

Physiotherapy Treatment in the Overall Management of Parkinson's disease
26 October, 2002; Vienna, Austria
Tel. 352 26 53 15 51, Fax. 352 26 53 15 52, E. mariella.graziano@internet.lu

European Federation of Neurological Societies Congress
26-29 October, 2002; Vienna, Austria
EFNS, Tel. 43 1 880 00270, Fax. 43 1 888 925581, E. headoffice@efns.org

12th World Congress of the International Society for Brain Electromagnetic Topography
27-29 October, 2002; Naples, Italy
Tel. 39 081 566 6504, Fax. 39 081 566 6523, E. isbet 2002@virgilio.it

Dementia, Mind, Meaning & Person
31 October - 1 November, 2002; Newcastle, UK
Tel. 0207 2352 351 x 142, Fax. 0207 2596 507, E. pcornell@rcpsych.ac.uk

November

2nd Neuro-Behavioural Rehabilitation of Severe Brain Injury: Theory & Practice Conference
London, UK
Conference administrator, Royal Hospital for Neurodisability,
Tel. 020 8780 4500 ext 5236,
E. conferences@rhn.org.uk

13th European Congress of Physical Medicine and Rehabilitation

28-31st May 2002, Brighton, UK

Three themes ran through this meeting in Brighton: clinical standards in rehabilitation medicine, measurement, and effectiveness. A European perspective was obtained, with a few Australasian touches. Despite great energy, it seems that everyone shares the problem of setting meaningful standards in terms that are actually useful both to clinicians undertaking the complex activity of rehabilitation and to those who fund health care. It was good for group bonding, but demoralising all the same to find that the ability of funders to mis-use clinically derived data is international: if the Barthel scale score doesn't change then rehabilitation isn't taking place.

I am beginning to feel old now I can remember conferences in rehabilitation when the message was "measure, measure and measure again" and battles would rage where the proponents of one scale would impugn the validity of rival scales. Such fun we had. In this meeting, a much more healthy nihilism about measurement was evident from the speakers. In part this was driven by the disturbing findings of the European PRO-ESOR project. This found that FIM scores mean different things in different parts of Europe and so are not comparable. This prompts me to speculate what on earth our functional scores really do measure. But the greatest challenge of all remains to find ways of defining and measuring clinical expertise: there can be no doubt that this exists, so it must be measurable.

There have been great strides in the establishment of the effectiveness of rehabilitation, particularly at a service level. Rigorous studies of specific interventions are now emerging too. An example was an elegant randomised study where patients with poor balance after stroke received balance training either with or without a blindfold. The idea was that removing the visual input would prevent visual compensation in balance tasks, and that such "visual constraint" would improve the underlying balance mechanisms, and this proved to be the case.

Inside the exhibition hall

But with aids, appliances, prostheses and the like: how should they be evaluated? What constitutes evidence of effectiveness? In a thought-provoking lecture, Professor Henk Stam from Rotterdam outlined how much the world of prosthetics resembles the world of the marketing of any other consumer goods or products. When I buy some toothpaste for myself, I don't usually read up on the RCTs demonstrating its effectiveness before making my choice, and I will be influenced by advertising or free gifts like anyone else. But what effect does the sponsorship of medical meetings by the companies that manufacture appliances have upon prescribing decisions, (at the expense of the taxpayer in most cases)?

A wonderful thing about large meetings is to see invention, innovation diversity and enthusiasm. I was interested in the apparently beneficial effects of magnetic fields, since in my ignorance I had thought this sort of treatment had disappeared either last century or the one before that. Hippotherapy, which is the treatment of people (with multiple sclerosis in this case) by horse riding, was under test. I noted that it improved the sexual function of men, but not women. Robotic physiotherapy was under early evaluation and development. It was not hard to see how stroke physiotherapy could be routinely robotically enhanced in a few years time. Functional electrical stimulation to enable cycling for aerobic fitness training in those with paraplegia looked like great fun and a marvellous success compared to the more usual disappointing effects of FES in walking. The next (14th) European Congress, in May 2004, will be in another cultural capital, this time Vienna, Austria.

Delegates were welcomed to the congress by 'Weapons of Sound', who played drain pipes and water butts and invited audience participation in the vocal backing!

Dr John Gladman,
Nottingham

A word from the BSRM President

This congress was organised by the BSRM together with the SRR to create one of the biggest forums of general rehabilitation practice and research ever seen in the UK. About 650 people attended the congress, including 400 doctors from all over Europe (joined by a few from Australasia and North America) and over 130 other health professionals from the UK.

Problems faced by those with disabilities, their families and carers not surprisingly are similar the world over. Strategies from health and social agencies seemed varied, but difficulties in enabling individuals to return to work in spite of illness or disability seem frighteningly similar in developed countries with responsibilities varying between employers and the state. As in the UK, some countries have difficulties with service provision relating to different policies being adopted by different local authorities. The need for interdisciplinary working was clear throughout all the plenary sessions. Visitors to the UK seemed interested at our community-based rehabilitation, which seems well developed compared to some European countries.

The conference was enhanced by many sponsoring organisations and companies, including some from the voluntary sector, which greatly contributed to the success of the conference **(see the special news review pages at the back of this magazine, where you can also find more information about the BSRM).** The BSRM is also grateful to the many individuals from the SRR and the BSRM who reviewed the hundreds of abstracts submitted.

Andrew Frank
BSRM President

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References:
1. Brashear et al, 2001.
2. Gordon et al, 2002.
3. Ward et al, 2001.
4. Barnes, 2001.
5. Goschel H, 1997.
6. Hatheway CL, Dang C, 1994.
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International Conference on Basic and Therapeutic Aspects of Botulinum and Tetanus Toxin

8-11 June 2002, Hannover, Germany.

Between the 8th and 11th of June several hundred basic scientists and clinicians from throughout the world gathered in Hannover to discuss the scientific and clinical aspects of botulinum and tetanus toxins. The goal of the conference was to provide an opportunity to share scientific and clinical experiences and to provoke further interest in neurotoxin research. Some of the sessions were joint sessions involving both basic scientists and clinicians, and as a clinician I was fascinated by some of the insights into the molecular and biochemical basis of botulinum toxin. For example, one presentation made the point that 7 out of 13 epitopes of botulinum toxin A (BTXA) and botulinum toxin B (BTXB) cross react. Not all are neutralising epitopes but they may boost the shared immune response. In light of this it was not overly surprising to learn (in a clinical session) that up to 25% of patients in one series who were switched to BTXB because of secondary non-responsiveness due to antibodies to BTXA had, within a year, also developed resistance and antibodies to BTXB. This makes it even more important to try to prevent antibody formation by making sure that patients are not reinjected too quickly and by keeping the dose of BTX to the minimum. Most patients who develop antibodies usually do so in the first four years.

A great deal of data on the results of key clinical trials which established indications for BTX therapy (such as cervical dystonia, focal limb dystonia and adult and paediatric spasticity) was presented. This was followed by papers and discussion on the mechanisms of BTX action and on the best way to target specific muscles (such as ultrasound for the iliopsoas for spastic legs in children and EMG guided injections for occupational cramps). Several sessions concentrated on the treatment of disorders of the autonomic nervous system especially hyperhidrosis and hypersalivation. These are now established indications for BTX use. The enhanced effect of BTXB on neurosecretory junction blockade was emphasised. BTX as a treatment of pain syndromes raised some debate. Disorders of the upper and lower GI tract (such as achylasia cardia and rectal fissures) are regularly treated by BTX and there is work ongoing in urological conditions. I was aware that BTX use in dermatology has shown a huge increase over the last few years, but I was slightly taken aback to learn that the increase over the last 3 years had been something in the region of 1500%!. The brow, periocular regions, lower face and neck are all now treatable. The muscles of the lower face are more sensitive to BTX and one speaker mentioned that it was not difficult to cause unwanted lip weakness. Ptosis and uneven eyebrows can follow injudicious upper face injections. BTX has been used to achieve relative facial symmetry after Bells palsy.

There is a great unresolved debate on the bio-equivalence between the different commercially available types of BTX. Not only is it unclear of what the conversion ratio is between the two BTXA products (it varies in different reports between 1:2 and 1:5) but also between BTXA and BTXB. To further complicate matters it is felt there is a different ratio between BTXA and BTXB when treating autonomic indications (with BTXB being perhaps 10 times more potent in this situation compared to motor condictions). The only way to establish these matters will be by carefully conducted randomised clinical trials which will need the co-operation and collaboration of different groups of investigators. Finally we were promised that new BTX preparations were in the pipeline and should be available before the next Toxin meeting in 2005.

Peter Misra, London

> "I WAS AWARE THAT BTX USE IN DERMATOLOGY HAS SHOWN A HUGE INCREASE OVER THE LAST FEW YEARS, BUT I WAS SLIGHTLY TAKEN ABACK TO LEARN THAT THE INCREASE OVER THE LAST 3 YEARS HAD BEEN SOMETHING IN THE REGION OF 1500%!"

Epilepsy - looking westward

3-6 April 2002, Exeter, UK

The British Branch of the International League Against Epilepsy held its annual scientific meeting at the University of Exeter between the 3rd and 6th of April 2002. Approximately 400 delegates attended, representing the many disciplines that now make up the British epilepsy community. The programme was a diverse one, ranging from Sudden Death in Epilepsy, the basic sciences of epilepsy, epilepsy nursing practice, hypothalamic hamartoma, vagal nerve stimulation, the older person with epilepsy, predicting the outcome of anti-epileptic drug treatment, the needs of women with epilepsy, cardiac disorders mimicking epilepsy and the management of people with learning difficulty and epilepsy. Only a fraction of the busy programme can be presented here.

On the first full day of the conference there was a workshop, devised by Liam Gray of the Neurosciences Department of Southampton University, on the relationship between basic science and clinical practice in epilepsy. The workshop debated three main questions: whether epilepsy causes lesions in the brain or brain lesions cause epilepsy, whether the brain has its own endogenous anticonvulsants and the effect of brain plasticity and gene sequences on epilepsy and vice versa.Participants in the workshop left with the feeling that we are on the edge of a far better understanding of the basic mechanisms of epilepsy (with the possibility of rational effective treatment) and that answering the question "why don't we all have epilepsy?" may be eventually more illuminating than trying to answer the question "why does this person have epilepsy?"

The Peter Chalk Centre at Exeter University, where the meeting was held.

On the same day there was a nursing workshop, devised by Lyn Greenhill from the Birmingham University Seizure Clinic, which addressed the sometimes controversial theme of advances in nursing practice in epilepsy care. Nurses no longer see themselves as devoted handmaidens of all-knowing physicians, but as independent practitioners who have a pivotal role in the management of people with epilepsy. A protocol was presented for nurse prescribing in epilepsy, which built on the covert prescribing that nurses already do, called for practical apprentice type learning and for prescribing in epilepsy to be protocol driven (as all prescribing should be). A similar apprenticeship model of learning (with agreed protocols) was presented for three areas of epilepsy in which nurses are starting to practice independently; fast track "triage" clinics for patients with new onset seizures, preconception and pregnancy clinics and Vagal Nerve Stimulation clinics. Audit of two "triage" clinics showed a trained nurse to be as accurate in diagnosis and management as the consultant. The workshop concluded that the relationship between physician and nurse should become a mutually supportive partnership.

Adam Fitzpatrick from the Manchester Heart Centre presented, with his colleagues in cardiology and neurology, a fascinating and disturbing seminar, which provoked much discussion, on those cardiac disorders which can be, and often are, mistaken for epilepsy. Possibly as many as 30% of people with epilepsy resistant to conventional anti-epileptic treatment, may have a primary cardiac disorder that may go unrecognised for years,and yet will often respond to simple treatment. There was much discussion whether the two conditions could be distinguished by careful history taking and examination but the gloomy conclusion was that there is so much overlap in terms of symptoms that the task is almost impossible. It was suggested that in those patients where seizures remain intractable and there is no conclusive electroencephalographic evidence of epilepsy then video EEG (and ECG) monitoring will be mandatory: for epilepsy specialists access to tilt table facilities will also be needed. This has resource implications.

The conference also heard evidence (from work of the Birmingham University group on the structure and function of the ovary in women with epilepsy, from the latest data from the Belfast run British Pregnancy Register and from the Liverpool group studies of intellectual development in children exposed to anti-epileptic drugs in utero) that leads to the conclusion that the time has come to manage women with epilepsy differently from men with epilepsy, particularly in terms of avoiding certain anti-epileptic drugs if at all possible in women with epilepsy.

In another seminar they also heard that the new science of pharmacogenetics is still a long way from predicting response to anticonvulsant drugs, but may be somewhat nearer to predicting those patients likely to respond with unpleasant side effects.

Dr Tim Betts,
Birmingham University Seizure Clinic

Phineas Gage and the beginnings of neuropsychology

Authors

Dr Andrew Larner is the editor of our Book Review Section. He is a Consultant Neurologist at the Walton Centre for Neurology and Neurosurgery in Liverpool, with a particular interest in dementia and cognitive disorders. He is also an Honorary Apothecaries' Lecturer in the History of Medicine at the University of Liverpool.

Dr John Paul Leach has recently been appointed to a consultant post at the Southern General Hospital in Glasgow, having trained in neurology and neurophysiology at the Walton Centre for Neurology and Neurosurgery in Liverpool.

1848 was a year of political revolutions in Europe. In the same year, in the field of neuroscience, a freak occurrence would also prove - eventually - to have a revolutionary impact. Few neurologists will be unfamiliar with the name of Phineas P Gage, nor with the extraordinary work-related accident which befell him on the afternoon of 13 September 1848 in Burlington, Vermont, USA.[1,2] Excavating rock with blasting powder, in his capacity as a railroad foreman, an accidental ignition caused a tamping iron approximately 1.1 m (43 inches) long, 3 cm thick at its widest point, and weighing 13 pounds, to smash through the left side of Gage's face, entering just below the cheekbone, and emerge from the top of his skull, landing some 25-30 yards away smeared with brain. Gage was thrown back, a few convulsive movements of the extremities were observed, but he was able to speak within a few minutes.

Fewer neurologists may be familiar with Dr John Martin Harlow, the railway physician who attended Gage within two hours of the accident. Harlow continued to treat Gage in the following days when death from infection seemed imminent. He then continued to observe the changes in Gage's personality, up to the time of his death from status epilepticus in 1861. Moreover, it was Harlow who persuaded the family to permit exhumation of Gage's skull five years after his death (no post mortem was performed). Harlow published his findings in two papers,[3,4] without which record Gage might not be remembered at all.

Gage's skull was subsequently donated to the Warren Anatomical Museum at Harvard University School of Medicine. Modern neuroimaging techniques have been used to study Gage's skull and reconstruct the probable path of injury caused by the tamping iron.[5] This has permitted more precise definition of the lesion location, and suggests that both left and right prefrontal cortices were injured. As Harlow's account records in detail the behavioural changes manifested by Gage after the accident,[4] and is still regarded as one of the best accounts of behavioural disorder following prefrontal damage, clinical-anatomical correlation is possible. From an efficient and capable work foreman, Gage became irreverent, capricious, profane and irresponsible, and showed defects in rational decision making and the processing of emotion, such that his employers refused to return him to his former position. Harlow argued that the frontal lobe lesion had caused a loss of planning skills.[4] These neurobehavioural changes, sometimes labelled "pseudopsychopathic" or "sociopathic", are now regarded as typical of orbitofrontal injury, having been observed in other patients with selective lesions of this area.[6] However, other case histories indicate the need to differentiate this clinical picture from that following injury to other parts of the frontal lobes. For example, a more recent report, with prolonged follow up, of a patient with frontal lobe injury due to an iron bar penetrating the skull documented prominent apathy, difficulties with planning, and lack of drive, yet stability of function within the domestic, professional and social setting (cf. Gage), associated with dorsolateral prefrontal injury.[7] Disinhibited, apathetic, and akinetic types of frontal lobe syndrome are described, associated respectively with orbitofrontal, frontal convexity and medial frontal lesions.

Although we accept the landmark status of Gage in the development of ideas relating to cortical localisation,[2] the contemporary response to Harlow's reports was, to say the least, muted.[1] However, the account did appear at a propitious time. Broca was publishing his observations correlating aphasic syndromes with focal brain injury (1861), and Fritsch & Hitzig's electrical stimulation studies of the exposed cortex were soon to follow (1870). Ferrier's experimental observations in monkeys (1878) largely confirmed Harlow's clinical findings in Gage.

Gage is unquestionably one of the most famous patients in neurological history, a fixture in neurological textbooks and the subject of many papers. (Regrettably these often err in their assertions about him, principally because they neglect the original Harlow reports.[8]) A cursory study of the history of medicine indicates that it is unusual for the names of patients, rather than their doctors, to be recorded for posterity (one eponymous exception which immediately springs to mind is Christmas disease). Why should it be, then, that Gage is remembered, and not Dr Harlow? Many speculations might be advanced: perhaps the extraordinary "truth-stranger-than-fiction" nature of the accident Gage suffered, the very fact that he survived, his memorable name, the fact that he was written up. More significant, however, may be the possibility, evident with the benefit of hindsight, that this case represents part of a paradigm shift, a "natural experiment" which demonstrated the possibilities of correlating particular personality and behavioural changes with injury to focal brain regions, and hence the correlation of function with location. This practice continues in modern neuropsychology, where detailed case histories may be compared with structural and functional neuroimaging findings to help elucidate the workings of the brain.[9]

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EDITOR'S CHOICE

Improving the outcome of spinal cord injury

When the spinal cord is injured, astrocytes form scars that act as physical barriers to axon growth. In addition there is a chemical barrier: the extracellular space of such scars contains molecules that actively inhibit axon extension, including chondroitin sulphate proteoglycans. In this elegant study Stephen McMahon's group, at King's College London, investigate the effects of inhibiting chondroitin sulphate proteoglycans on recovery from a spinal cord injury. Adult rats received a dorsal column crush at C4, as well as an intrathecal injection of chondroitinase ABC, which degrades chondroitin sulphate proteoglycans. The controls were rats with no spinal injury and rats with a spinal lesion who received placebo. Chondroitinase ABC treatment increased the number of fibre bundles approaching and crossing the lesion (by cholera toxin B-subunit labelling of median nerve projections for ascending tracts and biotinylated dextran amine injected into the motor cortex for descending tracts). This increased anatomical connectivity was accompanied by a greater preservation of the dorsal column potentials evoked by electrical stimulation of the motor cortex. Most importantly, chondroitinase ABC treatment was associated with improved function on behavioural tasks such as beam or grid walking, as well as an adhesive tape removal task (!). Lastly, (and it is hard not to smile when this antique test appears after such technological wizardry) the analysis of footprint traces from rats with inky feet shows that chondroitinase ABC preserves normal gait after animals with spinal lesions, unlike controls.

Chondroitinase ABC does not restore full anatomical connectivity across injured cord lesions. But it does so sufficiently to support a very real and useful improvement in function. So it now becomes a candidate for clinical trials of spinal injury treatment, along with blockade of NogoA, neurotrophic factor treatment and cellular grafting.-***AJC***

Bradbury EJ, Moon LD, Popat RJ, King VR, Bennett GS, Patel PN, Fawcett JW, McMahon SB.
Chondroitinase ABC promotes functional recovery after spinal cord injury.
NATURE
2002;416(6881):636-40

NERVE REPAIR

★★★ RECOMMENDED

Acute stroke: no Nogo = go?

Nogo-A, originally known as NI-250, is a myelin-associated glycoprotein, originally characterised by Martin Schwab and colleagues, which inhibits neurite growth and causes growth cone collapse. A monoclonal antibody (mAb) to this protein, IN-1, was produced some years ago, and has been shown to promote CNS functional regeneration following various experimental lesions in neonatal and adult rats, as a consequence of axonal regeneration and/or neuroanatomical plasticity of uninjured pathways. The effects of IN-1 in acute stroke have now been examined.

Adult rats underwent unilateral middle cerebral artery occlusion (MCAO); some received IN-1 given by hybridoma xenograft, others a control mAb, others no treatment (all received cyclosporin immunosuppression, necessary to block rejection of the xenograft). Although stroke volume examined eight weeks postlesion did not differ between the groups, the animals receiving IN-1 showed 80% recovery of prelesion behavioural performance in a forelimb reaching task (grasping sucrose pellets), whereas the recovery in controls reached only 50% of baseline values. Anatomical studies showed that neuroanatomical plasticity paralleled functional recovery, with the development of increased projections from the intact primary motor cortex to the contralateral red nucleus (the corticorubral projection in rats is mostly ipsilateral).

Of course caution is appropriate in interpreting these findings, since there are many claims for treatments that improve outcome from MCAO in experimental animals, some of which have failed to translate to the clinical arena. However this study does suggest that the CNS has regenerative potential which if exploited, by providing a permissive environment for axonal growth by blocking growth inhibitory factors, may lead to meaningful functional recovery.-***AJL***

Papadopoulos CM, Tsai S-Y, Alsbiei T, O'Brien TE, Schwab ME, Kartje GL.
Functional recovery and neuroanatomical plasticity following middle cerebral artery occlusion and IN-1 antibody treatment in the adult rat.
ANNALS OF NEUROLOGY
2002;51(4): 433-441

★★★ RECOMMENDED

Adult neural stem cells are useful

These two recent papers have demonstrated that adult neural stem cells do form functional neurons. There has been a long standing debate as to whether the cells labelled in the adult mammalian brain with markers of proliferation, such as BrdU, are of any functional significance. Last year it was demonstrated by Shors *et al* that inhibiting dividing cells in the adult brain of rodents could affect trace memory formation (Shors TJ *et al* (2001) Nature

410:314-315). However this was only circumstantial evidence to support the contention that adult neural stem cells (NSCs) can be incorporated into host circuits with functional effects. Now Gage and colleagues have shown that adult rodent NSCs can form functionally active neurons in vitro and Frisèn and colleagues have done the same in vivo.

Song *et al* took GFP labeled adult NSCs and studied them in vitro for their intrinsic electrical properties; capacity to respond to synaptic stimuli and the release of neurotransmitter. This is a beautiful, elegant and extensive study as is typical from the Gage laboratory, and is a tour de force of scientific work. In all cases the GFP NSC were shown to be similar to the primary embryonic neurons, although this was contingent on how the cells were grown - for example the nature of the substrate used in culture and the use of BDNF.

The study by Frisèn *et al* took a different approach using BrdU to label the endogenous NSC population, and then trace their connections using specific viral vectors linked to GFP. This demonstrated that BrdU positive cells could be incorporated into circuits, both in the olfactory bulb and hippocampus, and that, in the case of the olfactory system, they responded to olfactory odour stimulation.

These two studies are important in highlighting that adult NSCs can differentiate into electrically active neurons and become incorporated into functional circuitry in the adult mammalian brain. The question that now needs answering is what regulates this process physiologically and what is its role - ***RAB***

Song H-J, Stevens CF, Gage FH.
Neural stem cells from adult hippocampus develop essential properties of functional CNS neurons.
NATURE NEUROSCIENCE
2002 5: 438-445

Carlen M, Cassidy RM, Brismar H, Smith GA, Enqvist LW, Frisèn J.
Functional integration of adult-born neurons.
CURRENT BIOLOGY
2002 12:606-608

NEUROPSYCHOLOGICAL REHABILITATION

★★★ RECOMMENDED

Assessing money management in rehabilitation

The ability to carry out monetary transactions with competence is a crucial aspect of functional independence and therefore an important area for rehabilitation. In severe instances when a person is incapable of managing their own affairs an appointee may take over this role. But how is financial acumen to be assessed? Many people have difficulties handling money on a daily basis after brain injury and yet there have been few attempts to investigate this problem. Following a brief but useful review of previous attempts to incorporate monetary skills into assessment, this paper reports on the development of a specific tool: the Assessment of Functional Monetary Skills (AFMS). This is a structured assessment protocol for investigating various aspects of monetary understanding, and includes: identification of coin/note denomination and ability to carry out written and mental arithmetic in a financial context. In addition, there is a procedure for investigating how effectively people carry out real-life transactions, including paying of bills and writing cheques. The AFMS is presented as a means of identifying problems and measuring change in response to intervention, not a basis for any specific treatment. A case study is provided but there is little by way of useful clinical information to correlate with monetary performance. However, the issue is important and very common in rehabilitation. For this reason this is a paper that many therapists will want to read, if only to stimulate them to producing something more structured in their own practice.-***ADW***

Gaudette M, Anderson A.
Evaluating money management skills following brain injury using the assessment of functional monetary skills.
BRAIN INJURY
2002: 16: 2: 133-148

Disorders of everyday action may be caused by multiple impairments

Action in everyday contexts or 'naturalistic action' is belatedly attracting the attention of cognitive scientists. This paper is one of a number of contributions to a journal special issue on Everyday Action and has interesting implications for clinicians who are regularly confronted with similar problems. Forde and Humphreys contrast the performance of two patients, HG and FK, who have difficulties carrying out basic tasks such as making a cup of tea, preparing a sandwich, and wrapping up a gift. Both patients were disorganised and made many perseverative errors. In an earlier paper the authors suggested that HG's difficulties arose from a failure of inhibition of a specific action once it had already been performed (rebound inhibition). In contrast, FK was thought to show a deficit in the activation of components of action over the duration of a task (impairment in an activation gradient). Whereas HG improved when given one action to complete at a time, FK's performance did not improve with written and visual prompts, but deteriorated when interrupted. Through a series of experimental manipulations the authors argue that FK shows damage to a store of action sequences and to an executive system for monitoring performance. This paper is useful to therapists on three accounts. First, the method of investigating deficiencies in everyday tasks can be adapted for routine clinical use. Second, the detailed analysis of actions illustrates the complexity of routine behaviours and thus militates against oversimplifications in interpretation. Third, it suggests that at least some forms of the disorder are amenable to intervention and this may be dependent on the nature of the underlying deficit.-***ADW***

Forde E M E, Humphreys G W.
Dissociations in routine behaviour across patients and everyday tasks.
NEUROCASE
2002: 8: 151-167

Picture this - I must remember to E.T (phone home)

Evidence for effectiveness of intervention for cognitive deficits is often limited to single case experiments. The need for individualisation of treatment and the length of time that training takes limits the number of cases that can be studied in any one centre. A newly published memory training study has pooled resources from 7 centres in Europe so that the effect of using imagery as a strategy for improving memory in 21 brain-damaged patients was assessed. Imagery proved to be an effective and useful strategy for patients with mild to moderate memory impairment.

Patients with mild memory impairment such that it might prevent effectiveness and functioning at work were included in the study. Patients with severe memory loss or other cognitive deficits such as neglect, apraxia, agnosia and aphasia were excluded. The patients were randomly allocated to the imagery-training group or to a control group. The imagery group were taught to generate images of objects and actions rapidly until they could recall 8/10 items. They were also helped to apply imaging to their own daily living needs. The control group received the kind of memory training they would normally have received in their respective centre. This included various internal and external strategies such as face-name associations, keeping notebooks and calendars.

The design was ABA, with 4 weeks of baseline, ten weeks of training (3 times a week) and a three month follow-up period in which no training was given. A variety of memory assessments were used, imagery training was expected to lead to improved

performance on some of them. The results were in keeping with the researchers predictions. Imagery training significantly improved recall of everyday verbal materials, e.g. stories, appointments and the frequency of memory problems observed by relatives was reduced. What's more these effects lasted over the follow up period.

There is strength in numbers. This study will carry more weight than 20 reports of n=1 studies that might be produced over years. Rehabilitation research into cognitive deficits must benefit from collaborative studies such as this one.-***AJT***

Kaschel R, Della Sala S, Cantagallo A, Fahlböck A, Laaksonen R, Kazen M.
Imagery mnemonics for the rehabilitation of memory: a randomised group controlled trial.
NEUROPSYCHOLOGICAL REHABILITATION
2002: 12: 127-153

EPILEPSY

★★★ RECOMMENDED

Do seizures damage the brain?

This longstanding debate remains without a clear answer but the current study does move it forward. It has long been known that the hippocampus is damaged by seizures in animals and that severe acute insults can damage the hippocampus in humans. Studies are compounded by complicating factors such as head injury from seizures and bouts of status epilepticus. What is not known is whether recurring seizures themselves cause a progressive deficit.

In this study 24 patients with well-lateralised TLE were followed from diagnosis and subjected to repeat MRI scans with hippocampal volume measurements after 3.5 years. The diagnosis of TLE was made on the basis of EEG and clinical criteria and all patients had a normal initial MRI. They were 30 +/- 14 years of age, so not in the usual age group for hippocampal sclerosis (HS) to be the cause of their seizures.

Epilepsy was generally mild and 15 patients had 0-1 generalised tonic clonic seizures (GTCS) and 9 had 2-8 GTCS during the follow-up period. One patient developed clear signs of hippocampal sclerosis on MRI and the others developed signs of hippocampal volume loss, of the order of 10-25%, which correlated strongly with the number of GTCS during follow-up.

This study provides evidence that even quite mild epilepsy can be damaging to the hippocampus and supports the century old view of the imperative to treat early. The hippocampus is however, a uniquely sensitive structure and whether this can be extrapolated to extratemporal epilepsy or whether the generalised epilepsies carry the same kinds of risks is even less clear.-***MRAM***

Briellmann RS, Berkovic SF, Syngeniotis A, King MA, Jackson GD.
Seizure-associated hippocampal volume loss: A longitudinal magnetic resonance study of temporal lobe epilepsy.
ANNALS OF NEUROLOGY
2002;51:641-4

To stop frowning on EEGs…….

Presurgical localisation of epilepsy hinges on accurate recording of electrographic seizure onset. A number of factors may hinder recordings and commonly artefact arising from scalp muscles from ictal motor activity is responsible. Traditionally the way to overcome this is to insert electrodes intracranially. The authors reduced scalp muscle activity by injecting botulinum-A (BTX) 100 units between temporalis and frontalis muscles. A week later patients underwent EEG and were asked to perform various facial contortions. If there was still significant artefact on EEG, a further 50-100 units were injected into muscles responsible.

Twenty-four seizures were recorded in 3 patients, 12 before and 12 after BTX injection.

They were reported blind. Prior to BTX only one seizure was localisable (3 lateralisable) whereas afterwards 8 were localisable. There were no adverse effects and muscle activity returned to normal after 8, 11 and 15 weeks.

The authors should be congratulated on lateral thinking to try and solve a problem with a benign, readily available procedure, potentially avoiding highly invasive intracranial EEG. How widely applicable this will be remains to be seen.-***MRAM***

Eisenschenk R, Uthman B, Valenstein E, Gonzalez R.
Botulinum toxin-induced paralysis of frontotemporal muscles improves seizure focus localisation.
NEUROLOGY
2002;58:246-249

Stopping heart stop

The central nervous system has well-established effects on the heart. A hierarchy of autonomic control is recognised involving cortical levels of modulation. It is therefore perhaps not surprising that epilepsy can result in changes of cardiovascular physiology. However, the precise dynamics are not well understood and need to be elucidated in view of their potential role in sudden unexpected death in epileptic patients (SUDEP). Surges of sympathetic outflow have been postulated to occur during seizures, which may then contribute, to the pathophysiology of SUDEP. Temporal lobe epilepsy is particularly troublesome in causing changes in autonomic activity and case reports of ictal associated tachycardia or bradycardias are frequently documented. Interestingly interictal changes of sympathetic cardiovascular tone have also been demonstrated.

To address this relationship further, Hilz and colleagues have studied autonomic parameters before and after surgery in 18 TLE patients. Variability of heart rate and blood pressure were determined (power spectral analysis) incorporating changes attributable to respiration.

Each signal had a combination of high and low frequency analysis. Calculation of baroreceptor sensitivity was also performed derived from the relationship between these parameters. The standard measures of cardiovascular function did not change. Low frequency components of HR and BP showed an average reduction of over 40% following surgery. Baroreceptor sensitivity also changed. This supports the conclusion that sympathetic tone is augmented in TLE patients. This is a reassuring study and implies that surgery should be accompanied by a reduced risk of cardiovascular emergencies in epilepsy patients. -***JLR***

Hilz A, Devinsky O, Mauerer A and Dutsch M.
Decrease of sympathetic cardiovascular modulation after temporal lobe epilepsy surgery.
BRAIN
2002: 125:985-995

MULTIPLE SCLEROSIS

★★★ RECOMMENDED

INdependent COMparisons of INterferons - INCOMIN: Alternate day Interferon beta-1b versus weekly Interferon beta-1a

In a world where evidence based medicine requires very large randomised double blind placebo controlled studies, direct comparisons between two similar drugs from different manufacturers are rare. Even more so if such a study is completely independent of any sponsorship or links in some form or other to one of the firms concerned. It is therefore pleasing to see that the INCOMIN trial study group has been able to undertake a direct comparison study of two of the three available interferons for relapsing remit-

ting multiple sclerosis as they are currently licensed, guiding our prescription habits in an evidence based manner, albeit with relatively small numbers. The basic protocol employed in this independent study was a 2-year prospective randomised multi-centre study with 96 patients in the beta-1b, alternate day administration, (Betaferon) limb and 92 patients in the beta-1a, weekly (Avonex) limb of the study. Outcome measures were proportion of patients remaining relapse free, clinically and radiologically (no new proton density/T2 lesions). In those receiving alternate day therapy 51% remained relapse free compared to 36% receiving weekly treatment (relative risk 0.76, p=0.03) and similarly 55% developed no new radiological lesions compared to 26% (relative risk 0.6, p<0.0003). On these grounds alternate day therapy is superior in effect. However, unsurprisingly injection site reactions were significantly more common in the alternate day group but this did not impact on compliance and could be minimised by improved injection technique, the authors suggest. Significantly more patients in the alternate day group generated neutralising antibodies, which adds to the controversy of the role of these antibodies. The observed increased effectiveness in the presence of increased antibody formation would support the argument that these antibodies do not have any effect on the treatment response.

The study design does not allow comparisons to be drawn about which agent is more potent (and clearly does not involve the third commercially available interferon-beta, Rebif) but does suggest that the frequency of administration maybe crucial. ***-TH***

Durelli L, Verdun E, Barbero P, Bergui M, Versino E, Ghezi A, Montanari E, Zaffaroni M, and the Independent Comparison of Interferon (INCOMIN) Trial Study Group.
Every-Other-Day Interferon Beta-1b Versus Once Weekly Interferon Beta-1a For Multiple Sclerosis: Results Of A 2-Year Prospective Randomised Multicentre Study (Incomin)
LANCET
2002; 359: 1453-60

Type 1 diabetes mellitus (DM) and multiple sclerosis (MS) in Sardinia

This relatively simple cohort epidemiological study undertaken in Sardinian families with MS reveals a surprising finding when compared to studies on other populations but does raise some interesting observations about the genetics of MS in this population. Sardinians are at high risk of developing MS and DM. This study demonstrates that epidemiologically there is a link in this population between these two autoimmune diseases, with DM being three-fold more prevalent in patients with MS compared with their healthy siblings but importantly DM was found to be five-fold more prevalent than the general population. At first sight this observation may be at odds with most Northern European studies with respect to MS and DM where no such link has been observed. But on closer examination of HLA haplotypes in Sardinian and other Northern European populations, some sense can be made of this apparent contradiction. Coraddu *et al* found that the most prevalent HLA haplotype profile of the Sardinian population with MS was DRB1*0301-DQA1*0501-B1*0201 which is different from other MS populations where the haplotype (DRB1*1501-DQA1*0102-B1*0602) is more common. This latter haplotype in fact bestows protection against DM and susceptibility to MS, whereas the Sardinian haplotype is a known risk factor for DM and other autoimmune diseases such as coeliac disease, autoimmune thyroiditis, Addison's disease and atrophic gastritis. So, together with the HLA haplotype profile and epidemiological evidence from this study, common genes are implicated in the susceptibility to both diseases in this population and the genes may be located in or around the HLA region. ***-TH***

Marrosu MG, Cocco E, Spinicci G, Pischedda Contu P.
Patients With Multiple Sclerosis And Risk Of Type 1 Diabetes Mellitus In Sardinia, Italy: A Cohort Study.
LANCET
2002; 359: 1461-65

T cells attack MOG

We have yet to identify the antigen targeted by the immune system in multiple sclerosis (MS). Myelin basic protein (MBP) and proteolipid protein (PLP) are both major constituents of myelin in the peripheral and central nervous system. They are therefore not ideal candidate antigens for a condition confined to the CNS. Myelin oligodendrocyte glycoprotein (MOG) is a quantitatively minor constituent of myelin present exclusively within the central nervous system, and therefore an interesting protein to investigate in the context of MS.

Koehler *et al* recruited four sibling pairs discordant for MS, One of the MS affected sibs had been treated with Interferon-beta. All sibs within a given family were haplo-identical. MOG reactive T cell clones (TCC) were generated by culturing the cells in the presence of MOG proteins. TCCs were then incubated with antigen presenting cells and 11 synthetic MOG peptides (all representing portions of the extracellular domain of the MOG peptide) or recombinant MOG protein. The cytokines produced were quantified by the use of ELISAs and cell phenotype was established using flow cytometry.

A total of 235 TCCs reactive to MOG peptide were isolated in the cohort overall, although only four from the patient treated with Interferon-beta. All the TCCs were CD4+. Challenging the TCCs with the 11 MOG epitopes in proliferation assays revealed no single dominant epitope shared between subjects, or even haploidentical siblings. The cytokines produced by the TCCs on exposure to MOG varied between individuals. TCCs from one MS affected sibling produced a Th1 (cytotoxic- IFN-3and TNF-/) pattern of cytokines. This was not seen in the unaffected siblings in whom a mixture of profiles was identified - Th2 (predominately IL-4), Th0 (IL-4 and IL-6) and Tr1 (regulatory- IL-10). The pattern of cytokines produced remained consistent despite repeated stimulation.

This paper reports the presence of MOG reactive T cells in nor-

Complimentary Journals Reviewed

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Cerebrovascular Diseases, Neuroepidemiology
S. Karger AG - Medical and Scientific Publishers,Allschwilerstrasse 10, CH - 4009 Basel, SWITZERLAND.
Tel. 0041 61 306 11 11, Fax. 0041 61 306 12 34, E-Mail. t.nold@karger.ch www.karger.com

Cerebral Cortex
Oxford University Press, Great Clarendon Street, Oxford, OX2 6DP. Tel. 01865 267154, Fax. 01865 267985.

Clinical Rehabilitation, Multiple Sclerosis
Arnold, 338 Euston Road, London NW1 3BH. Tel. 020 7873 6339, Fax. 020 7873 6325,
E-Mail.arnoldjournals@hodder.co.uk,www.arnoldpublishers.com/journals

Current Opinion in Neurology
Lippincott Williams & Wilkins, 241 Borough High Street, London, SE1 1GB. Tel 0207 940 7564, Fax 0207 940 7530
Email. rmclachl@lww.co.uk, www.Lww.co.uk

Epilepsia
Blackwell Publishing, Commerce Place, 350 Main Street, Malden, MA 02148-5018, USA. Tel. 888 661 5800, Fax. 781 388 8270,
www.blackwellscience.com/epi

mal healthy individuals and those with MS (reduced in number in interferon-beta treatment). It identifies no single immunodominant epitope on MOG and demonstrates that TCCs from healthy and MS sibs produce different cytokine profiles on stimulation. The authors speculate that the loss of regulatory control of these MOG reactive T cells could result in demyelination. Unfortunately the cohort studied in this paper was too small to draw conclusions about the pathogenesis of MS, except to identify this as a protein worthy of further investigation. ***-ALC***

Koehler NK, Genain CP, Giesser B, Hauser SL.
The human T cell response to myelin oligodendrocyte glycoprotein: a multiple sclerosis family-based study.
JOURNAL OF IMMUNOLOGY
2002, 168:5920-5927

Chips in Multiple Sclerosis

★★★ RECOMMENDED

Gene chips are the technological cutting edge of gene expression analysis. One chip allows the simultaneous analysis of expression of tens of thousands of genes. They are relatively easy to use, but their results present a considerable bioinfomatics headache! Other gene expression techniques (such as SAGE) are harder to use, but have the advantage over chips that they can pick up unknown genes, whereas chips rely on a library of known genes and expressed sequence tags.

Lock *et al.* used Affymetrix chips to compare genes expressed in CNS lesions from 4 patients with MS, and two controls without neuropathology. The four MS samples were classified histologically into acute/active and chronic/silent lesions. Genes demonstrated to be up or down regulated were identified and analysed.

Differences in gene expression between MS and control samples were identified. Of the genes that were up regulated, a number of immune response genes were identified such as MHC class II, IgG and genes suggesting the activation of T cells, B cells, macrophages and complement. Genes reflecting proinflammatory cytokine activity were also up regulated in all MS lesions. There was an elevation in several stress related genes and genes reflecting astrocyte activity. Of the genes that were down regulated the most significant were those associated with myelin proteins and neuron specific genes such as proteolipid protein and neuronal growth protein.

Differing gene expression was identified between the acute and chronic lesions. Genes elevated in the acute lesions included variable-joining-constant region immunoglobulin (125 fold), a MAP kinase and various growth factors including insulin growth factor-1 and G-CSF. In the chronic lesions, integrin ⁄ was elevated. Various gene transcripts associated with Th2 or allergic response were also elevated including the histamine receptor H1, IgE receptor and IgG Fc receptor. In addition a number of matrix metalloproteinases (MMP) were elevated, IL-17 and various neuroendocrine molecules.

One of these proteins was tested therapeutically using an animal model of demyelination - experimental allergic encephalomyelitis (EAE). G-CSF (elevated 13 fold in active compared with chronic lesions) given prior to onset of EAE prolonged time to disease onset and reduced the severity of the acute phase of the disease. Also the role of IgG Fc receptor was tested, as its expression was elevated in chronic lesions; in Fc3receptor knockout mice the chronic phase of EAE became less severe.

This study demonstrates the power of gene chip analysis to monitor the dynamics of gene expression changes between tissues, and will probably be the best way to investigate the mechanisms of action of the susceptibility alleles identified by genome studies. Also, such studies may identify potential therapeutic targets for disease modification in MS. ***-ALC***

Lock C, Hermans G, Pedotti R, Brendolan A, Schadt E, Garren H, Langer-Gould A, Strober S, Cannella B, Allard J, Klonowski P, Austin A, Lad N, Kaminski N, Galli S J, Oksenberg JR, Raine CS, Heller R, Steinman L.
Gene-microarray analysis of multiple sclerosis lesions yields new targets validated in autoimmune encephalomyelitis.
NATURE MEDICINE 2002 May;8(5):500-8

Book Reviews

If you would like to review books for ACNR, please contact Andrew Larner, Book Review Editor, c/o AdvancesinCNR@aol.com

Localization in Clinical Neurology 4th edition

Authors: Paul W Brazis, Joseph C Masdeu, José Biller
Publisher: Lippincott Williams & Wilkins 2001
Pages: 596
ISBN No: 0-7817-2843-6
Price: £102.00

As an SHO considering whether or not to pursue a career in neurology, I noted my registrar (Hugh Willison) reading a weighty tome entitled Localization in Clinical Neurology. Evidently this was required reading for the budding neurologist, so I purchased a copy (3rd edition). Its now dog-eared pages, crumbling spine, copious marginalia, and multiple index additions attest to my frequent recourse to it over the years. I believe I have learned more from its pages than any other neurology text, hence it is one of my favourite books. That others feel similarly may be indicated by the fact that it is the only one of my neurology books ever to have been stolen (by person(s) unknown), which I was fortunate to recover quite by chance, lurking in a filing cabinet it had no purpose to be in. Does this new edition amount to a steal?

Uncompromisingly, the authors state at the outset, in a new chapter discussing the general principles of localization, that the "key to localization" and "the roadmap for a correct assessment" is neuroanatomy (so admirably served by the primer in ACNR). Chapters then proceed, as in previous editions, centripetally from peripheral nerves to cerebral hemispheres, the largest (more than one sixth of the book) devoted to the ocular motor system. The text is clear and coherent, perhaps reflecting the restricted authorship, now so unusual in major neurology books. The text is supplemented with line diagrams and tables, but there is no neuroimaging, congruent with the authors' hope, stated in the preface, that diagnosis be achieved at the least cost and avoiding unnecessary testing. The whole work remains, as originally conceived, primarily for the clinician, a manifesto for the importance of the clinical method supplemented by modern paraclinical (particularly imaging) methods, rather than vice versa.

More than any other neurology text with which I am familiar, this book conveys the scope of clinical phenomenology and its potential value in making inferences about the anatomical location of pathology, the critical step in focusing subsequent investigations. The major (and unforgivable) deficiency is the index: slimmed considerably from the previous edition, it misses page references to some topics and omits many headings. For those dipping into the book, rather than reading systematically (the majority, I would suspect), this will profoundly impair the utility of the book. At £102.00 it is not cheap but, index nothwithstanding, to my way of thinking it represents excellent value for money for the reader prepared to engage with it. Highly recommended.

AJ Larner

Neuropsychological sequelae of subarachnoid hemorrhage and its treatment

Authors: BO Hütter
Publisher: Springer 2000
Pages: 178
ISBN No: 3-211-83442-7
Price: £50

This book is claimed to be the first monograph on the subject of the neuropsychological sequelae of subarachnoid haemorrhage (SAH), stemming from the author's researches over the past decade in Aachen. The findings are disturbing. Although many patients are judged to make an excellent neurological recovery from SAH, cognitive and behavioural problems which impair quality of life and the ability to return to employment are common; four years post-bleed one-third of operated patients fulfil diagnostic criteria for post-traumatic stress disorder.

Impairments of short-term memory (i.e. attention) and cognitive slowing, without impairments of general intelligence as measured by IQ tests, are the most frequent long-term neuropsychological sequelae; aphasic language disorders may occur but are less common. These deficits are similar to those seen following mild closed head injury, as are the impairments in everyday life. Assessments performed in the acute or chronic stage suggest the pattern of deficits is static.

The pattern and severity of abnormalities correlates poorly with morphological damage seen with structural imaging (CT, MRI). Hence the morphological substrate of the observed deficits is attributed to diffuse damage of paracisternal grey substance, with fronto-basal emphasis, rather than a focal lesion dependent on aneurysm location. The prevalent idea that anterior communicating artery aneurysms are most prone to cause memory deficit and psycho-organic syndromes of Korsakoff type is rejected as a consequence of selective case reporting and small series, as opposed to systematic studies.

The similarity of findings from patients with aneurysm rupture compared with spontaneous non-traumatic SAH without a proven source of bleeding suggests that SAH causes nonspecific brain damage, independent of the location of the ruptured aneurysm. Hence bleeding per se is adjudged to be the main cause of cognitive impairment. A corollary of this finding is that surgery may have advantages over newer (and expensive) endovascular coiling techniques by removing subarachnoid blood. No additional damaging effects of surgical intervention were identified.

This is a challenging book which should be read by all involved in the management of patients with SAH. Regrettably the translation is not into idiomatic English, which makes for a rather bumpy read, and there is no index, deficiencies which might profitably be redressed in a second edition.

AJ Larner

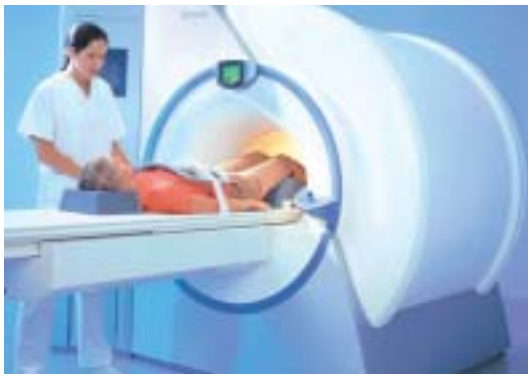
Siemens signs academic partnerships

Siemens is forging even closer partnerships with clinical research sites and academic institutions. For example, within the UK, neurological research will be carried out at the Functional Imaging Laboratory (FIL), London on a new MAGNETOM 3T Allegra and a 1.5T High Gradient MAGNETOM Sonata.

Siemens has also just announced they have formed a strategic alliance with the New York University Medical Centre. The contract features a seven-year agreement using the Iselin, NJ based vendor as the exclusive supplier of radiology equipment for the hospital's diagnostic and interventional radiology programmes.

The agreement covers 100 clinical imaging systems, as well as research units such as a 7-tesla MRI magnet, which will be housed at a new MR research facility located near NYU's mid-town Manhattan campus. NYU Medical Centre Manhattan, an affiliate Hospital for Joint Diseases, is also a party to the agreement.

For further information contact Mike Bell, Siemens Medical Solutions on Tel. 01344 396317.



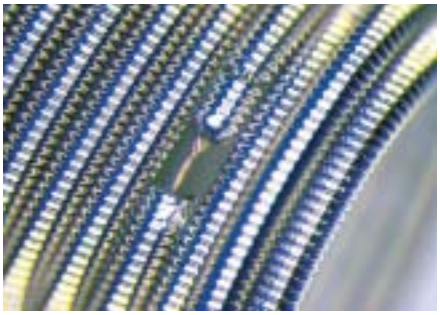
The Siemens MAGNETOM Sonata, Maestro class used for cardiac and neuro research.

VDS trial beats expectations

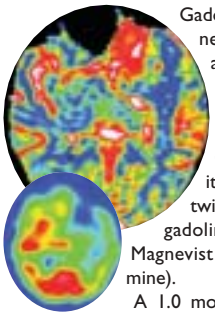
Dendron has announced that the trial of the variable detachment coil (VDS) is beating expectations. The product is unique in that it has three detachment points, therefore reducing the need to use extra coils in larger aneurysms and also providing a safe final coil – alleviating the risk of leaving part of the coil extending into the vessel.

The trial has been extended to three further sites as well as Hamburg and Glasgow. These are Zurich, Beijing and Ancona. It is planned to publish the results of this trial at the Symposium neuroradiologicum in Paris this coming August. The product will be added to the EDC II range which are freely available now.

Please contact Guy Tuck at Neurotechnics Ltd to receive a CD Rom of the latest Embolisation coil technology from Dendron. Tel. 01844 260777, Fax. 01844 260778, E-Mail. guy.tuck@neuro-technics.com



New MR contrast agent from Schering



Gadovist 1.0 (gadobutrol) is a new extracellular contrast agent developed by Schering for intravenous use in spinal and cranial MRI.

According to Schering, Gadovist is unique because its 1.0 molar concentration is twice that of routinely used gadolinium-based agents, like Magnevist (gadopentetate dimeglumine).

A 1.0 molar concentration not only offers the practical advantage of a smaller injection volume, but also provides a sharper bolus of contrast agent and enhanced image quality. This is said to make Gadovist a promising candidate for high dose applications and techniques that depend more heavily on bolus geometry, ie dynamic imaging and first pass techniques such as brain perfusion.

Gadovist is expected to become an important tool for radiologists in tumour diagnosis, stroke assessment and multiple sclerosis imaging.

The new contrast agent will be available in the UK in vials from July and pre-filled syringes later in the year.

For further information contact Chris Matthews at Schering Healthcare on Tel. 01444 232323.

READER OFFER

Clinical Neuroscience and Therapeutic Principles 3rd edition

Diseases of the Nervous System 2 Volume Set, Edited by Arthur Asbury et al

Cambridge University Press have just published the third edition of a neurology classic.

This two-volume reference encompasses epidemiology, pathology, pathophysiology, and clinical features of the complete range of neurological disorders. The basic principles of neurological dysfunction are covered at cellular and molecular level by leading international experts in the field. Disease mechanisms are reviewed comprehensively, with particular relevance to the principles of therapy.

Current, comprehensive and authoritative, this is said by Cambridge University Press to be the definitive reference for neurologists, neurosurgeons, neuropsychiatrists, and psychiatrists, indeed everyone with a professional or research interest in the neurosciences.

As a special introductory offer, readers of ACNR can order the 2 volume set at the introductory price of £250 (£295.00 after November 2002).

For further information contact Gurdeep Pannu at Cambridge University Press on Tel. 01223 312393.

Epilepsy Information Network

For many years the National Society for Epilepsy has recognised the importance of providing information and support to people with epilepsy within their own community. Following pilot schemes in Nottingham, it was decided to provide epilepsy information on a regional basis. This led to the creation of the Epilepsy Information Network just over a year ago, funded by the Community Fund (National Lottery) and UCB Pharma.

The Epilepsy Information Network provides information to people with epilepsy, their families, carers and others within the local community. It does this through Epilepsy Information Services in hospital-based neurology clinics around the country. The service offers people the opportunity to talk to trained volunteers in an informal setting. It is is now available in 25 clinics throughout the country, with more than 75 trained volunteers.

In future, it is hoped that volunteers will be able to take information into other settings, such as schools, help to raise awareness of epilepsy and reduce the prejudice that is still experienced by many people.

For further information contact the National Society for Epilepsy on Tel. 01494 601391.

Focus on Rehabilitation

Royal Hospital for Neuro-disability

The Royal Hospital for Neuro-disability is a national charity providing treatment and care for people with complex disabilities resulting from disorders or injuries to the brain. The Hospital founded the UK's first brain damage unit that has both a national and international reputation for its treatment of patients in vegetative state.

As well as long term care and day services, specialist units include a Profound Brain Injury Unit, Neuro-rehabilitation and Disability Management, Neuro-behavioural Rehabilitation, Transitional Living Unit, Huntington's Disease Service and a new Ventilator Unit.

The Hospital also runs nationally and university accredited courses from IT training, to specialist rehabilitation techniques, and BSc (Hons) Neuro-disability Studies. The programme of multidisciplinary conferences includes one on 1st October at Kensington Town Hall, London, to examine issues relating to violence, particularly in the work environment.

Information on this and other courses and conferences are available on the website: www.rhn.org.uk or contact the Royal Hospital on 020 8780 4500, email conferences@rhn.org.uk.

Royal Hospital for Neuro-disability
A national medical charity

A powerful movement in rehab

What can be more painful than seeing a patient's progress wane? Traditional rehabilitation can lead to frustration and become unbearable for many patients and their families. VIASYS healthcare, a leader in neurodiagnostics, has introduced what they believe to be a revolution in rehabilitation. MotoVate helps patients work for longer, gives direct feedback but most importantly, gets results.

MotoVate combines computer games with surface electromyography to give direct feedback to patients as they undergo therapy. Therapists place surface electrodes on targeted muscles; the patient can then be taught that contracting or relaxing muscles controls the game they have chosen. The system can be calibrated to work with the smallest of movements or made more difficult as treatment progresses. As the patients progress through the game, they see their clinical improvement in real time.

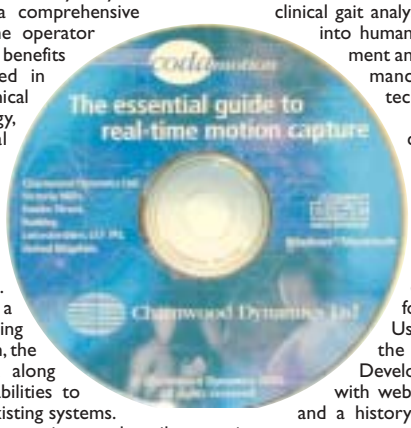
The compelling nature of computer games means that MotoVate can encourage patients to use almost any muscle. Such a valuable tool helps with many conditions including stroke, brain injury, cerebral palsy, orthopaedic injuries to name just a few and is ideal for use with children and the elderly alike.

For more information on MotoVate contact; Jane Glover, VIASYS Healthcare, Welton Road, Warwick. CV34 5XH. Tel 01926 838503, E-Mail. jglover@viasyshc.c.uk

FREE RESOURCE

Essential guide to real-time motion capture

Codamotion, from Charnwood Dynamics, is a real-time motion capture and analysis system. The company has launched a comprehensive CD-ROM that guides the operator through the features and benefits of a system that is used in diverse scientific and clinical areas, sports technology, biomechanics, industrial processes and animation.



The CD contains more than 150 screens with a logical navigation sequence, illustrated with more than 25 video sequences and animations. The contents include a products section providing an overview of the system, the hardware and software, along with the interfacing capabilities to enable integration with existing systems.

The Applications section describes Codamotion's use in a number of areas including clinical applications, scientific research, sport, animation and industrial processes. Also included is a selection of case studies, covering areas such as clinical gait analysis, biomechanics, research into human movement, the measurement and analysis of sports performance, industrial and space technologies and animation.

The resources section covers functions such as setting up a movement laboratory, the mathematics of segmental gait analysis, a movement analysis software demonstration and a full system explanation with a PDF form of the Codamotion User Manual. Also featured is the Codamotion Software Development Kit (SDK), along with web-links, a glossary of terms and a history of motion analysis techniques.

For more information, or a free copy of the CD, E-Mail. davina@charndyn.com

Lightwriter Communication Aids now on EAT Contract

Toby Churchill Ltd were exhibiting their range of communication aids at the exhibition in Brighton. The company is the only communication-aid manufacturer run by someone who is himself physically and speech-disabled, the user of a communication aid, and also the designer of the products. The company believe that this unique combination gives them a deeper understanding of the particular needs of the speech disabled and helps them design better products.

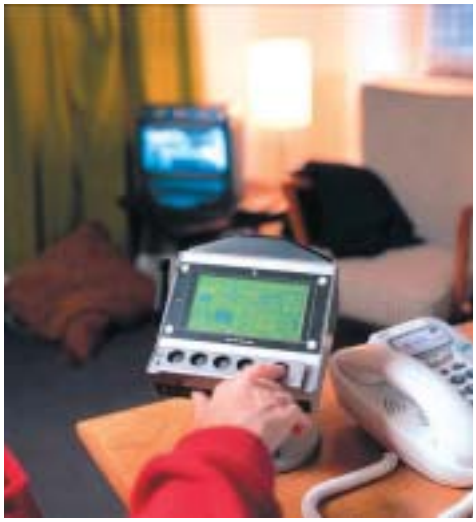
Lightwriters are small portable text-to-speech communication aid specially designed to meet the particular needs of people with speech loss and to cater with progressive conditions. Lightwriters are widely used by people with acquired speech disorders following laryngectomy, head injury, stroke, or with progressive neurological diseases such as Motor Neurone Disease, Parkinson's Disease, and Multiple Sclerosis, Lightwriters are also used by people with congenital speech disorders with conditions such as Cerebral Palsy.

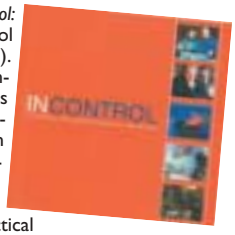
The Lightwriter range is now available on NHS Electronic Assistive Technology Contract.

For more information contact Toby Churchill Ltd: Tel. 01223 576117, Fax. 01223 576118, E-Mail. sales@toby-churchill.com

FREE RESOURCE

Need more information about environmental controls?





SRS technology are offering a free copy of *In Control:* The Ultimate Guide to Environmental Control Systems for Independent Living (normally £4.95). The book provides an overview of the environmental controls market, detail on how such systems operate and what they can be used for. Its non-technical, user-focused approach means the book is an excellent reference source for healthcare professionals who make recommendations and provide advice to clients about these systems.

Practical training: If you are looking for practical training, SRS also have the answer. A series of one day seminars throughout the UK will provide a comprehensive overview of the issues to be considered when assessing an individual's requirements for environmental controls. Dr Mohammed Sakel, a registrar based in Coventry, attended the first session. He says, "It was very instructive. Environmental Controls are an important part of our training, and this course provides a really good overview of all the products available and when they are most appropriate to prescribe. The information on alternative sources of funding was also useful. I would definitely recommend the course."

Alternative sources of funding: SRS can provide you with information about alternative sources of funding for environmental control systems. This is available at the one-day training sessions, or direct from SRS Technology.

For further information contact Rebecca Auterson on Tel. 01922 456882, or use the reader enquiry service included with this magazine.

Guillain-Barré Support Group

Guillain-Barré Syndrome (GBS) is not a specific illlness but a clinical syndrome, an aggregate of symptoms. It is an illness of the peripheral nervous system, a peripheral neuropathy. There are many causes – symptoms of weakness and/or altered sensations are typical as motor and/or sensory nerves become affected.

GBS is an acute illness. There are around 1000-1500 new cases every year in the UK, and apart from in the elderly population, it is the most common form of acute paralysis.

The GBS support group was founded in 1985 by Glennys Sanders to provide a lifeline to sufferers of GBS and CIDP, and to their families and friends. The group provides information about the illnesses and can provide local contacts, usually recovered patients, who visit patients and their families at hospitals and at home. In addition, the group continuously strives to increase awareness of the syndrome among the medical professions and the public. Over the years, large sums of money have been raised to fund research into GBS and for other projects.

For more information E-Mail. admin@gbs.org.uk or Tel. 01529 304615.

Optimising outcomes in spasticity management

At the ECPRM Professor Majid Bakheit, well known for his work with botulinum toxin, chaired a symposium sponsored by Ipsen Ltd.

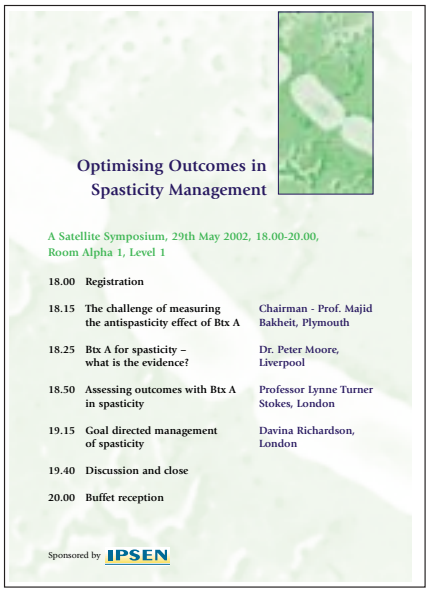
Dr. Peter Moore reviewed the evidence for botulinum toxin in the management of adult spasticity. Although there are consistent reports of spasticity being significantly reduced throughout the literature, demonstrations of this translating into functional patient benefit are sparse.

Professor Lynne Turner Stokes propounded the concept of active and passive function. In most clinical trials the outcomes measured are those of active function, but passive functional changes may have greater importance for the patient's QOL. She presented a case study, which illustrated a substantial cost saving following BoNT-A treatment, resulting in reduced carer burden.

Davina Richardson highlighted the value of individualised goal setting in rehabilitation and the need for all professionals involved in patient care to work together as a team.

These presentations were well received by an audience of some 170 and generated interesting discussion.

For more information contact Alex Obszanska-Homer, Ipsen Ltd on Tel. 01753 627777.



British Society of Rehabilitation Medicine

The BSRM is the UK professional organisation for practitioners in Rehabilitation Medicine and is devoted to: Promoting the development and good practice of Rehabilitation Medicine as a medical specialty; Enhancing undergraduate and postgraduate education in rehabilitation and disability issues; Supporting rehabilitation research; Liaising with related medical, paramedical and voluntary organisations to further these aims.

Membership is open to registered medical practitioners with an interest in disability and its management.

Membership benefits include: Reduced subscription to Clinical Rehabilitation; Reduced registration fees at BSRM meetings/courses; Complimentary copies of BSRM publications and newsletters; Participation in regional groups' events; Opportunities to contribute to national debates and influence decisions of statutory bodies on issues related to Rehabilitation Medicine; Membership of Special Interest Groups (Amputee Medicine & Electronic Assistive Technology).

Upcoming meetings:
10-13 September 2002 in Nottingham – '5th BSRM/University of Nottingham Advanced Rehabilitation Course'
25 November 2002 in London -'Practical Approaches to Managing Fatigue Problems in Rehabilitation'

For more information contact British Society of Rehabilitation Medicine, C/o the Royal College of Physicians, 11 St Andrews Place, London NW1 4LE. Tel. 01992 638865, or see www.bsrm.co.uk

Imagine needing
to go to the toilet.

But needing someone else
to do the dirty work.

REQUIP® ropinirole

FIGHTS PARKINSON'S. DEFENDS DIGNITY.

REQUIP (ropinirole) Prescribing Information
Presentation 'Requip' Tablets, PL 10592/0085, 0087-0089, each containing ropinirole hydrochloride equivalent to either 0.25, 1, 2 or 5 mg ropinirole. 0.25 mg tablets - 210 tablets starter pack, £43.12; 1 mg tablets - 84 tablets, £46.20; 2 mg tablets - 84 tablets, £92.40; 5 mg tablets - 84 tablets, £184.80. **Indications** Treatment of idiopathic Parkinson's disease. May be used alone (without L-dopa) or in addition to L-dopa to control "on-off" fluctuations and permit a reduction in the L-dopa dose. **Dosage** *Adults:* Three times a day, with meals. Titrate dose against efficacy and tolerability. Initial dose for 1st week should be 0.25 mg t.i.d., 2nd week 0.5 mg t.i.d., 3rd week 0.75 mg t.i.d., 4th week 1 mg t.i.d. After initial titration, dose may be increased in gradual weekly increments of up to 3mg/day, until acceptable therapeutic response established. Do not exceed 24 mg/day. Concurrent L-dopa dose may be reduced gradually by around 20%. When switching from another dopamine agonist follow manufacturer's guidance on discontinuation. Discontinue ropinirole by reducing doses over one week. *Renal or hepatic impairment:* No change needed in mild to moderate renal impairment. Not studied in severe renal or hepatic impairment - administration not recommended. *Elderly:* Titrate dose in normal manner. *Children:* Parkinson's disease does not occur in children - do not give to children. **Contra-indications** Hypersensitivity to ropinirole, pregnancy, lactation and women of child-bearing potential unless using adequate contraception. **Precautions** Caution advised in patients with severe cardiovascular disease and when co-administering with anti-hypertensive and anti-arrhythmic agents. Patients with major psychotic disorders should be treated with dopamine agonists only if potential benefits outweigh the risks. Ropinirole has been associated with somnolence and episodes of sudden sleep onset. Patients must be informed of this and advised to exercise caution while driving or operating machines during treatment with ropinirole. Patients who have experienced somnolence and/or an episode of sudden sleep onset must refrain from driving or operating machines. Caution advised when taking other sedating medication or alcohol in combination with ropinirole. If sudden onset of sleep occurs in patients, consider dose reduction or drug withdrawal. **Drug interactions** Neuroleptics and other centrally active dopamine antagonists may diminish effectiveness of ropinirole - avoid concomitant use. No dosage adjustment needed when co-administering with L-dopa or domperidone. No interaction seen with other Parkinson's disease drugs but take care when adding ropinirole to treatment regimen. Other dopamine agonists may be used with caution. In a study with concurrent digoxin, no interaction seen which would require dosage adjustment. Metabolised by cytochrome P450 enzyme CYP1A2 therefore potential for interaction with substrates or inhibitors of this enzyme - ropinirole dose may need adjustment when these drugs are introduced or withdrawn. Increased plasma levels of ropinirole have been observed with high oestrogen doses. In patients on hormone replacement therapy (HRT) ropinirole treatment may be initiated in normal manner, however, if HRT is stopped or introduced during ropinirole treatment, dosage adjustment may be required. No information on interaction with alcohol - as with other centrally active medications, caution patients against taking ropinirole with alcohol. **Pregnancy and lactation** Do not use during pregnancy - based on results of animal studies. There have been no studies of ropinirole in human pregnancy. Do not use in nursing mothers as lactation may be inhibited. Adverse reactions In early therapy: nausea, somnolence, leg oedema, abdominal pain, vomiting and syncope. In adjunct therapy: dyskinesia, nausea, hallucinations and confusion. Incidence of postural hypotension (commonly associated with dopamine agonists), was not markedly different from placebo, however, decreases in systolic blood pressure have been noted; symptomatic hypotension and bradycardia, occasionally severe, may occur. As with another dopamine agonist, extreme somnolence and/or sudden onset of sleep have been reported rarely, occasionally when driving (see 'Precautions' and 'Effects on ability to drive and use machines'). **Effects on ability to drive and use machines** Patients being treated with ropinirole and presenting with somnolence and/or sudden sleep episodes must be informed to refrain from driving or engaging in activities where impaired alertness may put themselves or others at risk of serious injury or death (e.g. operating machines) until such recurrent episodes and somnolence have resolved. **Overdosage** No incidences reported. Symptoms of overdose likely to be related to dopaminergic activity.

POM

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