

## EDITOR'S CHOICE

**Camel antibodies prevent amyloidosis**

Amyloidogenesis, the aberrant assembly of a protein or protein fragment into fibrils with subsequent plaque deposits, is a common pathogenic mechanism underlying many neurological diseases, including Alzheimer's Disease and prion diseases. This study involves the well-characterised human lysozyme protein. This protein may be amyloidogenic in its mutant form, and different point mutations in its gene causes non-neuropathic systemic amyloidosis. The authors investigate inhibition of amyloid fibril formation of a specific mutant lysozyme protein (D67H). They describe the novel use of antibodies derived from camelids (dromedaries). Camels uniquely produce functional antibodies devoid of light chains and are thus composed of heavy chains only making them more stable and soluble. They derived a camelid antibody fragment raised against the wild-type lysozyme protein and used this to inhibit in vitro mutant protein amyloid formation and aggregation.

An array of elegant biophysical data is presented to demonstrate that specific antibody binding to the mutant lysozyme prevents its aggregation in vitro by significantly reducing the mutant protein's ability to form a partially unfolded species; an event which is thought to be key in initiating aggregation and subsequent fibril formation. Interestingly, the antibody epitope does not include the site of mutation or any significant portion of the structure destabilised by the mutation. Thus, it is proposed that the stabilisation of the mutant lysozyme by the antibody interaction is a result of transmitted conformational changes, akin to the action of allosteric effectors at the active site of an enzyme. These long-range conformational changes are reported to restore global structural co-operativity to that of the wild-type protein.

This paper is interesting in terms of therapeutics because it demonstrates that preventing the formation of an aggregation-prone species by an antibody is a valid strategy for the treatment of the large family of amyloidogenic diseases. Moreover, it highlights that the antibody interaction need not impede the normal function of the protein as it may occur away from sites essential for functioning. The use of camelid antibodies in human therapeutics is novel; once humanised, they make attractive candidates for immunotherapies because of their small size, solubility, and simple but stable structure. – *LMS, SJT*

*A camelid antibody fragment inhibits the formation of amyloid fibrils by human lysozyme.*

Dumoulin M, Last AM, Desmyter A, Decanniere K, Canet D, Larsson G, Spencer A, Archer DB, Sasse J, Muyldermans S, Wyns L, Redfield C, Matagne A, Robinson CV, Dobson CM

NATURE

2003; 424: 6950: 783-788

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## NEUROIMMUNOLOGY

## ☆☆☆ RECOMMENDED

**Cannabis may prevent nerve death**

The political arguments for the legalisation of cannabinoids have included its potential therapeutic effects, fuelled amongst other things by the David Baker's Nature paper three years ago demonstrating their anti-spasticity effect in animals. The MRC UK trial of the effects of cannabinoids on spasticity in multiple sclerosis has come to an end. No doubt its results, when announced, will cause much medical and political wrangling.

Now, David Baker's group have added further fuel to the fire with an elegant demonstration that cannabinoids may prevent neuronal death in acute inflammation. He induced his established model of chronic relapsing EAE in normal mice and those knocked out for the cannabinoid receptor gene CB1. Each had a similar clinical course of acute EAE but afterwards the CB1 knock-outs were much more disabled and had lost more spinal cord axons. The only caveat to the interpretation that cannabinoids mediate neuroprotection is that the CB1 knock-outs had reduced axonal density prior to EAE suggesting a developmental failure. So CB1 agonists were given to acute EAE and acute experimental allergic uveitis in doses that had no immunosuppressive effect; there was no change in the inflammatory infiltrate but axonal/photoreceptor damage was reduced. The mechanism? Well, calcium fluxes induced by NMDA agonists were more prolonged in CB1 knock-outs and kainic acid induced seizures and death at much lower doses in these animals.

Taken together, these observations suggest that cannabinoids may reduce the excitotoxic effects of acute inflammation on axons. If translated to multiple sclerosis, this would mean that cannabinoids would not alter relapse frequency but would reduce the disability acquired as a result of each relapse. If cannabinoids are approved as a treatment of spasticity, there will be ample opportunity to test this hypothesis. – *AJC*

*Cannabinoids inhibit neurodegeneration in models of multiple sclerosis.*

Pryce G, Ahmed Z, Hankey DJ, Jackson SJ, Croxford JL, Pocock JM, Ledent C, Petzold A, Thompson AJ, Giovannoni G, Cuzner ML, Baker D.

BRAIN.

2003;126: 2191-202.

**Rehabilitation of acute relapses of multiple sclerosis.**

There is an ever increasing body of evidence supporting the benefit of rehabilitation in treating patients with Multiple Sclerosis (MS) - see Nov/Dec 02 issue of ACNR for a comprehensive review. However despite the common clinical pattern of relapse in MS few studies have looked specifically at the role of rehabilitation in managing relapses (indeed many have excluded them). This study looked at whether there is benefit of adjunctive multi-disciplinary team MDT rehabilitation (as opposed to "standard care" therapy) along with the standard 3 day treatment of intravenous Methylprednisolone (IVMP) for relapse in MS.

After randomisation the intervention group received a planned MDT assessment and then treatment depending on goals set during assessment. The primary outcome measures used were the Amended Motor Club Assessment (AMCA), which measures motor impairment, and Guy's Neurological Disability Scale (GNDS). Secondary ones used were the Barthel Index (BI), Human Activity Profile (HAP), and the SF-36. All were carried out on admission, and at one and three months later. A total of 40 patients completed the study, 20 in each arm.

There was no baseline difference between groups in patient characteristics or primary measures. At three months there was both a statistical and clinically significant change from baseline in the AMCA, GNDS, BI and HAP scores of the intervention arm. The SF-36 did not reach statistical significance in the intervention arm. The intervention group also received significantly more therapy (though this wasn't standardised) which was statistically correlated with the improved outcome measures. This group were also more frequently referred on for whatever available outpatient therapy so it is not possible to ascertain whether the community or hospital setting accounted for the benefits noted. Therapists included MS nurse specialists, physio-, occupational & speech and language therapists as well as orthotists. Rehabilitation physicians were not included as part of the MDT but thankfully there is other evidence in the literature to support their role in benefiting patients with MS.

– *JM*

*A randomised controlled trial comparing rehabilitation against standard therapy in multiple sclerosis patients receiving intravenous steroid treatment.*

J Craig, CA Young, M Ennis, G Baker, M Boggild  
 JOURNAL OF NEUROLOGY, NEUROSURGERY AND PSYCHIATRY.

2003;74: 1225-1230.

## PARKINSON'S DISEASE

## ☆☆☆ RECOMMENDED

**A double-blind study, trial of bilateral fetal nigral transplantation in Parkinson's disease**

This much awaited study, mentioned previously in ACNR when it was presented at the International Movement Disorder meeting last year in Miami, has now eventually been published in the *Annals of Neurology*. It involves the transplantation of 34 patients with advanced Parkinson's disease. The study was a prospective double-blind placebo controlled trial in which patients were randomised either to no transplant, transplant with small amounts of foetal tissue, namely one foetus per side or a four-donor per side group. Whilst there was clear PET study evidence of increased dopaminergic signal in the grafted donor transplant group this did not correlate with clinical improvement. The primary end point of the study did not improve and worryingly significant numbers of the patients developed dyskinesias that persisted after overnight withdrawal of dopaminergic medication (56%).

The study has clearly been well developed and was originally devised to address the question of the optimum amount of donor tissue that is required for optimal therapy. It is clear that whilst four-donor per side patients have done better than the one donor the overall analysis of the three groups shows no significant effect on the primary end point. However, post mortem studies clearly show that there are more dopaminergic cells surviving in the four-donor group compared to the one donor group, which fits in with the PET study. Furthermore, whilst there has been no overall benefit if one subdivides the patients into those with relatively mild disease with a UPDRS score of less than 49 there is clearly a significant benefit compared to those with more advanced disease.

The take home message for me in this study is that whilst transplantation has produced a negative outcome in this study if one actually addresses issues of patient selection one can clearly see that there are a group of patients who would benefit from the procedure. These tend to be those PD patients who have less severe disease and, therefore, probably have a lower risk of developing dyskinesias post transplantation. However in the current climate it would seem that this study coming on the back of the PD transplant study of Freed *et al* in 2001, will lead rightly to a period of re-evaluation before any further similar trials can be considered -RAB

*A double-blind controlled trial of bilateral fetal nigral transplantation in Parkinson's disease.*

Olanow CW, Goetz CG, Kordower JH, Stoessl AJ, Sossi V, Brin MF, Shannon KM, Nauert GM, Perl DP, Godbold J, Freeman TB.

ANNALS OF NEUROLOGY

2003;54(3):403-14

**Transfer of the von Hippel-Lindau gene to neuronal progenitor cells in treatment for Parkinson's disease**

One of the major problems in the use of neural stem cells for treating Parkinson's disease is their reluctance to turn into dopaminergic neurons. There have been a number of studies which have tried to rectify this, including using hypoxic culture conditions and erythropoietin. Yamada *et al* have taken a slightly different approach, capitalising on the von Hippel-Lindau gene which is known to be intimately involved with oxygen sensing (see ACNR 3.2). The authors take rat embryonic neural precursor cells and transduce them with von Hippel-Lindau gene and show that this greatly increases the neuronal and especially the dopaminergic yield from these cells. This is not only shown in vitro but in the standard 6 hydroxydopamine lesion model of Parkinson's disease. This effect of the VHL gene is enhanced by GDNF.

This study is important because it shows that it may be possible to increase dopaminergic yield and thus develop a cell therapy which can be used in Parkinson's disease clinically. However the study does have a few caveats - for example, the neural precursor cells are never passaged and therefore it is debatable the extent to which they are truly stem cells. Furthermore the net effect of the transplants is to produce large numbers of dopaminergic cells which have a modest effect on drug induced rotation and this coupled to the histology makes one wonder the extent to which these are fully functional nigral dopaminergic neurons.

Overall though this study offers encouragement to those who feel that stem cells therapies may be of value although clearly based on the above transplant study further work needs to be done in deciding which patients if any should receive such dopaminergic rich transplants -RAB

*Transfer of the von Hippel-Lindau gene to neuronal progenitor cells in treatment for Parkinson's disease.*

Yamada H, Dezawa M, Shimazu S, Baba M, Sawada H, Kuroiwa Y, Yamamoto I, Kanno H.

ANNALS OF NEUROLOGY

2003 Sep;54(3):352-9.

## PRION DISEASE

## ☆☆☆ RECOMMENDED

**Variant Creutzfeldt Jakob Disease is transmitted to the central nervous system via the sympathetic ganglia of the gut**

Variant Creutzfeldt Jakob Disease (vCJD) is thought to be caused by dietary exposure to the bovine spongiform encephalopathy (BSE) agent and there is now good experimental evidence from strain-typing studies that BSE and vCJD are linked to the same prion strain. However the oral route of human contamination and the pathways that lead to neuroinvasion are not known. Experiments in mouse scrapie models have demonstrated that cells from the lymphoreticular system are involved in the peripheral replication of prions, and that the sympathetic nervous system supports propagation from the gut lymphoid tissue to the central nervous system (CNS). This study demonstrates that a similar process occurs in man. They demonstrate, using immunohistochemical techniques, the accumulation of the abnormal disease-associated isoform, PrP<sup>Sc</sup>, in the neurons of sympathetic ganglia of three vCJD patients. These observations provide strong evidence to implicate the gut-associated sympathetic ganglia in the transmission of infectious prions to the CNS after oral exposure. If this is also the case for food animals infected with prion disease then removal of infected sympathetic nervous system tissues from contaminated carcasses in abattoirs should be addressed. In addition these findings also strengthen the case for peripheral prophylactic treatment of prion diseases prior to the stage where neuroinvasion has occurred. - LMS, SJT

*The sympathetic nervous system is involved in variant Creutzfeldt-Jakob Disease*

Haik S, Faucheux BA, Sazdovitch V, Privat N, Kemeny JL, Perret-Liaudet A, Hauw JJ

NATURE MEDICINE

2003; 9: 9: 1121-1123

## ALZHEIMER'S DISEASE

**Dopamine D2 receptors and cognitive decline in Alzheimer's disease**

Alzheimer's disease leads to impaired acetylcholinergic systems and these are often cited as one of the causes of cognitive decline, particularly relating to learning and memory. Certain drugs already target these systems. However, patients' brains post mortem also show decreased D2 receptors in both the hippocampus and amygdala compared to control brains. Here it is argued that D2 receptor availability is reduced in temporal regions in early Alzheimer's disease in vivo and that this is associated with patients' dysfunctional memory.

Post mortem studies have shown that D3 receptors are largely absent from extrastriatal temporal regions investigated here so although [11C]FLB-457 has high affinity for both D3 and D2 receptors, binding of the novel antagonist was taken to represent binding to D2 receptors specifically. Patients were given neuropsychological tests. It is not stated whether controls were. Fourteen patients in early stages of AD, and 11 age and sex matched controls underwent PET (Positron Emission Tomography). Medication history was known. Structural MRI brain scans used to map PET data showed cortical and hippocampal atrophy in AD patients compared to controls. PET results showed that D2 receptor binding potential in the right hippocampus was significantly positively associated with verbal memory performance on two tests and it was deduced that atrophy of the hippocampus was not the sole explanation. As the authors suggest, investigating dopaminergic systems alone and in conjunction with acetylcholinergic approaches could offer new opportunities for drug development. -LAJ

*Hippocampal dopamine D2 receptors correlate with memory functions in Alzheimer's disease.*

Kemppainen N, Laine M, Laakso M P, Kaasinen V, Nägren K, Vahlberg T, Kurki T and Rinne J O.

EUROPEAN JOURNAL OF NEUROSCIENCE

2003; 18: 149-154.

**Talking to relatives with Alzheimer's disease**

Many areas of speech and language therapy in neurological conditions have seen a shift in emphasis over the last few years to include training of carers in the management of communication disorders. This is based on the simple recognition that it takes (at least) two to tango, or in this case to communicate. As the authors of this study point out, people with Alzheimer's disease (AD) are often unable to modify their own communicative behaviour. While clinicians may offer intuitively appealing strategies, as yet these lack empirical support.

This study involved 'wireless audio-recorded interactions' between 18 people with AD and their carers during the course of everyday activities around the home. Carers' reports of the strategies they use were compared with their actual occurrence in interaction and then analysed in relation to the success or otherwise of conversations.

The results highlighted several strategies that carers reported using frequently but which occurred only rarely and others that they appeared to be unaware they were using. The least successful strategy was slowing the rate of speech, which was significantly associated with subsequent communication breakdowns. Using relatively simple grammatical constructions was much more successful, though it is somewhat more difficult to teach.

The recognition that carers' interactive style can serve to make communication either better or worse in AD has important implications when clinicians are prioritising their input. Identification of successful and unsuccessful strategies can only serve to make that process more effective. -RB

*Effectiveness of communication strategies used by caregivers of persons with Alzheimer's disease during activities of daily living.*

Small, J.A., Gutman, G., Makela, S. and Hillhouse, B.

JOURNAL OF SPEECH, LANGUAGE, AND HEARING RESEARCH  
2003; 46:2, 353-367.

### ☆☆☆ RECOMMENDED

#### Do antimuscarinic agents increase Alzheimer-type pathology?

To explore the hypothesis that muscarinic receptor antagonism might promote Alzheimer-type pathology (since cholinergic therapy seems to have beneficial effects in AD, promoting non-pathogenic APP metabolism), brains of non-demented Parkinson's disease (PD) patients were examined for plaques and neurofibrillary tangles (NFT) and the findings correlated with use of antimuscarinic drugs. These were prescribed for movement or bladder control (benztropine, orphenadrine, trihexyphenidyl; oxybutinin) or for depression (tricyclic antidepressants [TCAD]: amitriptyline, imipramine).

Cortical plaque density was significantly higher in those receiving chronic (> 2 years) muscarinic receptor antagonist treatment compared to the untreated and those receiving short-term (< 2 years) treatment. Although rarely observed, NFT were twice as common in the long-term as compared to short-term and untreated groups. No significant intergroup differences were found with TCAD use although there was a trend to increased pathology in chronic users. However, this may be an incidental finding since depression may be a risk factor for developing dementia in PD.

The data are consistent with the possibility that prolonged anti-muscarinic drug use may accelerate beta-amyloidosis and plaque formation. This may have implications for therapeutic use of anticholinergs as "tremorolytic" agents in PD. -AJL

*Increased Alzheimer pathology in Parkinson's disease related to antimuscarinic drugs.*

Perry EK, Kilford L, Lees AJ, Burn DJ, Perry RH.

ANNALS OF NEUROLOGY  
2003;54(2):235-238

## COGNITION

### Language function in corticobasal degeneration

Although originally described as a movement disorder (asymmetric parkinsonism, apraxia), it has been increasingly recognised that corticobasal degeneration (CBD) is also characterised by cognitive impairments, amongst which language dysfunction may be prominent, although no systematic studies have been reported.

In this study from Cambridge, ten patients with clinically diagnosed CBD (one confirmed pathologically) were assessed with various neuropsychological tests to probe language function. Although 8 of the 10 patients had no clinically apparent aphasia, testing showed phonologic and oral spelling impairments to be prevalent, as evidenced on tests of nonword reading, phoneme blending and phoneme segmentation. Semantic memory, word-picture matching, and naming were normal or only mildly impaired. Tests tapping visuospatial, constructional and frontal functions did show impairments, as previously defined in CBD.

The authors of this study suggest that the language dysfunction observed in CBD forms a continuum overlapping with cases of progressive nonfluent aphasia.

However, as with all studies involving clinically ascertained cases of CBD, there is a "but": CBD phenocopies are well described, with pathological substrates including Alzheimer's disease, Pick's disease, progressive supranuclear palsy, non-specific histology, and even Creutzfeldt-Jakob disease. It would seem that clinical phenotype reflects the neuroanatomical distribution of pathological change, rather than the precise histological nature of that

change. Hence it is doubtful whether careful language testing would prove helpful in the premortem diagnosis of CBD. -AJL

*Language function and dysfunction in corticobasal degeneration.*

Graham NL, Bak T, Patterson K, Hodges JR.

NEUROLOGY  
2003;61:493-499.

### The neuroanatomy of visual neglect

The neuroanatomical substrates of visual neglect have been debated. A role for the posterior parietal lobe has long been assumed, but recently a counter claim has been made suggesting damage to the superior temporal gyrus is crucial. Masud Husain and his colleagues have looked at this issue by studying a group (n = 35) of unselected right cerebral hemisphere stroke patients with and without neglect, and mapping their lesions with high resolution MRI protocols (i.e. these were not scans done for clinical purposes). Neglect was ascertained by abnormal performance on shape cancellation tasks, line bisection tasks, or both, corroborated by evidence from everyday behaviour.

In patients with middle cerebral artery territory infarcts (n = 24; 14 with neglect, 10 without) the critical area was defined as the angular gyrus on the lateral surface of the inferior parietal lobe. Superior temporal gyrus was involved in some but not all of these patients. In patients with posterior cerebral artery territory infarcts (n = 11; 5 with neglect, 6 without) the critical area was defined as the parahippocampal gyrus in the medial temporal lobe. These areas have known neurobiological connections. Inferior frontal areas, implicated in some cases of neglect, were neither necessary nor sufficient to cause neglect in this series of patients.

Although lesion volume might be a confounding factor, nonetheless this study suggests that lesions of the angular gyrus and parahippocampal gyrus are critical to the development of visual neglect. -AJL

*The anatomy of visual neglect.*

Mort DJ, Malhotra P, Mannan SK, Rorden C, Pambakian A, Kennard C, Husain M.

BRAIN 2003;126(9):1986-1997

## EPILEPSY

### When to scan and how to interpret the result

A couple of recent articles in the JNNP have served to remind us of the purpose and potential pitfalls of scanning patients with seizures. In the first of these, Wieshmann from the Walton Centre, Liverpool, retrospectively reviewed 495 scan results available from 919 outpatients seen in general neurology or specialist epilepsy clinics. The type of scan performed depended on the clinical presentation and suspected diagnosis, but overall was roughly equally divided between CT, MRI with 5mm slice width and MRI with 1.5mm slices. The results showed that about 18% of those with single seizures had a scan abnormality, and none of the patients with idiopathic generalised epilepsy (IGE) or non-epileptic attacks showed any abnormality (results roughly comparable to previous studies). Interestingly, about 40% of patients with IGE were none the less scanned, and potential reasons for this are discussed. The key learning point, however, was that even in this centre about 30% of patients with localisation-related epilepsy were not scanned. This is contrary to accepted guidelines, and important since in those that were scanned more than half the results were abnormal.

The second article by Alsaadi *et al* in California reminds us to cautiously interpret abnormal scans. They provide follow-up data on outcome after temporal lobe surgery on 15 patients with large non-neoplastic extra-temporal lesions on their scans. In only nine cases was hippocampal atrophy present. The surgery was performed on the basis of seizure semiology and EEG investigation both suggesting a temporal focus. All 6 of the patients with a large extra-temporal lesion but no hippocampal atrophy present on the MRI were improved by temporal surgery (without lesionectomy), four becoming completely seizure free. Overall nine of the 15 patients became seizure free, the other 6 gaining at least significant improvement. They remind us not to rush to conclusions on the basis of scan results, but to concentrate on the clinical assessment and other investigations since the abnormality seen on the scan may not be the seizure focus. These patients seem to do well without lesionectomy but with temporal surgery alone if this is felt to be the focus.

-AWM

*Clinical application of neuroimaging in epilepsy.*

Wieshmann UC.

JOURNAL OF NEUROLOGY, NEUROSURGERY AND PSYCHIATRY  
2003; 74; 466-470.

*Potentially misleading extratemporal lobe lesions in patients with temporal lobe epilepsy.*

Alsaadi TM, Bateman LM, Laxer KD, Barbaro NM, Austin EJ, Garcia PA  
JOURNAL OF NEUROLOGY, NEUROSURGERY AND PSYCHIATRY  
2003; 74 566-569.

## ☆☆☆ RECOMMENDED

### The anti-epileptic properties of nail varnish remover

Smell is of course the most potent stimulus to memory and this article about the anti-epileptic properties of acetone brought back vivid memories of my mother's nail varnish remover. I can hear all the male readers' Oedipal sighs of recognition.

The ketogenic diet has been used for refractory epilepsy for many years, especially in children. Its anti-epileptic properties are indisputable but the mechanism is unknown. This study was triggered by the observation that acetone levels are substantially elevated by the ketogenic diet. Dose-response tests were carried out in four rat models of epilepsy; maximal electroshock which models tonic seizures; subcutaneous PTZ test, a model of absence seizures; amygdala kindled seizures and a further model of atypical absences of Lennox Gastaut syndrome. Animals were then injected intraperitoneally with four different doses of acetone. In all four models acetone had a significant effect on seizures with a clear dose-response curve, and a potency similar to valproic acid, affording nearly 100% protection at the higher doses used. Cerebrospinal fluid acetone concentration paralleled the doses used.

This study provides evidence that acetone concentrations may be important in the anti-epileptic effect of the ketogenic diet. Patients should however be advised against illicit forays into their mother's make-up cabinets.

-MRAM

*Anticonvulsant properties of acetone, a brain ketone elevated by the ketogenic diet.*

Likhodi, SS, Serbanescu I, Cortez MA, Murphy P, Snead OC III, Burnham WM.

ANNALS OF NEUROLOGY  
2003;54:219-26.

### Autosomal dominant nocturnal frontal lobe epilepsy

ADNFLE is due to mutations of the nicotinic acetyl choline receptor and most sufferers respond well to carbamazepine. Leniger *et al* describe a new mutation with variable penetrance and a clear response to carbamazepine, shared by most patients with this condition. They expressed the ACh receptor in *Zenopus oocytes* and studied its electrophysiological characteristics. The mutant receptors showed no difference in the time-course of the current evoked by ACh but a marked increase in sensitivity to ACh. Suppression of ACh-evoked currents by carbamazepine was much greater in the mutant receptor preparation than in controls. This has been observed previously for other mutations and has been postulated to be an effect of the mutations on the sodium ion pore, affecting the binding properties of carbamazepine.

Varadkar *et al* describe 3 patients in one family whose ADNFLE was not responsive to a wide variety of anti-epileptic drugs, but eventually came under control with acetazolamide. When I worked with the group publishing this letter, we admitted a patient from abroad with nocturnal frontal lobe epilepsy characterised by curious attacks with singing at the onset. He is the only patient I have ever known to be controlled with acetazolamide monotherapy. ADNFLE had not been described at that stage but this article convinces me he suffered with the same condition. More important than the nostalgic meanderings of a time-expired reviewer is how this might relate to the mechanism of the mutation. Clearly something different is happening as these patients do not respond to carbamazepine. Perhaps this mutation inhibits carbamazepine binding but acetazolamide may indirectly affect sodium fluxes by its action on hydrogen ions. Its effect on ion channel disorders is well known. I await more frogs' eggs with interest. This is only the second form of rational prescribing in epilepsy that I know of. The other is ethosuximide for absence epilepsy, acting on T-type calcium channels in the thalamus, implicated in this condition. Both are of course genetic epilepsies, and are likely to have a purer mechanism than acquired epilepsy but they offer the hope that a magic bullet can be found for at least some of the epilepsies.

-MRAM

*A new Chrna4 mutation with low2 penetrance in nocturnal frontal lobe epilepsy.*

Leniger T, Kananura, C, Hufnagel A, Bertrand S, Bertrand D, Steinlein O.  
EPILEPSIA  
2000;44:981-5.

*Acetazolamide and autosomal dominant nocturnal frontal lobe epilepsy.*

Varadkar S, Duncan JS, Cross JH.  
EPILEPSIA  
2003;44:986-987.

## REHABILITATION

## ☆☆☆ RECOMMENDED

### Virtual sandwich making

Many patients recovering from head injury need to relearn kitchen skills. This can take a long time and teaching and supervising patient's practice in simple kitchen tasks is very labour intensive. Given the limited occupational therapy time available one way to provide more practice is to use a simulator. These days 3-D interactive images are used to train astronauts and surgeons to perform tricky procedures. Why not use them in rehabilitation of head injured subjects? Virtual reality kitchen environments offer the potential to allow patients to practice in the absence of a therapist and can provide information about performance to both the patient and therapist.

A group in the USA have developed software to create a virtual kitchen environment that can be used to make a virtual sandwich and prepare soup from a virtual can. The simulated environment was tested on 54 consecutive subjects with head injury and performance of virtual soup and sandwich preparation was compared with actual soup and sandwich making. Performance of both was assessed by scoring the time and errors observed in completing the task. In addition to the validity of the virtual meal preparation, the reliability of performance was assessed.

The virtual reality scores were found to be reproducible and consistent on repeat testing and the virtual kitchen task was found to be valid. When the groups' virtual reality performance was compared with actual kitchen performance a moderate and statistically significant correlation ( $r=0.63$ ) was found. In actual fact the patients' virtual performance scored higher than actual performance. The authors put forward a number of possible explanations for this: immersion in virtual reality could increase subject's attention; there could be more distractions in a real kitchen. It's also possible that most of the subjects being young were better at interacting with computer graphics than performing real kitchen tasks. There are a myriad of complex sensorimotor interactions involved in preparing a simple sandwich in a real kitchen with real food and kitchen tools and equipment. However despite the limitations in reality of the virtual reality kitchen the study showed it to be a promising tool for those who need practice in remembering the steps need to complete a simple kitchen task. There is at least one other advantage; virtual washing up is probably quicker than real.

-AJT  
*A virtual reality environment for evaluation of a daily living skill in brain injury rehabilitation.*

Zhang L, Abreu BC, Seale GS, Masel B, Christiansen CH, Ottenbacher KJ.  
ARCHIVES OF PHYSICAL MEDICINE AND REHABILITATION  
2003; 84: 1118-1124

## MOVEMENT DISORDER & SPASTICITY MEETINGS 2003-2004

**Dystonia in 2003** Saturday November 8th, 2003; Sheffield

**Management of the Advanced Parkinson's Disease Patient** Friday November 21st, 2003; Aintree

**Modern Management of Spasticity** Friday February 27th, 2003; Plymouth

**Advanced Management of Spasticity in the CP Child & Adult** Thursday 26th February, 2004; Edinburgh

*Each meeting is available to interested specialists at all levels, whether consultant, junior or specialist nurse.*

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