

## EDITOR'S CHOICE

## CHOREA

**Molecular mimicry in Sydenham's chorea**

The debate as to the exact mechanism underlying Sydenham's chorea is not known (see this issue page 19). However, the argument has always been that the streptococcal infection triggers antibodies which, by chance, also recognise components of the basal ganglia (so called "molecular mimicry" between host and pathogen). In this recent paper the identity of the offending antibody has been postulated to be against a mammalian lysoganglioside GM1 and N-acetyl- $\beta$ -D-glucosamine which is the dominant epitope of group A streptococcal carbohydrate. However whilst the exact identity of the neuronal epitope recognised by the anti-Streptococcal antibodies is not known, it is clear that these antibodies can bind to neuronal cells (in the form of a neuroblastoma cell line) and activate a calcium/calmodulin dependent kinase (CaM kinase II). How this effects the cellular function or causes the movement disorder and other features of Sydenham's chorea (and/or PANDAS) is not known, but does at least highlight how antibody mediated neurological disease may induce its effects. Thus about 320 years after its original description, Sydenham's chorea continues to generate new research and insight into autoimmune neurological disorders. -**RAB**

Kirvan CA, Swedo SE, Heuser JS, Cunningham MW.

*Mimicry and auto-antibody mediated neuronal cell signalling in Sydenham Chorea.*

NATURE MEDICINE

2003; 9: 914-920

**Benign hereditary chorea and the thyroid gland**

Benign hereditary chorea is an autosomal dominant condition where chorea starts young and progresses little during life. This paper, from Toronto, describes one affected family where chorea had been noted between 6 months and two years, and all were delayed in starting to walk between 2 and 5 years. In most cases there was some progression over time and FDG-PET on four affected members was normal. The report focuses on a mildly affected family member, who died at the age of 59 from leukaemia. At post-mortem, there was mild "fronto-parietal-temporal atrophy" (surely "cerebral atrophy" would have been a simple description!), and microscopically there was some non-specific astrogliosis. This form of chorea is associated with defects in the thyroid transcription factor 1 (TTF-1) gene and sure enough a novel mutation was found in this family, in part of the TTF-1 gene that is highly conserved. The predicted effect of the mutation is to shorten a loop in a stem-loop structure which would probably significantly inter-

fere with protein function.

TTF-1 is a transcription factor, exclusively expressed during embryogenesis and is important for the development of the thyroid gland, lung and pallidum. TTF-1 knockout mice die at birth and have loss of the normal cholinergic tract from pallidum to striatum. One phenotype in man, of a heterozygous mutation in TTF-1, has been described with congenital hypothyroidism, pulmonary abnormalities and choreoathetosis. -**AJC**

Kleiner-Fisman G, Rogaeva E, Halliday W, Houle S, Kawarai T, Sato C, Medeiros H, St George-Hyslop PH, Lang AE.

*Benign hereditary chorea: Clinical, genetic, and pathological findings.*

ANNALS OF NEUROLOGY

2003 Aug;54(2):244-7.

**Proliferating stem cells in Huntington's chorea?**

The role of neural stem cells in the repair of neurological disorders has been a hot topic in recent years, as has the ability of the endogenous neural precursor cell to repair acute CNS damage (see ACNR 2.5 page 25). However the response and role of these latter cells in chronic neurodegenerative conditions has been somewhat overlooked, even though exciting hypotheses in this area have been generated (see for example; Armstrong and Barker (2001) Lancet 358:1174-1176). However a recent paper by Richard Faull's group rectifies this issue by studying the proliferation of CNS cells in Huntington disease brains using the marker, PCNA (proliferating cell nuclear antigen) and double-labelling for markers of neuronal and glial differentiation. In this study they report that with disease progression there is an increase in cell proliferation which may imply increased neural precursor cell turnover and differentiation – an attempt by the degenerating brain to repair itself. This is clearly of great interest and has a number of important implications – not least how such a response is recruited and why it is ineffective in halting disease progression and expression. However, whilst this study shows cell proliferation in the degenerating HD brain, it does not convincingly show that these cells form surviving functional neurons. Indeed much of the proliferation may relate to the ongoing gliosis that is seen in advancing HD. Whatever the interpretation of the results as presented in this paper, this study is stimulating not only to the endogenous stem cell but conceptually to all those working on this and related neurodegenerative conditions. -**RAB**

Curtis MA, Penney EB, Pearson AG *et al.*

*Increased cell proliferation and neurogenesis in the adult human Huntington's disease brain.*

PNAS

2003; 100:9023-9027

**Genetic heterogeneity in Huntington's disease**

## ☆☆☆ RECOMMENDED

Most cases of Huntington's disease (HD) result from CAG trinucleotide repeat expansions in the important transcript 15 (IT15) gene on chromosome 4. However, a HD-like (HDL) phenotype may occur in the absence of such expansions. This study involved samples from 252 patients referred for IT15 gene testing which had proven negative. Sixty of the patients had been seen by movement disorder specialists and were clinically diagnosed as "typical" HD; less detailed clinical characterisation was available for the remaining 192 cases. Mutations were sought in other candidate genes: PRNP, encoding prion protein, an insertion in the octapeptide coding region of which has been associated with the HD phenotype in one family (HDL1); junctophilin-3 (HDL2); TBP, a TATA-binding protein, mutations in which have been identified in autosomal dominant cerebellar ataxia (SCA17); and DRPLA.

Two cases showed CTG repeat expansions in JPH3, both individuals were of African origin. Two cases showed CAG/CAA repeats in TBP, both of French origin. No CAG expansions in the DRPLA gene were identified and no insertions in the octapeptide coding region of the PRNP gene. All four patients with expansions were from the clinically typical HD group; no mutations were identified in the 192 other cases.

These findings indicate genetic heterogeneity in patients with the HD phenotype. Up to 6% of clinically "typical" HD patients without IT15 CAG expansions may harbour trinucleotide expansions in either TBP or JPH3. -**AJL**

Stevanin G, Fujigasaki H, Lebre A-S *et al.*

*Huntington's disease-like phenotype due to trinucleotide repeat expansions in the TBP and JPH3 genes.*

BRAIN

2003;126(7):1599-1603

**Panel of Reviewers**

**Roger Barker**, Honorary Consultant in Neurology, Cambridge Centre of Brain Repair

**Patrick F Chinnery**, Senior Lecturer in Neurogenetics and Honorary Consultant

Neurologist, University of Newcastle upon Tyne and Newcastle Hospitals NHS Trust

**Alasdair Coles**, Wellcome Advanced Fellow, Dunn School of Pathology, Oxford and Dept of Neurology, Cambridge

**Amanda Cox**, Research Registrar, Addenbrooke's Hospital, Cambridge

**Tom Foltynie**, Neurology Research Registrar, Cambridge

**Richard Hardie**, Consultant Neurologist and Director of Neurorehabilitation, Headley Court Medical Rehab Unit

**Tim Harrower**, SpR in Neurology, Addenbrooke's Hospital

**Lucy Anne Jones**, Research Associate (Cognitive Neuroscience)

**Andrew Lerner**, Consultant Neurologist, Walton Centre for Neurology & Neurosurgery, Liverpool

**Simon J G Lewis**, Honorary Clinical Research Fellow, Cambridge Centre for Brain Repair

**Mark Manford**, Consultant Neurologist, Addenbrooke's Hospital, Cambridge, and Bedford Hospital

**Peter Martin**, Consultant Neurologist, Addenbrooke's Hospital, Cambridge

**Brian McNamara**, Consultant Neurophysiologist, Cork, Ireland

**Wojtek Rakowicz**, SpR Neurology, National Hospital for Neurology and Neurosurgery, London

**Julian Ray**, Consultant Neurophysiologist, Addenbrooke's Hospital, Cambridge and Queen Elizabeth Hospital, Kings Lynn

**Robert Redfern**, Consultant Neurosurgeon, Morrision Hospital, Swansea.

**John Thorpe**, Consultant Neurologist, Addenbrooke's Hospital, Cambridge, and Peterborough

**Ailie Turton**, Research Fellow, Burden Neurological Institute, Bristol

**Andrew Worthington**, Brain Injury Rehabilitation Trust, Birmingham

For more information on joining our panel of reviewers,

E-Mail [AdvancesinCNR@aol.com](mailto:AdvancesinCNR@aol.com) or Tel. Rachael Hansford on

0131 477 2335.

# Journal Reviews

## MULTIPLE SCLEROSIS

### ☆☆☆ RECOMMENDED

#### Myelin antibodies and multiple sclerosis

Thomas Berger and his group in Innsbruck have long been interested in the presence of antibodies in the serum and CSF of patients with multiple sclerosis that react against myelin basic protein and myelin oligodendrocyte glycoprotein. Their research seems to have borne fruit in a clinical study that has made it into the *NEJM*.

A total of 103 patients were studied with a first demyelinating event and typical demyelinating lesions on an MRI brain scan as well as oligoclonal CSF bands. Such patients are likely to have a second demyelinating episode in the future and so become classified as clinically definite multiple sclerosis. In the fifty odd months of follow-up during this study, 65 patients had such a second episode. Of these, 56 (86%) had serum antibodies at presentation to MBP, MOG or both. In contrast, such antibodies were found in only 7 of the 38 (18%) people who did not convert to MS. It turns out that serum anti-MOG antibodies alone generate a relative risk of 32, compared to without antibodies, of developing MS; anti-MOG and anti-MBP antibodies together increase this to 76, but anti-MBP antibodies alone are not associated with an increased risk. The time to first relapse was much quicker for those with positive myelin antibodies (7-14 versus 45 months). At baseline, those patients with serum myelin antibodies had significantly greater numbers of enhancing MRI lesions, however in a Cox-proportional hazards model, the risk of developing MS was significantly associated with anti-myelin antibodies but not active MRI lesion load.

Fascinating results no doubt, and potentially of real usefulness in managing the patient with an isolated demyelinating syndrome. One quibble is that there were no illustrations of the immunoblot technique used to detect the anti-myelin antibodies. Interpretation of these blots is not always easy. In particular, it seems that positive immunoreactivity was judged by the naked eye. This probably ought to be validated by a more objective technique before taking these tests into the clinic. Biologically, we do not yet know whether these anti-myelin antibodies are pathogenic or whether they simply reflect increased tissue damage. Matters are further confused by the ideas of Michal Schwarz and others on the protective effects of anti-myelin antibodies. -AJC  
Berger T, Rubner P, Schautzer F, Egg R, Ulmer H, Mayringer I, Dilitz E, Deisenhammer F, Reindl M.

*Antimyelin antibodies as a predictor of clinically definite multiple sclerosis after a first demyelinating event.*

NEW ENGLAND JOURNAL OF MEDICINE

2003;349(2):139-45.

## EPILEPSY

### Anticonvulsants... like rabbits from a hat

With a bewildering array of drugs at our disposal, we like to think that with evidence-based practice, training and long clinical experience we can select exactly the right anti-epileptic drug to suit the patient sitting in front of us. Well think again! The authors studied 26 patients in an open-labelled trial of clobazam as first-line therapy over 24 weeks. Only 25 were available at follow-up, of whom 16 were seizure-free. The patients were not entirely typical of UK practice; 5 had ring-enhancing lesions on CT, presumably neurocysticercosis. These all became seizure-free but then these lesions may frequently spontaneously regress anyway. Two of four others with complex partial seizures were well controlled and both patients with juvenile myoclonic epilepsy were well controlled.

The dose of clobazam ranged from 20-80mg daily with a mean of 27mg. 16% of patients were sedated but generally not severe, although one suspects that the patient on 80mg was too fast asleep to complain. This is a small and short study and of course clobazam is particularly prone to habituation effects which may cause late relapse in a higher proportion of patients than more conventional monotherapy drugs. However, on the face of it this study shows remarkably similar efficacy to just about every other monotherapy study in the history of epilepsy – about 60% seizure-free and somewhat better at generalised than focal seizures. This supports Professor Martin Brodie's hypothesis that you could choose a drug from a hat and get more or less the same results in terms of efficacy. Don't tell that to the patients but perhaps the SANAD study will help us restore our mystique. -MRAM

Mehndiratta MM, Krishnamurthy, Rajesh KN, Singh G.  
*Clobazam monotherapy in drug naïve adult patients with epilepsy.*

SEIZURE

2003;12:226-228

## Photosensitivity & book covers

This is one of those papers drawing your attention with an impressive title verging on neurophilosophy. It then goes on to talk about "phase clustering analysis" (PCI), which is where the head nods, the lids become leaden and theta rhythms appear. But I must struggle on, this may be taking me one step closer to unlocking the meaning of life, the universe and everything. PCI is a term used by the authors to describe the degree of phase synchronisation of the different rhythms of the brain as measured by magnetoencephalography (MEG). The authors stimulated 10 patients with photosensitive epilepsy with stroboscopic stimuli at various frequencies, some of which did and some did not produce a pathological photoparoxysmal response (PPR). On the MEG, they found that gamma region (30-120Hz) harmonics of the stimulation frequency were particularly revealing. When photic stimulation did not produce a PPR the PCI was the same in the gamma region as in the fundamental frequency or in controls. Before a PPR occurred the index was increased, suggesting much greater synchronisation in the harmonics than in the fundamental frequency. The increase in PCI was 85% sensitive and 80% specific in predicting PPR. The changes were widespread and sensitivity was greatest with red and blue flashes, reflecting the greater potential of these stimuli to induce a PPR. Phase synchrony at higher frequencies has been postulated to be important in visual processing and the authors suggest that a loss of normal controls over this process may underlie the PPR.

The authors suggest that on a more practical level the predictive role of the PCI for PPR may be useful in diagnosis without exposing the patient to a risk of triggering a photic induced seizure. This would only be realistic if EEG rather than MEG could be used and the test is proven to have satisfactory sensitivity and specificity in less highly selected patients. So did the paper live up to the title? It certainly told me something I didn't know but I have learned never to buy novels with a picture of a pretty woman on the cover, I should transfer this knowledge to my academic reading. -MRAM

Parra J, Kalitzin SN, Iriarte J, Blanes W, Velis D, Lopes da Silva FH  
*Gamma-band phase clustering and photosensitivity: is there an underlying mechanism common to photosensitive epilepsy and visual perception.*

BRAIN

2003;136:1164-1172.



## Project Grants

Applications are invited for grants to a maximum of £60,000 to undertake basic or clinical research in the UK into the causes and treatment of epilepsy for a period of up to 3 years.

Requests for equipment up to £10,000 can also be submitted.

## Epilepsy Research Foundation Fellowship

Applications are also invited for the Epilepsy Research Foundation Fellowship. The Fellowship is for the personal support of young researchers entering the field, for example those undertaking a 3 year PhD or a 2 year MD. Candidates must be graduates in medicine or one of the allied sciences and should be resident in the UK. The research could be of either a clinical or laboratory nature.

For more information and an application pack please contact Mrs Camilla Young, Research & Information Executive, Epilepsy Research Foundation, PO Box 3004, London W4 4XT. Tel: 020 8995 4781. Applications have to be received by Friday 24th October.

For more information about The Foundation visit our website at [www.erf.org.uk](http://www.erf.org.uk) where, if you wish to be kept informed of our activities, you can register your interest in epilepsy research.

## PARKINSON'S DISEASE

## ★★★ RECOMMENDED

**Slow, slow, quick, quick, slow – auditory cues for walking with Parkinson's disease**

Walking is a major problem for people with Parkinson's disease (PD). They commonly experience difficulty with both temporal and spatial parameters of gait. They may freeze and have difficulty initiating walking or controlling speed; moving very slowly or having involuntary quickening of step, and they often walk with small steps. Therapists have often used extrinsic sensory cues such as lines or obstacles on the floor to help patients with PD to keep walking or to increase stride length. However these visual cues are restricted to therapy or home environment. Auditory cueing using a portable system offers the opportunity for widening the environment in which PD patients can walk. In a study reported in *Clinical Rehabilitation* patients were shown to modulate their cadence (number of steps per minute) with respect to the rate of beat supplied by a pocket sized digital metronome.

The cadence, velocity and stride length of eleven patients with early stage PD were recorded on an electronic walkway within a physiotherapy gym. The patients were all studied after taking their medication. They walked first at their preferred pace and then with the metronome set to 85%, 92.5%, 107.5% and 115% of the mean of preferred pace. The mean velocity and cadence increased relative to baseline values at cue rates of 107.5% and 115% of preferred pace cadence and decreased at the 85% cue rate. Stride length was not affected by the variations in cue rate.

This is a promising and simple aid for walking and as the authors point out, it will be interesting to see if benefits extend to more chronic patients and to environments outside the hospital. –AJT  
Howe TE, Cody FWJ, Ashton VJ, Oldham JA.

*Auditory cues can modify the gait of persons with early stage Parkinson's disease: a method for enhancing parkinsonian walking performance?*

CLINICAL REHABILITATION

2003; 17: 363-367

## COGNITION &amp; MOVEMENT

**Premier planning - an fMRI study**

The dorsal and dorsolateral prefrontal cortex are involved in solving problems requiring effort. These areas are implicated in higher executive processes, being involved in planning and utilising working memory to support complex tasks. The extent to which the areas are involved differs between individuals and in this functional Magnetic Resonance Imaging (fMRI) research, it is demonstrated that individuals who are better than others at solving an electronic "Tower of London" (TOL) planning task have different patterns of brain activation from those who are less effective.

Solving the TOL task involves mental manipulation and a number of other cognitive abilities including planning, working memory and attentional control to work out the most efficient way (minimum number of moves) to recreate a tower of coloured balls from distributed starting positions.

All eleven volunteers showed dorsolateral prefrontal cortex activation which was bilateral as well as other bilateral activations in the anterior and posterior cingulate and parietal regions. However, the six people who performed best on the task were found to have a more widely extended activation in the left dorsolateral prefrontal cortex. The five more standard performers (<70% correct) demonstrated a greater extent of anterior cingulate activation, an area whose function is still debated. It is speculated that differing patterns of dorsolateral prefrontal cortex activation reflect differences in "strategy selection" or "attentional capacity" across performers, and these notions would benefit from further investigation. Studying and comparing activation patterns in clinical populations where executive processes are challenged may help further delineate intact function. –LAJ

Cazalis F, Valabrègue R, Pèlègrini-Issac M, Asloun S, Robbins T W, Granon S

*Individual differences in prefrontal cortical activation on the Tower of London planning task: implication for effortful processing.*

EUROPEAN JOURNAL OF NEUROSCIENCE

2003; 17: 2219-2225

**Think yourself better**

The idea that imagining a motor task has physiological effects on the motor system has recently been demonstrated by a number of authors utilising transcranial magnetic stimulation (TMS). An increase in primary motor cortex excitability during imagery of target muscle contraction, for example, has been shown to decrease motor threshold and increase the amplitude of the motor evoked potential amplitude of the target muscle, compared to rest conditions. However, the relative contributions of supraspinal and spinal changes responsible for this behaviour remains unknown. This study from New Zealand not only supports the notion that the modulation is principally supraspinal, but the temporal effect is also comparable to the actual motor task. Eight subjects had TMS studies performed on 2 hand muscles (APB target muscle, ADM control muscle), whilst alternating randomly between three different conditions; rest, isometric contraction of their thenar muscles (pressing the thumb downwards onto a table), and motor imagery of the same contraction. Performance of the task was performed in time with a metronome (1Hz) allowing analysis division into 'on' and 'off' periods. In both active and imagined motor tasks an increase in MEP amplitude was observed and was significant only during the active 'on' phases ( $P<0.05$ ). The tentative conclusion is that motor imagery and

Web Browser

Web Address	Details
<b>PRODUCT INFORMATION</b> <a href="http://ambion.com">ambion.com</a>	<b>Ambion (Europe) Ltd:</b> The RNA resource from the RNA company. Information, research papers, developments, technologies, protocols, products, and manuals for RNA manipulations.
<a href="http://camb-labs.com">camb-labs.com</a>	<b>Cambridge Laboratories:</b> Information on our range of neurology products and useful backgrounders on various neurological disorders. Links to key neurological organisations and patient associations are provided.
<a href="http://vnstherapy.com/international">vnstherapy.com/international</a>	<b>Cyberonics Europe:</b> Up to date information on Vagus Nerve Stimulation Therapy - the effective and tolerable treatment for refractory epilepsy, includes clinician and patient resources plus contact details for Cyberonics.
<b>PUBLISHERS</b> <a href="http://dunitz.co.uk">dunitz.co.uk</a>	<b>Martin Dunitz Ltd:</b> Part of the Taylor & Francis Group, Martin Dunitz publishes top quality, high level medical books in areas such as cardiology, neurology, psychiatry, oncology and urology.
<a href="http://acnr.co.uk">acnr.co.uk</a>	<b>ACNR magazine:</b> Download free PDF's of articles past and present and link to other sites of interest.
<b>CONFERENCES</b> <a href="http://epdaconferences.org">epdaconferences.org</a>	<b>European Parkinson's Disease Association:</b> 5th European PD Association meeting.

**To list your web site in the Web Browser  
call Rachael on 0131 477 2335.**

## Journal Reviews

actual movement appear to modulate corticospinal activities in similar ways both temporally and spatially. Perhaps we should be using our imagination in neurorehabilitation. -JLR

Stinear SM and Byblow WD.

*Motor imagery of phasic thumb abduction temporally and spatially modulates corticospinal excitability.*

CLINICAL NEUROPHYSIOLOGY

2003; 114; 909-914

### ALZHEIMER'S DISEASE

#### ☆☆☆ RECOMMENDED

#### Alzheimer's disease: another possible CSF biomarker

Although clinical criteria for the diagnosis of Alzheimer's disease (AD) may achieve a sensitivity and specificity of around 80%, nonetheless the availability of additional biomarkers remains a research priority. Since there is evidence for a long preclinical phase in AD, which would seem the optimal time to initiate disease-modifying treatment, a biomarker for early diagnosis is particularly desirable.

Having previously demonstrated a decline in sulfatide (ST), a sulphated galactocerebroside of oligodendroglial origin, in AD grey and white matter in an autopsy study, investigators from the Memory and Aging Project at Washington University, St Louis, looked for this compound in CSF using electrospray ionization mass spectrometry. Two groups of volunteers were studied, those with incipient dementia (defined as CDR = 0.5, which probably corresponds to what others describe as "mild cognitive impairment"; n = 20) and normal individuals (CDR = 0; n = 19). A 40% decline in the absolute value of CSF ST was noted in the incipient dementia group, whereas phosphatidylinositol (PI) was unchanged; ST/PI ratio was accordingly lower in the CDR = 0.5 group, and this was statistically significant.

Encouraging as these data are, they will require corroboration. It will need to be shown that the changes are specific to AD, since the ST decline may reflect non-specific axonal damage and degeneration. Other CSF biomarkers for AD have been reported (such as reduced Ab; elevated tau; neuronal thread protein), but have not achieved widespread adoption into clinical practice. For the time being, the jury must be out on the utility of CSF ST as a biomarker for AD. -AJL

Han X, Fagan AM, Cheng H *et al.*

*Cerebrospinal fluid sulfatide is decreased in subjects with incipient dementia.*

ANNALS OF NEUROLOGY

2003;54(1):115-119

### VASCULITIS

#### Treating vasculitis

Cerebral vasculitis, often discussed at clinico-pathological conferences, is so rare that few neurologists are comfortable with its management. It

makes sense then to look at how physicians manage systemic vasculitides. Amazingly, the European Vasculitis Study Group has managed to perform an open randomised clinical trial on the maintenance treatment of 144 patients with ANCA-associated vasculitis (Wegener's granulomatosis and microscopic polyangiitis).

All patients were given oral cyclophosphamide (2mg/kg/day for most patients) and a reducing dose of prednisolone (starting at 1 mg/kg/day) for twelve weeks. They were then randomised to receive either continued cyclophosphamide or azathioprine (1.5mg/kg/day). At 12 months after starting treatment, all patients were put onto azathioprine. So the trial was, in effect, of the consequences of early switching from cyclophosphamide to azathioprine: would the benefit in terms of reduced exposure to cyclophosphamide's toxicity be at the cost of earlier return of vasculitis? There was no difference between the groups on any measure: relapse of vasculitis, an index of vasculitis damage, adverse events, renal function or inflammatory markers. -AJC

This all seems pretty clear: switch your vasculitis patients from cyclophosphamide to azathioprine at 12 weeks and they will be no better off. A truly helpful study.

Jayne D and the European Vasculitis Study Group.

*A randomised trial of maintenance therapy for vasculitis associated with antineutrophil cytoplasmic autoantibodies.*

NEW ENGLAND JOURNAL OF MEDICINE

2003;349(1):36-44.

### PAIN

#### GABA and your pain threshold

Ohara's group in San Francisco study pain in rats. They are particularly interested in the *rostral agranular insular cortex* (RAIC) which is one of the few cortical areas consistently activated by painful stimuli. Increasing the concentration of GABA in this area, using vigabatrin or genetic manipulation, resulted in analgesia of the rats' paws that was mediated by increased activity in descending spinal inhibitory pathways. This turns out to be mediated by RAIC neurons with GABA A receptors projecting to the locus coeruleus. On the other hand, RAIC GABA B neurons innervate the amygdala. Selective blockade of GABA B receptors resulted in ipsilateral hyperalgesia.

So the cerebral cortex contains pathways that raise or lower pain thresholds. It may be that chronic pain states are caused by activation of a pain-inducing circuit that includes the amygdala. Inhibiting the amygdala just might be a useful treatment. -AJC

Jasmin L, Rabkin SD, Granato A, Boudah A, Ohara PT.

*Analgesia and hyperalgesia from GABA-mediated modulation of the cerebral cortex.*

NATURE.

2003;424(6946):316-20.

## Complimentary Journals Reviewed

We would like to thank the following publishers who have provided us with complimentary review subscriptions to their journals. For subscription details please contact the relevant publisher direct.

#### Cerebrovascular Diseases, Neuroepidemiology, Neuroembryology

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. rmlacl@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