British Association for Cognitive Neuroscience (BACN) Conference

1-3 September, 2008; Swansea, UK.

View of Swansea Bay and the University Campus.

The annual conference of the British Association for Cognitive Neuroscience (BACN) was held from September 1st - 3rd at the University of Swansea (picture). The association is home to UK cognitive neuroscientists from a variety of backgrounds, ranging from psychophysiologists (BACN emerged from the British Psychophysiology Society) to those with a background in neuroimaging. The Association prides itself on the friendly and supportive atmosphere of its annual meetings and is particularly welcoming to scientists at the start of their career. International visitors this year travelled as far as from Taiwan and Kenya.

The first symposium was devoted to the auditory basis of language learning impairments, especially those associated with specific reading disability (SRD) and specific language impairment (SLI). Dr Halliday (UCL, Oxford) showed impaired auditory processing in SRD but preserved ERP evidence for auditory cortical maturation. Dr Baker (UCL) reported that ERP indices of delayed auditory processing in SLI were correlated with reduced basal ganglia grey matter density. Dr Hamalainen (Cambridge) reviewed behavioural and ERP studies of sound processing in SRD and concluded that deficits in sound onset perception were the most consistent deficit. A keynote from Prof Scott (UCL) reviewed recent progress in mapping brain networks for speech comprehension and their link to speech production. Of interest was the sensitivity of the left anterior temporal cortex to speech intelligibility and the involvement of a posterior superior temporal region to sensorimotor integration, which supports the notion of a dual stream model of speech perception.

They reported altered brain function (EEG) and slower speed of cognition but normal neurological functions in those children living above 3500m

The second symposium was dedicated to recent advances in cognitive neurophysiology (ERP and EEG). Representatives from major ERP system manufacturers demonstrated their newest developments, ranging from automated artefact correction methods (Gutberlet, Brain Products), low resolution electromagnetic tomography (van de Velde, ANT) to multimodal image registration and volume conductor models for EEG source localisation (Fuchs, Compumedics Neuroscan). The developers of Statistical Parametric Mapping (SPM) gave an introduction to Dynamic Causal Modelling (DCM), a novel SPM extension for hypothesis-driven exploration of electrophysiological and neuroimaging data (Kilner, UCL). The plenary talk by Prof Stam (Amsterdam) was dedicated to the emerging application of modern network theory to disruption of functional brain networks in human brain diseases such as Alzheimer's disease, schizophrenia and epilepsy.

Among the numerous high quality open-platform presentations, the study by Dr Hogan and colleagues (Southampton, UCL, Universities of Granada and Western Australia, Univalle and UPSA Bolivia) deserves a mention. They used modern cognitive neuroscience methods (psychometrics, ERP and EEG) in a large-scale field study in Bolivia to evaluate the adaptation of cognition to high-altitude living in infants and children. They reported altered brain function (EEG) and slower speed of cognition but normal neurological functions in those children living above 3500m.

This year's BACN conference was jointly organised with the Welsh Institute for Cognitive Neuroscience, which held its inaugural meeting in Swansea. Its symposia included advances in the cognitive neuroscience of memory. The plenary lecture was given by Dr Wilding (Cardiff) on ERP studies of memory retrieval. Of particular interest was also the report by Vann and colleagues (Cardiff, Bristol, Manchester) on a large cohort of patients with colloid cysts and variable degree of fornix and mamillary body damage which resulted in selective loss of memory recall with preservation of recognition abilities.

Torsten Baldeweg,
UCL Institute of Child Health,
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The next Annual meeting will be held from 21st-23rd September 2009 in London, at the UCL Institute of Child Health. Symposia will cover topics such as neural plasticity in cognition and advances in multimodal neuroimaging.
Those interested in hosting a symposium at this meeting should contact T.Baldeweg@ich.ucl.ac.uk

ABN Autumn Scientific Meeting
A fond farewell to biannual ABN meetings

10-12 September, 2008; Aviemore, UK.

Falling asleep on the outskirts of London and waking in the Scottish highlands on board the Caledonian Sleeper was a perfect start to the last 'old-style' ABN conference, held in the beautiful setting of Aviemore.

A stroke symposium reflected the current political importance of this area, and the increasing engagement of neurologists in stroke medicine. Dr Malcolm Macleod discussed the reasons for the failure of translation from successful treatments in animal models of stroke into clinical benefits in patients. He dramatically illustrated the impact of low power, lack of randomisation and blinding and failure to model co-morbidity in animal models. These problems, equally significant in animal models of neurodegeneration, suggest the need for radical changes in the approach to pre-clinical therapeutic studies. Dr Ed Littleton presented the results of an audit of the introduction of a 24 hour thrombolysis service. The audit found that paramedics and A&E triage nurses find it difficult to use the 'FAST' assessment system appropriately, and suggests that models of thrombolysis delivery need to be carefully designed to avoid negative impacts on neurology training.

The short scientific papers given by members were of consistently high quality. Dr J Jones presented three-year follow-up data from the trial of alteluzumab (Campath) in early active multiple sclerosis. A clear reduction in progression of disability in the treated group may herald an important breakthrough in MS treatment from the ongoing Phase III trials. Dr Sarosh Irani described the clinical features and natural history of sub-acute encephalopathy associated with NMDA receptor antibodies in a cohort of 31 patients. This syndrome appears to have a very distinctive phenotype. Presentation with psychiatric symptoms is followed by seizures, reduced conscious level, autonomic instability and movement disorder. Further studies of antibody levels in disease control groups will establish the specificity of the diagnostic assay.

The ABN medal was presented to Dr John Morgan-Hughes. He provided an inspiring overview of his scientific legacy, which is particularly remarkable for having been achieved whilst working as an NHS clinician in a small research group.

A highland banquet and celidh, as well as a mini-triathlon, allowed delegates to make the most of their time in Scotland. Despite looking forward to the new format of a five day annual conference, many will look back fondly on our last small and traditional ABN meeting.

Biba Stanton, ABN Trainees Committee Secretary, Royal Free Hampstead NHS Trust.

delegates at the ABN

The Association of British Neurologists' 2008 autumn meeting in Aviemore was followed by a unique sporting event. Some 23 members of the Association took part in the first ever 'ABN mini-triathlon', which benefitted from glorious sunshine, spectacular scenery and the stunning backdrop of the Cairngorm Mountains.

Competing over a 'modified super-sprint' distance, the entrants swam sixteen lengths of the hotel pool, before exiting the hotel past startled onlookers, to pick up their pre-hired mountain bikes from the car park. They then cycled over a 6.5 km course which included a fairly punishing uphill component, a short rocky technical section – which clearly favoured experienced mountain bikers - and a fast forest track back to the hotel for the cycle-run transition. A final 2.5km run through the woods of the Rothiemurchus estate returned the competitors to the finish line at the Hilton Coylumbridge.

The event was won by Dr Richard Davey, consultant neurologist in Wakefield with a time of 30 minutes 30 seconds. Dr Ursula Schultz from Oxford was a close second, arriving at the finish line some 58 seconds later. Entrants included a past President of the ABN, Professor Charles Warlow, who completed the entire course in a commendable 61 minutes. All the finishers were awarded a medal and a commemorative T-shirt.

Finishers of the Triathlon.

European Federation of Neurological Societies (12th Congress)

23-26 August, 2008; Madrid, Spain.

With the profusion of neurological congresses around the world, many dedicated to specialist and subspecialist interests, it is perhaps inevitable that a general neurological congress will not be the forum at which investigators will wish to announce startling new findings. It may be said that the emphasis is more on encouraging us, the foot soldiers of neurology, to retain the information which is already in the public domain, with any gain of new information being a bonus. Hence, the arena of focused workshops and satellite symposia, amongst which the following proved helpful to my waning cognitive powers of factual retention. The limitations of functional imaging in the trigemino-autonomic cephalalgias, showing activation of the neural pain matrix, were emphasized, prior to a 'stimulating' account of the possible place for neurostimulation in these conditions. One literature review has suggested >60% efficacy in chronic drug-resistant patients, but the drawbacks are many: weeks to months before improvement occurs, the risk of adverse effects from surgery, the generator or the electrodes, and the current absence of any double-blind studies (1 apparently ongoing in France). The latter will require homogeneous patient selection criteria, agreed assessment methods and long-term follow-up.

A lecture on advances in genetics in movement disorders demonstrated how these findings have increased understanding of disease pathogenesis, for example in Parkinson's disease, specifically in terms of mitochondrial dysfunction and misfolded protein toxicity. Parkin, PINK1, and DJ1 all encode proteins which normally protect neurones from oxidative stress and regulate mitochondrial morphology, whilst α-synuclein and LRRK2 proteins become misfolded and aggregate. The possible importance of autophagy, a constitutive lysosomal mechanism to protect neurones, was introduced: knockout of this process in animal models leads to neurodegeneration, which may be relevant in the rare Kufor-Rakeb disease.

Some conditions which are only occasionally seen in the general neurology clinic, and hence in congress symposia, made welcome appearances. A focused workshop on myotonic dystrophy covered the genetics of DM1, wherein the correlation between increased trinucleotide repeat size in the DMPK gene and disease severity does not necessarily permit accurate prognosis, with some families showing a variable phenotype despite the same number of repeats. Missed diagnosis of both DM1 and DM2 seems common because the presentation is often to other, non-neurological, specialties, in DM1 including ophthalmology, cardiology, O&G, and paediatrics, although neurologists are not immune from error, the differential diagnosis of DM2 encompassing inflammatory myopathies, mitochondrial myopathies, acid-maltase deficiency, FSH dystrophy, fibromyalgia and iatrogenic myopathy. In view of the systemic nature of DM1, a plea was made to rename the disorder as 'Batten-Gibb syndrome' since these individuals described the systemic features in 1909, the same year that Steinert emphasised the muscular problem which has formed the basis for disease nomenclature ever since.

Treatment of Friedreich's ataxia, hitherto entirely symptomatic, was the focus of a drug-company sponsored symposium. Idebenone may have effects on the cardiomyopathy and possibly also the neurological features. The increased understanding of disease pathogenesis, stemming from the identification of the underlying genetic mutations and the functional roles of frataxin, has prompted the possibility of disease-modifying treatment, for example with iron chelation.

As a medical student in the last century, I got interested in the possible viral pathogenesis of multiple sclerosis. The subject still lives, with a symposium on herpes viruses looking at their potential causative roles in MS (EBV, HHV6, VZV), Behçet's disease (HSV1), and Bell's palsy (HSV1). Furthermore, it has been noted that similar brain areas are injured in herpes simplex encephalitis and Alzheimer's disease, with anecdotal reports of HSV1 infection in dementia brains, and in vitro and in vivo evidence of increased Aβ production associated with HSV1. CSF PCR remains the gold standard for diagnosis of herpes simplex encephalitis, although may be negative if testing is very early or late in the disease course. The role of steroids remains uncertain, no randomised study having yet been performed, although a retrospective study (JNNP 2005;76:1544-9) found poor outcome in patients who did not receive steroids.

Amongst the more than 1500 scheduled poster presentations, I noted two describing parkinsonism of late onset in type 1 Gaucher's disease: this may apparently look identical to idiopathic Parkinson's disease. In a French national prospective study, nearly a quarter of the patients developed parkinsonism. For those seeking advances in the treatment of neurological disease, three posters looked at the use of prolonged-release ropinirole (PREPARED study) which seems to produce better symptom control and levodopa sparing in advanced PD than standard ropinirole (I have already had enquiries from a patient).

A careful study (double-blind, placebo-controlled, crossover) from Newcastle suggested a possible role for levetiracetam in the treatment of MS intention tremor, but I was less convinced by a report from elsewhere of transcranial magnetic stimulation for MS ataxia. A trial from Iran of rivastigmine for memory disorder in MS found equal improvement in both treatment and placebo-control arms of the study, perhaps inevitable in a brief (12-week) study; the severity of the pre-treatment impairments in the MS patients did not appear to be mentioned. In a case study from Greece, rituximab was reported to be useful in neuromyelitis optica, in agreement with a larger study from the Mayo Clinic now being published (Arch Neurol).

For those for whom all this activity was too much, and a brief snooze required at the back of one of the lectures rooms, solace was at hand in the form of a poster documenting 'Inspiration from dreams in neuroscience research', relevant to two Nobel Prize Winners, Otto Loewi and John Eccles. As a Nature paper from 2004 stated, sleep inspires insight!

The History of Medicine session focused on the work of Santiago Ramon y Cajal, describing how his painstaking studies using the Golgi stain allowed him to develop the neurone theory, in succession to the reticular theory of Golgi, wherein the neurone was viewed as an autonomous unit in contact but not in continuity with other neurones, an infinitely fragmented system. The history tour visited the old Hospital de San Carlos, where there are several atmospheric lecture theatres including the Aula Ramon y Cajal where he used to teach; there is also a garden dedicated to him and a statue, the latter somewhat solemn and linear. Another Spaniard, lesser known outside his own country, Pedro Lain Entralgo (1908-2001), formed the subject of Ivan Iniesta's lecture which reviewed many of the works of this medical historian, and to whom the final words of this review may be given: 'the history of medicine is memory at the service of hope'.

AJ Larner, Walton Centre for Neurology and Neurosurgery, Liverpool, UK.

WCTRIMS

17-20 September, 2008, Montreal, Canada.

As the biggest demyelination show in the world rolled into Quebec this September, Montreal struggled a little with the infrastructure required to support the hoards but her charm just about won through in the end. Despite its size, the meeting itself was a surprisingly modest affair. There were no scientific fireworks declared here, but WCTRIMS offered a nice review of the progress that has been made on several fronts over the past 12 months.

The teaching courses were popular and successful. It's a reflection of how far things have come in the past year that the advances in our understanding of aetiology; both in determining relevant environmental exposures, and even more strikingly the genetic contributors to susceptibility, are now part of "teaching" sessions rather than being trumpeted from on high as "key breakthroughs". It is also to the great credit of the investigators involved that the important lessons learned during the long struggle to reach this point have led to a sober and realistic view of how far we still have to go, and our ability to take those next steps.

In descriptive pathology, Esther Breij received a frosty reception from the audience in response to her inability to replicate the heterogeneity of the Luccinetti lesional classification system. 'Different selection criteria' was the uneasy but diplomatic conclusion. Perhaps MS is yet one disease? The great pathogenic debate of our times remains as an uneasy stand-off between the primary inflammatorists and the primary degenerates. However the debate as presented here meekly conceded the premise that inflammation drives the disease and resolved to a question of whether it primarily targets glia versus simultaneously targeting glia and neurons. Regardless, the more fundamental inflammatorists declaring MS to be a self-limiting disease may have overstepped the mark and were met by a gloriously Gallic non plussed response from the gathered audience. Happily, this response was also given to the other lot when their case was put forward. The Quebec charm may have contributed, or perhaps a communal sense was evidenced that descriptive pathology may still have the upper hand in declaring lesions that the MRI doctors miss, and the final say in taxonomy, but is fundamentally limited by its cross sectional approach. The natural historians can help, as can the therapists, but there was little news from either to further illuminate. The therapists tell us that Copaxone has now mirrored the BENEFIT, CHAMPS and ETOMS Trial results in delaying time to second event; and that the quest for oral DMTs is nearing a position of having something to say for itself, but the repair doctors still have nothing meaningful to offer to patients. For them (and I am one), achieving a more fundamental understanding of how remyelination occurs (and why it fails) remains the issue – there were no breakthroughs to be found in Montreal but steady progress in the roles of OPC guidance molecules, axo-glial interactions that contribute to axonal injury, and the metabolic microenvironment determinants of injury response.

The natural historians were not completely silent, telling us that while prognostication for the individual patient remains challenging, being non-white and young predicts a more severe early disease course. Interestingly, it seems that disease course is relatively stereotyped in both site and severity during the initial attacks; perhaps reflecting undiscovered genetic disease course modifiers. The Ebers group presented their evidence that the HLA DRB1*01 allele may have a beneficial effect on disease course through examination of allelic discordance in sib-pairs. This (admittedly limited) progress was briefly encouraging, however the mighty MSBase team were subsequently to confirm our worst suspicions that early disease is indeed the hardest for which to prognosticate, and that EDSS in the mid-ranges remains a lottery for the long-term outcome even at advanced disease duration time points. At least they were able to console us with news that (as we intuitively always suspected) patients who remain relatively free of disability, or who are heavily disabled at advanced disease durations, tend to remain as they are.

But with statements such as the last, one cannot get away from the limitations of our assessment measures. Poor responsiveness to real change 'at the ends of the ruler' used to measure that change might account for predictability in a fundamentally unpredictable disease. So are we any better, or will we be any better in the future at measuring our patients' disease burden? Not really is the conclusion from the evidence presented here. There are no new clinical tricks, and our MRI surrogates still present problems. Maria Pia Sormani tackled the problem by using clever statistics to bridge the clinico-radiological chasm; establishing 'ecological correlation' between accumulation of new T2 lesions and annualised relapse rates in the published trials, but concluding that we haven't yet reached the stage where 'causal correlation' can be established at an individual patient level. This leaves us in an interesting position where measuring T2 lesion load isn't pointless, but neither is it yet validated as clinically meaningful! The speaker's frustration was clear about the difficulties in advancing this work due to the possessiveness of investigators and companies over outcome data. Our intellectual isolationism means that replicating these promising initial efforts for atrophy measures is presently beyond even what the redoubtable Dr Sormani and her team can face. As an imaging footnote, the MR modalities embarrassingly still labelled as 'new' (MRS, MTR etc.) continue to search for their role as useful and interpretable endpoints. We will see.

In the absence of anything exciting to report, the therapists offered a fascinating meta-perspective on why there is nothing exciting to report – it seems that all the relapses have gone! The annualised relapse rate in placebo arms of DMT trials has fallen from around 0.8 in the pivotal studies to current levels of around 0.3. As a result, it has become hard in these difficult times to prove that our wonderful new treatments work, further compounded by the fact that those pesky ethicists won't let us use placebo arms anymore. So what is an MS researcher to do? The development of new 'platform' based study designs (where lengthy trials are performed to test the addition of novel vs placebo treatments onto existing best practice) seemed too sensible to ever catch on. The audience quietly reflected on the prospects of big Pharma accepting this vision for a brave new

world; regrettably we may have to waste a lot more time and money before desperation permits that kind of mature approach in developing better treatments for our patients.

Shamefully, cognitive dysfunction and rehabilitation remain the cinderella subjects of MS research. The relevant session was scheduled on the Saturday morning when most of the delegates had succumbed to fragility following a very fine Gala dinner the previous evening, opting instead to take refuge amongst Montreal's soothing diversions. A pity; if there was hope of new clinical endpoints that might take us forward, they were likeliest to be found here. Furthermore, those delegates who did attend found the draw of the competing "late breaking news" session too hard to resist. The last chance for fireworks went something like the following: regular high dose oral steroid courses further reduce relapse rates if you're still having them whilst on conventional DMT but are they not well tolerated (quel surprise), rituximab reduces MRI disease in PPMS but only if you have MRI disease to begin with, dosing with 40mg of Glatirimer Acetate is no better than 20mg and probably less well tolerated, phase III studies with anti-sense DNA molecules to silence VLA-4 will probably happen over the next 5-10 years, and that HHV-6A can induce a disease similar to MS in Marmosets.

Nevertheless, perhaps the real benefit of such an international gathering of MS professionals is to take an international view. A review of the current variation in availability of existing therapies was sobering. If "postcode prescribing" is problematic at a local level, the issue is compounded at an international level. Unsurprisingly, the rest of the world do not, and cannot, do as you do. On a purely immediate basis we could achieve much for the world's MS patients by addressing the global availability of existing therapies. As we heard here, the emerging generics are often more problematic than they might initially appear – being neither cheaper nor necessarily of equivalent safety and efficacy as their branded counterparts. WCTRIMS remains the only forum through which issues such as this can be highlighted and ultimately tackled.

Peter Connick
September 2008, Montreal, Canada.

PREVIEW Dementias 2009

February, 2009; London, UK.

The 11th national conference for all those working with patients suffering from dementia will be taking place in London in February next year. The 2-day conference, organised in association with the British Journal of Hospital Medicine, will give delegates a review and update on current developments in the dementias; in the fields of research, investigations, clinical care and service and policy issues.

The conference is aimed at all professionals involved with dementia, including old age psychiatrists, neurologists, geriatricians and physicians with an interest in the elderly; mental health service workers and team members, community nurses, hospital nurses and practice nurses.

Programme advisors Professor Tom Arie, CBE, Professor Emeritus of Health Care of the Elderly, University of Nottingham and Professor Alistair Burns Head of School of Psychiatry & Behavioural Sciences, Professor of Old Age Psychiatry, University of Manchester, have put together a programme of speakers from all over the country. Professor Arie and Professor Burns have worked together producing the programme for this national conference since the first conference took place in 1999.

The first day will begin with a key-note speech from Professor Ray Tallis, University of Manchester, looking at the philosophical aspects of dementia and consciousness. Following a range of talks on clinical topics, the day will conclude with a discussion on 'The best paper on dementias that I have read in the past year', with contributions from all speakers on day 1.

Professor Sube Banerjee, Professor of Mental Health and Ageing at the Institute of Psychiatry, London, will open the second day of the conference with a talk on the National Dementia Strategy: where are we now? Following talks on Psychotherapy and dementia and An overview of nursing care of people with dementia, Professor Roy Jones, Director of the Research Institute for the Care of Older People in Bath, will outline drugs which are currently in clinical trials, and look at the potential these may offer for future treatments.

In the afternoon of day 2, Professor Edzard Ernst, Laing Chair of Complementary Medicine from Peninsula Medical School, Exeter, will outline the place of complementary medicine in the treatment of patients with dementia, and then Professor Elaine Perry, Professor of Neurochemical Pathology, Institute for Ageing and Health, Newcastle University will talk about Plant power: the potential of phytotherapeuticals. These will be followed by a discussion of case histories and opinions on alternative treatments, which should make for an interesting debate.

The conference will provide participants with an update on ongoing clinical, research, organisational and policy developments that are taking place in the field of dementia, a forum to share and exchange views with eminent faculty speakers, a chance to look at progress in old age psychiatry and its service provision, and an update on the management of clinical conditions and practices associated with dementia, e.g. agitation and depression, as well as the chance to debate and discuss 'alternative therapies' for dementia.

Rebecca Linssen, Editor,
British Journal of Hospital Medicine.

For further information, or to book a place, go to www.mahealthcareevents.co.uk or phone 020 6501 6762