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ADVANCES IN CLINICAL NEUROSCIENCE & REHABILITATION

In this issue

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APO-go© Apomorphine hydrochloride
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Consult Summary of Product Characteristics before prescribing. **Uses** Treatment of motor fluctuations ("on-off" phenomena) in patients with Parkinson's disease which are not sufficiently controlled by oral anti-Parkinson medication. **Dosage and Administration** Apomorphine hydrochloride is administered subcutaneously either as an intermittent bolus injection or by continuous subcutaneous infusion. Its rapid onset (4-12 mins) and duration of action (about 1 hour) may prevent an "off" episode which is refractory to other treatments. Apomorphine should be initiated in the controlled environment of a specialist clinic. The patient should be supervised by a physician experienced in the treatment of Parkinson's disease (e.g. neurologist). Please refer to the Summary of Product Characteristics for full details before initiating therapy. Treatment with domperidone (typical dosage 20mg three times a day) before and during apomorphine HCl therapy is essential. The optimal dosage of apomorphine HCl has to be determined on an individual patient basis; individual bolus injections should not exceed 10mg and the total daily dose should not exceed 100mg. Do not use if the solution has turned green. The solution should be inspected visually prior to use. Only clear, colourless and particle free solution should be used. **Contraindications** Children and adolescents (up to 18 years of age). Known sensitivity to apomorphine or any other ingredients of the product. Respiratory depression, dementia, psychotic disease or hepatic insufficiency. Intermittent apomorphine HCl treatment is not suitable for patients who have an "on" response to levodopa which is marred by severe dyskinesia or dystonia. **Pregnancy and lactation** Apomorphine should not be used in pregnancy unless clearly necessary. 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Since apomorphine may produce hypotension, care should be exercised in patients with cardiac disease or who are taking vasoactive drugs, particularly when pre-existing postural hypotension is present. Neuropsychiatric disturbances are common in Parkinsonian patients. APO-go should be used with special caution in these patients. Apomorphine has been associated with somnolence and episodes of sudden sleep onset, particularly in patients with Parkinson's disease. Patients must be informed of this and advised to exercise caution whilst driving or operating machines during treatment with apomorphine. Haematology tests should be undertaken at regular intervals, as with levodopa, when given concomitantly with apomorphine. Patients should be regularly monitored for the development of impulse control disorders. 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Neuropyschiatric disturbances (including transient mild confusion and visual hallucinations) have occurred during apomorphine therapy and neuropsychiatric disturbances may be exacerbated by apomorphine. Positive Coombs' tests, haemolytic anaemia and thrombocytopenia have been reported in patients receiving apomorphine. Local and generalised rashes have been reported. Eosinophilia has occurred in only a few patients during treatment with apomorphine HCl. Patients treated with dopamine agonists, including apomorphine, have been reported as exhibiting signs of pathological gambling, increased libido and hypersexuality, compulsive spending or buying, binge eating or compulsive eating, (especially at high doses). Apomorphine is associated with somnolence. Yawning and breathing difficulties have been reported, as has peripheral oedema. Apomorphine has been associated with sudden sleep onset episodes. *Prescribers should consult the Summary of Product Characteristics in relation to other side effects* **Presentation and Basic NHS Cost** APO-go ampoules contain apomorphine hydrochloride 10mg/ml as follows: 20mg in 2ml – basic NHS cost £37.96 per carton of 5 ampoules. 50mg in 5ml – basic NHS cost £73.11 per carton of 5 ampoules. APO-go pens (disposable multiple dosage injector system) contain apomorphine hydrochloride 10mg/ml, as follows: 30mg in 3ml – basic NHS cost £123.91 per carton of 5 pens. APO-go Pre-filled syringes contain apomorphine hydrochloride 5mg/ml, as follows: 50mg in 10ml – basic NHS cost £73.11 per carton of 5 syringes. **Marketing Authorisation Numbers:** APO-go Ampoules: PL 04483/0072 APO-go Pens: PL 04483/0073 APO-go Pre filled syringes: PL 04483/0074 **Legal Category** POM **Date of last revision:** April 2015 For further information please contact: Britannia Pharmaceuticals, 200 Longwater Avenue, Green Park, READING, Berkshire, RG2 6GP

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The Academy of Medical Sciences announces new Fellows for 2015

ACNR's founding Editor, Professor Roger Barker, has been elected a Fellow of the Academy of Medical Sciences. He is Professor of Clinical Neuroscience and Honorary Consultant Neurologist, Addenbrooke's Hospital and Department of Clinical Neurosciences, Cambridge, UK. Professor Barker is one of 48 researchers from across the UK who have been recognised for their contribution to the advancement of medical science. Academy Fellows are elected for excellence in medical research, for innovative application of scientific knowledge or for their conspicuous service to healthcare. See the full list at http://www.acmedsci.ac.uk/more/news/new-fellows-2015/.

The 2015 Andrew Wilson Award

The 2015 Andrew Wilson award for services to people suffering from Restless Legs Syndrome (now known as the Willis-Ekbom disease) was presented to Professor K Ray Chaudhuri by Daragh Brogan, the Chief Executive of the only UK RLS charity, RLS;UK/Ekbom Society. Professor Chaudhuri set up the educational academic group RLS:UK with a multi disciplinary committee in 2000. He led several trials on RLS in the UK as well as setting up the only dedicated RLS clinic at Kings College and Kings College Hospital, London. Professor Chaudhuri also worked closely with Eileen Gill who ran a telephone advice service for RLS sufferers in the UK from the 1980's. Prof Chaudhuri's team with Dr Anna Sauerbier now offer a specific RLS remote advice service with a monthly telephone clinic service from Kings. Professor Chaudhuri is also leading a world first and UK based study addressing non motor symptoms of RLS and validating a RLS-non motor questionnaire in a NIHR portfolio adopted study.

Honour for Professor Hardy

Professor John Hardy, UCL Institute of Neurology, will be awarded this year's "Hartwig Piepenbrock-DZNE Prize" honouring his contributions to the study of Alzheimer's disease. The award ceremony will take place on World Alzheimer's Day, September 21, 2015, in Bonn, Germany. Professor Hardy has made ground-breaking findings on the molecular causes of this brain disorder. His discoveries provide the basis for therapeutic approaches and potential medicines. Every two years the "Hartwig Piepenbrock-DZNE Prize" honours outstanding contributions to the study of neurodegenerative diseases. The prize is endowed by the Piepenbrock Group. The winner is chosen by an international committee under the coordination of the DZNE.

Mike Zandi, Editor.

How can we help augment brain recovery after stroke or other brain injury effectively and with finite resources? The issues of dosage, intensity, timing and nature of neurorehabilitation are increasingly debated in the rehabilitation community. Nick Ward, Kate Kelly and Fran Brander from the National Hospital tackle these issues in the context of upper limb motor recovery after stroke in our first article, further introduced by David Werring. Robotic technologies hold great promise in enabling us to deliver effective therapies of sufficiently high intensity and dosage which otherwise would be difficult to provide. We still need significant financial investment to enable us to provide more with less.

In our second article, Seyed Sajjadi and Jeremy Brown from Cambridge provide a solid clinical approach to the assessment process in suspected dementia, focussing on the art of clinical examination. The authors provide a helpful discussion adjudicating the turf wars of currently available short cognitive screening tools. This theme is developed by Andrew Larner who writes on mirror symptoms and signs.

Roger Barker writes an account of Alastair Compston's Festschrift occasion in July this year, which was a hugely enjoyable celebration of a phenomenal career in clinical neuroscience. I, along with at least half of the current ACNR editorial board, have benefited immensely from having known DASC as a colleague and mentor over the years, and would like to add a personal thank you here.

Tom Isaacs of The Cure Parkinson's Trust reflects on receiving his own diagnosis of Parkinson's Disease age 26, and shares his method for developing a research charity which has been highly innovative and effective in taking novel potential therapies to clinical trial. Collaboration and strong patient-involvement are two of the secrets of success shared here.

Sophie Russell, Stuart Vernon and Emma Tallantyre of the Association of British Neurologists Trainees (ABNT) describe their own attempts to provide high dosage and intensity (and free) training in clinical neurology to junior medical training doctors through e-learning and mentorship programmes.

This issue ends with our usual reviews, including journal reviews by Roger Barker and a book review by Andrea Cavanna, and we hope you enjoy reading it.

Mike Zandi, Editor
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Editorial board and contributors

Mike Zandi is Co-Editor of ACNR, Senior Clinical Research Associate in the Department of Clinical Neurosciences, University of Cambridge, and Honorary Consultant Neurologist at Addenbrooke's Hospital and Cambridgeshire and Peterborough NHS Foundation Trust. He is working on psychiatric presentations of autoimmune encephalitis, and the development of clinical trials and biomarkers for NMDAR and other antibody-associated neuropsychiatric disorders.

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Roger Barker is Consulting Editor of ACNR, Professor of Clinical Neuroscience at the University of Cambridge and an Honorary Consultant in Neurology at The Cambridge Centre for Brain Repair. His main area of research is into neurodegenerative and movement disorders, in particular Parkinson's and Huntington's disease.

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CRIT/07/2015/368 Date of preparation: July 2015

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It is recommended to gradually decrease the dosage. *Elderly:* Doses of 10-20 mg daily. Treatment requires low initial doses and gradual dose increments under careful observation. *Children:* Children require low initial doses with gradual dose increments under careful observation. It is recommended that normally treatment should be started at 5mg daily. A maintenance dose of 0.3 to 1mg/kg body weight daily is usually sufficient. No dosage recommendations can be made in children under 6 years of age. ***Treatment of anxiety:*** Please refer to the SPC for information on dosage and administration. **Contra-Indications:** Patients with hypersensitivity to benzodiazepines or any of the excipients of clobazam; patients with any history of drug or alcohol dependence, myasthenia gravis, severe respiratory insufficiency, sleep apnoea syndrome, severe hepatic insufficiencies, the first trimester of pregnancy and in breast-feeding women. Clobazam must not be used in children between the ages of 6 months and 3 years, other than in exceptional cases for anticonvulsant treatment where there is a compelling indication. **Warnings and precautions:** Amnesia may occur with benzodiazepines. In case of loss or bereavement psychological adjustment may be inhibited by benzodiazepines. Use with extreme caution in patients with personality disorders, myasthenia gravis, spinal or cerebellar ataxia or sleep apnoea; chronic or acute severe respiratory insufficiency; impaired renal or hepatic function; reduce dose if necessary. Use of benzodiazepines may lead to the development of physical and psychological dependence therefore the duration of treatment should be as short as possible. Patients with rare hereditary problems of fructose intolerance should not take this medicine. Consult SPC for further information. **Interactions:** Clobazam may interact with antipsychotics (neuroleptics), hypnotics, anxiolytics/sedatives, antidepressant agents, narcotic analgesics, anticonvulsant drugs, anaesthetics and sedative antihistamines; lithium; alcohol; carbamazepine, muscle relaxants, analgesics and nitrous oxide. Drugs that inhibit the cytochrome P-450 enzyme (mono-oxygenase) system (eg cimetidine). Phenytoin and valproic acid - dosage of clobazam should be determined by monitoring the EEG and the plasma levels of the other drugs checked. **Fertility, Pregnancy and Lactation:** If prescribed to a woman of childbearing potential, she should be warned to contact her physician regarding discontinuation of the product if she intends to become pregnant or suspects that she is pregnant. If the product is administered during the late phase of pregnancy, or during labour at high doses, effects on the neonate such as hypothermia, hypotonia, moderate respiratory depression and difficulties in drinking "floppy infant syndrome", may occur, they may have developed physical dependence and may be at risk for developing postnatal withdrawal symptoms. Benzodiazepines are found in the breast milk and should not be given to breast feeding mothers. **Effects on ability to drive and use machines:** Sedation, amnesia, impaired concentration and impaired muscular function may adversely affect the ability to drive or to use machines. **Undesirable effects:** Clobazam may cause sedation, leading to fatigue and sleepiness, especially at the beginning of treatment and when higher doses are used. Drowsiness, dizziness or dryness of the mouth, constipation, loss of appetite, nausea, or a fine tremor of the fingers have been reported. These are more likely at the beginning of treatment and often disappear with continued treatment or a reduction in dose. Paradoxical reactions, such as restlessness, irritability, difficulty in sleeping, anxiety, delusion, nightmare, hallucinations or suicidal tendencies may occur, especially in elderly and in children. In this event, treatment with clobazam must be discontinued. Anterograde amnesia may occur, especially at higher dose levels. Amnesia effects may be associated with inappropriate behaviour. Clobazam may cause respiratory depression, especially if administered in high doses. Isolated cases of skin reactions, such as rashes or urticaria, slowing of reaction time, ataxia, confusion and headaches, disorders of articulation, unsteadiness of gait and other motor functions, visual disorders (eg, double vision), weight gain, or loss of libido may occur, particularly with high doses or in long-term treatment. These reactions are reversible. Pre-existing depression may be unmasked during benzodiazepine use. Tolerance and physical and/or psychic dependence may develop, especially during prolonged use. Discontinuation of the therapy may result in withdrawal or rebound phenomena. Abuse of benzodiazepines has been reported. When used as an adjuvant in the treatment of epilepsy, this preparation may in rare cases cause restlessness and muscle weakness. Consult SPC for further information. **Product Licence Number:** PL 00156/0322 (5 mg/5 ml), PL 00156/0323 (10 mg/5 ml). **Product Licence Holder:** Martindale Pharmaceuticals Ltd T/A Martindale Pharma, Bampton Road, Harold Hill, Essex RM3 8UG. **Basic NHS Price:** £90.00 (5 mg/5 ml); £95.00 (10mg/5ml). **Legal Category:** POM. Further information: Martindale Pharma, Bampton Road, Romford, RM3 8UG. Tel: 01277266600. **Date of Preparation:** July 2015.

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1. Tapclob 5mg/5ml Summary of Product Characteristics and Tapclob 10mg/5ml Summary of Product Characteristics. Available at https://www.medicines.org.uk/emc /
2. MHRA. Antiepileptic drugs: new advice on switching between different manufacturers' products for a particular drug. Letter to healthcare professionals from the Commission on Human Medicines November 2013.

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Nick S Ward, MBBS BSc MD FRCP,
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Introduction to the ACNR Stroke Series

Upper limb impairment is one of the most important challenges for clinicians, researchers and stroke survivors. Improving outcomes is a key goal. In this next article in our stroke series, Nick Ward, Kate Kelly and Fran Brandner – from the innovative Queen Square specialist upper limb clinic team - offer a clear and concise summary of recent developments and promising new directions. They make a strong case for increasing the amount and intensity of neurorehabilitation, as well as outlining new approaches to augment the response to interventions. This article reminds us of the importance of working as a multidisciplinary team in stroke neurorehabilitation, and of the challenges in translating neuroscience findings to pragmatic and effective treatments.

David Werring, Reader in Clinical Neurology, UCL Institute of Neurology, National Hospital for Neurology and Neurosurgery, Queen Square, WC1N 3BG.

The future of stroke rehabilitation: upper limb recovery

The impact of stroke-related impairment around the world remains high.[1] In particular, residual upper limb dysfunction after stroke is a major clinical, economic and societal problem. In the UK alone, the economic burden of stroke is estimated at over £5 billion a year and so improving outcomes after stroke is an important clinical and scientific goal. Nearly three-quarters of stroke survivors experience upper limb symptoms after acute stroke and in the first six months only 20% or so achieve some functional recovery.[2,3] Management of the upper limb after stroke can be complex, requiring approaches that avoid complications, promote recovery and provide compensatory strategies in varying combinations depending on severity and time post-stroke.[1]

The wrong dose of rehabilitation?

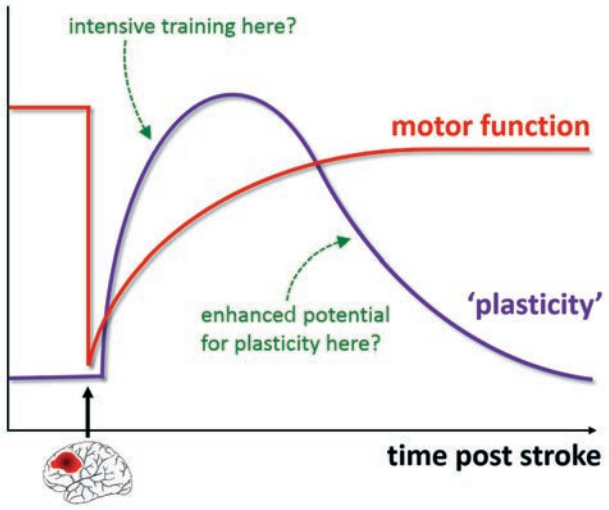
There is concern that the dose and intensity of upper limb rehabilitation after stroke is too low. During early inpatient rehabilitation, the time spent engaged in activities, especially functional upper limb movements, is surprisingly low.[4,5] Several studies have examined whether increasing the time spent on upper limb therapy makes a difference. For example, an additional two to three hours of arm training a day for six weeks reduced impairment and improved function by clinically meaningful amounts when started one to two months after stroke,[6] but anything less than this does not appear to provide much benefit on average.[7,8] It seems likely that when it comes to upper limb therapy, more is better.

However, the intensity (amount of activity), as well as the overall dose (time spent in therapy) is important. Data from work in rodent models of stroke suggest that changes in synaptic density (a marker of the neuroplastic reorganisation that is the substrate for recovery) in the primary motor cortex occur after hundreds but not tens of repetition.[9] In human stroke patients, the typical number of repetitions in a therapy session can be much lower.[4] It may be the case that there is a threshold of activity below which the neuroplastic reorganisation of surviving motor networks supporting recovery is unlikely to occur.[10]

How to increase the dose of rehabilitation?

One way of increasing dose is to implement a treatment programme that patients can administer themselves. The self-administered 'graded repetitive arm supplementary program' (GRASP) has the advantage of being flexible enough to use in patients with a range of impairments. When started early after stroke in an in-patient setting, four weeks of GRASP led to improvements in upper limb function compared to patients undergoing an education programme. These gains were maintained at five months post-stroke. GRASP is easy to administer, cost-effective and feasible to implement in a number of health care settings on a large scale.[12]

Constraint-induced movement therapy (CIMT) also increases the dose of functionally relevant training. Patients are required to wear a sling or mitten restricting use of the unaffected upper limb resulting in increased use of the affected hand/arm in functional tasks. CIMT led to improvements in the performance of functional tasks compared to standard (less intense) treatment.[13] Despite its apparent simplicity, it is not always tolerated well if worn for six hours per



A change in the potential for experience dependent plasticity after stroke has implications for (i) when intensive neurorehabilitation training should be delivered and (ii) when 'plasticity-enhancing' interventions might be used.

day (standard protocol) and so modified protocols have been used, although less well studied.

The use of robotic technology in guiding highly specific training regimes might also allow a sufficient number of repetitions to be delivered in a motivating environment. Some devices allow weight support of the arm, so that skilled movements can be practiced even in the presence of significant shoulder weakness. Most clinical trials have been small and have involved chronic stroke patients. Two relatively large studies of upper limb robotic training in chronic stroke patients have recently been carried out.[14,15] Both achieved high numbers of repetitions but only improved impairment by a few points compared to usual (less intense) therapy, and results were not greatly different to standard therapy matched for dose. It is likely that robotics and other technology such as virtual-reality based rehabilitation will find use as adjunctive therapy, rather than replacement for hands-on therapy. In other words, technological solutions provide a way of providing massed practice, but hands-on therapy is crucial for turning benefits into functional gains. Advances in devices that can be used and monitored in a patient's own home will also be required before technological approaches to neurorehabilitation have a substantial impact.

What is the best time for neurorehabilitation?

One of the interesting things about stroke is the response to focal injury in the brain. There is evidence from animal models that a number of changes at molecular, cellular and systems levels reflect an upregulation of the potential for experience-dependent plasticity.[16] In particular, (i) widespread activation of genes normally seen during development and (ii) shifts in cortical excitability that support long-term potentiation and cortical map reorganisation. These changes probably support what has been termed 'spontaneous biological recovery' which refers to rapid, generalised improvement in impairment in the first few months after stroke and is in contrast to modest gains made in the chronic phase.[17] Limited evidence suggests the same critical window exists after stroke in humans. If so, this would provide a compelling reason to deliver the highest dose and intensity of neurorehabilitation in the first few weeks and months after stoke in order to effect the biggest improvement in the widest range of functional tasks (figure). Concerns over very early (within 24 hours) neurorehabilitation persist,[18] but early assessment and planning should start as early as possible, taking each patient's clinical status into consideration. Understanding the mechanisms underlying spontaneous biological recovery could provide novel therapeutic targets with the goal of enhancing, prolonging or even re-opening the critical period during which spontaneous biological recovery is most likely.

Enhancing plasticity

Training works through mechanisms of experience-dependent plasticity,[16] and there is now interest in enhancing the potential for plasticity to increase the efficacy of motor-skills training after stroke. A key determinant of the potential for plasticity in adults is the balance between cortical inhibition and excitation.[19] Reduced GABAergic-inhibition and/or enhanced glutamatergic-excitation can enhance long-term potentiation and facilitate downstream changes in neuronal structure, allowing remapping of sensorimotor functions to surviving cortical regions.[16] Knowing the profile of these longitudinal changes is crucial because it will impact on plasticity-mediated recovery, influence when training is best delivered and when plasticity-enhancement might be attempted.[20]

Several approaches to plasticity-enhancement for promoting the effects of training are of interest in stroke, including neuropharmacological and non-invasive brain stimulation (NIBS). These approaches and others, including mental imagery, action observation, bilateral movements, somatosensory stimulation and aerobic exercise, might be thought of as ways of 'priming' the brain (and specifically the motor cortex) just prior to more specific motor training.[21] Whilst brain stimulation has yet to repay early enthusiasm based on small studies, the neuropharmacological approach holds more realistic promise. The interest in selective serotonin reuptake inhibitors in promoting motor recovery after stroke is highlighted by the FLAME study[22] in which fluoxetine 20mg daily, started five to ten days after ischaemic stroke and continued for three months, enhanced upper limb motor recovery at three months. Dopamine-agonists are also currently under investigation in RCTs.[23] However, the implementation of strategies for post-stroke plasticity-enhancement in phase III trials lacks clear mechanistic rationale and is therefore premature. Without understanding 'who' and 'when' to treat based on mechanistic approaches, these trials are unlikely to succeed in delivering novel treatments into routine clinical practice.[24]

Summary

Management of the upper limb after stroke can be complex. At present the dose of upper limb neurorehabilitation is too low. Here we have outlined the rationale and approach for increasing both dose and intensity of treatment. Novel approaches to enhancing the potential for experience dependent plasticity may be available soon, if the required level of evidence comes from appropriately stratified clinical trials. Despite these potential advances, it is important to remember that reduced impairment needs to translate into functional improvements in everyday tasks, and that ongoing home based exercise or therapy programmes need to be embedded in self-management programmes[25] if patients are to truly benefit.

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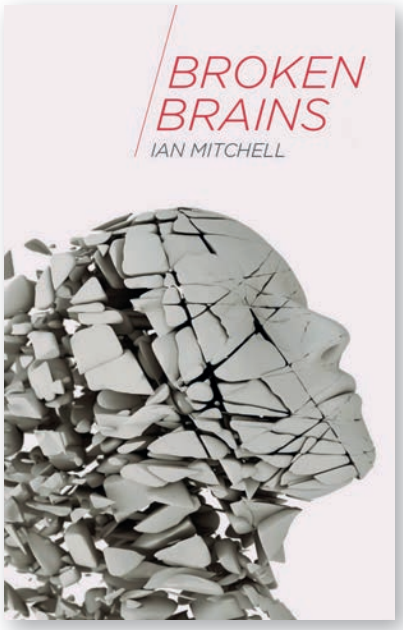
Broken Brains

Author: Ian Mitchell. **ISBN:** 9781137366832. **Published by:** Palgrave MacMillan. **Price:** £17.99. **Pages:** 248

Reviewed by: Andrea E Cavanna, Consultant in Behavioural Neurology, Department of Neuropsychiatry, BSMHFT and University of Birmingham, UK.



Conversing with Hippocrates on the brain

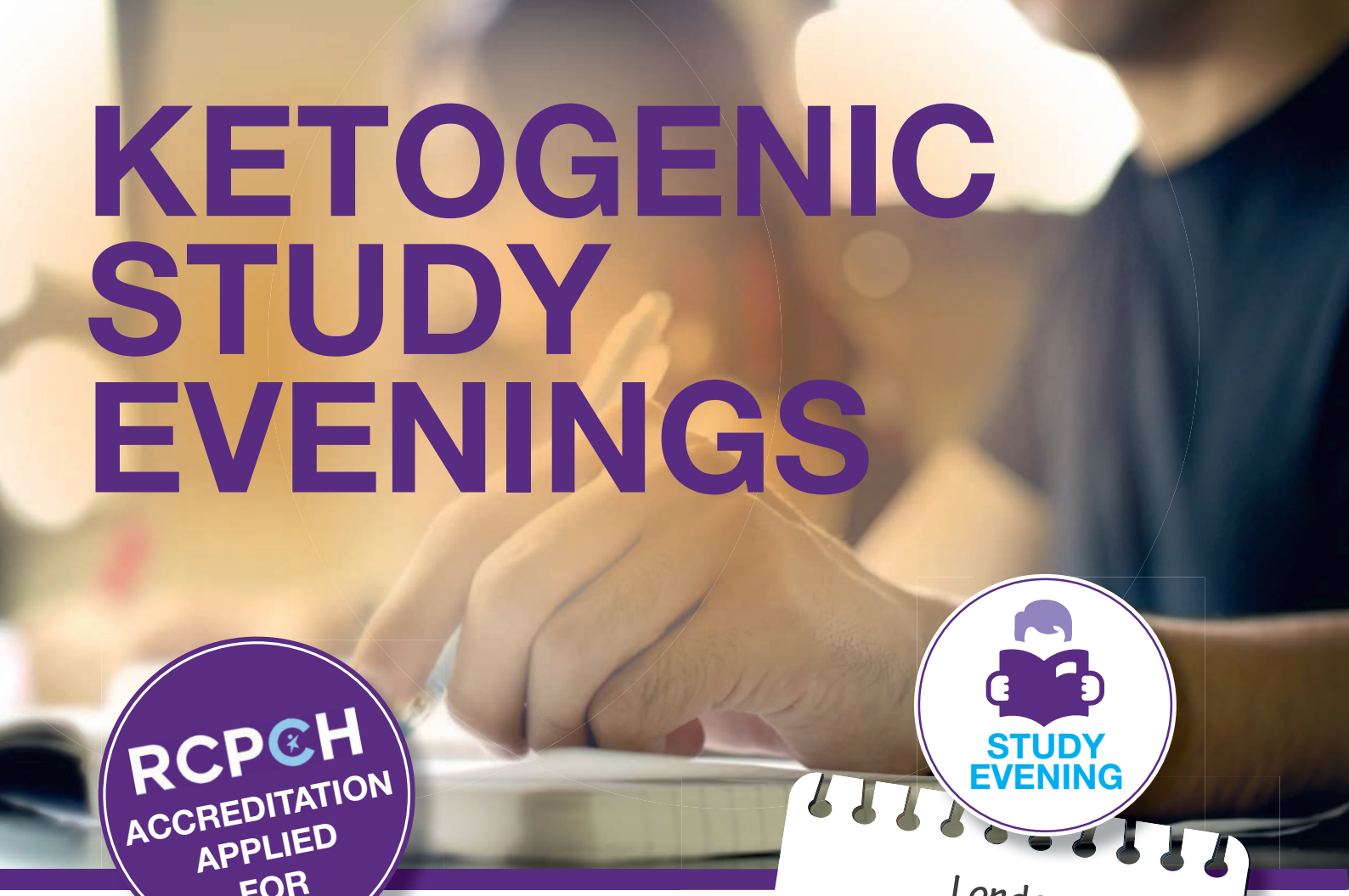
It is not often that you meet an eminent author who invites you to join him for tea and biscuits and then regales you with an exceptionally interesting and intimate conversation about the mysteries of the brain. This is what *Broken Brains* feels like to its readers – a real treat for anyone who shares the author's interests in Neuroscience.

Ian Mitchell is Senior Lecturer in the School of Psychology at the University of Birmingham with a genuine passion for the brain. He has published extensively on a range of brain-related topics, including the neurobiology of Parkinson's disease and psychopathy, programmed cell death and social cognition. This original book encompasses a number of puzzling conditions which illustrate brain function in health and disease, while maintaining both the overview and the reductionist viewpoint of modern neuroscience. Its underlying philosophy is projected to future advances in the brain sciences without neglecting the most valuable lessons of the past. Indeed, echoes of early Hippocratic writings resound on many of its pages: "And men ought to know that from nothing else but from the brain come joys, delights, laughter and sports, and sorrows, griefs, despondency, and lamentations. And by this, in a special manner, we acquire wisdom and knowledge, and see and hear, and know […] what are bad and what are good, what are sweet, and what unsavoury [...] And by the same organ we become mad and delirious, and fears and terrors assail us [...] All these things we endure from the brain, when it is not healthy". Just like his illustrious predecessor, Ian Mitchell masters the art of writing in a succinct and accessible way, without sacrificing scientific rigour. His narrative style is informative and entertaining, filled with engaging personal anecdotes from his wife's experience as a renowned neurosurgeon and his own early career as an accomplished researcher.

The main goal of *Broken Brains* is to introduce readers to the consequences for our behaviour and personality when brain circuits break down. This is achieved by means of a grand tour through neuropsychiatric disorders familiar to the author, including Parkinson disease, Tourette syndrome, depression and psychopathy.

A few features of the book deserve special mention. Each of the twelve chapters is closed by an up-to-date commented list of references, which often includes websites where readers can find more introductory material on the topic. Among the recommended websites there are links to the most popular and entertaining TED talks, thus making the reading experience truly engaging and interactive. Clear summaries inform the reader of what to expect in each chapter, whilst informative diagrams and box texts effectively illustrate the more challenging concepts. These are always interspersed with narrative entertainment, to ensure that learning about the secrets of the brain becomes a memorable and pleasurable experience. Finally, the glossary included at the end of the book is a useful appendix for readers who, despite lacking a professional background in neuroscience, could not resist the fascination of the brain.

As the author explicitly states, *Broken Brains* is primarily intended for university students beginning their studies in Psychology, Neurobiology, Medicine and allied disciplines. However, the book's non-technical style makes it accessible and of interest to sixth formers, as well as the larger public.



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Clinical assessment of patients with dementia

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There has been a great increase in interest in the clinical assessment of dementia and in particular in the early diagnosis of dementia in the last few years. We present a method for assessment of patients with cognitive problems based on our experience in the Cambridge memory clinic and teaching on the Cambridge Dementia Course. There have been great advances in the use of neuroimaging and other biomarkers in the diagnosis of dementia but the diagnosis of dementia remains a clinical one based on the clinical assessment of the patient.

Assessing cognitive function requires 4 stages:

1. History from the patient
2. History from a reliable informant (usually taken separately)
3. Physical examination of the patient
4. Cognitive examination of the patient

In reality, there is always some mixing up of these stages. The detail and responses to questions in the patient's history provides an informal assessment of their memory. Language problems often become apparent as the patient speaks.

1. History from the patient

Because many patients with dementia have reduced insight, it is often difficult to establish the usual features of a neurological history such as the onset of problems and progression, and the informant interview is often more informative.

Important parts of the history include:

- A brief autobiographical sketch, including maximum educational achievement and work history, provides an estimate of their premorbid cognitive abilities. This knowledge is helpful in tailoring subsequent autobiographical interview for assessing their episodic memory.
- Past medical and psychiatric history may provide useful information. For instance, if the patient has atherosclerosis or major psychiatric disease this influences the differential diagnosis.
- Many medications prescribed for the elderly including beta blockers, sodium valproate, and amitriptyline can cause cognitive problems which are often reversible.
- Alcohol consumption is sometimes minimalised or hidden.
- A family history of dementia will be common in any individual coming from a long-lived pedigree but a history of onset of Alzheimer's disease (AD) at an age younger than 60 years or behavioural variant Frontotemporal dementia (FTD) in a first degree relative is likely to be significant.

2. History from an informant

The importance of the informant's account cannot be over emphasised, not only due to the effect of possible cognitive impairment on the patient's recollection of the relevant parts of the history but also on their insight into their current problems. Often organic cognitive problems are suspected when the patient's relative is more concerned, whereas a worried patient and a less concerned informant would normally be associated with "worried well" patients. Self-repetition and repeated questioning are the hallmarks of the episodic memory impairment seen in AD. Tactless remarks, loss of empathy, and sweet tooth are features commonly volunteered by the relatives of behavioural FTD sufferers. Features of REM sleep behavior disorders are frequently noticed by partners of patients with dementia with Lewy body (DLB).

3. Physical Examination

Routine physical examination is normal in most patients presenting with dementia. There are sometimes important signs. Some such as papilloedema or a visual field defect will change the differential diagnosis dramatically making a cerebral tumour much more likely. More often in a memory clinic, parkinsonian features will support a diagnosis of dementia with Lewy Body, an apraxic gait would suggest a vascular or mixed dementia, supranuclear gaze palsy would suggest progressive supranuclear palsy or a related condition or a cortical sensory loss would suggest corticobasal syndrome.

Some unconventional signs can be helpful: the "Head turn sign" is a useful feature seen in organic amnesia and denotes the patient's reliance on their partner during consultation. Patients with visuospatial problems or "truncal" apraxia may have difficulty navigating to their seat and sit on it askew.

4. Cognitive Examination

4.1. Short Cognitive Tests (SCTs)

Over the years, many SCTs have been developed. It is crucial to remember that they are aids to the examination of the patient, not diagnostic tests. If time is no object then the Addenbrooke's Cognitive Examination version 3 (ACE-III) allows a relatively full assessment of the patient and is the test of choice in most memory clinics. The Mini mental state examination (MMSE), despite its many limitations, remains popular but is now restricted by copyright. The Montreal Cognitive Assessment (MoCA) and Test Your Memory (TYM) are more recent innovations which have clear advantages over the MMSE and are quicker to administer than the ACE-III. These are all multi-domain tests which assess several cognitive skills. Other tests such as abbreviated mental test score (AMTS) and GP assessment of cognition (GPcog) are much more limited in scope and whilst widely recommended, are too brief to allow a proper assessment of a patient's cognition. There is no one test that is universally appropriate for all settings

Table 1: Popular global cognitive assessment tools

Test	Description (cut-off point for dementia)	Advantage	Disadvantage
AMTS[1]	Brief 10 item assessment tool (6-8/10)	Short screening tool for identification of cognitive problems, easy to use on general medical wards and in primary care setting	Insufficient for more detailed assessment of cognition
MMSE[2]	Scored out of 30, The most widely used cognitive assessment tool (24/30)	Widely recognised test, objective scoring criteria, brief	Over reliance on verbal cognitive function, not able to detect cognitive impairment in non-Alzheimer dementia, not sensitive to mild cognitive impairment, copy right restrictions apply
MOCA[3]	Scored out of 30, aimed at detection of MCI, takes about 10 minutes to complete (26/30)	Relatively comprehensive albeit brief assessment tool, not biased towards particular cognitive domain	Not suitable for patients at the more advanced stages of dementia
TYM[4]	Scored out of 50, can be self-administered	Sensitive tool for detection of Alzheimer's disease, clear margin between the scores of patients and controls, freely available	Not suitable for detection of MCI
ACE[5]	Scored out of 100, ACE-III is the most recent version of the test (82-88/100)	Robust validation in various neurodegenerative conditions, appropriate for longitudinal studies, sensitive to subtle cognitive impairment and diagnosis of less common forms of dementia	Not particularly sensitive to behavioural impairments and executive dysfunction
CERAD-NP	Comprising 6 tests: MMSE, VF, BNT, VLM, CP, WLR, WLR-c	Good combination of tests to detect AD and MCI with pathologically confirmed disease in the studied subjects	Insensitive to executive function deficits and behavioural impairment, not accessible free of charge, variable scoring systems with no universally agreed total score
DRS-2[6]	Comprising 24 subtests in five categories of attention, memory, conceptualisation, construction, initiation/perseveration; maximum score 144	Varied combination of tests to assess different cognitive domains	Time consuming, not suitable for assessments with time constraint
ADAS-Cog[7]	Consists of 11 tasks measuring the disturbances of memory, language, praxis, attention and other cognitive abilities	Widely used in clinical trials	Not useful in non-Alzheimer's dementia, subjective scoring with no quantitative criteria
Functional scales			
CDR[8]	Numeric scale used to quantify the severity of symptoms of dementia (0: none, 3: severe) based on the clinicians assessment of 6 cognitive domains	Provides a global measure for the degree of cognitive impairment, good inter-rater agreement demonstrated in previous studies of AD patients	Time consuming to conduct the assessment, insensitive to longitudinal change, utility for non-Alzheimer's dementia is not established
Bristol activities of daily living scale[9]	Carer filled assessment, 20 items covering common aspects of daily life	Provides a dementia specific measure of functional impairment, sensitive to longitudinal change	Not suitable for patients at the early stages of dementia

Abbreviations: AD: Alzheimer's disease, MCI: minimal cognitive impairment, AMTS: abbreviated mental test score; MMSE: mini mental state examination; MOCA: the Montreal cognitive assessment; TYM: test your memory, ACE-R: Addenbrooke's cognitive examination-revised, CERAD-NP: consortium to establish a registry for Alzheimer disease-neuropsychological battery, VF: verbal fluency, BNT: modified Boston naming Test, WLM: word list memory, WLR: word list recall, WLRc: word list recognition, CP: constructional praxis, CR: constructional recall, DRS: dementia rating scale-second version; ADAS-cog: Alzheimer's disease assessment scale-cognitive subscale, CDR: clinical dementia rating

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and even for each given situation, different tools have their own weaknesses and benefits. Table one provides a summary of the most popular assessment tools and their main pros and cons.

The combination of an experienced clinician's assessment and a poor score on a short cognitive test is usually sufficient to diagnose dementia. Some patients, however, need a more thorough assessment.

4.2. Problem oriented cognitive assessment

The symptoms mentioned by the patients or their informants during history taking provide diagnostic clues. It is worth remembering that symptomatology in this context has anatomical but not pathological importance as symptoms reflect the involved areas of the brain as opposed to the presumed pathology affecting those areas.

4.2.1. Attention and orientation:

Preserved attention and orientation is a prerequisite for normal cognitive function and impaired orientation is a hallmark of delirium.

– 4.2.1.1 Orientation: Time and place orientation are useful clinically; in AD orientation for time is lost before orientation to place. Time orientation should be assessed by asking questions about date, time of the day, day of the week, month of the year, season, and year. Orientation to place can be tested by asking the names of the hospital, ward, town, or home address.

– 4.2.1.2 Attention can be tested by spelling a 5 letter word such as "world" backwards, forward and backward digit span, serial 7s, and recitation of the months of the year or the days of the week in reverse order. In aphasic patients one should opt for less language specific tests such as digit span. Normal forward digit span is considered 6 +/-1 and backward digit span is normally one less than forward.

4.2.2. *Declarative memory:* This is divided into episodic and semantic memory.

– 4.2.2.1. Episodic memory: Loss of episodic memory is a cardinal feature of AD. The history provides a valuable test of episodic memory; patients are often unable to provide the details of their past medical problems such as dates of operations, etc. Informal autobiographical interview in context of history taking is another effective way of exposing memory lapses. By asking patients questions about life events in both recent and remote past, one can expose memory deficits that may surprise relatives. Patients are often unable to recall recent important news, destination of holidays, or comment on their favourite soap operas. Other complaints such as forgetting appointments or needing shopping lists may reflect poor attention rather than poor memory and are less discriminatory.

– 4.2.2.2 Semantic memory: This is the part of memory that comprises our knowledge about the surrounding world that is not necessarily linked to life events. Conditions such as semantic dementia and some forms of limbic encephalitis involve the anterior temporal lobes and selectively involve semantic memory. Patients who suffer from semantic memory deficits speak fluently and an initial impression can be of normal speech. Semantic paraphasias may provide a diagnostic clue. Asking the patient to repeat a word and then to define it is one way to expose semantic impairments. Patients with semantic dementia have no problems in repeating but are unable to define words like caterpillar, barrister or xylophone. Semantic dementia should be suspected when the patient scores very poorly on naming line drawings or mispronounces irregular words such as pint and dough (surface dyslexia).

4.2.3 Language

Assessment of language starts from the first moments of the consultation. By listening to the patient whilst they provide the history, a trained ear can detect a number of impairments including phonological errors, grammatical mistakes, anomia, and speech abnormalities such as dysarthria and apraxia of speech. Some patients will have an abnormal rhythm of speech (dysprody). Many of these impairments are best appreciated by listening to the patients' connected speech during an informal interview. A more formal approach complements the informal listening. Language assessment should include testing reading and writing.

– 4.2.3.1. Anomia is a hallmark of aphasia. Anomia or "word finding difficulty" can easily be assessed objectively by asking the patients to name common objects in the consultation room or at their bedside. A watch is a useful aid as it contains components of varied word frequency, therefore difficulty, such as hands, winder, strap, buckle, etc. to expose more subtle anomia. Anomia is non-specific and needs further assessment.

– 4.2.3.2. Comprehension difficulty can be due to a number of factors. Single word comprehension difficulty is a relatively uncommon cause and can be assessed by asking patients to point to objects by either their names or description. Syntactic problems can be identified by asking patients questions put in a syntactically complex structure eg "touch your left ear when I hold up 3 fingers".

– 4.2.3.3. Impaired repetition can be either at single word level or a problem with sentence repetition. Isolated sentence repetition problems would normally suggest an impairment of the phonological loop component of the working memory. Single word repetition difficulty is usually due to problems with articulation in context of either dysarthria or apraxia of speech. Differentiating speech apraxia from aphasia can be difficult and often debatable.

4.2.4. Visuospatial impairment

Visuospatial impairment can be suspected by seeing the patient missing the chair whilst trying to sit or struggling to find their way out of the consultation room. Features in the history such as minor road accidents or parking problems may imply problems with spatial judgement.

– 4.2.4.1. Visual neglect can be noticed in patients who do not comb one half of their hair or do not shave half of their face. Neglect can be tested by asking the patients to bisect a line or copy a double–headed daisy. Hemi-neglect implies damage to the contra-lateral parietal lobe. Simultagnosia is another feature of non-dominant parietal lobe damage that can be detected in tasks such as letter or shape cancellation in which patients are asked to cancel particular letters that are written in different sizes and shapes.

– 4.2.4.2. Construction apraxia, despite the terminology, is widely accepted as a useful marker of visuospatial impairment. The most widely utilised way of assessing this is by asking the patients to copy relatively complex shapes such as inter-locking pentagons or wired cubes. Alternatively, by seeing the patients drawing a clock face with hands pointing at a particular time, one obtains valuable information about their executive and visuospatial function.

– 4.2.4.3. Prosopagnosia can be tested by asking the patient to identify famous faces either in a formal test or from a celebrity magazine. It is an unusual feature that suggests posterior, non-dominant or bilateral hemisphere disease.

4.2.5. Apraxia

Apraxia is the inability to execute motor responses despite intact basic motor functions. A number of different types of apraxias have been described but it

suffices to mention that presence of apraxia would indicate damage to the supplementary motor area and should be tested by the following:

– 4.2.5.1. Orobuccal apraxia: ask the patients to do a number of well learnt actions such as blowing, kissing, and yawning. Impairment in these actions is commonly seen in various types of aphasia.

– 4.2.5.2. Limb apraxia: ask the patients to demonstrate how they would stir sugar in a cup of coffee or ask them to mime to various gestures (both meaningful and meaningless)

4.2.6. Executive function

Executive function which traditionally localises to the frontal lobes can be tested in many different ways for example: asking the patient to estimate answers (How far is it from Cambridge to London?) or interpret proverbs. The value of such tests in localising problems is debatable, careful observation of the patient's behaviour is usually more valuable.

Conclusion

The clinical assessment of a patient with dementia can be divided into 4 stages. The assessment requires time and some expertise and is aided by the use of short cognitive tests. A system to allow thorough assessment of patients is presented. Investigations such as neuroimaging, neuropsychological testing and cerebrospinal fluid testing should be determined by the initial clinical assessment of the patient.

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Neurobiology of Brain Disorders

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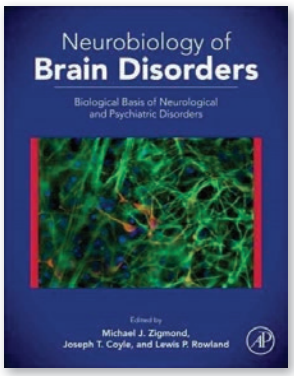

This is a textbook aimed at scientists, students, post doctoral and research fellows in neurology, neurobiology and psychiatry. Notably, the royalties earned from its sales are to be spent on the noble cause of making the book available, free of cost, to trainees in the developing world.

The book throws light on the often mysterious biological basis of neurological and psychiatric disorders. It has a very detailed list of the contributors and extensive cross referencing to published research in peer reviewed journals. The preface contains an impressive world history of the sciences of psychiatry and neurology.

Treating neurological and psychiatric disorders is a very complex task. This book very clearly explains the interface between neurobiology and disorders of the brain, as important for formulating diagnoses and treatments.

All the chapters of this book are colour coded and the topics are complemented with tables, illustrations, photographs, slides, radiological images and statistics. The sections are well written in easy to understand language catering for readers at various career grades. The topics are well presented, starting from basics and progressing to recent advances. At the end of every chapter, attention is given to unanswered questions in the field, identifying further research challenges.

In Psychiatry, there are chapters on developmental disorders such as ADHD, autistic spectrum disorder, Rett syndrome, diseases of higher function, stress, addictions, sleep disorders, post-traumatic stress disorder, obsessive-compulsive disorder, schizophrenia, depression and suicide.

As a psychiatrist, I would like to reflect on the chapter on pain, as I see many patients with relapses in their psychiatric illness when their pain is not well controlled. Pain may be a neurological condition but in general is seen as a symptom rather than a disease in itself. Pain is a subjective phenomenon, and this further complicates its treatment. It is extremely important to all branches of medicine, not to mention the patients, that pain is understood better and treated more effectively.

From the neurology point of view, myasthenia gravis, muscular dystrophy, spinal cord injury, traumatic brain disease, epilepsy, Parkinson's disease, Alzheimer's disease, Huntington's disease, stroke, prion disease, multiple sclerosis and amyotrophic lateral sclerosis are included in this book. Chapters on infectious and immune mediated diseases of the nervous system (and pain) are additional attractions.

I am pretty sure that my neurologist colleagues will be very interested to know the key role of the brain in response to stress, which may be a psychiatric illness. The brain is the key organ of the stress response as it assesses stressful stimuli, and determines the behavioural and physiological response to stress. The chapter on stress gives a compelling account of the neuroanatomical changes occurring in brain structures, especially in hippocampus and amygdala, and physiological responses in cortisol metabolism, as a consequence of stress. An understanding of the organic processes of the brain that occur with stress provides a basis for pharmacotherapy and non-pharmacological treatment in stress disorder, in particular the insight that depression and anxiety disorders may be seen as a loss of resilience and that this has a bearing on neural plasticity.

Analysis of the burden of neurological disease, the ethical basis of neuroscience, the role of stress in health and health disparities among different races are further, somewhat unexpected, highlights of the book.

This is more of a reference book than a read-through. It is recommended especially for an approach that encompasses the scientific basis of brain medicine in the widest sense.

Neurological Signs: Mirror Phenomena

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Larner AJ. ACNR 2015;15(4):14.

"I've had the experience of finding myself unexpectedly before a mirror and not recognising myself..."
André Malraux *La Condition Humaine* (published in English as *Man's Fate*)[1]

The speaker of these lines is an ageing Chinese academic, Old Gisors, who habitually smokes opium, a habit which might possibly be relevant to his strange sensory experiences. A number of mirror phenomena are described in the neurological literature,[2] of which those with a cognitive flavour are briefly considered here (i.e. neither mirror movements nor the "mirror dystonia" sometimes encountered in writer's cramp are discussed).

Mirror Sign and Mirrored Self-Misidentification

The experience reported by Old Gisors, a failure to recognise ones' own reflection in a mirror, may be described as the "mirror sign". In addition to this failure, patients may sometimes develop a delusional belief that their reflection is in fact that of a stranger, which has been termed "mirrored self-misidentification",[3] a response which might contribute to the "phantom boarder sign" (the belief that there is someone else living in the house).

Rather little seems to have been published on these signs, but the articles which have appeared generally indicate that it is a reflection (no pun intended!) of cognitive decline,[3] for example in Alzheimer's disease (AD)[4,5] or dementia with Lewy bodies.[6] Mirror sign may perhaps be a consequence of visual agnosia, and has been noted in a patient with the posterior cortical atrophy variant of AD who also had visual hallucinations.[7] Unusually mirror sign may occur as a focal deficit at the onset of a progressive dementing illness, indicative of non-dominant hemisphere dysfunction. In addition to perceptual (face processing) impairments, affective and reasoning deficits may also contribute to the pathogenesis of mirror sign.[8] Dementia is not, however, a *sine qua non*: mirrored self-misidentification has also been noted in an elderly patient with a right dorsolateral frontal infarct, bilateral frontal encephalomalacia consistent with previous head trauma, and posterior periventricular ischaemic lesions but without dementia. Based on these observations, the authors suggested that the right dorsolateral prefrontal cortex may be important for self-recognition.[9]

Mirror Agnosia, Mirror Apraxia, Mirror Ataxia

Mirror agnosia and mirror apraxia are related phenomena, as may be mirror ataxia.

Mirror agnosia is a deficit in which patients are unable to use mirror knowledge when interacting with mirrors (a definition which might also encompass mirror sign and mirrored self-misidentification). Also sometimes known as the "looking glass syndrome", or "Ramachandran's sign" after the first description,[10] patients are unable to point to the real object when it is seen in a mirror. They may attempt to reach "into" the mirror even when the actual location of the target has been shown, suggesting an inability to distinguish between the real and virtual images. This reaching for the virtual object has been termed mirror apraxia.[11] Reaching for the real object but with increased errors of direction has been termed mirror ataxia.[12] Parietal lobe lesions with associated hemispatial neglect may underlie these signs, with dissociation of retinotopic (allocentric) space and body schema (egocentric space). A lesion study suggested different areas of parietal lobe might underpin mirror ataxia (postcentral sulcus) and mirror agnosia (posterior angular gyrus and superior temporal gyrus).[12]

Mirror Hallucination

The visual hallucination of seeing ones' own face, autoscopy, has been termed mirror hallucination since there is left-right reversal as in a mirror image. This has been described in association with epilepsy, migraine, and parieto-occipital space-occupying lesions.[13]

Mirror Writing

Mirror writing is a mirror image of normal writing, hence in English it runs from right to left with characters back to front. In double mirror writing (*écriture en double miroir*) script is also inverted top to bottom (script goes up the page) as well as being mirror reversed. Mirror writing may occur spontaneously, more often in left-handers, as well as in a variety of pathological situations, mostly associated with left hemisphere damage. Leonardo da Vinci is perhaps the most celebrated historical mirror writer.[14]

Mirror writing should perhaps not be included here since it is most probably a motor phenomenon, akin to mirror movements, rather than a cognitive phenomenon, although it is reported to occur on occasion in the context of cognitive impairment or dementia. That said, in my experience of asking people with cognitive complaints to write sentences (e.g. when administering the Mini-Mental State Examination or the Addenbrooke's Cognitive Examination and its subsequent iterations, ACE-R and ACE-III) I do not recall ever having seen a mirror sentence produced.

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The Festschrift of Alastair Compston

Report by: Roger A Barker, Professor of Clinical Neuroscience, University of Cambridge and Honorary Consultant Neurologist at Addenbrooke's Hospital, Cambridge.

In a hot lecture theatre in the old LMB in Cambridge in July, the career and achievements of Alastair Compston were celebrated in a 16 lecture 9 hour bonanza – of which two were video recorded from San Francisco (Steve Hauser) and Australia (Simon Broadley). The day involved a series of short talks introduced by two chairs who delivered some personal, and often revealing, recollections on Alastair, with the whole meeting suffused with good humour and personal warmth and admiration but not without some gentle mocking.

So what did we discover outside of what we already knew about Alastair's contribution to the genetics of MS and the taking of Campath-1H to the clinic?;

1. That many of the current Professors of Neurology in the UK had spent formative times undertaking research with Alastair and this included Messers Sawcer, Wood, Chandran, Scolding, Robertson, Zajicek with many others in the audience such as Chris Shaw. Several of this distinguished team spoke about how he had shaped their future research careers such as Nick Wood and his huge contribution to the genetics of Parkinson's disease. In addition, looking across at the audience of several hundred revealed that a significant proportion of the current neurological community in the UK have been in receipt of a major input from DASC.
2. That Alastair had not only been involved with MS in the way described, but also had made significant contributions in other auto-immune diseases, most notably Myasthenia Gravis. This was all beautifully summarised in a talk by Angela Vincent where she went on to discuss the plethora of new auto-immune diseases that are now well recognised.
3. While Alastair has been involved in the antibody therapy of MS, it has not been restricted to this domain with Siddharthan Chandran and Neil Scolding discussing in vitro modelling of axon-glial interactions and the development of stem cell based treatments for demyelinating disease.
4. Many who know Alastair will also know of his passion for books – especially ones that are very old and written in languages that are archaic at best. It was therefore a delight to hear from someone who has a similar disorder (described as medicobibliomania), Jan van Gijn about how this comes about and how it can be cured. His three solutions were firstly, to turn away, abstain and simply retreat to being a wise thinker through the Socratic method; buy the ultimate of all old medical books (De humani corporis fabrica by Vesalius, a cool £265,250); or thirdly actually try reading them all!! Jürg Kesselring and Klaus Toyka celebrated Alastair's European presence, including early morning haggling in bookshops on the Rue Jacob in Paris.
5. The contribution that Alastair himself has made to the neurological literature was also covered with many references to his editing roles in McAlpine's textbook on MS – that inspired much of what Hans Lassmann has done and spoke about. In addition his 10 year editorship of Brain was put into historical context by the current Editor, Dimitri Kullmann who explained how the journal originated out of cases seen at the National. Simon Shorvon then followed up with a history on how neurology was practised in the first half of the 20th century, which would leave a lot to be desired by the current EU directive on working conditions.
6. The initiatives that have taken place in Cambridge under Alastair were also touched upon perhaps most clearly by James Fawcett discussing the origins, trials and tribulations of the Cambridge Centre for Brain Repair, and Trevor Robbins on the development of a specifically designed overarching Cambridge Neuroscience structure. These all highlighted Alastair's capacity to think big and have visionary concepts on how to develop and make fields of neurobiology and neurology flourish and with this has come many successful careers.
7. Finally we were treated to the development of Campath-1H for MS and the brave decisions that needed to be made en route for it to become a licensed drug for MS. This initially involved the academic development of this agent in human trials in MS, building on the seminal work of Herman Waldmann, who spoke about this and his current work on regulatory T cells. There then followed a talk by Mark Enyedy on the commercial development of the drug and the bravery, tenacity and guile needed to persuade big Pharma to take this on as a money earner. This having been achieved, the final talk by Joanne Jones discussed some of the new interesting questions that the use of this agent has thrown up around the development of autoimmune diseases. This talk also encapsulated all that Alastair has done in many ways, bringing on young scientists in an environment that encourages and recognises the importance of such work.

The day then concluded with a very special dinner at Jesus College, where Alastair is a fellow, with talks by John Walton (born 1922) and Alasdair Coles (born much later) – the latter pointing out many of Alastair's outstanding qualities, not least his editing skills which on one occasion extended into correcting quotes within the text, some of which were from scripture. Now that is some legacy!

looking across at the audience of several hundred revealed that a significant proportion of the current neurological community in the UK have been in receipt of a major input from DASC

Ten years of searching for a cure: Tom Isaacs, President and Co-Founder of The Cure Parkinson's Trust

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Having been diagnosed with Parkinson's at the age of 26, it took me at least three years to really accept the condition as part of who I am. At the time, I had no idea how the remorseless assault that Parkinson's has on mind and body would lead me to a place where Parkinson's embraces almost everything I do. Although coping with my own advancing Parkinson's has defined the path of most of my working life, oddly, it has never been my inspiration. I don't believe Parkinson's inspires anyone. Certainly, Parkinson's has only ever been a destructive and soul sapping force in my life.

So how has the task of finding better treatments for Parkinson's made me more passionate, more determined and more fulfilled in my life than I ever thought possible? The answer to this question is simple. It's the people. My involvement with Parkinson's has been motivated solely by the brilliance of scientists, the generosity of philanthropists, the selflessness of those friends or family with Parkinson's and, above all else, the incredible ability of the human spirit to overcome extreme adversity of health. It is the knowledge that these people are out there; that there is the ability, the resource and the will to make a difference and improve the lives of those of us who have Parkinson's, which has given both me and all my colleagues at The Cure Parkinson's Trust our sense of purpose, enthusiasm and commitment.

I was told I had Parkinson's in 1996. Like most, I went through a period of sadness, anger and denial, but in 1999 I decided I would walk from John O'Groats to Lands End to raise funds for research into Parkinson's. I was staggered by the amount of support I received and three years later felt the urge to attempt the bigger challenge of walking 4,500 miles around the coastline of Britain. The walk, "Coastin'" provided the platform for everything that was to follow and led to my meeting seven extraordinary people without whom The Cure Parkinson's Trust simply would never have come into being. The "magnificent seven" were my wife, Lyndsey; Professor Andrew Lees, who at the time was my Neurologist, the other three original "movers and shakers" Sir David Jones, Sir Richard Nichols and Air Vice Marshal Michael Dicken, fellow people with Parkinson's; Professor Steven Gill from Frenchay Hospital, Bristol; and a remarkable and industrious force of nature in the form of Helen Matthews with whom I have now been working for thirteen years.

Two years after "Coastin'", we set up The Cure Parkinson's Trust determined to help the push towards a cure in any way we could.

Although none of us really knew much about setting up a new charity, we did know what we wanted to achieve and the type of people who could enable us to realise our goals. A key appointment was Dr Richard Wyse who became involved after chairing a meeting on delivery mechanisms for us in Windsor. His determination to defeat Parkinson's remains as strong today as it was ten years ago. His capacity to read and retain information and to drive new science forward so that it has the best opportunity to be converted quickly into new treatments, has shaped much of our research strategy and we have been fortunate that he has been so committed to our cause.

It was Richard who was responsible for master-minding our Linked Clinical Trials programme (LCT) which is now in it's fourth year.

This initiative provides the means to bring treatments already in use in other conditions and to assess their application and effectiveness in Parkinson's. Every year, Dr Wyse produces dossiers which make the case for any number of compounds which, from the data available, suggest that they might have a mode of action which could benefit people with Parkinson's. The dossiers are prioritised by twelve of the most renowned Parkinson's specialists from around the world in order of their likely impact and ability to slow, stop or reverse the condition.

The first Linked Clinical Trial that took place was on a treatment for diabetes called Exenatide undertaken by Dr Tom Foltynie at UCL London. This not only generated enormous interest in the potential of similar GLP-1 agonists for use in Parkinson's, but also defined the template for other LCT studies that were to follow. The LCT initiative is now also backed by the Van Andel Research Institute whose Associate Director, Professor Patrik Brundin also chairs the LCT Committee. Over seventy compounds have been assessed since 2012 and twenty novel approaches to treating Parkinson's have now been prioritised and are at varying stages of development and further analysis. The six most recent examples of prioritised compounds going into trial are:

1) Simvastatin – a trial about to start at 25 UK centres under the leadership of Dr Camille Carroll from Plymouth University.

2) Deferiprone – a pan-European study, funded by the EU, commencing in January 2016 involving 300 patients.
3) Liraglutide – another treatment for diabetes is under way at Cedar Sinai Hospital in Los Angeles.
4) Mitochondrial target – one of the prioritised compounds which has been shown to have an effect on dysfunctional mitochondria is due to move into a clinical trial in London and Boston in the Autumn.
5) Ambroxol – we expect to start funding a clinical trial in the UK in the very near future.
6) N-Acetyl Cysteine – the trial protocol is being finalised and a study is expected to start in California soon.

The Cure Parkinson's Trust funds both pre-clinical and clinical research. Our Research Committee is chaired by Dr John Scadding and supported by some of the UK's most inspirational scientists and clinicians. Their "can-do" attitude and ability to select the most important projects for the charity to fund has allowed us to grow and acquire a reputation for delivering excellent science with the capacity to accelerate tangible differences to the way Parkinson's is treated.

From the Trust's inception we believed that it was critical that we made sure every research project we supported was evaluated by and relevant to people living with Parkinson's. As we were founded and led by people with Parkinson's, we have remained true to these guiding principles. The involvement of people with Parkinson's in every aspect of our work has led to the growing importance and influence of our advocacy arm, Parkinson's Movement (PM). This year PM has created a Clinical Trials Charter to help deliver better communication within clinical trials. It has also hosted Research Club events, conducted patient-designed experiments, supported recruitment drives for clinical trials and later this year, will be designing a rating scale for new apps and devices to evaluate them in terms of their usability.

One of the most important pieces of work in which our involvement has been pivotal, has been our support of the work of Professor Steven Gill in Bristol. On the fifth day of my walk around the coast, a news story broke announcing the results of a pilot study infusing a growth factor, GDNF (glial-cell line derived neurotrophic factor) which showed remarkable improvements to the five patients involved. I was in Essex at the time and some 3,000 miles later, I met Steven Gill at the service station at the end of the Severn Bridge. It didn't take a scientist to see the potential of his work and having met the man I was convinced that Gill, GDNF and the work needed to improve the delivery of this molecule into the brain had to be supported. It was the closest thing I had seen to a cure.

It took ten years from that M4 service station to get GDNF back into trial – that's some traffic jam even by M4 standards! Nevertheless, the results of the phase II study are due in mid to late 2016 and we are delighted to be funding this trial jointly with Parkinson's UK.

The last ten years has been an extraordinary journey. We have funded and facilitated millions of pounds worth of research. We have been responsible for uncovering scientific discoveries which could lead to a breakthrough. We have met and brought together some truly inspirational and generous people, scientists, fundraisers and people with Parkinson's. I still maintain that one day I will be able to insert the words "used to" when I say "I have Parkinson's".

The Cure Parkinson's Trust

www.cureparkinsons.org.uk
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Next Generation Neurology: E-learning

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The Association of British Neurologists Trainees Innovative E-Learning Programme: aiming to promote confidence and engagement with neurology prior to specialisation.

Background

The term neurophobia, coined by Ralph Jozefowicz in 1994,[1] refers to a fear of neurology encountered amongst medical students. A recent national survey of UK medical students confirms that students continue to find the subject of neurology and the ability to draw up a neurological differential diagnosis significantly more difficult compared with other specialties.[2] We have recently conducted a survey of 108 Foundation and Core Medical Trainees (CMT) from 19 deaneries across the United Kingdom. Results revealed that 48% describe themselves as being neurophobic, therefore demonstrating that neurophobia is not just confined to medical students. Overall, 78% felt they were under-confident managing neurological conditions that may present on the acute medical take (self-rated confidence level of two or less on a four point scale). Thematic analysis of free text responses from the 52 self-identified neurophobes highlighted three areas of particular concern: lack of clinical exposure and experience during medical school and/or early training, lack of skill base to effectively elicit clinical signs and form differential diagnoses, and a perception of neurology being a complicated speciality requiring expert support and rapid specialty takeover. [Unpublished]

The Association of British Neurologists (ABN) continues to play a key role in campaigning for disorders of the nervous system to feature centrally on UK undergraduate curricula.[6] Recent evidence from the USA supports the premise that undergraduate exposure to teaching of the neurosciences correlates directly with the likelihood of medical graduates subsequently enrolling in a neurology specialist training programme. The competition ratio for ST3 neurology applications has been relatively stable over the last three years,[3] but with typical rates of around two applications per post, there is room for improvement if we seek to expand our specialty. A recent article in the BMJ highlighted the urgent need to expand neurology services in the UK, given that there is only one neurologist per 90,000 people (compared with a European average of one per 15,000), and an estimated 12 month wait for outpatient neurology services.[4] As it stands in the UK at present, we must acknowledge that a high proportion of the one in five patients who present to the acute take with a disorder of the nervous system, are not received by a Neurologist.[5] Their initial management tends to be provided by junior doctors on an acute medical unit, the same population who our survey suggests feel under-confident or neurophobic.

It seems that the neurology training needs of junior doctors are not being fully met by current teaching methods during medical school or junior training posts. Long term solutions to this problem (e.g. adapting medical school curricula, increasing the number of neurology posts in junior rotations) seem largely to be no more than theoretical pledges at present. The ABN and ABN Trainees (ABNT) committees remain committed to try to bridge this gap. Launched one year ago, the ABN Mentor Scheme provided 40 aspiring Neurologists, currently in junior training posts, with the opportunity to be mentored by a local Neurologist or neurology trainee.[12] However, the ABNT feel that further initiatives are required to maintain engagement and recruitment into neurology.

E-learning

E-learning, defined as 'learning conducted via electronic media',[7] has been traditionally used to deliver distance-learning and computer assisted instruction.[8] E-learning formats for the delivery of medical education range from plain electronic text, to wholly interactive, virtual reality platforms. The World Health Organization (WHO) recently commissioned a review of evidence for e-learning in healthcare, conducted by Imperial College London. The findings suggested that e-learning resources should complement, rather than replace traditional learning methods for teaching healthcare professionals,[9] but that e-learning enhances the convenience and accessibility of educational resources. Student satisfaction appears to be higher for e-learning than for traditional learning methods and data exists to validate e-learning as a means of improving test-scores.[9] In our survey of Foundation and core medical trainees, only 24% report using interactive e-learning resources to revise for professional exams. The remainder predominantly cited lack of availability, and cost of available resources as reasons for not utilising interactive e-learning cases as a revision tool. In addition to the Medical Royal College of Physician (MRCP) exam cost of £1,495, our survey indicated that 50% of junior doctors spent an additional £100 or more on revision resources. [Unpublished] We suggest that a lack of freely available, open access neurology resources further inhibits motivation to dedicate revision time to the speciality.

Student-centred Learning

Developing a comprehensive, evidence-based, curriculum-centred online learning resource for junior doctors represents a significant challenge. While a range of subscription-based online question banks for MRCP exams exist, we endeavoured

to generate a non-profit, open-access resource. Evidence from undergraduate practice shows that asking students to write their own exam-style questions, and to review and respond to those of their peers, can be a hugely successful way of encouraging learning.[10] The Peerwise initiative (https://peerwise.cs.auckland.ac.nz) had high rates of student uptake and generated large volumes of formative learning material. This demonstrates how valuable learning resources can be developed without the need for high-level investment from time- and resource-poor departments. Interestingly, the students also reported that they found the process of question writing, answering and commenting on peers' questions to be a useful learning technique.[10]

Innovative e-learning

When authors ET and SV were paired as ABN mentor and mentee, we, along with a colleague (SR), decided to embark on a project that collaborated with the ABNT to enhance neurology training for junior doctors, and to offer an opportunity to engage with neurology ahead of specialisation. We suggest that the enthusiasm of junior doctors who are already interested in neurology can be employed in this project to develop a resource that is relevant and accessible to any junior doctor, regardless of their specialist interest. We have devised an innovative and interactive e-learning programme that will cover all neurology outcomes of the CMT curriculum through a series of 20-30 modules. Learning modules will be developed around clinically relevant scenarios that we expect junior doctors to face in their current medical practice. Our e-learning modules will utilise a basic and accessible computer format (PowerPoint) and will require participants to prioritise patients and combine academic knowledge with clinical acumen, principally through single best answer questions.[11]

So far, 23 topics have been allocated to junior doctors who will work in conjunction with a senior neurology mentor. The project will be led by the junior colleague, who will research the topic and devise a module that simulates an on-call shift, ward or outpatient clinic experience, dealing with neurology based presentations. The role of the neurology mentor will be to aid learning, highlight relevant resources and to ensure clinical accuracy. Once the e-learning module material is received by the Innovative E-learning team, it will be sent for further peer-review by one of the ABNT committee, before it is transformed into an e-learning format and uploaded to the ABNT website (www.abnt.org.uk/elearning.php). E-learning modules will be freely available for individuals or as a teaching resource worldwide, with accreditation given to the contributors.

Lack of maintenance to e-learning sites has been cited as an obstacle to the longevity of open-access online teaching resources. In fostering a supportive mentoring ethos we would expect that the management of each case will be passed down through generations of junior mentees, further facilitating ongoing learning and supervision in the speciality.

Summary

We envisage that the ABNT Innovative E-learning project will provide a comprehensive, interactive e-learning platform for junior doctors to access free of charge. In developing this programme as a grassroots initiative we hope to achieve sustainability, and motivate junior doctors to feel confident managing acute neurological disorders and consider neurology as an inspiring and supportive speciality.

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Neurturin and Parkinson's Disease – the latest chapter

Reviewer: Roger A Barker, Professor of Clinical Neuroscience, University of Cambridge and Honorary Consultant Neurologist at Addenbrooke's Hospital, Cambridge.

Parkinson's disease (PD) is characterised by the loss of dopamine cells in the substantia nigra and as such many restorative therapies have been developed to try and repair this network. This has involved using cellular transplants as well as growth factors – administered either as direct infusions or via viral delivery systems. One such approach has involved the GDNF like factor – Neurturin (NTN) – delivered using an AAV2 system in patients with advancing PD. This, in open label studies, showed promise but in a double blind placebo controlled trial failed at its primary end point at 12 months – although at the unblinded 18 month time point there was some signal of efficacy.

As a result a new study was set up that sought to deliver NTN into the nigra and putamen of slightly earlier stage PD patients. This new study has now been reported to have also failed as was indicated by a press release two years ago. This new paper detailing the trial results has just been published along with another one reporting on four cases from the trial that came to post mortem.

The clinical trial involved 48 patients of whom 23 received the active treatment with a primary end point at 15 months of change in UPDRS in a practically defined off state. Several secondary measures were also looked at along with safety. The main finding was that the active treatment showed no efficacy and there were no significant adverse effects.

The second study looked at four patients who died from unrelated causes – two of these deaths happened soon into their treatment with this agent and two many years later, one of whom turned out to have MSA. In all cases the volume of distribution of the NTN was the same at about 20% with little evidence for a major effect on the TH system either at the level of cell bodies or fibre sprouting – paralleling the clinical response which was seen in the trial.

So what does all this mean – Is this approach not useful? I think before one concludes that this is the case, there are three major issues that need to be considered;

1. Were the patients given this therapy the correct group of patients, given that the dopaminergic system is already majorly affected at the time of diagnosis?
   It is well known that by the time a patient with PD presents with motor deficits about 50% of the dopaminergic neurons and 80% of their fibres are already lost. Furthermore, within a few years of diagnosis there is a near complete loss of dopaminergic fibres within the striatum of PD patients and thus it may be that only those individuals early in the disease course may be amenable to treatment. This is addressed in Figure 3 of the paper, where those closest to disease onset have a greater response to the NTN – as such there may be merit in doing a new trial in newly diagnosed de novo PD cases.
2. Does NTN work as you would expect in the alpha synuclein diseased human adult PD brain compared to rodent and non human primate animal models of PD?
   Recently there has been work from the Bjorklund lab suggesting that GDNF does not work in the presence of alpha synuclein pathology because of changes in the GDNF receptor signalling pathway, which can be rescued using Nurr 1. If true in the PD brain, then it implies that GDNF like factors such as NTN may have a muted response compared to that seen in animal models of PD that use non alpha synuclein approaches such as neurotoxins. As such new trials may want to employ agents that upregulate Nurr 1 expression.
3. Was the right dose given over the right volume of distribution to allow meaningful effects to be seen?
   Looking at the histology in patients in receipt of NTN, there is a question as to whether the volume of distribution would be sufficient to generate the necessary extent of putamenal innervation required to see an effect. As only 20% of the putamen received the agent presumably at different concentrations, this seems likely. Thus higher doses using convection enhanced delivery systems may have improved on this, and may be a way to consider taking this agent forward.

Overall this paper shows that NTN has no significant benefit in PD patients when given at this dose in this way at this stage of the disease – although new trials to look at this further can clearly be designed given some of the issues that this trial has thrown up. Indeed whether this means that all similar growth factors will be equally ineffective is unclear, but in the next 12 months or so we should know at least what effects GDNF has when given either as a direct infusion into the brain or delivered via a different viral vector system to the PD striatum.

Olanow CW et al (2015) Gene delivery of neurturin to putamen and substantia nigra in Parkinson Disease: A double-blind, randomized controlled trial. Ann Neurol. Epub.

Bartus RT et al (2015) Post-mortem assessment of the short and long term effects of the trophic factor neurturin in patients with α-syncleinopathies. Neurobiol.Dis. 78:162-171.

Keep an eye on the prion – the spreading pathology of MSA

Reviewer: Roger A Barker, Professor of Clinical Neuroscience, University of Cambridge and Honorary Consultant Neurologist at Addenbrooke's Hospital, Cambridge.

Over the last 50 years the origin of prion diseases has become more secure even if the mechanism by which the abnormal protein accumulation kills cells is still unresolved. These disorders include genetic conditions such as Gerstmann-Straussler-Scheinker disease as well as sporadic diseases such as CJD. Of late there has been a great deal of interest in whether other, more common, neurodegenerative disorders of the CNS may have a similar basis – namely that the pathogenic protein that lies at the core of the condition can act in a prion like disease. This has been explored in most detail with tau and alpha synuclein and are the subject of two papers from the Pruisner lab that have just been published in PNAS.

These studies involve in vitro studies using human embryonic kidney cells along with the in vivo work involving the Tgm83 +/- mice that express alpha synuclein (A53T). In each case the cells/animals are "inoculated" with "prions" purified from the brains of patients dying with PSP, MSA or PD. In the first study they show that both MSA and PSP brains can infect cells in vitro, while PD brain extracts did not display such behaviour. This was then confirmed in the second paper with respect to MSA versus PD synuclein extracts in the mouse model. The authors therefore conclude that "alpha synuclein is the first human prion to be identified, to our knowledge, since the discovery a half century ago that CJD was transmissable".

This is a bold statement although fits with an emerging literature showing that alpha synuclein can spread from cell to cell and seed pathology in some instances. Thus this finding adds to that existing literature, although does draw a distinction between the alpha synuclein "strains" found in PD and MSA which again has been suggested by other studies (e.g. Peelaerts et al Nature 2015). Thus these papers are of great interest to those working in this field, although as far as I know, it has still not been shown that anyone has developed an alpha synucleinopathy from exposure to "infected" human tissue as has been the case for CJD.

Woerman AL, Stöhr J, Aoyagi A, Rampersaud R, Krejciova Z, Watts JC, Ohyama T, Patel S, Widjaja K, Oehler A, Sanders DW, Diamond MI, Seeley WW, Middleton LT, Gentleman SM, Mordes DA, Südhof TC, Giles K, Prusiner SB. Propagation of prions causing synucleinopathies in cultured cells. Proc Natl Acad Sci U S A. 2015 Sep 1;112(35):E4949-58

Prusiner SB, Woerman AL, Mordes DA, Watts JC, Rampersaud R, Berry DB, Patel S, Oehler A, Lowe JK, Kravitz SN, Geschwind DH, Glidden DV, Halliday GM, Middleton LT, Gentleman SM, Grinberg LT, Giles K. Evidence for -synuclein prions causing multiple system atrophy in humans with parkinsonism. Proc Natl Acad Sci U S A. 2015 Aug 31. pii: 201514475

Peelaerts W, Bousset L, Van der Perren A, Moskalyuk A, Pulizzi R, Giugliano M, Van den Haute C, Melki R, Baekelandt V. -Synuclein strains cause distinct synucleinopathies after local and systemic administration. Nature. 2015 Jun 18;522(7556):340-4.

To list your event in this diary, email brief details to Rachael Hansford at Rachael@acnr.co.uk by 6th October, 2015

2015

September

Paediatric Oncology Solid Tumours Study Day
14 September, 2015; London, UK
www.royalmarsden.nhs.uk/paedsolidtumours
T. 020 7808 291/2924,
E. conferenceteam@rmh.nhs.uk

How to Develop a True 7 Day Stroke Rehabilitation Service
16 September, 2015; Birmingham, UK
T. 01732 897788,
E. nichola.cadwallader@sbk-healthcare.co.uk
http://sbk-healthcare.co.uk/home/event/1048/#eventpage

Stroke Rehabilitation Service Delivery
17 September, 2015; Birmingham, UK
T. 01732 897788,
E. nichola.cadwallader@sbk-healthcare.co.uk
http://sbk-healthcare.co.uk/home/event/1045/#eventpage

Epilepsy 2015
ILAE UK Chapter SpR Teaching Weekend
19-20 September, 2015; Oxford, UK
E. Juliet.solomon@ucl.ac.uk
www.activateevents.com/epilepsy2015

ILAE British Chapter Annual Scientific Meeting
23-25 September, 2015; London, UK
www.ilae-ukconf.org.uk

October

The 8th Practical Cognition Course
1-2 October, 2015; Newcastle, UK
www.practicalcognition.com
T. Ann Fitchett 0191 208 8320,
E. ion@ncl.ac.uk

37th Clinical Neurology Course
5-6 October, 2015; Edinburgh UK
www.ed.ac.uk/schools-departments/clinical-brain-sciences/postgraduate-training/edinburgh-clinical-neurology-course
E. Judi.Clarke@ed.ac.uk

Ketogenic Study Evening
15 October, 2015; Taunton, UK
Jacqui McAleer, E. jmassociates1@me.com

Ketogenic Study Evening
28 October, 2015; Stirling, UK
Jacqui McAleer,
E. jmassociates1@me.com

November

Ketogenic Study Evening
9 November, 2015; Dublin, Ireland
Jacqui McAleer,
E. jmassociates1@me.com

Examining the utility of music interventions in neurological disorders of older people
Monday 16 November, 2015; RSM London, UK
Royal Society of Medicine, London
Lucy Church,
E. rsmprofessionals@rsm.ac.uk
T. 0207 290 3928,
www.rsm.ac.uk/livemusicnow

Modern Thinking in MS Management
7pm Friday 20 November -
16:40 Saturday 21 November, 2015;
The Palace Hotel, Manchester, UK
www.modernthinkinginms.com

11th Essential Neuro MRI Course
Saturday 21st November, 2015;
Liverpool Medical Institute, UK

One day intensive course in how to interpret MRI Brain & Spine6 Cat 1 CPD
Contact: Sam Pickup
T. 0151 709 9125
E. essentialcourses@hotmail.com

Consultant PD Masterclass – Sheffield
Module 1 - 2, 3rd & 4th June 2015
Module 2 - 26th November 2015
(Both modules must be attended)
www.parkinsonsacademy.co.uk for further details.

Ketogenic Study Evening
25 November, 2015; Liverpool, UK
Jacqui McAleer,
E. jmassociates1@me.com

The 2nd British Symposium on the History of Neurology and Psychiatry
A commemoration of the centenary of the death of Sir William Gowers
November 25th, 2015; Institute of Neurology, London, UK
Programme and registration details: Liz Beckmann at www.hnps.co.uk2016

History of Neurology and Psychiatry in London
November 26th, 2015
Institute of Neurology, Queen Square, London, UK
Programme and registration details:
Liz Beckmann at www.hnps.co.uk2016

23rd Annual Meeting of the European Charcot Foundation
26-28 November, 2015; Milan, Italy
www.charcot-ms.org

December

BNPA Neurology & Psychiatry SpRs Teaching Weekend
11, 12 13 December, 2015; Oxford, UK
E. admin@bnpa.org.uk
T.0560 438 3951,
m. 07940 591096

2016

February

Is it criminal? Acquired brain injury, challenging behaviour and rehabilitation Partnerships in Care Brain Injury Services Conference 2016
24 February, 2016; Cambridge, UK
www.partnershipsincare.co.uk or contact samantha.coburn-kett@partnershipsincare.co.uk

The Brain and Behaviour Conference

Conference details: 12 March 2015,Stoke-on-Trent, UK. ***Report by:*** Dr George El-Nimr, Clinical Lead for Neuropsychiatry Services, Clinical Tutor and Academic Secretary for the Faculty of Neuropsychiatry at the Royal College of Psychiatrists.

Professionals working with patients with brain injury and disease travelled from all over the country to attend our 5th UK National Neuropsychiatry Conference. This was held at Stoke-on-Trent Moat House on the 12th March 2015. The conference which was fully subscribed provided a platform for academics, clinicians and service users to enhance cross-fertilisation of thinking. The conference was supported by a number of statutory, private and voluntary organisations and received excellent feedback.

Following introductions from Dr George El-Nimr, event organiser, Dr John Murphy, Associate Specialist in Psychiatry and Honorary Lecturer gave his perspective as a former patient who survived a severe head injury back in the 80's. Dr Murphy talked about his rocky journey and the success he achieved through hard work and support from family and relevant services. Dr Murphy gave a first-hand experience of specific symptoms such as hemineglect and impaired social emotions. He explained to the conference delegates how he was eventually able to return to his role as a clinician and educator. Similarly, Sam Dawson who works as an administrator for the NHS offered further insight into what it actually means to look after someone with a brain disease that is increasingly robbing them of their personality and independence.

Dr El-Nimr then gave an overview on brain and behaviour issues. He particularly explained the current models of studying brain, mind and consciousness and how thinking around those issues has evolved over the years. Dr El-Nimr presented a number of curious phenomena related to body image, cognitive capabilities and mystical experiences, some of which could be difficult to explain within the traditional brain/mind dichotomy. Dr El-Nimr explored puzzling questions such as: "do we need our eyes to see?", "can our somatosensory cortex be stimulated through stimulation received from other bodies or even the environment?", "how can brain injury be associated with gaining new skills?".

Dr Barrett, retired Consultant Neuropsychiatrist and the founder of North Staffordshire Neuropsychiatry Services, gave an inspiring talk on the history of psychosurgeries. 2015 marks the 80th anniversary of the first "prefrontal leucotomy", the surgical destruction of the brain tissue as a treatment for psychiatric disorders. Dr Barrett highlighted that by 1965 an estimate of 70,000 patients, worldwide, had gone through similar procedures. In his presentation, Dr Barrett examined cases, events and the major players in an attempt to understand how psychosurgery became a mainstream procedure and what lessons could be learnt.

Dr Salman Haider, Research Fellow in Neurology, presented a research perspective on Huntington's disease. It was highlighted that the genetic predictability of HD provides an opportunity for early therapeutic intervention many years before overt symptom onset and at a time when reversal or prevention of neural dysfunction may still be possible. It was clear that understanding of HD pathogenesis is evolving, and there are a number of candidate therapeutics with potential disease modifying effects that are currently being tested. New data to understand the neurobiology of the preclinical phase of neurodegeneration in HD was presented along with an overview of recent advances, working towards HD gene silencing in humans.

Key messages:

- It is important for science and humanities to work together to enhance a better understanding of the brain / mind problem.
- Neurosurgery continues to have a place in managing specific mental health problems.
- There are a number of candidate therapeutics with potential disease modifying effects that are currently being tested in Huntington's disease.
- Evidence of the effectiveness of comprehensive, multidisciplinary brain injury management does exist but this is yet to be fully translated into practice.
- Taking a good history is critical to reaching an accurate diagnosis of most sleep disorders, especially in the absence of sophisticated sleep equipment.
- Non-motor symptoms of Parkinson's disease tend to be poorly recognised, often misunderstood and left untreated.
- Good grasp of the Mental Capacity Act, Mental Health Act and other related legislation is essential when managing patients with brain damage.
- Understanding behavioural changes in patients with epilepsy can be of significant diagnostic value.
- Challenging behaviour frequently presents as a consequence of traumatic brain injury and requires multidisciplinary bio-psycho-social management approach.
- Disentangling the effects of motion and emotion in Tourette Syndrome can be challenging and the role of the Neuropsychiatrist is crucial to fine tune the management of motor and emotional aspects.

Dr Alex Ball, Consultant in Rehabilitation Medicine in North Staffordshire, then delivered a talk on how comprehensive services for brain injury can be achieved. Dr Ball highlighted the fact that in order to achieve the best possible outcomes for patients, tailored intervention should begin as early as possible. The redesign of major trauma services in England has brought about welcome changes to acute phase management in some centres but as yet has little impact on longer term community provision and has not benefited those with non-traumatic brain injuries. The challenges around writing a business case were highlighted given the fact that the financial benefits are not immediate. Evidence of the effectiveness of comprehensive, multidisciplinary brain injury management does exist but this is yet to be fully translated into practice. Issues around services for patients with severe disability following brain injury were also discussed. This was particularly highlighted by a carer who contributed towards Dr Ball's session discussing practical difficulties in looking after loved ones with such a severe degree of disability.

The conference offered a selection of workshops for delegates to choose from. A workshop run by Dr Selsick, Consultant Neuropsychiatrist and Lead Consultant Psychiatrist of the Insomnia Clinic at the Royal London Hospital, emphasised that clinicians may feel that they cannot manage sleep disorders without specialist diagnostic equipment found in sleep clinics. However, a good history was thought to be critical to reaching an accurate diagnosis of most sleep disorders. The workshop looked at a few sleep disorders that are commonly encountered, but frequently missed in general medical and psychiatric practice.

A session on Non-motor Manifestations of Parkinson's disease was run by Dr Sridharan, Consultant Neuropsychiatrist in North Staffordshire. In the context of that workshop, the fact that non-motor symptoms of Parkinson's disease are poorly recognised, often misunderstood and left untreated was highlighted. It was also acknowledged that non-motor symptoms can manifest from the pre-motor phase of the illness and can often complicate the advanced phase. The impact on quality of life and prognosis was discussed. Various assessment and management issues were also explained.

Mr Feery, Barrister, ran a workshop on Brain Disease in the Court Room. The workshop explored some of the medicolegal issues that

are involved in the context of brain injury and related measures. Issues related to the Mental Health Act and Mental Capacity Act with particular relevance to brain damage were discussed with conference delegates and their questions were addressed accordingly.

A workshop on Epilepsy and Behaviour was run by Dr Bagary, Consultant Neuropsychiatrist from Birmingham. Dr Bagary talked about various behavioural changes that can take place in the context of epilepsy. How those behaviours can be of diagnostic value along with management issues were also discussed.

Dr Mike Dilley, Consultant Neuropsychiatrist, gave a key note talk on Brain damage and challenging behaviour. The emphasis of the talk was on pharmacological management issues. Dr Dilley presented current evidence in relation to agitation, aggression and impulsivity amongst other related symptoms in the context of brain injury. Management of acute and chronic phases were also discussed and relevant advice was given in relation to clinical management. Dr Dilley highlighted the fact that challenging behaviour frequently presents as a consequence of traumatic brain injury. Commonly, more clinical attention is paid to agitation and aggression, but there are a range of behaviours that can be difficult to manage in people with traumatic brain injury. Dr Dilly reviewed a range of challenging behaviours commonly seen after traumatic brain injury and also touched on the relevance of psychosocial approaches to management in this respect.

Professor Cavanna, Consultant in Behavioural Neurology, gave a talk on Tourette's Syndrome and other tic disorders. Professor Cavanna discussed current diagnostic criteria and management issues. The fact that up to 90% of patients with Tourette's syndrome present with psychiatric disorders, including OCD, ADHD, impulsivity, anxiety and depression was highlighted. Disentangling the effects of motion and emotion can be challenging and the role of the neuropsychiatrist was thought to be crucial in order to fine tune treatment interventions and improve patients' health related quality of life.

Conference presentations and videos were made available for delegates after the events.

BANA National Conference & AGM

Conference details: 27 June 2015, London, UK. ***Report by:*** Debra Nash, CEO of BANA.

London's summer heat was just rising when the British Acoustic Neuroma Association (BANA) arrived in the capital to host its 23rd National Conference and AGM on 27 June 2015. Delegates were luckily not deterred, and for the day the Wesley Hotel, close to Euston station, became our conference home.

After an introductory welcome, one of BANA's new Patrons, Mr David Moffat, Consultant Neuro-otologist and Skull Base Surgeon, delivered a keynote presentation to the 70 delegates, who were members of the charity and their guests. In an interesting delivery, Mr Moffat began by charting the history of acoustic neuroma discovery and the developments of surgical practice to the present day. Of much interest to those present, Mr Moffat went on to approach the leading questions posed at diagnosis and the management options. He presented a number of studies, and his audited findings, on schwannoma size and data relating to such symptoms as hearing loss, facial palsy and tinnitus; thus providing the patient with an evidence base for each of the current three options in management. This enables the patient to make an informed decision on their management.

The focus of BANA's conference this year was research, instigated in part by the Board's first medical member trustee, Dr Michael Maslin; formerly a Research Scientist at the University of Manchester, and now an International Clinical Trainer with the Interacoustics Academy. Dr Maslin's presentation explored BANA's charitable objectives and the Board's motivation to invest more focus on the research field, chronicling his own involvement with the charity to becoming a serving Trustee. Swapping hats, he then demonstrated the potential for research to help those with acoustic neuromas from the perspective of his role with Interacoustics, the conference's main sponsor this year.

Mr David Moffat

Dr Michael Maslin

Dr Roland Schaette

Professor Andrew Forge

The afternoon session was dedicated to some of the research work of University College London's Ear Institute, represented by Dr Roland Schaette and Professor Andrew Forge. Dr Schaette presented an interesting and detailed lesson to the delegates on his specialist field of tinnitus. He explained the correlation between tinnitus, the brain and hearing loss, noting studies in which hearing loss is temporarily induced to understand the associations. It was explained that tinnitus might arise as a side-effect of the brain trying to compensate for hearing loss. When the auditory brain increases the gain of its neural circuits due to lack of input from the ear, there can be over-amplification of spontaneous neuronal activity/neuronal noise which is then heard as tinnitus. Whilst Dr Schaette advised that a cure for tinnitus is not currently available, the concepts of current research directions were inspiring to those present.

Professor Forge concluded the day's events with a stimulating visual presentation on his research in the therapeutic potential of the regeneration of hair cells in the inner ear. Taking the lay audience through the inner workings of the ear at microscopic level, viewed at intervals in 3D with the help of distributed glasses, he illuminated delegates' understanding of deafness and vertigo, two principal symptoms of the acoustic neuroma condition, by explaining the structures and purpose of the hair bundles, hair cells and supporting cells in generating sound, and how damage may occur. While it was acknowledged that regeneration of hair cells will not cure deafness for acoustic neuroma patients, Professor Forge was keen to support BANA and present to the delegates, as a thank you to acoustic neuroma patients, whose anonymous tissue following translabyrinthine surgery has been utilised within his research work.

BANA's AGM concluded the day's events for member delegates, with two more trustees formerly adopted onto the Board of Trustees; Business Consultant Phil Whiley, and Mr Simon Lloyd, Consultant Skull Base Surgeon and Auditory Implant Surgeon. An overview of BANA's first full year under its new management structure showed a positive turnaround for the charity, and the day was considered an informative and successful one by those in attendance.

The First Congress of the European Academy of Neurology

Conference details: 23 June 2015, Berlin, Germany. ***Report by:*** David B Vodušek, Chair EAN Liaison Committee, Hannah Cock, Chair EAN Education Committee, Paul Boon, Chair EAN Programme Committee.

The European Academy of Neurology (EAN) held its 1st Congress in Berlin, Germany, from 20-23 June that was attended by 6400 participants from 106 countries who took part in 8 Symposia, 25 Teaching courses, 23 Focused workshops, 5 Hands-on courses, 3 Interactive sessions, 5 Special Sessions and showed 1546 posters. Furthermore, 2 Scientific Satellite Symposia took place at the Charité, as well as 17 Industry Satellite Symposia.

EAN was set up last year following a merger between the European Federation of Neurological Societies (EFNS) and the European Neurological Society (ENS). The new society unifying all European neurologists is well placed to make major contributions to neurological health care in Europe. This includes playing a coordinating role in education and training in neurology, in neurological practice, and in defining uniform diagnostic and therapeutic standards for patient care in Europe. EAN also has enormous potential for promoting scientific research in neurology as well as the neurosciences in general. It is becoming more and more obvious that neurological diseases have major public health relevance. More than 220 million people in Europe[1] suffer from some form of neurological disease – a ticking time bomb for health care systems due to the sheer numbers and costs involved. The incidence of many conditions such as Alzheimer's and stroke will further increase in an ageing society. This scale and impact of neurological disease in Europe is underestimated and often overlooked, an important health care policy message that came out of the 1st Congress of the European Academy of Neurology.

The main message from this congress is that our members want us to cover the whole spectrum of Neurology and that we need to represent this at the highest level with the most outstanding speakers from all fields. We are happy that the congress was a meeting point of all neurological subspecialties, and both the education programme and scientific presentations covered the whole spectrum of Neurology. Neurology is in the privileged position to have not only a unified voice for Neurology in Europe but also many sub-specialty societies, with the EAN congress being the ideal place for the neurological generalist to meet the neurological specialist, and for specialists to update their general neurology knowledge.

The congress sessions provided much new and breaking content and they were overall well attended. Particularly, the congress highlights session was packed. Among these highlights were presentations on improvements in the understanding of immunological mechanisms of neurological disease and the increasing success of determining and validating biomarkers for neurological conditions such as multiple sclerosis, Alzheimer's disease and epilepsy. Several large clinical trials were reported to show positive outcomes. Among the hands on courses that were strongly promoted at this congress, the electrophysiological course was particularly successful. EAN has clearly chosen in favour of an e-poster environment. Only e-posters were available during the congress, which was met with enthusiasm by most and some comments for refinement and improvement by others. Last but not least, the epilepsy and Parkinson village were organised for the first time and proved to be a wonderful learning experience that will be continued during the Copenhagen congress.

Professor Gunther Deuschl, President of EAN.

Participants gather around the e-posters presenting new research, and providing an ideal environment for generalists and specialists to interact.

This congress was not only about science, it was an event with many faces.

Among the several social, educational and scientific sessions, the programme included a new event entitled "Challenges for women in Neurology: sharing experiences". For European Neurology at least the overt recognition that some women still face unacceptable challenges to progressing their academic or hospital careers represents an innovative idea.

Successful female colleagues in neurology and neuroscience shared professional and personal experience related to their career route. Those on the panel at this inaugural meeting were Angela Vincent, Oxford (UK), Dorota Religa, Stockholm (Sweden), Valeria Caso, Perugia (Italy) and Ana Verdelho, Lisbon (Portugal). The audience included men and women at different career stages, providing a platform for open constructive discussion and sharing experiences, and was particularly enriched by the professional experience of two Egyptian Neurologists. They shared the difficult situation of being women, who want to pursue an academic career in their country, without any type of support and often substantial barriers. Overall the meeting reinforced what we already know – the need to ensure equal opportunities for women Neurologists in academic and hospital careers, and the value in providing opportunities (for both genders) to openly discuss barriers and strategies to overcome these. There remains a striking disparity between the proportion of women enrolled as students in medical schools and the proportion of women who hold senior faculty positions, which may further discourage women from pursuing academic careers, and this needs to change.

Ensuring EAN is in touch with the needs of patients is also an important part of the EAN vision. In line with this a Public Awareness Day was organised around the theme Diagnosing, Treating and Managing Headache and Sleep Disorders at the Neurology Lecture Hall in the Alte Nervenklinik at the Charité Campus. The meeting was a joint initiative by EAN and EFNA – European Federation of Neurological Associations, the European umbrella patient group for neurological illness. The event was moderated by Wolfgang Oertel. After the opening by Gunther Deuschl, President of EAN, the topics headache and restless legs syndrome (RLS), and how these can be diagnosed, treated and managed effectively, were presented: Uwe Reuter spoke about the various forms of headache, their causes and triggers, possible treatment, and coping tips. Claudia Trenkwalder presented RLS, its symptoms, cause and treatment.

For both topics, patients had been invited to talk about how they managed their conditions, and how these disorders had greatly impacted on their home, work and social lives. Following the personal testimonies a lively general discussion was led by David B. Vodušek and Wolfgang Oertel.

As it is EAN's foremost task to improve neurological patient care in Europe, it will endeavour to promote scientific research and ongoing educational events leading towards the second EAN Congress that will take place in Copenhagen, Denmark on May 28-31, 2016.

1. *Calculation includes EU-27 plus Switzerland, Norway and Iceland;* Olesen et al, *The economic cost of brain disorders in Europe.* European Journal of Neurology 2012;19:155-16.

European Stroke Organisation Conference (ESOC) 2015

Conference details: 17-19 April, Glasgow, UK. ***Report by:*** Dr Duncan Wilson MbChB, Brain repair and rehabilitation, Stroke research Group, UCL Institute of Neurology, Queen Square, London WC1N 3BG. ***Acknowledgment:*** I would like to thank Dr David Werring for reviewing the draft prior to submission.

"Smoked or baked towel". It was only after the third time repeating himself I finally realised what I was being asked "Small or big towel". I was at the hotel gym reception; the thick Glaswegian accent was going to take some getting used to.

I arrived in Glasgow, disconcertingly sunny, concerned I may have caught the wrong train. It was the inaugural European stroke organisation conference, in its infancy after splitting from the European stroke conference. 2700 attendees, 160 scientific oral presentations, 1100 posters; this was clearly going to be a success.

The conference was arranged into parallel sessions run over three days divided into: general interest, focused clinical topics, focused research topics, care/patient organisation, scientific communications, teaching courses and industry supported symposia. With so many parallel sessions it is impossible to cover the whole conference, so I will present some personal highlights.

No other sub specialty within Neurology has accelerated as fast as vascular neurology over the past four years. The introduction of non vitamin K oral anticoagulants (NOACs) has changed the face of stroke prevention in atrial fibrillation (AF) and continues to do so. More recently the endovascular trials have caused a sea change in hyperacute stroke care, whilst intracerebral haemorrhage (ICH) understanding, management and prevention is also a burgeoning research topic. All three topics had major roles at the conference.

Endovascular treatment (thrombectomy) in addition to routine IV thrombolysis for major proximal anterior circulation occlusions was further confirmed as a new standard of care. Four positive endovascular trials were announced at the international stroke conference earlier this year in Nashville Tennessee, and ESOC continued the trend: two further trials were announced (ESCAPE and REVASCAT), whilst MR CLEAN and SWIFT PRIME released sub analysis of their trials.

In keeping with the four recently published endovascular trials both ESCAPE and REVASCAT were positive and strikingly similar. ESCAPE shows that endovascular thrombectomy is 2.6 times more likely to yield a good clinical outcome compared with tPA alone with a number needed to treat of 4[1] whilst REVASCAT odds ratio was 1.7 for the same outcome with a NNT of 6.[2] Despite these excellent results and the very good recanalisation rates achieved in all the recent endovascular trials, a poor outcome (mRS 3-6) still remains prevalent. A shift in focus now turns to neuro-protective agents or other adjunctive strategies to salvage more penumbra.

NOACs continue to make headlines: a recent meta analysis showed that they are superior to VKA in preventing cardioembolic stroke whilst having markedly lower ICH risk (RR 0.49).[3] Phase IV registry data for Dabigatran was presented showing very similar results to those seen in the RCT, suggesting RCT data is applicable to the "real world".[4] Lastly, a small case series from our team at Queen Square was presented comparing NOAC ICH with warfarin ICH: interestingly NOAC ICH cases had smaller haemorrhage sizes and better clinical outcomes when compared with warfarin ICH cases.

Despite only representing a small proportion of stroke, ICH is a major cause of stroke mortality. As such there was significant interest in this topic. The clinical dilemma of restarting oral anticoagulants (OAC) for AF prevention after ICH was the topic of two talks. A Danish registry of 1032 patients with follow up over 2.4 years revealed a lower incidence of ischaemic stroke (IS) (HR 0.37) and mortality (HR 0.37) for those who restarted OAC without an increase risk of major bleeding (HR 0.67). This data supports a similar finding by German group whose results were recently published in JAMA.[5] Preliminary results from an unpublished multi-centre study revealed the marked variation in centres in restarting OAC in patients with AF after ICH (7%-72%). Clearly a randomised controlled trial (RCT) is needed, to this end the protocol for APACHE-AF was presented. More work is also needed to define subtypes of ICH (e.g. cerebral amyloid angiopathy, CAA) which may respond differently to exposure to antithrombotic drugs.

Further presentations on ICH included;

1. Meta analysis on ICH cases in alteplase RCTs. Findings revealed a delay in treatment, increasing age and baseline NIHSS score was not associated with an increased odds of ICH although there was an absolute increase in ICH with increasing NIHSS scores.
2. A sub analysis from INTERACT 2 shows a very interesting association between ICH risk and the temperature in the preceding 72 hours. Low temperatures (especially below 0) show higher risk of ICH. This was somewhat independent of systemic blood pressure (BP), the author suggesting a 'mammalian diving response' may be implicated, perhaps by raising cerebral perfusion pressure.
3. Cavernomas and unruptured intracranial arterio-venous malformations (AVMs) trials (ARUBA) were presented, the clear take home message being avoid intervention in unruptured AVMs and cavernomas. Conservative management yielded a risk reduction of 73% vs. intervention in unruptured AVM management,[6] probably the largest treatment effect (or non treatment effect) ever seen in stroke!

Other topics which came up frequently were cerebral amyloid angiopathy (CAA) and, closely related to this, cerebral microbleeds (CMBs). The expanding clinical spectrum of CAA led the Boston group to look at the different pathological, genetic and imaging phenotypes of CAA with ICH and CAA without ICH. The CAA with ICH phenotypes showed increased cortical superficial siderosis (cSS) in particular disseminated cSS and increased levels of apolipoprotein epsilon 2, whilst non ICH CAA phenotypes were associated with apolipoprotein epsilon 4. Interestingly both groups had similar "vasculopathic changes" (changes associated with ICH) in their blood vessels suggesting there are other pathological changes associated with ICH risk that are yet to be discovered.

The effect of CMBs on stroke risk in a population based cohort (Rotterdam study) was presented. Subjects with CMBs in a strictly lobar distribution (suggestive of CAA) were found to have a 5.25 times risk of ICH compared to those without CMBs, but did not carry an increased risk of IS, whilst those subjects with CMBs in a non lobar distribution were found to be at risk of both ICH (OR 5.77) and IS (2.6). Lastly a meta-analysis was presented revealing CMBs increased the risk of spontaneous ICH by roughly two in thrombolysis, however clinical outcomes were not examined so this should be considered hypothesis generating only.

Stroke is an exciting field with excellent research opportunities for both neurology trainees and medical trainees. Next years meeting is in Barcelona, Spain and I would strongly suggest you attend.

References

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Association of British Neurologists Annual Meeting

Conference details: 19-22 May 2015, Harrogate, UK. ***Report by:*** Seán J Slaght, Neurology Consultant, University Hospital Southampton.

The Association of British Neurologists was welcomed to Harrogate for this year's annual meeting. In his opening address as outgoing President of the association, Geraint Fuller informed us that the People of Yorkshire divided people into three types; those who come from Yorkshire, those who want to come from Yorkshire and those with no ambition at all!

The meeting started with a session on Neurosurgery. The treatment of Normal Pressure Hydrocephalus is always controversial, but Richard Edwards, from Bristol, gave some very compelling reasons why we should at least consider it. Caroline Hayhurst from Cardiff described the recent change in management of low grade gliomas, with the evidence that early aggressive treatment results in better long term outcomes than the traditional watch and wait. The session was rounded off by William Taylor from Glasgow, who told us when he would operate on himself.

The Holmes lecture from Prof Anthony Lang (Toronto, Canada), talked of his work on Corticobasal Syndrome, updating us on the underlying pathology, diagnosis and the hope for future treatments.

The ABN lecture took us through neurological infectious diseases, the challenges of Global health and the bureaucracy of research. Jeremy Farrar described his career, starting with Neurology, moving onto running an infectious disease unit in Vietnam for 18 years, before returning to the UK to take the helm of the Wellcome trust. He described how it could take 611 days to go from initially having a research question to enrolling your first patient in a clinical trial – a time scale that is too long to tackle modern day emerging health problems such as the Ebola epidemic.

The day was rounded off with parallel sessions. The advent of commissioning and the challenges and potential rewards this may bring were explored in an important managerial session.

The second day kicked off with an early start with several special interest groups holding parallel breakfast meetings.

The main sessions started with a review of ion channels, from a reminder of their structure and function from Dimitri Kullman, the psychiatric consequences of their disfunction from Belinda Lennox and neuromuscular channelopathies with Nicholas Davies.

The ABN medallist this year was Andrew Lees, with a citation from William Gibb. Prof Lees described his extensive career in movement disorders.

The day was finished off with the annual general meeting and more special interest groups. An excellent opportunity to either catch up with friends and colleagues who share your interest; or delve into an area of neurology that you have less experience with. I attended the Infectious Diseases special interest group and learned a great deal in excellent, interactive case discussions.

Geraint Fuller with ABN medallist, Andrew Lees.

Alastair Compston with Anthony Lang.

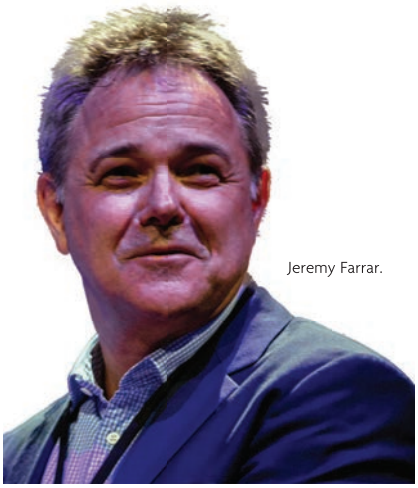
The final day saw the ever-popular case presentation competition, sponsored by ACNR. The standards were exceptionally high, with the prize going to Dr Alexander Rossor from London with his description of a case of Brown Violetta Van Laera syndrome – self treated with mushy peas! Look out for this case report in a future issue of ACNR.

The morning was rounded off with a teaching session in the Psychiatric borderlands of neurology, including the acutely agitated patient, Autism spectrum disorder and Psychosis.

The final sessions of the day were new themes for the ABN. Nicholas Fox and Robert Hadden told us how they would approach the patient with cognitive impairment and generalised sensorimotor neuropathy. Very didactic sessions, but always good to see how the experts do it. Just to prove that neurologists no longer rely solely on steroids the afternoon was concluded with a roundup of the treatments for MS (Neil Scolding), CIDP (Michael Lunn) and Myasthenia (Jon Sussman).

The meeting was brought to a close with the awarding of prizes: best platform presentation went to Dr Joseph Masters, best Audit to Dr Amy Edwards, case presentation competition to Dr Alexander Rossor and best poster to Dr Salwa Kamourieh.

All in all an excellent meeting in a wonderful setting.



Jeremy Farrar.

Association of British Neurologists Trainee Afternoon

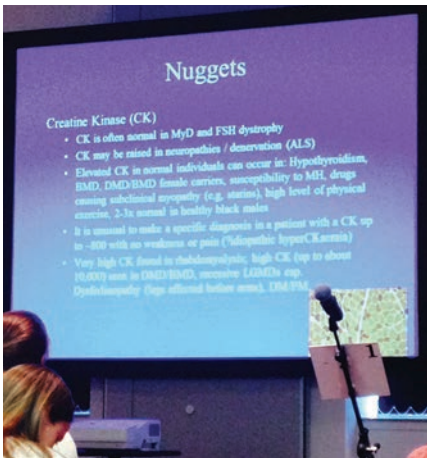
Conference details: 19 May 2015, Harrogate, UK. ***Report by:*** Chinar Osman, Neurology SPR, Southampton General Hospital.

I attended the Association of British Neurologists trainee afternoon on Tuesday 19th May 2015 in Harrogate. I must say I found it to be very useful and relevant to clinical practice. It was a mixture of cases with interactive small group discussions.

The first part entailed small group teaching sessions on muscle diseases. We were divided into four groups depending on our level of training. The sessions were delivered by Professor Doug Turnbull from Newcastle, Dr Paul Maddison from Nottingham, Dr Mark Busby from Leeds and Dr John Walters from Swansea. They were rotating between groups and presenting cases for discussion. The first case was a patient with a diagnosis of chronic progressive external opthalmoplegia. They explained the different genetics in this condition, which can have an effect on prognosis. For instance, if the patients have a large single deletion in mitochondrial DNA, this can increase the chance of serious cardiac conduction abnormalities and the 3243 mutation carries a poorer prognosis. The second case was rhabdomyolysis in a 27-year-old patient with learning difficulties and scapula winging who was found to have a limb girdle muscular dystrophy. We discussed the importance of history taking in muscle patients and also the need to establish if there are any clues in the history regarding the 'second wind' phenomenon, which can affect patients with McArdle's disease. The third case was a patient who was found to have a laminopathy where the nuclear laminar and associated proteins such as emerin are affected. Once again, this case highlighted the importance of genetic testing for various genetic subtypes, which can cause significant cardiac abnormalities such as LGMD1B. The fourth case was a patient with chronic fatigue and aches with mild calf hypertrophy and a persistently raised CK. A muscle biopsy with immunohistochemistry showed dystrophin, highlighting the importance of performing immunohistochemistry to look for muscle integrity.

The second session was a lecture by Dr Gillian Sare from Nottingham on 'Moving Towards Consultancy'. This was a well-delivered and relevant talk. It outlined important interview skills as well as being an eye opener of what one needs to do to prepare for consultancy.

Following a well-deserved coffee break, the third session was again small group teaching sessions on dizziness in the general neurology clinic. The sessions were delivered by Dr Geraint Fuller from Gloucester, Dr Nicola Giffin from Bath, Dr Ralph Gregory from Poole and Dr Mark Lewis from Leeds. They were rotating between groups and presenting cases for discussion. The first case was a patient with acute vertigo with BPPV who had a positive Hallpike. We were shown how to do the Dix Hallpike and the therapeutic Epley manoeuvre. The second case was a Parkinson's patient complaining of dizziness. We discussed different mechanisms of dizziness in Parkinson's disease, varying from polypharmacy to postural hypotension and postural instability. The third case discussion was on how to differentiate between peripheral and central causes of vertigo. If the patient had a negative head thrust test with direction change nystagmus and a skew deviation then it is likely to be a central cause. The fourth case was a case of vestibular migraine with a combination of vertigo, balance disturbance with migraines. It is still under-diagnosed and the management is similar to migraines. There is also no strong evidence of risk of stroke if you are a migraine sufferer unless you are female and on the combined oral contraceptive pill.



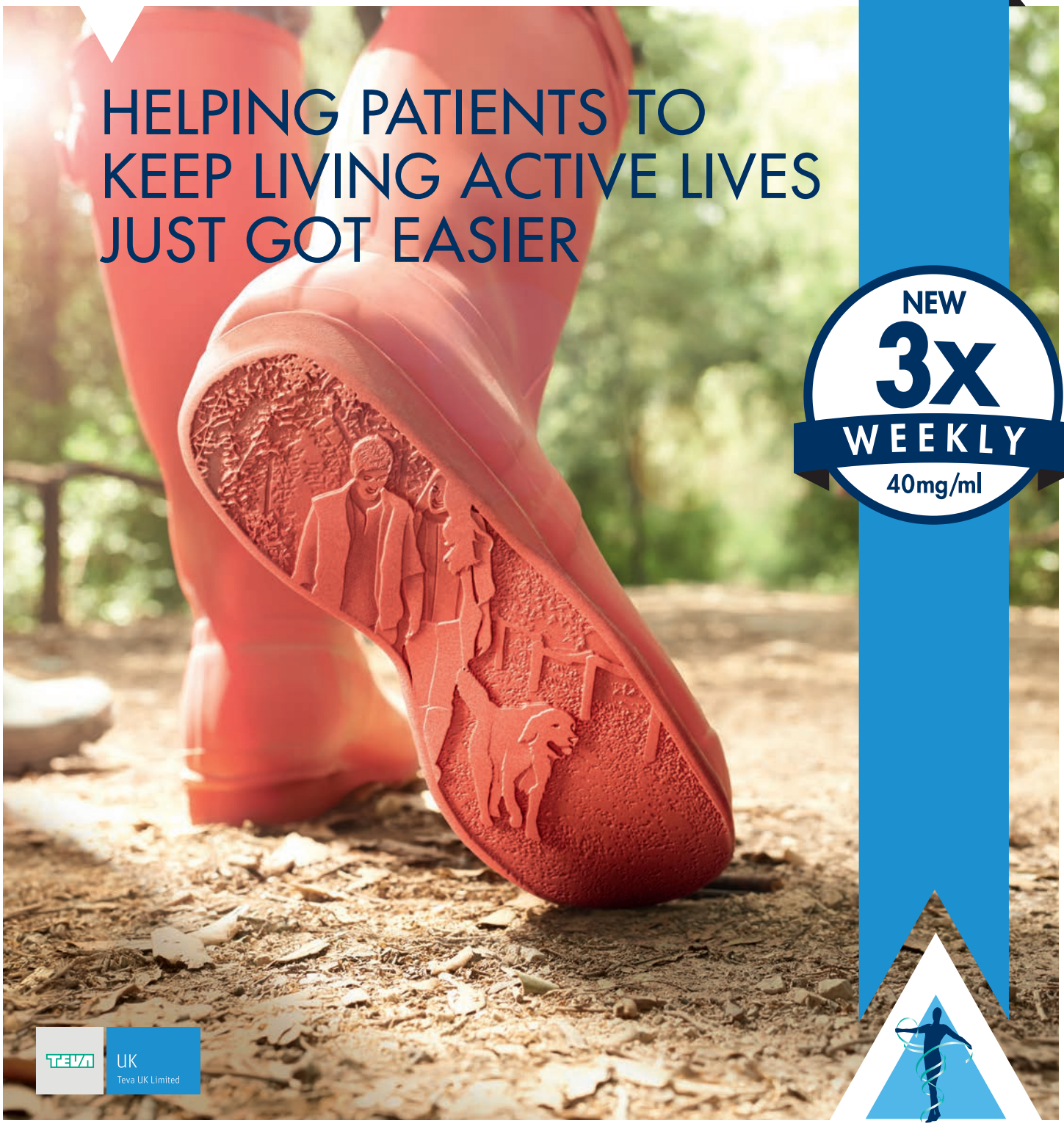
During the second part of the afternoon we were joined by the foundation/core medical trainees and had a lecture by Prof Doug Turnbull and Dr Paul Maddison on red flags in muscle disease and top tips for neurology examination. This was primarily aimed at muscle diseases and I felt was slightly high powered for the foundation trainees. 1 in 4000 have a mitochondrial disease and the commonest mitochondrial disease is Leber's Hereditary Optic Atrophy and 3243 mutations. Patients with MELAS (Metabolic encephalopathy lactic acidosis and stroke like episodes) have 3242A mutation in 80% and they need optimum seizure control. If patients have a POLG mutation and have seizures one must avoid sodium valproate. Patients with 3243A mutations can have gastrointestinal muscle involvement, thus impeding peristalsis, so it is important to prevent constipation. We were also taught about the importance of distribution of weakness to help establish a diagnosis. For instance, in inclusion body myositis, the distribution of weakness is variable and can be asymmetric, with early weakness of knee extensors and ankle dorsiflexion and the weakness of wrist and finger flexors is disproportionate to the extensors. Therefore, they complain of dexterity loss and grip strength. Finally, they discussed the significance of CK in certain conditions and the importance of always checking thyroid function tests in a suspected high CK as hypothyroidism can raise CK.

Following some light refreshments, Professor Alastair Compston delivered a lecture on 'Translational Neurology in Action – Campath-1H'. The history of which backdates to 1984 (The year I was born!) where its original intention was to treat leukaemia. This was the first human monoclonal antibody (CD52) used as a treatment for multiple sclerosis (MS), with the first MS cohort treated in 1991 and it was soon found to be beneficial in early relapsing remitting MS (RRMS). However thyroid autoimmunity is a common (30%) complication after two years of treatment. In 1999 patients were being treated very early in the disease and it showed a good response with expanded disability status scale (EDSS) improvement. Later named Alemtuzumab this was trialled in RRMS in phase II trials, which showed superiority over Rebif (interferon beta-1a). Alemtuzumab improved natural history for up to 15 years post therapy. The current aim is to help identify patients in advance who could be at risk of autoimmunity following treatment.

We then had a talk on 'Running a Multicentre Study' by Professor David Burn from Newcastle who explained all the important components of running a study and was an insight into real research.

The last talk was 'Lessons I've learned from my PhD and beyond' by Dr Jon Rohrer from London. This was a great way to end the evening as it helped guide us on how to approach research and the important factors to consider.

So all in all this was certainly a packed and useful trainee session which was a good kick start to the meeting ahead!



IT'S ABOUT GOOD DAYS, NOT LOST DAYS

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