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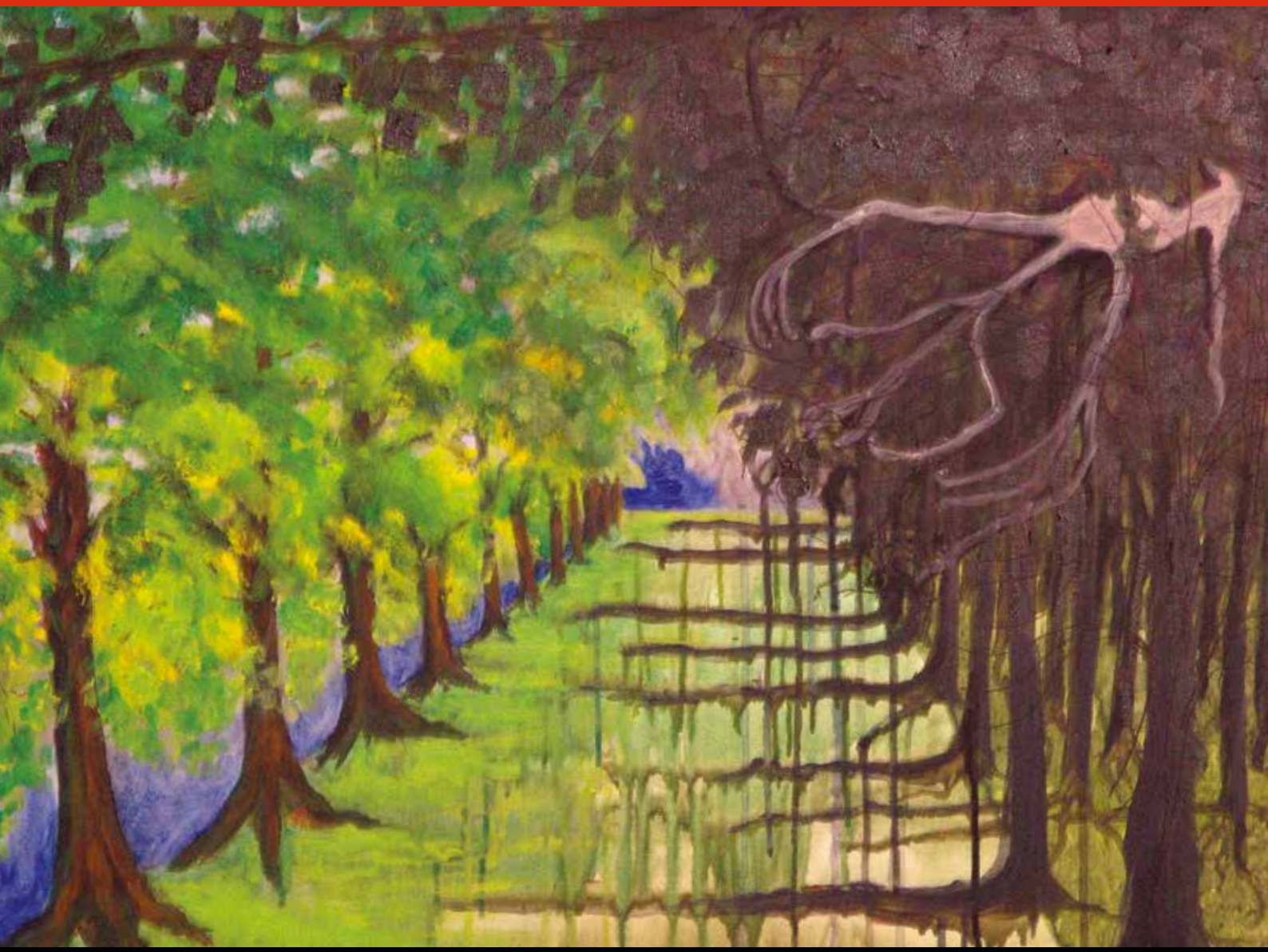

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Front cover picture: The cover picture this issue was painted by Ann Eastman. The painting is a personal expression of the pain that Ann has experienced as a sufferer of Trigeminal Neuralgia. Find out more at http://www.tna.org.uk

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Mike Zandi, Co-Editor.

As neurologists we are increasingly confronted with the issues of genetic testing and screening, and the need to interpret test results and provide guidance to our patients (and their families). In this edition of ACNR we have Nigel Laing from the University of Western Australia write on the issues surrounding preconception carrier screening in neurological disease, with particular attention given to next generation sequencing, and the ethics of screening. Jesse Dawson and Frances McGrane from Glasgow review the potential of vagus nerve stimulation to aid cortical reorganisation and induce helpful plasticity changes for upper limb rehabilitation after stroke, reflecting on evidence in tinnitus, animal models and clinical studies. Wouter Peelaerts from Leuven writes a brief update on the pathogenesis of synucleinopathies, providing context and discussion around his own groups' *Nature* publication in 2015 on α-synuclein assemblies with different structural properties, or 'strains', and the ensuing consequences (Peelaerts, et al. Nature 2015).

Kirstie Anderson, from Newcastle, introduces our new series of sleep neurology articles on page 12, and co-authors with Seán O'Dowd the first on sleep and Parkinson's Disease. This is a comprehensive review with a useful diagnostic flowchart and provides an update on therapies and recent research themes. The rest of this issue of ACNR is full of conference reviews and previews, commentary and book reviews. We hope you enjoy the edition and consider submitting to the journal.

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What is the role for preconception carrier screening in neurology?

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Key take home messages:

- One of the current hottest topics in clinical genetics is whether countries should implement population-wide preconception carrier screening.
- Preconception carrier screening identifies recessive diseases that individuals are carrying before those individuals have children.
- Preconception carrier screening implemented for specific populations with high carrier frequencies for certain diseases, has significantly reduced the incidence of the diseases in those populations.
- Current discussion centres on whether new genetic knowledge and technologies, especially next generation sequencing, can be used to make preconception carrier screening available to entire populations. This would allow anyone who wishes to undergo such screening to avoid having children with genetic diseases.

The sixty-year-old dogma calculated by Newton Morton[1] is that each of us is carrying 3-5 lethal recessive diseases. The trouble is that most of us don't know which 3-5 lethal recessive diseases we are carrying and we don't know which 3-5 lethal recessive diseases our partner is carrying. Therefore, when we shuffle the packs of our genes in our children, like Forrest Gump's box of chocolates, we don't know what we are going to get. We play when we have children, what I have called "genetic roulette."[2] If one of the 3-5 lethal recessive diseases that you are carrying matches one of the 3-5 lethal recessive diseases that your partner is carrying, then there is a one in four chance of a child with a lethal recessive disease. A large percentage of genetic diseases (usually stated as one third[3]) are neurological. These include spinal muscular atrophy, where the carrier frequency is 1:40 to 1:50[4,5] and the special case of Duchenne muscular dystrophy, where, because it is an X-linked recessive disease, only the mother needs to be a carrier for 1:4 of the children to be affected.

I have been involved in molecular diagnosis of Duchenne muscular dystrophy since 1987 and, in that nearly 30 years, I have lost count of the times where, after identifying a boy with Duchenne, we have shown that the mother, unknown to her, was a carrier. This story is repeated all over the world. Would the mothers of Duchenne boys, or the mothers and fathers of children with spinal muscular atrophy, or other severe neurogenetic diseases, like to know they are carriers before having children?

There has been a great deal of rhetoric about how the genomics revolution is going to change health and medicine, with the buzz catchphrase of "personalised medicine" hauled out at every opportunity. But, what might some of the practical implementations of genomic personalised medicine be? Preconception carrier screening might be one of them.

A well-known example of preconception carrier screening targeted at a population with high frequency of a recessive disease, is screening for carrier status for Tay-Sachs disease in the Ashkenazi population. This screening significantly reduced the incidence of Tay-Sachs disease in that group of people.[6] Reduction of the incidence of thalassaemia in Mediterranean countries is another success story of preconception carrier screening.[7] Screening for multiple recessive diseases in a geographically restricted population within the Netherlands,[8] is a use of targeted preconception carrier screening that might not readily spring to mind.

The US National Institutes of Health,[9] the American College of Medical Genetics (ACMG)[10] and the American College of Obstetrics and Gynaecology (ACOG)[11] recommended around the turn of the millennium that population screening for carrier status for cystic fibrosis should be made available. Individual experts in the field have also recommended implementation of preconception screening, stating for example that "carrier screening for various serious disorders should be available."[12] In 2011, the UK Human Genetics Commission concluded that there was no ethical impediment to preconception carrier screening being offered in a population-screening programme.[13] There appears therefore to be no ethical or policy reasons to block population-wide preconception carrier screening being implemented. Nevertheless, population-wide carrier screening programmes remain the exception rather than the rule.[14] Why might this be?

Most of the successful programmes have been implemented for population groups with high carrier frequencies of single founder mutations and therefore the programmes could be highly effective in reducing the incidence of disease using laboratory methods targeted to detect a small number of mutations. Programmes for whole multi-ethnic populations are not so simple to implement.

The best practice example of a population-wide pan-ethnic preconception carrier-screening programme appears to be that in Israel. A decade

or more ago, Israel initiated programmes for diseases prevalent in its Ashkenazi and non-Jewish populations, but also population-wide pan-ethnic carrier screening for recessive diseases, such as cystic fibrosis and spinal muscular atrophy, which are common in all ethnic groups.[15] The Israeli programme is now providing pre-conception carrier screening to more than 60,000 individuals a year[16] but still, significantly, is largely based on founder mutations.

Expanding programmes to entire populations, especially the outbred populations of most countries, introduces the technical challenge of having to screen genes for a far higher number of disease-causing mutations. An illustration of this is that carrier screening for Tay-Sachs disease in the Ashkenazi population requires analysis for only one variant and has a sensitivity of basically 100%, but screening for the 23 cystic fibrosis variants recommended by the ACMG or ACOG, has a sensitivity of only 80%.[17]

Next generation sequencing provides the possibility of screening large numbers of genes, including the entire exome, simultaneously. Bell et al in 2011[18] explored the possibility of carrier screening using next generation sequencing of a targeted panel of disease genes. Their panel consisted of 437 genes responsible for 448 severe recessive childhood diseases.[18] Interestingly, the average number of severe recessive diseases carried by the individuals they tested was 2.8: close to the dogma of 3-5. The Bell et al result[18] is based on only 437 genes and many more disease genes for severe recessive disorders have been identified since, including by my own Group.[19,20] Others have since further explored the use of next generation sequencing for preconception carrier screening.[21,22] However, whether we are ready to implement such screens has been questioned,[17] as has whether screening more and more genes is in fact better.[23]

Problems with next generation sequencing-based carrier screening include:

1) The large number of "variants of unknown significance" identified, how to interpret them and how to calculate the residual risk after screening.
2) Some of the mutations that cause common severe genetic diseases that should be screened for, such as spinal muscular atrophy and myotonic dystrophy, are not readily detected by next generation sequencing technologies. One would thus have to run multiple procedures for each individual to cover all the diseases that should be screened.

Another major issue is residual risk. The fact that the pathogenicity of many variants in the human genome remains unknown (i.e., of uncertain significance) means that when screening disease genes using next generation sequencing, it will not be possible to predict for many findings whether the variant will in fact cause disease in the next generation. It is recommended that only variants of known pathogenicity should be used in screening.[23] Preconception carrier screening cannot therefore guarantee a child free of genetic disease, including those diseases that are screened for.

Preconception carrier screening also cannot prevent genetic disease resulting from de novo mutation, which is a major cause of severe genetic disease.[24] The risk can only be reduced.

Another issue that needs to be considered in relation to prevention of genetic disease is that the long-term clinical effectiveness of many current therapies for genetic diseases is unknown, and it may take decades to determine the effectiveness of presently experimental therapies. The best treatment for genetic disorders may well be prevention.

Prior[17] suggests that we need to implement pilot studies to research preconception carrier screening, including which genes should be screened, population attitudes to screening and counselling requirements. Best practice preconception carrier screening programmes will vary in the different health systems around the world. This becomes especially obvious when it is considered that preconception carrier screening is an issue for both developed and developing countries.[25] Provision of preconception carrier screening by commercial entities, which is already happening in many countries,[23] might work better in countries with more private health systems than in those with more state-provided healthcare. Pilot programmes therefore need to be run in multiple countries.

Preconception carrier screening has the potential to significantly reduce the morbidity and mortality from genetic disease in all societies. It poses however major questions that each country has to grapple with. Answering those questions will require a greater spend on researching prevention of genetic disease.

Finally, you may like to ask yourself a few questions. If you were having children now or were planning to have children in the future, would you like to be able to do as much as you can to avoid passing a severe genetic disease to your children, including using preconception carrier screening? Or, do you think we should continue to play genetic roulette, as generation after generation has done up until now? Should we use the new genetic knowledge and tools we have to take control over the genetic legacy we leave our children, or should we not?

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Vagus nerve stimulation and upper limb rehabilitation

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The Upper Limb and Stroke

Arm weakness is common after stroke and its treatment is recognised as an area of considerable need.[1] Approximately 85% of patients with stroke present with arm weakness[2] and 60% of stroke survivors with poorly functioning arms at one week do not recover meaningful function by six months.[3] Arm weakness is a major factor contributing to disability following stroke.[4] Current treatment for arm weakness typically comprises intensive, task-specific and repetitive rehabilitative interventions or occasionally methods such as constraint induced movement therapy and robotic therapy.[5] A recent meta-analysis and large-scale trials show the effects of current treatments for arm weakness to be modest.[6,7] Improvement in arm function should improve quality of life for stroke survivors, reduce co-morbidities associated with loss of independence, and reduce cost to the health care system.[8]

Neuroplasticity and Recovery

Neuroplasticity is the brain's ability to form new neural pathways in response to injury or disease. It has been a target for the treatment of many neurological disorders including epilepsy and tinnitus. Recent studies have suggested that augmentation of neuroplasticity is required to more fully recover motor function.[9] Novel techniques that drive the growth of new neural pathways related to motor function are needed; vagus nerve stimulation (VNS) may achieve this.

Vagus Nerve Stimulation

VNS is the delivery of small electrical impulses to the vagus nerve (Figure 1). VNS activates neurons in the basal forebrain and locus coeruleus and results in the release of acetylcholine and norepinephrine. These neurotransmitters are known to facilitate the reorganisation of cortical networks.[10] VNS is already used to treat patients with medically refractory epilepsy, with studies showing a reduction in seizure frequency of 50% in 24.5 to 46.6% of patients.[11,12,13] In excess of 75,000 patients with refractory epilepsy have been implanted with VNS devices.[14] The concept of using VNS to restore normal neuronal activity / drive neuroplasticity is under investigation in other chronic neurological conditions.

In noise induced tinnitus, cochlear trauma can lead to a disorganised auditory cortex resulting in chronic symptoms.[15,16,17] The severity of tinnitus is related to the degree of map re-organisation in the auditory cortex.[15,16,17] In pre-clinical studies, pairing auditory tones with brief pulses of VNS has been shown to cause re-organisation of auditory cortex maps specific to that tone.[18] Further, noise-exposed rats were noted to have a significant reduction in startle response, presumably due to tinnitus, and pairing VNS with multiple tones reversed this effect.[18] Thus, VNS paired with a specific stimulus may drive neuroplasticity specifically for that stimulus, thereby restoring auditory cortex architecture and reducing tinnitus. Studies suggest that VNS may help humans with tinnitus.[19] Ten patients known to have unilateral or bilateral tinnitus for over a year received four weeks of VNS paired with auditory tone therapy (using MicroTransponder Inc's Serenity© system). Subjective and objective primary outcome measures were identified in the form of the Tinnitus Handicap Inventory (THI) and the Minimum Masking Level (MML). In patients who had not been taking drugs which could interfere with VNS (muscarinic antagonists, noradrenergic reuptake inhibitors and γ-amino butyric acid agonists), a significant fall in THI of 28.17% was seen following VNS paired with auditory tones.[19] Three out of five such patients had a clinically meaningful decrease in THI (44.3% decrease).[19] Similar results were seen in the MML test which detects the lowest level of noise required to "drown out" the tinnitus. Results of a recently completed and larger, double blind and randomised study of VNS paired with auditory tones in tinnitus are eagerly awaited. Another study looked at the use of transcutaneous vagus nerve (t-VNS) stimulation in tinnitus. When used in combination with sound therapy t-VNS was found to modulate auditory cortical activation, resulting in reduced tinnitus and tinnitus associated distress.[20]

Following on from the work in tinnitus, it is hypothesised that VNS paired with upper limb rehabilitation could drive neuroplasticity specific for upper limb tasks and improve outcomes for stroke survivors. Recent animal studies have shown that VNS paired with motor rehabilitation improves forelimb function after stroke more than either rehabilitation or VNS alone.[21,22,23] Pairing VNS with motor tasks induces plasticity in the motor cortex that is specific to the paired movement and is not seen with motor training alone (Figure 2).[24] The timing and amount of VNS appear important to ensure optimal results are achieved; delaying VNS until after rehabilitation and significantly increasing the amount of VNS delivered results in a poorer outcome.[21,23] Similar results have been seen in experimental models of haemorrhagic stroke; a 77% recovery in function was seen in the VNS plus rehabilitation group as opposed to a 29% recovery in the rehabilitation only group, which was sustained six weeks after VNS was stopped.[22]

The first in-human evaluation of VNS paired with upper limb rehabilitation was recently completed using MicroTransponder Inc's Vivistim© system. VNS treatment for stroke involves high intensity repetitive rehabilitation

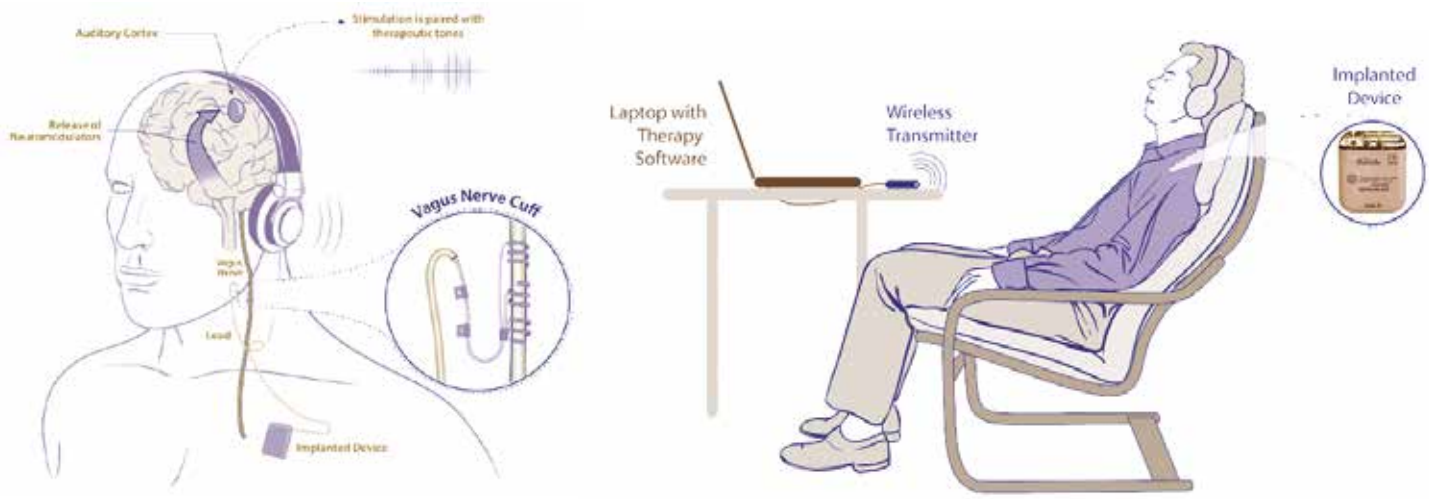


Figure 1: © Images copyright of MicroTransponder
The stimulation electrodes of the leads are placed on the left vagus nerve in the left carotid sheath, and the lead is then tunnelled subcutaneously to a subcutaneous pocket created in the left pectoral region where it is attached to the pulse generator. A wireless control interface is used to communicate with the VNS device and deliver stimulation during therapy sessions.

tasks and each movement task is paired with a 0.5 second train of VNS (0.8 mA). Each two hour long therapy session typically involves 400 such stimulations. Twenty-one patients with an ischaemic stroke and upper limb weakness were randomised to six weeks of VNS plus rehabilitation or rehabilitation alone. The per-protocol analysis included participants who attended at least 12 of the 18 therapy sessions and were not on medications that could interfere with VNS. The upper extremity Fugl-Meyer (FMA-UE) score was used to compare outcomes in the two groups, although the primary objective was to assess safety and feasibility of treatment. A clinically significant improvement was defined as a change in FMA-UE score of six or more. In the per-protocol analysis the mean change in FMA-UE score was 9.6 points in the VNS group and 3.0 points in the rehabilitation only group. Six (66·7%) achieved a clinically meaningful response on the FMA-UE score in the VNS group compared to 4 (36·4%) in the rehabilitation only group (p=0·17).[25] The study confirmed that VNS paired with rehabilitation is feasible and did not raise safety concerns.[25] A further randomised double blind and sham controlled study is under way.

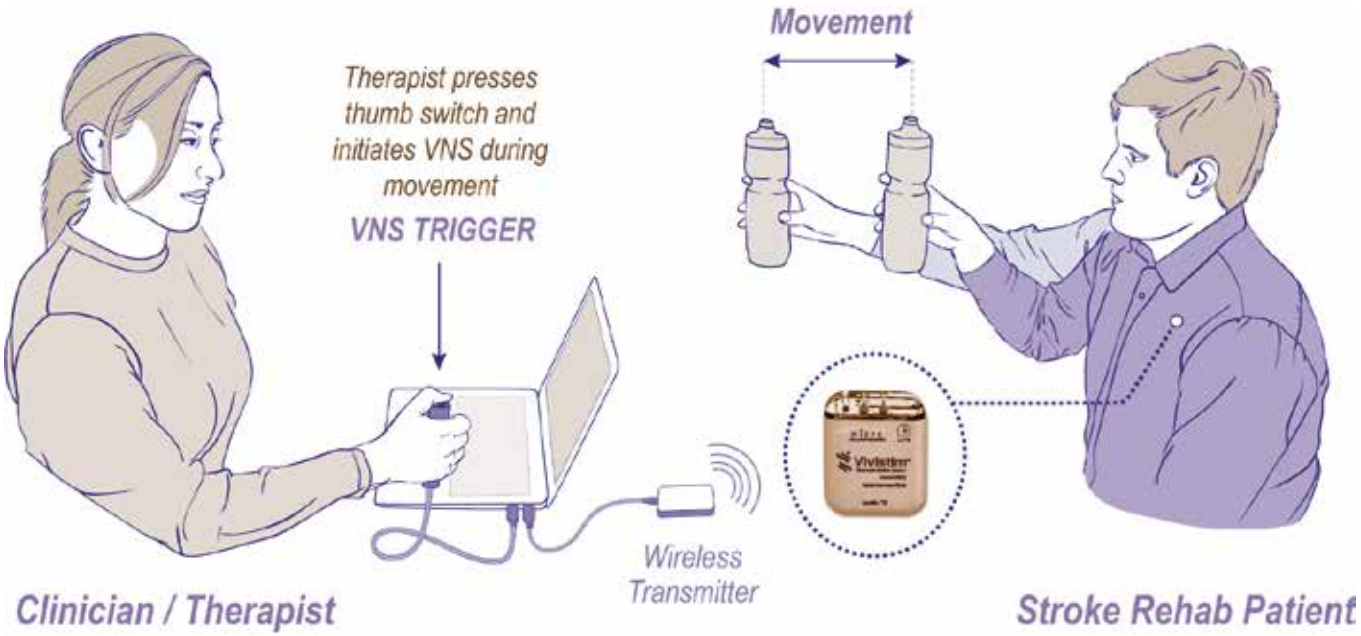
Suitability of VNS Therapy After Stroke

Clearly further study is needed. VNS is already used safely and effectively in patients with medically refractory epilepsy and in the stroke stimulation paradigm, only approximately 1% of the VNS given in epilepsy is used (the device is only active during therapy). This may further reduce the risk of adverse events. Little additional set up time is required and therapists can be readily trained to deliver VNS therapy in contrast to techniques such as transcranial magnetic stimulation. One of the main disadvantages is that surgery is required, which will exclude some patients and carries small risks of infection, vocal cord palsy or anaesthetic complications. The use of t-VNS has not yet been explored after stroke but has been studied in both tinnitus and epilepsy.

Summary and Further Research Implications

Animal studies have shown that VNS paired with rehabilitation therapy for the upper limb augments upper limb specific neuroplasticity and improves forelimb function. A small pilot study in humans has shown promising improvements in upper limb function and confirmed it is an acceptably safe and feasible treatment for further study. Further research is needed to assess efficacy as the recent clinical pilot study was small.

Figure 2: © Images copyright of MicroTransponder
Vagus nerve stimulation is manually triggered by the therapist using a push button while the patient performs a task.



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Putting a strain on the brain

An update on synucleinopathy pathogenesis

Wouter Peelaerts

After a predoctoral research internship at the Laboratory of Neurogenetics at the National Institutes of Health (NIH), Washington D.C., USA, with a focus on familial PD-linked proteins, Wouter was awarded with a PhD scholarship from the FWO Flanders and is currently a Doctoral Researcher/Neurobiologist at the lab for neurobiology and gene therapy of Professor Veerle Baekelandt at the KU Leuven, Belgium. By using viral vector technology the aim is to develop and characterise new rodent models to gain new basic insight in the pathogenesis of PD, which will help to design and explore new rational, therapeutic strategies. Specific research interest involves studying the role of α-synuclein protein aggregation in PD. Our recent work has shown a new and exciting role of different types of α-synuclein aggregates that link α-synuclein pathology to multiple neurodegenerative diseases.

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Recent and exciting developments are providing new clues as to how different synucleinopathies such as Parkinson's Disease (PD), Multiple System Atrophy (MSA) and neocortical Lewy Body Dementia (LBD) might originate. Synucleinopathies comprise a large group of heterogeneous neurodegenerative disorders and although they present with distinct clinical phenotypes, they all share α-synuclein (α-SYN) protein deposits as a common histopathological hallmark. α-SYN proteinaceous inclusions are found at specific predilection sites within the nervous system and their post-mortem confirmation is crucial for diagnosis of PD, DLB or MSA. In PD and DLB, α-SYN inclusions are found in neuronal cell bodies and axons, which are termed Lewy Bodies (LB) and Lewy Neurites (LN), respectively. Patients that suffer from PD show predominant parkinsonism[1] while patients with DLB exhibit progressive cognitive impairment as a predominant feature next to motor-related deficits or other core features.[2,3] The clinical and histopathological features of MSA, however, are notably different compared to PD and DLB. In the central and peripheral nervous system of patients with MSA, α-SYN does not only deposit in neurons but also in oligodendroglial and Schwann cells causing crescent-shaped glial cytoplasmic inclusions and filamentous Schwann cell cytoplasmic inclusions.[4,5] Compared to PD and DLB, this translates to distinct symptomatology with corticospinal tract dysfunction, cerebellar ataxia and autonomic dysfunction that can exist next to a parkinsonian syndrome.[6] The heterogeneity of synucleinopathies is also illustrated by the observation that these symptoms can overlap between patients, adding complexity to the diagnosis of these neurodegenerative diseases.

The reason why a single pathognomonic histopathological component is found in different diseases with different symptomatology has been a mystery for over several decades. In a link with prion diseases, researches hypothesised that differences in the α-SYN aggregation process resulting in different α-SYN aggregated structural isoforms might explain such a clinical heterogeneity. In transmissible encephalopathies or prion diseases such as bovine spongiform encephalopathy (BSE) or Creutzfeld Jakob's Disease (CJD), different clinical phenotypes are observed because self-sustaining infectious protein particles, or prions, have the ability to encode structural information and replicate. These aggregated prion assemblies bear unique fingerprints and after exposure to the central nervous system (CNS) they incite specific biological and neurotoxic profiles. The pathogenic prion protein therefore bears intrinsic pathogenicity via a protein-based strain-encoded mechanism causing strain-specific symptomatology.

With this concept of prions in mind, researchers asked whether α-SYN was also able to form strains and propagate in a similar manner. α-SYN is a small and flexible protein of only a few kilodaltons that can readily aggregate in vitro from an unfolded, unstructured protein into megadalton β-sheet-rich fibrillar aggregates that consist out of several thousands of α-SYN molecules (Figure 1). In an initial study performed by Bousset and colleagues it was shown that when α-SYN assembles under different aggregation conditions, it is able to aggregate into distinct high-molecular weight fibrillar polymorphs.[8] The resulting two α-Syn fibrils were extensively characterised and appeared structurally different in various biophysical assays. They had the ability to encode structural information and faithfully propagate between cells, which suggested that these α-SYN fibrils behaved as strains. The morphology of these two strains was examined by electron microscopy and it was shown that one strain appeared straight while the other was more twisted. This led the researchers to label these two types of strains as 'fibrils' and 'ribbons', respectively. Both fibrils and ribbons furthermore responded very different in biochemical and functional assays, indicating that the structural variations of the α-SYN strains were responsible for the different biological phenotypes that they induced.

An important step in proving the relevance of these α-SYN strains for synucleinopathy pathogenesis was to inoculate these strains in brain and study their potential pathogenicity in vivo. By using an experimental rat model that allowed to examine the inoculation of fibrils and ribbons in native and α-SYN overexpressing backgrounds, it was shown that the two synthetic α-SYN strains exhibited distinct histopathological, neurotoxic and behavioral phenotypes.[9] Ribbons induced aberrant Lewy neurite-like inclusions in dopaminergic cells of the substantia nigra pars compacta, a severely affected midbrain nucleus in PD, while this was virtually absent for fibrils. In contrast, fibrils induced motor impairment in absence of clear dopaminergic cell death indicating that α-SYN aggregates have to ability to impair synaptic activity and motor impairment before overt neurodegeneration takes place. When the two α-SYN strains were inoculated in the brain of rats that overexpressed α-SYN, neurotoxicity increased drastically for animals that were exposed to fibrils. This, however, was not the case for animals exposed to the other strain or even oligomers, which are smaller variants of aggregated α-SYN that are assumed to play an important role in several neurodegenerative diseases. Another remarkable finding was that in α-SYN overexpressing conditions, ribbons induced a second histopathological feature. Next to neuritic inclusions, ribbons promoted sparse α-SYN inclusions in oligodendroglial cells, the histopathological hallmark

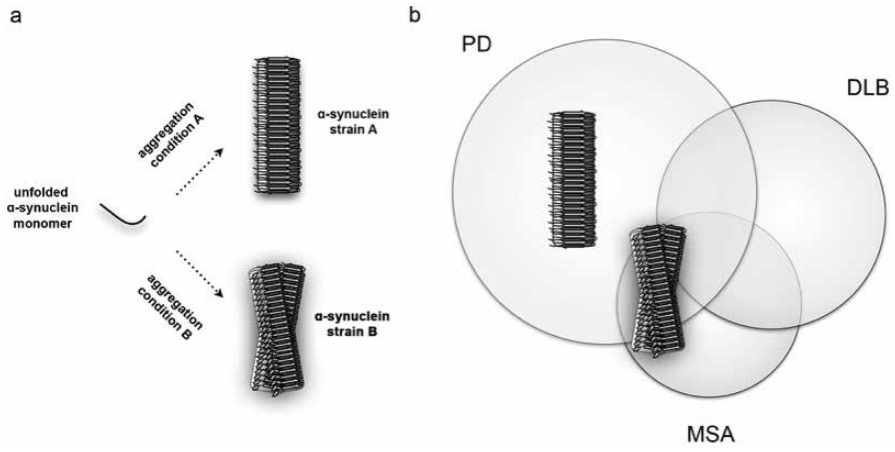

Figure 1. The potential role of α-synuclein strains in synucleinopathies. α-SYN is a small and flexible protein that is highly expressed in neurons of the central and peripheral nervous system where it negatively regulates synaptic activity after binding to the membrane of synaptic vesicles15. a. In the cytosol, α-SYN exists as a disordered protein without secondary structure16. In this unfolded and disordered state, different α-SYN molecules can bind and clump together forming large neurotoxic aggregates that are rich in β-sheet content. Under different environmental conditions, α-SYN can form distinct aggregates or strains that have the ability to replicate in a way that is similar to prions. These strains can multiply and spread throughout the CNS via anatomically connected regions and show different histopathological, neurotoxic and functional profiles after exposure to the central nervous system of experimental animal models. b. α-SYN strains could therefore provide a basis to explain how a single protein is able to induce distinct clinical profiles in a heterogeneous group of neurodegenerative diseases.

of MSA. This was not observed for other conditions and reveals that strains can differentially promote different types of proteinaceous inclusions. These results therefore demonstrate that unique structural assemblies promote disease pathogenesis with different outcomes in histopathology, neurotoxicity and symptomatology.

By using synthetic strains, these experiments provided a proof-of concept as to how synucleinopathies might originate. To further examine whether the brain of patients with PD or MSA indeed contain different types of α-SYN aggregates – the strains, the group of Stanley Prusiner assessed whether brain isolates derived from PD and MSA patients possessed 'prion-like' properties.[10] They indirectly showed that brain isolates derived from patients with PD and MSA, which contain α-SYN aggregates, might indeed be very different. In various cellular and in vivo assays, the isolated α-SYN-enriched fractions were able to accelerate α-SYN aggregation similar to what is observed for prions. These brain fractions furthermore induced strain-specific effects by lowering the incubation time during second passage experiments after inoculation of MSA-derived isolates in transgenic mice. These effects were only observed for post-mortem brain isolates derived from patients that were diagnosed with MSA but not with PD and indicates that the structural ensemble of α-SYN within the brain of these two groups of patients might indeed be very different.

Prions can invade the CNS from the periphery and subsequently spread to anatomically connected regions.[11] A horizontal transfer of prions can therefore occur between individuals, although only in extremely rare conditions, as result of blood transfusions, organ transplantation, injection of growth hormone extracts, exposure to improperly sterilised medical material or eating BSE-contaminated food.[7] In parallel with this, several independent research groups assessed whether misfolded α-SYN might also spread in a similar pattern for the periphery to the CNS. Strikingly, administration of α-SYN aggregates into the blood, muscles or stomach of rodents successfully resulted in transmission of aggregated α-SYN to the CNS.[9,12,13] Synucleinopathy patients very often present with clinical symptoms that indicate a peripheral involvement. Lewy pathology is also present in the enteric nervous system of patients and a long prodromal stage precedes the typical symptoms that characterise PD, DLB or MSA. These findings collectively suggest that the spread of α-SYN is not restricted to the CNS but extends far beyond.

A complete understanding of how α-SYN misfolds and aggregates into different strains with central and peripheral involvement could lead to the development of new diagnostic tools and therapeutic strategies. PET tracers already exist to detect Aβ plaques in the brain of Alzheimer's patients and solving the structure of α-SYN strains might yield new opportunities to develop tracers for synucleinopathies as well. In addition, aggregated α-SYN particles are present in the blood of PD patients.[14] The exact properties of these aggregates, however, are unknown. If strains would propagate systemically, then immuno-based assays (e.g. ELISA) might yield interesting opportunities to detect different types of aggregates by analyzing cerebrospinal fluids or blood samples. The identification of disease-specific strains could furthermore allow differentiating between PD, DLB and MSA patients, who often show overlapping symptoms. Therapeutic strategies involve directly tackling α-SYN aggregation via blocking α-SYN aggregation, promoting the clearance of α-SYN aggregates or immunization therapies. The existence of strains thus not only helps us to understand why synucleinopathies are so different, it also holds great promise in our continuous efforts to improve diagnostic tools and therapeutic strategies.

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Introduction to the sleep series

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Among other pragmatic observations, the Hippocratic teachings state that "sleep and watchfulness, both of them when immoderate constitute disease". Only four things go wrong with sleep - my patients sleep too much (hypersomnia), too little (insomnia), things go bump in the night (parasomnia/restless legs) and they sleep at the wrong time (circadian rhythm disorder). Primary sleep disorders are all common, 10% of UK men over 40 have obstructive sleep apnoea, 5% have troublesome insomnia, at least 2-3 % of adults have some form of parasomnia and the prevalence figures for all these conditions double for those over 65 or those with severe psychiatric disease. However symptoms are often attributed to other daytime conditions rather than thinking of problems within sleep itself.

The enjoyment from sleep clinics comes from most patients having conditions that are easy to diagnose and treat, often with significant improvement in quality of life and other long term conditions. Possibly the lack of sleep medicine as an accredited sub-speciality in the UK is the reason that the average medical student receives little or no sleep medicine education. Even neurologists and psychiatrists have limited exposure to sleep disorders. This is despite the immediate and chronic impact on all aspects of brain function after sleep disturbance of any cause. In particular consolidation of new memories (separate to a simple decrease in attention) and normal mood are the key things we really need sleep for. Aspects of physical health such as hypertension, diabetes, obesity, longevity all suffer too.

So this series of articles tries to highlight sleep problems seen in general neurology and rehabilitation clinics and a simple approach to tests and treatment. Those of us who see patients with Parkinson's Disease at any stage already know that poor sleep is a prominent and early non-motor symptom but an overview of the clinical presentation of different sleep problems, research updates and a simple guide to therapy is within this first article.

By far the commonest cause of significant daytime sleepiness is sleep apnoea, obstructive from obesity and central largely from the pain clinic (look up the simple and evidence based STOPbang questionnaire for those over 40 who are sleepy).

Narcolepsy is different with patients truly "seized by somnolence" and the exciting advances in both understanding of the molecular biology and newer therapies available will be described by Dr Reading.

Distinguishing the bumps in the night can be challenging, the patient has good reason to be an unreliable witness so Dr Dennis will explain the key aspects of history and management for those with nocturnal seizures.

Those with traumatic brain injury have many long term problems and also many reasons to have both acute and chronic sleep disturbance and a framework for diagnosis and management will be provided by Dr Singh.

Finally circadian rhythm disorders have been on the rise since the Industrial Revolution (the real start of shift work) rapidly followed by the electric light bulb and its immediate ability to disrupt 50,000 years of evolutionary biology whereby every aspect of physical and mental health evolved around a 24 hour light dark cycle. Our cellular clocks are aligned by the master time keeper within the hypothalamus – the suprachiasmatic nucleus. More severe circadian rhythm disorders are increasingly recognised as part of the molecular clockwork of severe psychiatric illness rather than simply a consequence of lack of employment and decreased activity, so spotting and fixing broken clocks will be our final article.

Dr Kirstie Anderson,
Section Editor.

Sleep and Parkinson's Disease

"…the sleep becomes much disturbed. The tremulous motion of the limbs occurs during sleep, and augment until they awaken the patient, and frequently with much agitation and alarm…"

Sleep disturbance has long been recognised as an integral component of Parkinson's Disease (PD), as evidenced by the above excerpt from James Parkinson's seminal 1817 paper, "An Essay on the Shaking Palsy". While his description seems to allude, counterintuitively, to tremor worsening during sleep, it is plausible that instead Parkinson was describing one or more of the primary sleep disorders which are now known to be associated with Parkinson's Disease: REM sleep behaviour disorder and/or restless legs syndrome.

Sleep dysfunction is a salient non-motor complaint afflicting 42-98% of patients with PD,[1] but for decades has been something of a "Cinderella" symptom in terms of the attention it garnered, both in the clinic room and in research literature. This is slowly changing and in this review we will attempt to describe some of the common sleep disturbances encountered by PD patients in the pre-motor, early and advanced phases of the disease, with a focus on clinical management, as well as highlighting some of the emerging research themes in the field. As an important preface, it is essential that any

evaluation of sleep in a patient with PD should consider the contribution of motor symptoms such as nocturnal hypokinesia, dystonia or dyskinesia as well as non-motor symptoms of pain, nocturia and sialorrhoea; and the neurologist should be vigilant for symptoms of depression. A thorough analysis of the patient's medication regime is also warranted.

REM Sleep Behaviour Disorder (RBD)

RBD, now widely recognised in clinical practice as a hallmark of the α-synucleinopathies, was first described by Schenck only thirty years ago.[2] This syndrome is characterised by dream enactment behaviour; in normal circumstances, complex inhibitory neuronal circuitry results in skeletal muscle paralysis during REM sleep. Aberrant α-synuclein aggregates interfere with brainstem control of this process, leading to disinhibition of spinal muscles – it is now recognised that this process can occur decades before the evolution of motor parkinsonism.[3]

Clinically, the patient's bed-partner will typically witness purposeful, often violent, movements which can result in injury to either the patient or the bed-partner. Loud vocalisation usually accompanies the motor phenomena. The patient can usually be roused easily, and will classically describe dreams with violent or threatening themes. Interestingly, the aggressive nature of the dream enactment is often at odds with the patient's waking personality. RBD tends to manifest most reliably in the second half of the night, since the proportion of time spent in REM sleep accumulates overnight. A careful clinical history should be taken to exclude mimics of the condition – most notably non-REM parasomnias (history of earlier life sleepwalking; symptoms occurring earlier in the night; patient often rises from bed with eyes open, but is difficult to rouse and will have little or no recall if awoken; can leave the bedroom), periodic limb movements in sleep (PLMS) (a non-REM phenomenon in the early hours of sleep, with slow rhythmic dorsiflexion of the great toe and ankle and flexion of the knee, these movements can be large amplitude), or rarely dream-enactment symptoms generated in the context of a sleep-related breathing disorder such as severe obstructive sleep apnoea (OSA); these patients would often have other symptoms of daytime sleepiness. A definitive diagnosis of RBD requires polysomnographic (PSG) evidence of REM sleep without atonia (see Figure 1). In the general population, the prevalence is estimated at 0.5%, with a preponderance of older, male patients, where it can run an insidious course; although it is generally held that it is under-diagnosed in older females, who due to longer life expectancy, are more likely not to have a bed partner.[4] Recognition of RBD is important in those without motor symptoms, it should alert the neurologist to monitor for the emergence of extrapyramidal signs, as it is a harbinger of neurodegenerative disease

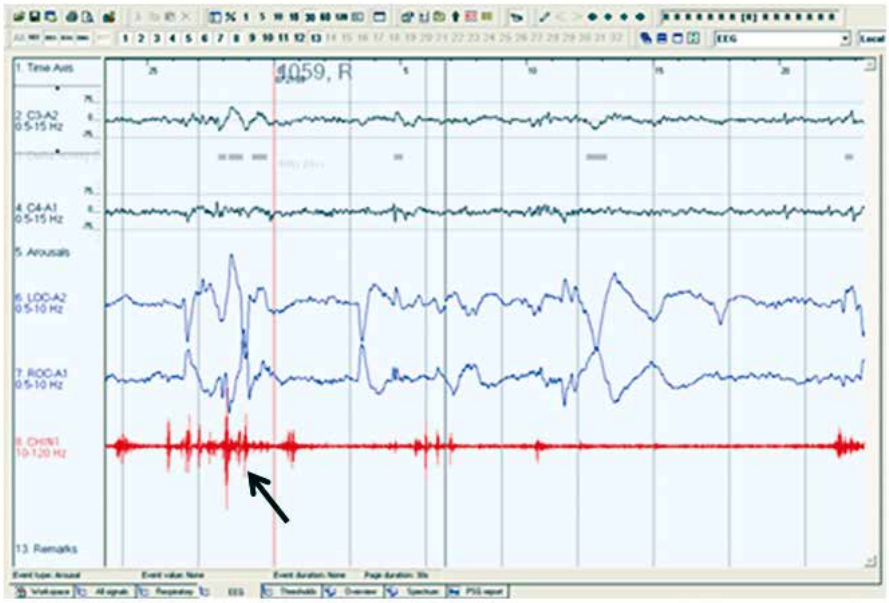

Figure 1. Loss of EMG chin atonia lead during REM sleep is characteristic of RBD. Leads 2 and 4 of the trace demonstrate the EEG features of REM sleep, accompanied by phasic activity of the extraocular muscles (Leads 6 and 7). In normal circumstances, this is accompanied by a quiet chin electromyography trace, "atonia"; here phasic activity is recorded in the muscle during REM sleep (black arrow).

in up to 91% of patients over 14-year follow up.[5] Estimates of the prevalence in patients with known PD vary from 27% in unselected cases[6] to 46% in those with subjective sleep complaints[7] and the syndrome can manifest at any stage of the disease. Identification of RBD in PD is important for two reasons – firstly, it portends a poorer prognosis;[8,9] secondly, it can cause significant morbidity which is potentially avoidable, as it typically responds very readily to pharmacotherapy. Both melatonin (3-12mg) and clonazepam (0.5-1.0mg) are effective treatments for RBD – most centres now use the former as first line therapy given its equivalent efficacy, with a much more favourable side effect profile.[10] It is important to note that many antidepressant treatments (ADTs) are associated with some dream enactment, which usually remits when the ADT is withdrawn; however an emerging literature suggests that in some cases, the ADT unmasks an underlying incipient neurodegenerative disease, manifesting as prodromal depression and RBD.[11]

Restless Legs Syndrome (RLS) and Periodic Limb Movements in Sleep (PLMS)

RLS is a common neurological disorder, which is a clinical diagnosis made on the basis of fulfilling certain essential criteria. These criteria can be summarised as an urge to move the legs, accompanied by an unpleasant feeling in the legs, which is induced or exacerbated by inactivity; these symptoms exhibit a diurnal pattern and are partially or wholly relieved by movement. Other medical or behavioural factors must be excluded. The recent revision of these criteria acknowledges that an episodic variant exists.[12] PLMS is a sleep-related movement disorder, defined by criteria laid out by the American Academy of Sleep Medicine, which stipulate the frequency and duration of the limb movements captured on PSG. Approximately 80% of patients with RLS exhibit PLMS,[13] although the reciprocal relationship is not quite as robust. As RLS responds to dopaminergic therapy, a common pathophysiology with PD has often been postulated, although neurodegenerative features are not seen at autopsy in RLS.[14] Methodological differences have led to the publication of conflicting data relating to prevalence of RLS in PD cohorts, but there does appear to be an excess in PD versus age-matched healthy controls.[15] Recently, severe RLS in middle aged to older men has been associated with risk of subsequent development of PD,[16] but in general RLS tends to follow the onset of parkinsonism rather than precede it.[17] PLMS are frequently recognised in PD, even in the absence of symptomatic RLS, and are important to identify as they are associated with poorer subjective sleep and poorer quality of life.[18] A number of studies have also highlighted a relationship between PLMS and PD severity.[18,19] An important clinical point is that PLMS can vary significantly from night to night, hence a negative overnight PSG may not refute the diagnosis in the setting of a convincing history; this difficulty can be overcome by serial domiciliary lower limb actigraphy over a number of consecutive nights.

The phenotype of RLS in PD appears to differ somewhat from idiopathic RLS. PD patients develop RLS at an older age than the idiopathic group, and have a far lower rate of family history of RLS.[20] It is important to recognise the possibility of RLS mimics in the PD population; various motor and sensory phenomena, particularly in the "OFF" state may at first glance appear to represent RLS

symptomatology, but a rigorous application of the IRLSSG criteria will typically distinguish RLS from these. It is also important to be aware of the propensity of certain adjunctive treatments in PD to unmask or exacerbate RLS; many antidepressants,[21] in particular mirtazapine[22] (commonly used in the PD cohort) have been implicated; there are also data demonstrating worsening of RLS with the administration of exogenous melatonin.[23] The relationship between RLS and dopaminergic therapy in PD is ambiguous; although an evidence-based treatment in idiopathic RLS, some authors have suggested that long duration of dopaminergic therapy in PD is deleterious from an RLS perspective.[14] Akin to PLMS, RLS in PD is associated with increased non-motor symptoms, poorer quality of life and greater daytime fatigue,[24] and as such, should be recognised and treated expeditiously. In those with ferritin levels below 50mcg/l, iron supplementation should be instituted. Consideration should be given to the addition of a small evening dose of a dopamine agonist if this is not already a component of their PD regimen. The other line of treatment of particular utility in this cohort is an alpha-2-delta agonist such as gabapentin or pregabalin.

Excessive Daytime Somnolence (EDS)

EDS is a symptom frequently volunteered by PD patients or their carers in the clinic. Whilst the evaluation of EDS can be confounded by the use of dopaminergic and other psychotropic drugs with disease progression, data from incident cohorts[25] have identified greater rates of daytime napping in early PD patients than controls, and EDS is also diagnosed more frequently in de novo drug-naïve patients than controls.[26] Larger cross-sectional studies have reported EDS in 51% of functionally independent, non-demented PD subjects.[27] Higher sleepiness scores are associated with a less favourable motor phenotype[28] and sleepiness indices worsen with time,[29] and as cognitive impairment and dementia ensue.[30]

EDS is readily quantified in clinic by means of the self-completed Epworth Sleepiness Scale, wherein patients rate the likelihood of falling asleep in eight everyday situations; a score greater than 10 is considered abnormal. Clinicians should be vigilant for EDS amongst PD patients, particularly those that drive. Complaints of daytime sleepiness should prompt a thorough review of nocturnal symptoms which may predispose to fragmented sleep and consequent EDS. In particular, obstructive sleep apnoea and other sleep disordered breathing (SDB) conditions should not be missed as a common and reversible cause of EDS. OSA is at least as common in PD as in age-matched controls;[31] furthermore PD patients tend to sleep in the supine position more frequently than controls,[32] which will worsen any underlying SDB. Suspicion of SDB in a PD patient warrants at least overnight home oximetry studies to determine if this is contributory to excessive sleepiness. Continuous positive airways pressure (CPAP) should be instituted where OSA is identified.

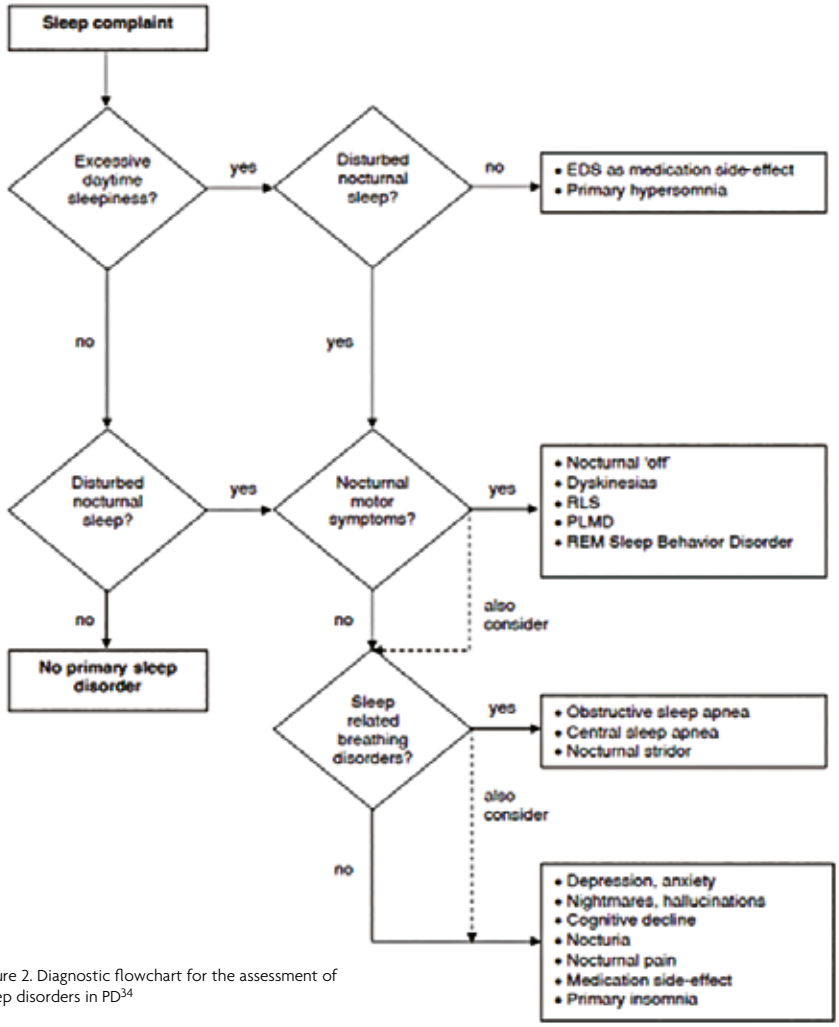

Figure 2. Diagnostic flowchart for the assessment of sleep disorders in PD[34]

Nocturia is another under-recognised nocturnal symptom in PD with significant potential to fragment sleep and if identified, warrants further assessment, as it will often respond in appropriate cases to a selective urinary antispasmodic. Similarly, troublesome sialorrhoea can respond well to low-dose tricyclic agents or clonidine. Motor symptoms affecting sleep should prompt a review of the timing and nature of dopaminergic treatments – addition of a controlled release levodopa preparation at bedtime can often ameliorate these significantly.

In the absence of a clear secondary cause of EDS, subjective improvements can be seen with modafinil (although these were not borne out on objective measures of sleep latency in trials);[33] headaches and nausea are common adverse effects and the prescriber should be mindful of potential deleterious cardiovascular effects in an elderly cohort.

Class I evidence for many of the above strategies is lacking, but many guidelines encompass these approaches. Figure 2 provides a useful algorithm for an approach to EDS and other sleep symptoms in PD.[34]

Research Directions

Sleep dysfunction is increasingly attracting attention in the realms of neurodegenerative research. The observation that sleep deprivation in transgenic mice leads to increased production of β-amyloid plaque[35] has prompted much interest in sleep in Alzheimer's disease (AD) research, and there is compelling evidence that sleep facilitates β-amyloid clearance via the recently described "glymphatic" system.[36] Sleep fragmentation has been implicated in increasing the risk of AD[37] and micro-architectural sleep alterations are well recognised in PSG studies of the condition.[38] Similarly, there are emerging data pinpointing early alterations in sleep structure in PD as a potential biomarker for the later development of PD dementia.[39] A burgeoning body of evidence from longitudinal, prospective cohorts indicts poor-quality sleep as a risk factor for dementia.[40] In our centre, unfavourable actigraphic measures of sleep obtained at baseline in an incident PD cohort eloquently predicted the decline into cognitive impairment and subsequent PD dementia (manuscript in preparation) (see Figure 3). The debate continues as to whether poor sleep initiates or hastens neurodegeneration, or whether disrupted sleep is merely a hitherto under-recognised prodromal feature. The possibility that poor sleep either accelerates or triggers neurodegeneration raises the tantalising possibility that early intervention with strategies to consolidate sleep and/or stabilise circadian rhythm may be neuroprotective, and will undoubtedly form the basis for further research.

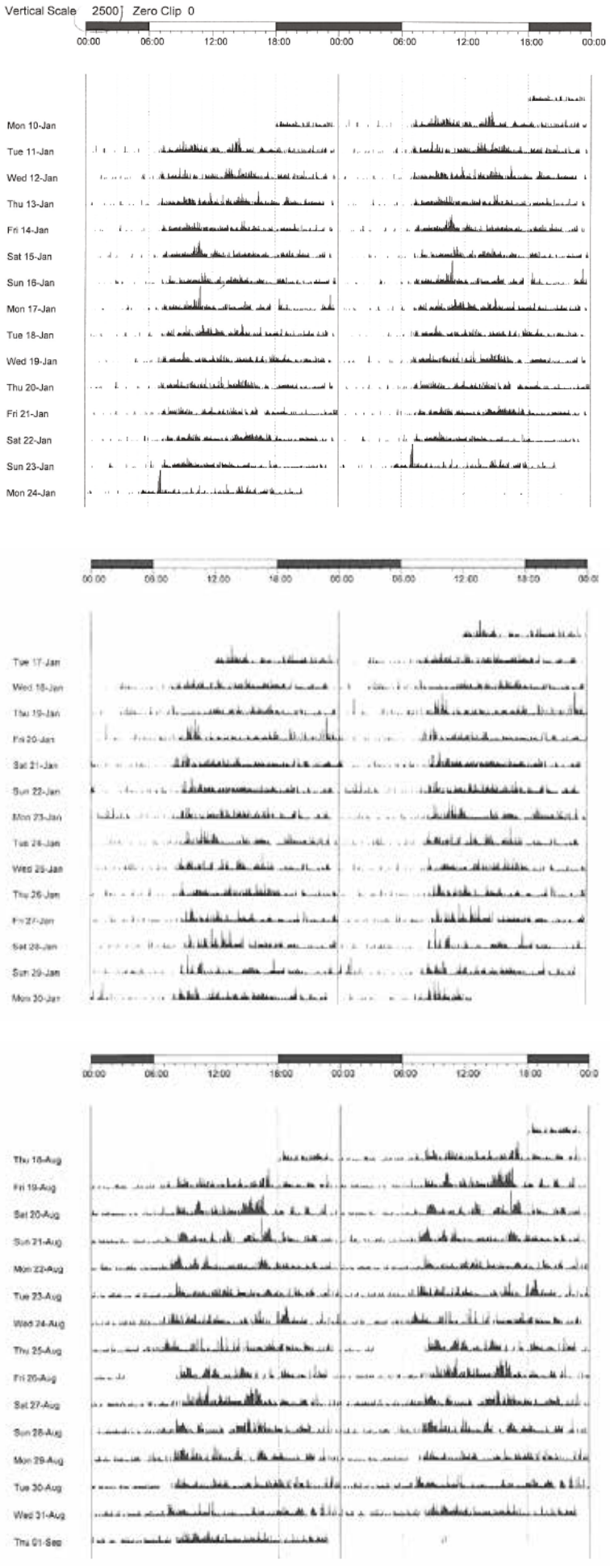

Figure 3. Baseline 24 hour wrist accelerometry patterns of three individuals with incident Parkinson's Disease.

A. (top image). A 59-year-old lady, cognitively normal at baseline; a clear circadian distinction is evident with high levels of daytime activity contrasting with minimal nocturnal activity, consistent with high quality sleep. She remained cognitively normal at three-year follow-up.

B. (middle image). A 66-year-old lady, cognitively normal at baseline; the sleep-wake pattern is less robust, with nocturnal muscle activity indicative of sleep fragmentation. At three-year follow-up, she had developed mild cognitive impairment.

C. (bottom image). A 65-year-old gentleman, with mild cognitive impairment at baseline. The distinction between sleep and wake is increasingly difficult to identify. At three-year follow-up, he had frank Parkinson's Disease dementia.

Learning Points:

1. Patients who develop REM sleep behaviour disorder (RBD) in the absence of other neurological symptoms should be monitored for the evolution of extrapyramidal signs; up to 90% will develop a neurodegenerative disease.
2. Those patients who do manifest RBD as a component of their PD tend to have a poorer prognosis from both a motor and cognitive perspective.
3. Melatonin is as efficacious as clonazepam for RBD and is better tolerated.
4. Antidepressants can provoke RBD, which is usually reversible upon withdrawal.
5. Restless legs syndrome (RLS) is common in PD and should be treated to reduce the impact on sleep disturbance and quality of life. The clinician should be vigilant for the tendency of drugs such as mirtazapine or melatonin to provoke or exacerbate RLS.
6. Excessive daytime somnolence in PD should be recognised as a debilitating symptom and secondary causes such as obstructive sleep apnoea should be sought and treated.

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ABN annual conference 2016

Brighton has been called the UK's "hippest city", and the "the happiest place to live in the UK". So what better place to turn to the Bard and "As You Like It" for our inspiration?

All the world's a stage, and all the men and women merely players

Our stage this year is the Brighton Centre, our theme is 'the seven ages of man', and our players include members of the British Paediatric Neurology Association who have worked with us to produce an exciting programme with talks that have relevance to adult and paediatric neurologists across the full life-span. So you will find lectures ranging from genetic counselling to the neurology of normal ageing.

They have their exits and their entrances

We are pleased to have supported the 'entrance' of many young researchers with the ABN abstract bursary for junior researchers, which resulted in a 20% increase in abstracts and the award of almost 100 bursaries. Our poster exhibition this year will include a separate section featuring the work of ABN fellows and our pre-meeting training and development day on Monday 17 May will again offer specific sessions for foundation doctors, specialist registrars and junior researchers. We will also be holding our regular 'Need to Know Neurology' session for GPs.

And one man in his time plays many parts

The success of the ABN conference depends on the contributions of many different men and women. We are delighted to announce that Alastair Compston is the 2016 ABN Medallist and will give a lecture entitled: "A Tale of Three Cities" on Wednesday 18 May. Our invited speakers include Ingrid Scheffer, Paediatric Neurologist and Professor at the University of Melbourne and Florey Institute of Neuroscience and Mental Health, who will deliver the 22nd Gordon Holmes lecture: 'Epilepsy genetics comes of age" and David Pencheon, Director of the NHS Sustainable Development Unit, who will give the Practical Neurology lecture: 'Addressing Armageddon – and avoiding the 8th age of mankind…'.

The negotiation of employment contracts has dominated many discussions this year. We have allocated a special session on 'Update on new junior doctor and consultant contracts' including contributions from Johann Malawana, Chair, UK Junior Doctors Committee, BMA and Trevor Pickersgill, Chair, UK Consultants' Conference.

The Special Interest Groups will once again run their own meetings over three different sessions during the conference, allowing delegates to choose from 12 different areas of interest. As mentioned above the plenary sessions will address topics across all seven ages of man whilst the parallel sessions will again follow cross-cutting themes with sessions focused on: disease natural history, disease pathophysiology, diagnostics, disease management, as well as audit and training.

We hope you enjoy the meeting in the vibrant setting of Brighton.

Phil Smith

Professor Smith qualified in General Medical in Liverpool and wrote an MD thesis on Breathing During Sleep in Mscular Dystrophy. He trained in Clinical Neurology in Liverpool, Newcastle-upon-Tyne and Cardiff. After four years as Consultant in Cornwall he returned to Cardiff in 1996 to develop interests in epilepsy and education.

He became ABN President in 2015 and was President of the International League Against Epilepsy UK Chapter (2008-11). He co-edits *Practical Neurology* and has a busy commitment to training as Sub-Dean for Assessments, and Associate Medical Director for Quality for the Royal College of Physicians.

	Tuesday 17th May	
0900	**Opening and Welcome: President, President Elect**	
0915	**Plenary session 1** Topic: Pre-conceptual / pregnancy Chairs: Phil Smith, Jean-Pierre Lin Speaker(s): 1. Reproductive choices in neurological disease - Mary Porteous, Edinburgh 2. Management of anti-epileptic drugs in pregnancy - JP Leach, Glasgow 3. Imaging the developing brain in utero: Neonatal imaging sciences - Mary Rutherford, London	
1045	**Coffee & Exhibition**	
1115	**Parallel session 1:** Scientific: Platform presentation Topic: Audit and Training Chairs: Richard Davenport, Heather Angus-Leppan	**Parallel session 2:** Scientific: Platform presentation Topic: Disease natural history Chairs: Waqar Rashid, Kevin Talbot
1230	**Lunch & Exhibition**	
	Genzyme Symposium **MS**	**Shire Symposium** **Fabry & Gaucher**
1400	**Gordon Holmes Lecture** Introduction: Dimitri Kullman Speaker: Ingrid Scheffer, Melbourne Australia Title: Epilepsy genetics comes of age	
1445	**Plenary session 2** Topic: Transitional neurology Chairs: Mary Reilly, John Livingston Speaker(s): 1. Learning disability - Michael Absoud, London 2. Neuromuscular disease - Ros Quinlivan, London 3. Epilepsy - Phil Smith, Cardiff	
1615	**Coffee and Exhibition**	
1645	**Parallel Session 3:** Business Session Topic: Update on new junior doctor and consultant contracts Chair: Ralph Gregory, Alex Foulkes Speaker: Johann Malawana, Chair, UK Junior Doctors Committee, BMA Trevor Pickersgill, Chair BMA Welsh Consultants Committee and UK Consultants Conference	**Parallel Session 4:** Scientific: Platform presentation Topic: Disease Pathophysiology Chairs: Nicola Giffin, Martin Rossor
	Special interest case discussions: Parallel sessions of case based presentations of Special Interest Groups of the ABN	
1800	Cognition | Myasthenia Gravis | Autonomic | Movement disorders | Traumatic brain injury	
1900	**Drinks reception** **ABNT Dinner**	

	Wednesday 18th May		
0715	**Special interest case discussions:** Parallel sessions of case based presentations of Special Interest Groups of the ABN		
	Multiple Sclerosis and Neuro-inflammation	Epilepsy	British Neurotoxin Network the contribution of the Botulinum toxin in neurology over the last 30 years
0830	**Plenary session 3** Topic: Neurology in young adulthood Chairs: Geraint Fuller, Alex Sinclair Speaker(s): 1. Inborn errors of metabolism in later life: diagnosis and treatment – Chris Hendriksz, Manchester 2. Movement disorders in young adults - Nick Fletcher, Liverpool 3. What an adult neurologist needs to know about cerebral palsy - Neil Wimalasundera, London		
1000	**Coffee & Exhibition**		
1030	**Parallel Session 5:** Scientific: Platform presentation Topic: Diagnostics Chairs: Colin Mumford, Anette Schrag	**Parallel Session 6:** Scientific: Platform presentation Topic: Disease management Chairs: Paul Worth, Richard Peatfield	
1200	**Lunch & Exhibition**		
	Novartis Symposium **MS**	**Eisai symposium - Has the neurologist a role to play in improving treatment compliance to Anti-Epileptic Drug?**	
1330	**Poster session with discussants**		
1430	**ABN Medallist lecture** Chair: Alasdair Coles Speaker: Alastair Compston, Cambridge Topic: A Tale of '*Three*' Cities Citation: Neil Scolding, Bristol		
1515	**Coffee and Exhibition**		
1545	**AGM**		
1645	**Neuro-ophthalmology video session:** Topic: Eye movement disorders and the seven ages of man Chair: Gordon Plant Richard Bowman: From birth to the teens – the mewling, puking & whining years Simon Hickman: From 15-50 – the lover, soldier and fair round belly years Diego Kaski: 50 and over - the spectacles, shrunk shank and second childishness years Discussion and video quiz		
1800			
1900	**Gala Dinner - Brighton Exhibition Centre**		

	Thursday 19th May			
0730	**Special interest case discussions:** Parallel sessions of case based presentations of Special Interest Groups of the ABN			
	BNSU	Myology	Neuro-critical	Peripheral nerve
0900	**Case presentation competition** Chairs: Trevor Pickersgill, Gareth Llewelyn			
1015	**Practical Neurology Lecture** Introduction: Phil Smith, Geraint Fuller Speaker: David Pencheon, NHS Sustainability Unit Topic: Addressing Armageddon – and avoiding the 8th age of mankind			
1100	**Coffee and Exhibition**			
1130	**Plenary session 4** Topic: The neurology of ageing Chairs: John-Paul Leach, Nigel Leigh Speaker(s): 1. Epidemiology of ageing – Carol Brayne, Cambridge 2. Clinical parameters of normal ageing – Jonathan Schott, London 3. The pathology of ageing - Paul Ince, Sheffield			
1255	**Lunch and Exhibition**			
	6 top posters Discussant: Mary Reilly		**TevaUK Symposium** **MS**	
1415	**Late breaking news** Chair: Mary Reilly			
1435	**How I would approach a patient with.....** Chairs: Jacqueline Palace, Tom Hughes One discussant: • A stroke-like presentation in an 18 year old - Hugh Markus, Cambridge One discussant: • White matter lesions on the MRI scan of a 15.5 year old - Evangeline Wassmer, Birmingham Two discussants contrasting cases of ages approx. 10 versus approx. 40 years (to include cross-discussion after each presentation): • Muscle weakness - James Miller, Newcastle & Mark Roberts, Manchester • Ataxia - Mark Wardle, Cardiff & Peter Baxter, Sheffield			
1635	**Prize presentations and close**			

Trainees' Preview of the Brighton 2016 ABN Meeting

Alexander Foulkes
is a Neurology ST6 in the southeast London deanery and Chair of the ABNT Committee.

Andrew Barritt
is a Neurology ST4 in KSS deanery, based at Hurstwood Park.

From fish and chips by Brighton pier to the trendiest bars and night clubs, Graham Greene novels to hipster street markets, the diverse microcosm that is Brighton has just about everything you'd ever need for a fantastic city break. And as if Brighton couldn't provide enough to keep you busy all year round, the ABN annual meeting's return there in 2016 coincides with the Brighton Festival and the Brighton Fringe.

The conference venue itself, the Brighton Centre, is on the sea-front right in the centre of town, perfectly placed for you to spill out after a long day's thinking and listening to draw in the fresh sea air and unwind. Take a stroll along the historic promenade and enjoy the evening sun on the shingle and the pier, or head inland for the cafés and bars of The Lanes and around the Pavilion – from trendy to quirky, you'll find something that suits.

But before you think you're off to Brighton for a holiday, don't forget the fabulous line-up for the Annual Meeting itself! Kicking off with the ever-popular ABN Trainees' sessions on Monday 16th May, we have kept the formula of previous years for the first half, with small-group teaching on CNS inflammation: starting with diagnosis, differentials, mimics and red flags, we process through, imaging, DMARDs and symptomatic treatment such as for paroxysmal symptoms, pain and mood.

For the second half of the afternoon we step into new territory for the Trainees' day with a double session on Leadership, courtesy of the Faculty of Medical Leadership and Management. We hope you will find this interesting and inspiring, as well as of direct practical use. We finish the Trainees' afternoon in the experienced hands of Nigel Leigh as he takes us through his favourite clinical signs and shares other tips and gems.

All of this runs parallel with an excellent set of talks and case studies for medical students and foundation year and CMT doctors interested in neurology. There will be plenty of advice and insight into what neurologists do, where we fit in the wider neuro family and how to join in – do encourage your junior colleagues to come along.

The early-evening research workshop has also become well-established over the last few years and returns with some great speakers on choosing a research question and setting up research studies.

And so the first day draws to a close. Sound exhausting? So relax and enjoy the fellowship of trainees from around the country, friends old and new, at the Trainees' Dinner. For me this has always been one of the highlights of coming to the ABN annual meeting, stepping over the deanery boundaries and meeting new people.

The final event specifically for trainees is the Trainee Forum. This is our opportunity as trainees to get together en masse to discuss issues amongst ourselves, and I would encourage you all to come along, even if it is at the breakfast slot the morning after the Trainees' Dinner!

As a phrase "The Seven Ages of Man" brings a number of different images to mind. But it also brings together the ABN and the British Paediatric Neurology Association, in what should be a fantastic overview of neurological disorders from pre-natal diagnosis right through to the nature of ageing itself.

About Brighton itself

Brighton has been a popular destination since the mid-18th century, when it became the go-to for London's rich and famous. Indeed Brighton Pavillion, built between 1787 and 1823, was commissioned by George IV when he was Prince Regent to be his palace by the sea from which to enjoy all the best that Brighton had to offer. As riotous as it looks on the outside, a trip inside is well worth the effort for the ridiculously over-the-top décor, followed by a cream tea in the Pavillion balcony café or an ice cream in the picturesque gardens.

A stroll along the sea-front also comes highly recommended: anything from a Jack Russell on a skateboard to a stag in drag may pass by as you explore the Palace Pier, the Wheel and the exciting i360 development which is set to be the World's tallest moving observation tower (although sadly due to open a matter of weeks after the conference). Alternatively, perch on the beach and watch a glorious sunset over the eerie shell of the burnt out West Pier. For those wishing to absorb the sights on a morning jog, the promenade may take you several miles east past Kemptown, the Marina and under the chalk cliffs towards the St Dunstan's Blind Veterans UK building, or west past Hove Lawns and yield distant views of Worthing Pier on a clear day.

If you've a penchant for shopping don't miss the boutique shops of The Lanes, a network of alleyways constituting the original centre of Brighthelmston fishing village just next to the conference venue. Nearby also are a multitude of welcoming cafés such as The Blackbird, Julian Plumart Patisserie and Sugardough Bakery and excellent restaurants Cote Brasserie (French), Food For Friends (vegetarian), Chilli Pickle (Indian), Alfresco (Italian and on the beach!) and Hotel du Vin which also has a mean cocktail bar.

There are plenty of bustling nightlife venues with sea-front bars and nightclubs surrounding the conference centre. Within Kemptown, the centre of Brighton's gay and lesbian community, are located the likes of Legends, Amsterdam Hotel and Revenge. More centrally along the lower promenade of King's Road are The Fortune of War, Coalition, Digital and Ohso Social Beach Bar, amongst others, which can keep The Seven Ages of Man rocking into the early hours. Although Shakespeare's Seventh Stage of 'mere oblivion, sans teeth, sans eyes, sans taste, sans everything' is to be avoided. Do remember that there are breakfast SIG Meetings to enjoy!

The natural beauty of the South Downs and surrounding area are definitely worth a venture further afield should the opportunity present. Within an hour's drive are Devil's Dyke, the medieval Arundel Castle, the intricate mosaics of Fishbourne Roman Palace and the Seven Sisters Country Park with stunning views along the Sussex coastline.

Offending behaviour: children and young people with acquired brain injury

By Louise Blakeborough MSc, on behalf of United Kingdom Acquired Brain Injury Forum (UKABIF)

Worldwide studies show that the incidence of brain injuries amongst young offenders in custody is significant (Williams 2012). The 2012 Children's Commission report 'Nobody made the connection' stated that the prevalence of Traumatic Brain Injury (TBI) among the general population was between 5% and 24%, compared with rates of 65% to 76% amongst populations in youth custody (Hughes et al 2012). In a systematic review Hughes et al (2015) found the prevalence of TBI among incarcerated youths ranged from 49% to 72%, and there was consistent evidence of a higher prevalence of TBI among incarcerated youths; this disparity was more pronounced as the injury severity increased.

Because of the hidden elements of Acquired Brain Injury (ABI), young offenders entering the Youth Justice System (YJS) receive little or no treatment. Their differing needs and difficulties are not diagnosed or acknowledged, not understood or not taken into account when professionals are preparing cases and considering sentencing. The overall number of young people re-offending is decreasing annually, however in 2013/14 the re-offending rate increased 36.1% (Youth Justice Statistics 2013/14). In 2012/13 approximately £247 million was spent on the detention of young offenders by the Ministry of Justice and Youth Justice Board. Detention of these individuals results in a huge cost, personally, socially and financially.

The United Kingdom Acquired Brain Injury Forum (UKABIF) launched its latest Manifesto 'Life After Brain Injury Manifesto for Children, Young People and Offending Behaviour' to highlight the urgent requirement to identify brain injury problems early, ideally before children and young people enter the YJS. If children and young people can be identified as being 'at-risk' and are then supported, this may then prevent any offending behaviour occurring and/or reduce the likelihood of re-offending.

Key messages:

- Brain injury is a significant variable in offending behaviour. Long-term brain injury in childhood and young adulthood is associated with an increased tendency of offending behaviour and, relative to the general population, there is a high prevalence of brain injury amongst young offenders in custody. Acquired Brain Injury is linked to earlier, repeated offences, a greater total time spent in custody and more violent offending
- Children and young people with Acquired Brain Injury are often failed by the health service, social care, education system and the youth and criminal justice system
- Acquired Brain Injury in children and young people should be considered a chronic health condition with associated ongoing, often life-long symptoms. It must be managed early to avoid long-term disability and to ensure rehabilitation is at its most effective. It must also be monitored long-term for problems arising post-injury
- Young people are not screened routinely for an Acquired Brain Injury until they enter a secure estate, by which time a cycle of re-offending may be triggered
- Children and young people in the Youth Justice System results in major personal, social and economic consequences

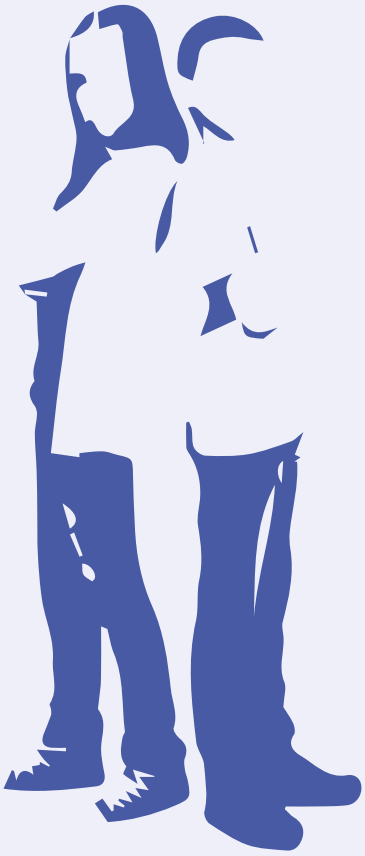
Consequences of brain injury in children and young people

Loss of memory, loss of concentration, decreased awareness of one's own or others emotional state, poor impulse control and particularly poor social judgment are all consequences of brain injury. It is also associated with greater mental health problems, higher rates of depression or mood disorder and/or childhood developmental disorders. Brain injury is potentially more damaging in younger people because of the potential to disrupt cognitive development which can lead to an increased tendency for offending behaviour.

Early identification, intervention and management

Early identification, intervention and management of brain injury is key to reducing offending behaviour and re-offending and/or help to manage the factors that contribute to the criminal behaviour.

There are two tools available for assessing brain injury; the Comprehensive Health Assessment Tool (CHAT) and the Brain Injury Screening Index (BISI®), the latter developed by The Disabilities Trust Foundation (DTF). A specialist brain injury Linkworker Service has been established by the DTF for prisoners in HMP Leeds and piloted with young offenders in Young Offender Institutions. The service works with those individuals identified using the BISI as having a brain injury, to address their problems, assist in their engagement with rehabilitation programmes and generally improve re-offending outcomes. The Linkworker provides one to one interventions for a caseload of young people with brain injury using psychoeducation and goal setting. The Linkworker works with agencies and staff to enable the young person to engage with services and rehabilitation programmes inside the prison and in the community. Brain injury awareness training is also provided to prison staff and Youth Offending Teams to aid engagement in their programmes and achieve better outcomes. Support literature is provided to staff and young people on the effects of brain injury and 'tips and tricks' on support and self-management (http://www.thedtgroup.org/about-us/publications/the-foundation)



Ash (not the patient's real name) was referred to the Linkworker service on being admitted into custody.

He was identified as a vulnerable prisoner due to ongoing investigation into historic head injuries which led to impulsive and erratic behaviour. It emerged that Ash had sustained multiple head injuries, the first occurring when he was very young and the second more recently. As a result of these injuries Ash suffered seizures and struggled with memory problems, processing information and dealing with multiple tasks. He also experienced episodes of uncontrollable anger during which he was unaware of what he was doing.

The Linkworker secured an appointment with an NHS Neurology team and accompanied him to support and share information with the consultant. The Linkworker subsequently contributed to a pre-sentence report, explaining the link between Ash's cognitive, emotional and behavioural problems and his brain injuries. As a result Ash received anger and memory interventions support.

Ash now independently uses techniques learnt to improve his memory; he writes lists of things he needs to do, leaving them on his shoes so that he remembers to take them with him. Ash feels this has improved his independence and ability to manage his memory impairments on a day to day basis (http://www.thedtgroup.org/media/134598/annual-review-2015.pdf).

The recent position paper from the British Psychological Society (2015) proposes six 'Calls to Action' including early intervention, screening and rehabilitation, training and guidance, commissioning, data sharing and further research. UKABIF would like to see increased awareness and training about the prevalence of ABI amongst children and young offenders throughout the youth and criminal justice system, and an acceptance and understanding of the need for assessment and management in hcommunity e.g. Youth Offending and Probation Teams and custodial settings. An easy-to-use assessment tool e.g. BISI should be used to facilitate the identification of those children and young people with ABI who are 'at-risk' of offending. Having identified the relevant individuals, guidelines for the management of children and young people with an ABI who are 'at-risk' of offending should be developed for use in the health and education system and social services.

UKABIF MANFESTO RECOMMENDATIONS

- Increased awareness and training is required about the prevalence of Acquired Brain Injury amongst children and young offenders throughout the youth and criminal justice system, together with an understanding and acceptance of the need for early assessment and management. Brain injury should be a key consideration when making decisions about children and young people on arrest

- Long-term, ongoing monitoring of children and young people with an Acquired Brain Injury is required. Early intervention is essential, by trained professionals within the school and healthcare environments, when problems arise that highlight individuals who may be 'at-risk' of offending behaviour

- An assessment tool should be used in schools to facilitate the identification of those children and young people with Acquired Brain Injury who are 'at-risk' of offending

- Practical guidelines are required for the management of children and young people with an Acquired Brain Injury who are 'at-risk' of offending for use across all sectors; health, education and social services

For further information or copies of the Manifesto, please contact:
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ABN Special Interest Group in Cognition Winter meeting

Conference details: 4th December, Imperial College, London, UK. ***Report by:*** Jonathan Knibb, Consultant Neurologist, Brighton and Sussex University Hospital; Paresh Malhotra, Senior Clinical Lecturer Imperial College, London and Consultant Neurologist at Imperial College Healthcare NHS Trust; Daniel Blackburn, Consultant Neurologist and Honorary Senior Lecturer, Sheffield Institute for Translational Neuroscience, University of Sheffield.
Conflict of interest statement: The authors declare that there are no conflicts of interest. ***First Published online:*** 13th April, 2016.

On 4th December, the ABN special interest group for cognitive disorders met at Imperial College, London for an afternoon of talks, debate and catching up with like-minded clinicians. It was well attended by both senior and junior neurologists, albeit with a bias towards those based in the south of England. A format of twenty-minute talks, as well as a striking variety of presentations from proof-of-concept proposals through to summaries of a career's work, proved effective in preventing attention from sagging.

Localisation of function in the brain has traditionally focused on the roles of individual brain areas in specific activities. Modern functional imaging research has started to analyse patterns of activation across the brain, networks which relate to generic states of brain activity across tasks. Prof Richard Wise and Fatemeh Geranmayeh (Imperial College) discussed the roles of three of these in language recovery after stroke: the default-mode network which is deactivated during specific tasks, the right and left fronto-temporo-parietal networks which are active in sustained attention, and the cingulo-opercular network which is active in processing multiple cognitive demands and the salience of stimuli. They proposed that speech therapy has been too narrowly focused on language, and should also engage aspects of the networks which support re-learning in general.

Continuing the theme of differential activation of networks in different kinds of task, Kanch Sharma (Bristol) drew our attention to the roles of amine neurotransmitters. Noting that the dopamine system is active in tasks requiring divided attention and executive control, and that caffeine acts primarily through the dopamine system, he presented a series of experiments investigating the effect of caffeine on executive and attentional tasks in healthy people. There were some interesting dissociations between tasks which will be well worth following up.

Updated criteria for Alzheimer's disease include biomarkers to add certainty to diagnosis. Amyloid PET ligands have recently become available for diagnostic use, and are now licensed in the UK. Alternatives included CSF examination for amyloid and tau. Biomarkers are not required for the vast majority of individuals with suspected Alzheimer's disease. Chris Carswell (London) described the first fifty patients who have been scanned using florbetapir at Charing Cross Hospital. This included patients who had previously had CSF biomarkers. There was not 100% concordance between florbetapir PET imaging and CSF results. The presented data

suggested that amyloid PET imaging has a role in particularly difficult/atypical cases, especially young onset, but should be implemented using a multi-specialty MDT approach. Further research is required on how best to implement biomarker detection for improving AD diagnosis in routine clinical practice.

Dan Blackburn (Sheffield) sparked an interesting debate on the subject of functional cognitive disorders. His survey of cognitive neurologists revealed a lack of consensus on how the concept should be defined, or even whether it was a useful one at all; some audience members argued that we give a 'functional' label to medically unexplained symptoms in other fields, and a clear diagnosis helps the patient; others felt that these symptoms were different in nature from other functional neurological disorders, and indeed medicalising them at all might not be the right thing to do. He went on to discuss the role of conversation analysis, and in particular looking at the approaches patients take to describing their problems in the consultation. There is evidence that this is a useful approach in differentially diagnosing pseudoseizures from epilepsy, and Dan presented evidence that it may also be useful in the cognitive clinic.

Apathy is a major problem for people with neurological disorders, and for their carers. In Parkinson's Disease, reduced motivation can be seen separately from depression (and is different from the apathy without distress which occurs for example in fronto-temporal dementia). Kinan Muhammed from Oxford described an interesting approach to this, using the fact that the expectation and experience of reward cause consistent changes in pupil size. He has found that this response is smaller in people with Parkinson's Disease who report apathy, but not in those without apathy, and that this is mitigated by dopaminergic medication, suggesting that these patients' lack of motivation may be related to a reduced sensitivity to reward.

Peter Jenkins (Imperial College) suggested that damage to the dopaminergic system might contribute to cognitive impairment following traumatic brain injury (TBI): typical impairments include executive function, attention and cognitive speed, all of which are modulated by dopamine, and dopaminergic nuclei and tracts are often damaged by TBI (as shown by volumetric MRI, diffusion MRI and DaTscan). He made a convincing prima facie case for testing dopaminergic treatments to relieve post-TBI cognitive dysfunction. Those who use neuropsychological tests will also find it interesting that his subjects engaged enthusiastically with tests on a tablet computer which they undertook at home in their own time, and on the other hand that repeated administration of the tests could avoid an alarming degree of test-test unreliability.

The common neurodegenerative diseases have the unusual property of being only weakly heritable except for a small proportion of cases associated with single dominant gene mutations. Jon Rohrer (Institute of Neurology) gave an update on the progress of the GENFI collaboration, an international database of patients with fronto-temporal dementia due to mutations in MAPT, GRN or C9ORF72. This promises to be a valuable resource for understanding these conditions and how they relate to their sporadic counterparts.

Cerebrovascular disease is an important cause of cognitive impairment, and no known medical treatment can relieve the symptoms. Mathilde Pauls (St George's) plans a proof-of-concept study using a single dose of a phosphodiesterase type 5 inhibitor (tadalafil) to try to increase cerebral perfusion in those with vascular cognitive impairment, using MRI with arterial spin labelling to measure the outcome. There was some debate over whether ongoing hypoperfusion really contributes to vascular cognitive impairment; cognitive tests are also planned as part of the study, so the question will be addressed empirically.

The climax of the afternoon was Prof Karalyn Patterson's explanation of the clinical and

neuropsychological features of semantic dementia, a condition which we have gradually come to understand over the last forty years – in significant part thanks to her own hard work and insight – and which has revolutionised our understanding both of what semantic memory is and of how the brain achieves it. Through clinical vignettes, Prof Patterson illustrated the way the condition attacks conceptual understanding in a way which is both uniform across individuals and remarkably specific: patients can recall events, navigate complex routes and enjoy sudoku, while at the same time they may hold an umbrella closed over their head, ask why the horse (actually zebra) has stripes, and draw a peacock with four legs. Perhaps most strikingly, two patients used unusual words in conversation ('petroleum', 'euphoric') but were baffled when five minutes later they were asked what that word meant.

The meeting was enthusiastically received; we hope that future meetings will keep up this standard, and if so they will be of interest to those with an interest in neurodegenerative diseases as a whole, not just their cognitive presentations.

First Dementia Masterclass

Conference details: 2 March, 2016; Manchester, UK. ***Report by:*** Sarah Gillett, Managing Director, Neurology Academy.
Correspondence to: sarahgillett@neurologyacademy.org ***Conflict of interest statement:*** Sarah Gillett is the Managing Director of the Neurology Academy.
First Published online: 15th April, 2016.

There are around 80,000 people with dementia in the UK and the numbers of people affected is expected to double by 2040 with economic costs likely to treble from the current estimated costs of £26 billion a year (Alzheimer's disease Society 2014).

The North West of England has approximately 89,000 people affected with dementia, the second highest in the country, with projected increases of more than 101,000 people in the region by 2021 (Alzheimer's Society 2014). Within care homes one in three adults die from dementia with the majority living in care homes at the time of their death.

With these statistics there is, without doubt, a real need to ensure the workforce is appropriately educated to manage the demands of this rising health problem and this has prompted the development of the Dementia Academy and Dementia MasterClasses through the existing Neurology Academy. This innovative programme builds on 14 years of success in Parkinson's disease education and extends this widely acclaimed and unique model of education to an area that is impacting significantly on health and social care services.

Spearheaded by Dr Ira Leroi, Clinical Senior Lecturer and Honorary Consultant in Psychiatry, University of Manchester Mental Health and Social Care Trust Institute of Brain, Behaviour and Mental Health, Sue Thomas, Chief Executive of NHiS Commissioning Excellence, and Tony Burch GP Trainer London, Manchester is an appropriate place to launch the Dementia Academy and first Dementia MasterClass. The aim of the Dementia Academy is to increase awareness, provide training opportunities and ensure competence for clinicians working with people who will have or develop dementia. The first meeting held on 2 March focused principally on GPs and provided education on how to diagnose, treat and manage dementia from 'forgetting my keys' to advanced care needs.

The meeting was opened by ex-Greater Manchester Chief Constable Sir Peter Fahy, who spoke of his personal experiences of his mother who had dementia. He highlighted that dementia is everyone's business and that we will need to work in an integrated way to manage the impact this condition brings.

Professor Alistair Burn, NHS England National Clinical Director for Dementia provided a keynote address outlining the fact that the interest in dementia was ignited by the publication of the National Dementia Strategy in 2009, energised by the first Prime Minister's challenge on dementia in 2012 and fuelled by a raft of developments such as the hospital dementia scheme, the primary care detection initiative, the creation of Dementia Action Alliances across the country, reduction in the prescription of antipsychotic drugs by 50% and the creation of one million dementia friends. He said support for people with dementia was rated in the top five in importance by the NHS Citizen's Jury in 2015.

For NHS England, the prevailing focus for the last year has been the fulfilment of the ambition that two thirds of the estimated number of people with dementia have a formal diagnosis and post-diagnostic support.

The ready availability of the national diagnosis rate coupled with the absence of a corresponding simple metric for post-diagnostic support have inevitably resulted in a focus on the former. The successful achievement of the diagnosis rate of 67% at the end of November 2015 has allowed conversations to move to post-diagnostic support and beyond.

He stated much of the focus to date has been toward primary care, emphasising the long-term nature of dementia, the need to get things right for patients in primary care – including prompt assessment and treatment – and the issue of whether GPs should be empowered to initiate anti-Alzheimer medication. He outlined the acronym DEMENTIA which should be used to guide dementia reviews (see https://www.england.nhs.uk/2016/03/alistair-burns-18/).

The next speaker, Dr Ross Overshott, gave a very enlightening interactive overview of dementia outlining diagnostic issues. Small group work followed, highlighting three differing stages of dementia potential management scenarios. During the meeting the 'Wall of inspiration' allowed sharing of resources to support better management of dementia and included resources from the voluntary sector, local clinical commissioning group pathways and guidelines as well as phone apps that could assist crisis issues.

Further group work in the afternoon focused on issues like driving, legal issues, carer support and the Memory Assessment Service.

Rounding up the meeting a panel presentation from Greater Manchester police, Manchester ambulance service and an acute hospital liaison clinician clarified for attendees what issues each of these services found most pressing and outlined how GPs might prevent or better support some of these issues from arising. For example, PC Adele Owen highlighted issues of people with dementia getting lost, which had prompted the purchase of bracelets which revealed a persons first name and an emergency contact phone number when scanned with an NFC enabled phone. Dan Smith from the ambulance service highlighted their most important need was for a baseline measure of patients as when they received a 111 call they were often unsure if the person was in a crisis situation requiring hospital admission or just needed extra home support.

Throughout the day, Sue Thomas collated information on the dementia pathway process as one of the main outputs for the meeting will be an interactive integrated dementia pathway.

The next meeting will be for secondary care clinicians to gain education on holistic dementia management as well as contributing to elements of the integrated care pathway.

The next meeting will be held on 15 June 2016 for secondary care clinicians to gain education on holistic dementia management as well as contributing to elements of the integrated care pathway. To participate in further meetings visit the Dementia Academy webpage; alternatively you can access presentations and reports from previous meetings on the Dementia Resources page.

To participate in further meetings or access presentations and reports see Dementia Resources.

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Faculty of Neuropsychiatry Conference

Thursday 15 - Friday 16 September 2016
RCPsych, London

Following on from the great success of our 2015 meeting, we are pleased to announce the 2016 Royal College of Psychiatrists' Faculty of Neuropsychiatry annual conference.

The conference will explore ways of utilising Neuropsychiatry as a platform where Neuroscience and humanities can be integrated to produce a high quality, evidence-based service for our patients.

Lessons from history, research and current practices from various countries will be presented. The intended rather broad theme of the event will cover a variety of clinical, legal, service developments and research issues.

Topics include: Neuropharmacology, Epilepsy, Parkinson's disease, Huntington's disease, Sleep Disorders, substance misuse related brain damage, Memory Disorders, Immunological Brain Diseases, Functional Neurological Disorders and Neuro-investigations. The programme will also include presentations from colleagues from different countries in the context of a session entitled "Neuropsychiatry from around the globe". In addition to key note talks, seminars and trainees' presentations, a thought provoking debate will be one of the highlights of the second day!

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www.rcpsych.ac.uk

For booking and sponsorship queries please contact Virali Shah on 020 3701 2622 or virali.shah@rcpsych.ac.uk

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- Deep Brain Stimulation, Professor Tipu Aziz
- Evidence for exercise, Fiona Lindop
- Preventing falls, Dr Emily Henderson
- Sleep and dysfunctions, Professor K Ray Chaudhuri
- Palliative care, Dr Robin Fackrell

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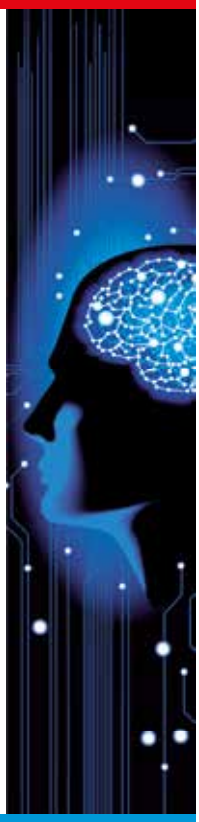

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British Neuropsychiatry Association

Conference details: Conference details: British Neuropsychiatry Association 11-12 February, 2016, Royal College of Surgeons, London, UK.
Report by: Dr Biba Stanton, Royal Free London NHS Foundation Trust, Pond St, London, NW3 2QG, Dr Boyd Ghosh, Wessex Neuroscience Centre, Tremona Road, Southampton SO16 6YD. ***Conflict of interest statement:*** The authors declare that there are no conflicts of interest. ***First Published online:*** 13th April 2016

The British Neuropsychiatry Association (BNPA) brings together psychiatrists, neurologists, neuropsychologists and other professionals interested in the brain and mind. Its annual meeting aims to increase, integrate, and disseminate understanding of the relationships between brain function and human behaviour. This year, the two key themes of the meeting were language and neurodevelopmental perspectives on adult disorders. An eclectic range of talks illuminated these themes from a variety of perspectives, both clinical and academic, but space only allows discussion of a few of these. Three clinical highlights have been chosen that might change your practice, and three fascinating scientific presentations that may tempt you to find out more about a new area.

Past and present Presidents of the BNPA

Clinical highlights

1. The genetics of epilepsy, Prof Sanjay Sisodiya
In discussing the genetics of epilepsy, Sanjay Sisodiya gave a clear overview of an enormously complex field. In particular, he drew attention to examples of where a genetic diagnosis can have real treatment implications for someone with epilepsy. Dravet's syndrome, caused by mutations in the SCN1A sodium channel gene, should be suspected in cases previously labelled as "vaccine encephalopathy". There is typically a history of febrile seizures and apparent developmental regression and then stabilisation. These patients are made much worse by sodium channel blocking anti-epileptic drugs.

2. Adult ADHD, Prof Philip Asherson
Philip Asherson convinced the audience that ADHD is not only a valid diagnostic entity in children, but also an under-diagnosed problem in the adult population which might come to the attention of both psychiatrists and neurologists. There is very significant comorbidity with other psychiatric disorders and emotional instability may be part of the syndrome, along with more classical features of inattention. There is high quality evidence for the efficacy of both amphetamines and atomoxetine in adults with ADHD.

3. Primary progressive aphasias, Dr Jonathan Schott
Jonathan Schott gave a systematic account of the clinical and radiological hallmarks of the three subtypes of primary progressive aphasia, and the correlation with underlying neuropathology. Progressive non-fluent aphasia causes effortful speech, orofacial apraxia and phonemic paraphasias, with subtle left posterior fronto-insular atrophy and can be caused by a range of different pathologies. Semantic dementia causes fluent, circumlocutory speech, surface dyslexia, and often behavioural disturbance, with obvious left anterior temporal atrophy and underlying TDP-43 type C pathology. In logopenic aphasia, there are word-finding pauses, severe anomia and impaired sentence repetition with subtle left peri-sylvian or parietal atrophy and almost always Alzheimer disease pathology.

Research highlights

1. Gut microbes and brain function, Prof Ted Dinan
Ted Dinan is an academic psychiatrist with a long-standing interest in the role of gut microbiota in stress-related disorders. He explained that mice in a "germ-free" environment show an altered cortisol response to stress and abnormal behaviour, and that mice subjected to the maternal separation model of depression develop a narrowed gut microbiota. Faecal transplants to rats from depressed subjects (but not controls) cause anhedonia and an inflammatory response. Specific probiotics may improve behavioural measures of anxiety in animal models.

2. Face, brain and behaviour, Prof Peter Hammond
Peter Hammond, a computational biologist, achieved the remarkable feat of making mathematical modelling both comprehensible and clinically relevant. His work on 3-dimensional facial photography provides a new diagnostic tool for suspected fetal alcohol syndrome. Fascinatingly, deletions and duplications in the same genomic region may have "opposite" effects on facial morphology.

3. Bilingualism and the brain, Prof Thomas Bak
Thomas Bak provided an overview of language as an introduction to the second day of the meeting, but his work on the clinical relevance of bilingualism was particularly intriguing. Being bilingual seems to delay the onset of dementia by several years, and to improve functional recovery following stroke. A two week foreign language course in healthy individuals can improve performance in unrelated cognitive domains.

This year's JNNP guest lecture by Prof Francesca Happe provided an authoritative overview of autism spectrum disorders and highlighted the fascinating combination of strengths and weaknesses that autism presents. People with autism seem to lack "central coherence", the

L-R: Nils Muhlert, Jessica Eccles and Yee Sung Yeoh receiving their Alwyn Lishman prizes from Alwyn Lishman for their members platform oral presentation.

drive to pull information together for the "big picture", but have very strong attention to detail. The BNPA medal was awarded to Chris Frith, whose talk on the benefits of group decision making prompted BNPA president Alan Carson to comment that he seems to be achieving more in retirement than most of us do in our peak years! Founding member of the BNPA Professor Alwyn Lishman delighted delegates by speaking on the history of the organisation.

Finally, the meeting was rounded off with a debate between Alasdair Coles (Cambridge) and Anil Seth (Sussex) discussing the motion "Is there still room for a soul in the modern concept of the psyche". Alasdair was working to an early advantage, with 50 people for and 25 against the motion prior to the debate. He built on this with a description of the soul to include that part of us which communicates with the divine and not necessarily an immortal part of us that lives on after our death. Anil, by comparison, built on the concept that the popular description of the soul was of something separate from the body, and that this division was not helpful for advancing our knowledge of the brain. In the end, Alasdair's technical argument regarding definitions lost out to Anil's more persuasive holistic argument – resulting in Anil winning 30 to 25 votes, a close and entertaining debate.

The BNPA meeting is not just for neuropsychiatrists, but for those of all disciplines interested in the grey area between brain and mind. The next annual meeting in February 2017 is sure to be equally stimulating.

UK Acquired Brain Injury Forum's 7th Annual Conference

Conference details: 11 November 2015, London, UK. ***Report by:*** Louise Blakeborough. ***First Published online:*** 4 February 2016

Professor Michael Barnes, UKABIF Chair welcomed over 200 delegates to the United Kingdom Acquired Brain Injury Forum's (UKABIF) 7th Annual Conference at the headquarters of the Royal College of General Practitioners in London's Euston Square. Delegates from all fields of brain injury attended from the interdisciplinary rehabilitation team, commissioners, case managers, personal injury lawyers, social care workers, voluntary organisations, care providers and also individuals living with a brain injury.

In her introduction to current and future commissioning Professor Lynne Turner-Stokes said: "Specialist rehabilitation is a critical component of the acute care pathway and without it the benefits of early acute care can't be realised". Professor Turner-Stokes addressed delegates wearing several 'hats' including Chair of NHS England (NHSE) Clinical Reference Group for commissioning specialised rehabilitation services for patients with highly complex needs, and the Clinical Reference Panel for development of case mix and tariffs for rehabilitation, and Director of the UK Rehabilitation Outcomes Collaborative (UKROC). The diversity of rehabilitation makes planning and service provision challenging and complex. Professor Turner-Stokes discussed the tariff which is based on a 5-tier weighted bed day payment model using rehabilitation complexity scores. From 2015/16 the tariff will be related to Category A patients for a maximum of 180 days, unless an extension is agreed. Professor Turner-Stokes also presented new data from UKROC which provides compelling evidence to justify rehabilitation services. Analysis of UKROC data collected over four years from 52 specialist (Level 1 and Level 2) rehabilitation services in England was used to calculate the life-time savings. For the 3592 patients reviewed, the life-time saving was £2.74 billion, of which £1.95 billion were in the highly dependent group. "These are real savings to NHS Continuing Care and few interventions can claim this level of cost saving in this group of patients" concluded Professor Turner-Stokes.

In February this year, ten local authorities and 12 clinical commissioning groups (CCGs)

for Greater Manchester (GM) and NHSE announced an agreement to devolve responsibility for the new health and social care budget to a new GM partnership which will oversee a budget of £6 billion. Kate O'Sullivan, Lead Comissioner Complex Care, Citywide Commissioning and Quality Team, Manchester North, Central and South CCGs Manchester Vanguard discussed how plans are progressing but emphasised: "It's early days and there's a lot of work to do to ensure health and social services can interact successfully, but progress is good".

The treatments and outcome tools available for neurobehavioural rehabilitation were reviewed in the afternoon.

Professor Nick Alderman, Director of Clinical Services, Brain Injury Services, Partnerships in Care and Dr Sara da Silvo Ramos, Research Fellow, The Brain Injury Rehabilitation Trust (BIRT) concluded that no single outcome measure is suitable for all brain injury rehabilitation services and that a 'basket' of measures is required. The Independent Neurorehabilitation Providers Association (INPA) is looking currently at what measures should be in the 'basket'. Dr Michael Dilley, Consultant Neuropsychiatrist at The Wolfson Neurorehabilitation Centre, St Georges Hospital, London gave an excellent review of the wide range of drugs used for treating many aspects of neurobehavioural brain injury including memory and cognitive impairment, executive function, disorders of attention, apathy and aggression.

UKABIF launched its third Manifesto 'Life After Brain Injury: Children, Young People and Offending Behaviour' to raise awareness and improve services for those with ABI. "We need to identify young people who are 'at-risk' of offending and keep them out of the Youth Justice System" said Professor Michael Barnes. Long-term brain injury in childhood and young adulthood is associated with an increased tendency of offending behaviour and, relative to the general population, there is a high prevalence of brain injury amongst young offenders in custody. All professionals involved with young people need to work together to recognise, understand and manage this problem as the evidence-base suggests that the incidence of brain injuries amongst young offenders in custody is significant. Offending behaviour and ABI is a European problem said Dr Éric Durand from the Fondation Hospitalière Sainte Marie in Paris. In France 61% of prisoners re-offend within five years and this is now a top priority for the French Ministry of Justice. The prevalence of TBI amongst prisoners in France is between 41% and 60%. Dr Durand presented the results of two studies; in the first study a self-reported questionnaire was completed by offenders (juveniles, males and females) on admission to Fleury-Mérogis prison in Paris, over a three month period. A total of 1148 questionnaires were completed and 30.6% reported a history of TBI; males were the highest with 32%, and 86% had sustained their first TBI before their first imprisonment. The second study, which is ongoing, is looking at 40 children (36 boys and four girls) who were treated in a rehabilitation department following a significant ABI, and who subsequently became offenders. "We know TBI is linked to criminal behaviour so it is important to screen for ABI when individuals arrive in prison" concluded Dr Durand.

UKABIF presented three Awards at the conference. Two winners were selected for the UKABIF Lawyer of the Year; Ann Allister from Carpenters Solicitors and Deirdre Healy from Irwin Mitchell. Dr Miles Rogish, Consultant Clinical Psychologist at York House, the Brain Injury Rehabilitation Trust's independent hospital in York, was named UKABIF Clinician of the Year and the UKABIF 2014 Award for Inspiration was presented to Nick Verron, who despite a devastating brain injury, raised an amazing £3000 for UKABIF in August this year.

The Encephalitis Society Annual Conference: Trials and Tribulations

Conference details: December 2015, London, UK. ***Report by:*** Dr Michel Toledano, Neuro-infection Clinical Fellow, Charing Cross and Chelsea & Westminster Hospitals. Edited by Dr Ava Easton, The Encephalitis Society. ***Conflict of interest statement:*** The authors have no conflicts of interest to declare.
First Published online: 13th April 2016.

Being familiar with the Encephalitis Society's work through word of mouth as well as their highly informative website, I was looking forward to attending this year's Professional Seminar. I had high expectations for the afternoon and I am happy to report that the event far exceeded those expectations.

The stimulating talks were delivered by a multidisciplinary panel of international experts and topics ranged from cutting-edge research to moving patient testimonies. Equally diverse was the audience in attendance which included neurologists, psychiatrists, nurses, neuropsychologists, as well as patients and their families. This coming together of diverse perspectives greatly enhanced the depth and reach of the afternoon's discussions and created a sense of community and shared purpose, often lacking at academic meetings.

The afternoon started with a very warm welcome from Dr Ava Easton, CEO of The Encephalitis Society and Professor Tom Solomon, Director, Institute of Infection & Global Health, University of Liverpool. Their brief introduction tracked the history of the society from its humble beginnings as a small group of like-minded individuals aiming to increase awareness about a neglected disease to its current standing as a major player in the field. The society celebrated its 21st year in 2015 and has now become a large multi-disciplinary network dedicated to improving the care of patients with encephalitis by supporting innovative clinical research and by continuing to educate the medical community and public at large about this often devastating disease, in addition to continuing to support patients and their families.

The first speaker was Dr Belinda Lennox, Oxford University Hospitals NHS Trust, presenting "What do Psychiatrists have to offer in the management of Autoimmune Encephalitis." Dr Lennox explained that although autoimmune encephalitis often presents with neuropsychiatric disturbances such as hallucinations, paranoia, movement disorders, autonomic dysfunction, and seizures, there may be a subpopulation of patients with acute psychosis as the sole manifestation of the disease. This is an important group to recognise, as their psychosis may respond to immunotherapy. Dr Lennox shared data from studies demonstrating NMDAR and VGKC antibodies in up to 6% of patients presenting with acute psychosis. Although this suggests a possible autoimmune basis, it is unclear whether the antibodies are clinically significant. In order to answer this question, Dr Lennox showed data from a small case series demonstrating good response to immunotherapy in antibody positive patients presenting with acute psychosis. A randomised controlled study comparing immunotherapy vs antipsychotics in this patient population is currently in the works. Finally, Dr Lennox emphasised the need for neurologists and psychiatrists to work together to ensure that patients with neuropsychiatric symptoms are adequately assessed in order to rule out a possible autoimmune basis for their presentation.

Professor Tom Solomon and Dr Belinda Lennox


Dr Domingo Escudero

Next, Dr Ruth Backman, University of Liverpool presented "Results of a cluster randomised controlled trial promoting early management of patients with suspected Encephalitis." Dr Backman detailed the results of a study evaluating an intervention package designed to improve the management of patients with suspected encephalitis upon arrival to the hospital. The theoretically informed intervention package included a variety of educational materials and training sessions targeting health staff responsible for the initial evaluation and management of those with suspected encephalitis. Twenty-four UK hospitals participated in the study which ran for 12 months. A composite primary outcome measure consisted of initiation of Aciclovir within 6 hours and performing a lumbar puncture within 12 hours of admission. The results of the preliminary analyses were discussed and will be the subject of a full publication.

Dr Julia Granerod discussed two recent epidemiological studies carried out at Public Health England. The first study aimed to assess the role of neuroimaging in the early management of encephalitis and the agreement on scan interpretation in a well-defined series of suspected encephalitis cases. The second study aimed to quantify increased risks of specific outcomes among encephalitis cases, including epilepsy, psychiatric sequelae, cognitive problems, headache, and alcohol abuse, compared to the general population. Results from these two studies will soon be published.

Next, Dr Cristina Fernandez, University of Liverpool, discussed 'DexEnceph', a long-awaited randomised control trial evaluating the role of corticosteroids in the management of HSV encephalitis. Dr Fernandez pointed out that despite adequate anti-viral treatment, HSV encephalitis is still associated with significant mortality and morbidity. She explained that brain inflammation occurring secondary to the viral infection could be an important contributing factor to poor outcomes. There is retrospective data suggesting that corticosteroids reduce brain swelling and improve outcomes in HSV encephalitis. DexEnceph will recruit 90 adults across the UK over 4 years. Half will receive dexamethasone along with standard treatment and half will receive standard treatment only. All participants will be followed for 18 months with the aim of determining whether corticosteroids improve memory and functional outcomes.

Just before the break, Dr Mildred Iro,

Oxford University, provided detail on IgNITE, a phase III randomised placebo controlled study aiming to assess the role of intravenous immunoglobulin (IVIg) in the management of children with encephalitis. Dr Iro explained that past studies have suggested a role for IVIg in encephalitis irrespective of whether it is autoimmune or viral in aetiology. However, no randomised controlled trial has ever been conducted to assess its efficacy. IgNITE will look to recruit 308 children and randomise them to receive either IVIg or placebo, in addition to standard therapy. All subjects will be followed for 12 months and outcomes assessed using standardised scales, imaging, and inflammatory markers.

The first talk following the break was given by Dr Domingo Escudero, Hospital Germans Trias i Pujol, Barcelona, Spain, who delivered a lucid and moving account of his struggles with NMDAR encephalitis. A neurologist himself, Dr Escudero first developed symptoms in 2006 before NMDAR encephalitis was described and was misdiagnosed with atypical schizophrenia. He vividly portrayed the fear and sense of loss he felt as his thinking became increasingly disordered and he became dependent on others for the most mundane of tasks. Without appropriate treatment, recovery was painstakingly slow and he doubted that he would ever return to work. He eventually did recover only to relapse in 2011. This time however, he was appropriately evaluated and diagnosed with NMDAR encephalitis. Recovery was hastened with immunosuppression but he did relapse again in 2014 requiring escalation in treatment. Despite these setbacks Dr Escudero is back at work and has become active in the larger encephalitis community sharing his story in both medical and lay platforms. Dr Escudero ended his talk by highlighting the crucial role played by organisations such as The Encephalitis Society, in providing accurate and up to date information to the public, particularly as patients and their families turn to the internet to gain knowledge about health and disease.

In the last scheduled talk of the afternoon, Janet Hodgson, Consultant Clinical Neuropsychologist, shared the experience of The Encephalitis Society Neuropsychology Service (ESNS). The ESNS provides neuropsychological support for adults through a variety of delivery modes including face–to-face, telephone, and videoconferencing. She explained that unlike patients with traumatic brain injury, patients with encephalitis are usually discharged home without rehabilitative follow-up, in part due to the absence of visible disability. Once in the community, patients can struggle gaining access to neurorehabilitative care in a timely manner. The ESNS was created to fill this need. Between April and September of 2015, a total of 26 patients were referred to the ESNS and outcomes were positive based on self-report as well as a battery of standardised measures. Ms Hodgson finished by describing future marketing efforts aimed at increasing referral to this unique, and much needed service.

As part of her concluding remarks, Ava Easton, CEO, spoke proudly of the many achievements of The Society and the events commemorating its 21st birthday, including the publishing of new guidelines for professionals as well as new educational materials for iBook, the growing reach of World Encephalitis Day, and the unprecedented success of a Road Show, which covered 21 cities in the UK in 21 days, and disseminated the society's message via the hashtag "#ShowYouKnow".

The seminar concluded with the announcement of a new Award to be launched in 2016 by The Encephalitis Society: "Outstanding Achievement Award for Excellence in Encephalitis Healthcare". Professionals will be able to make nominations for the award from Spring 2016.

Finally the prizes were awarded to the winner and runner-up of The Society's Medical Student Essay Prize: Roshni Bhudia (Winner) for the essay: Diagnosis of NMDA Receptor Autoantibody Encephalitis, and Mitchell Burden (Runner-Up) for the essay: Current public awareness of encephalitis and its importance in improving health outcomes.

A wine and cheese reception, allowing opportunity for networking, followed the talks.

For free professional membership of The Encephalitis Society and to be kept up to date with research and future conferences, please visit www.encephalitis.info

Preview: Pain Therapeutics 2016

Conference details: 23-24 May 2016, Holiday Inn, Kensington Forum, London UK. www.pain-therapeutics.co.uk ***First Published online:*** 10th February, 2016.

SMi's 16th annual Pain Therapeutics conference will hone in on the latest innovations and novel approaches to pain therapy and analgesic drugs as well as look at the practicalities of using animal models and translational biomarkers in pain research.

Aimed at an audience of senior specialists in neurology, CNS, clinical sciences and pharmacology, Pain Therapeutics 2016 will keep attendees at the forefront of scientific breakthroughs to adapt to the growing need towards minimising opioid dependency and new drug discovery.

Presentations from a selection of leading pharmaceutical companies currently developing novel analgesic treatments including Glenmark, Pfizer, GSK, Grunenthal and Nektar Pharmaceuticals, will provide delegates with an understanding on key topics such as drug development mechanisms, neuropathic pain, severe chronic pain, sodium channels, industry challenges, plus much more! An interactive panel discussion on medical incidents in experimental clinical trials will be just one of the highlights at the conference.

Unrivalled Speaker Line-up Includes:

- Andrea Houghton, Executive Director, MSD (Merck & Co Within The Usa)
- Catherine Stehman-Breen, VP Clinical Sciences, Regeneron Pharmaceuitcals Inc
- Chao Chen, Therapy Area Head, Glaxosmithkline
- Thomas Christoph, Senior Director, Head Of Pain Pharmacology, Grunenthal GmbH
- Richard Butt, Senior Director, Research Project Leader, Clinical Research, Pfizer
- Shaloo Pandhi, Global Program Medical Director, Novartis
- Neelima Khairatkar Joshi, Senior Vice President, Glenmark Pharmaceuticals
- Stephen Doberstein, Senior Vice President & Chief Scientific Officer, Nektar Therapeutics
- Geert Jan Groeneveld, Research Director Neurology & Pain, Centre for Human Drug Research
- Steven Kamerling, Therapeutic Area Head For Pain, Inflammation And Oncology, Zoetis
- Praveen Anand, Professor of Neurology, Imperial College London

Reasons to Attend:

- Explore different strategies to minimise risk of opioid dependency
- Discover Pfizer's achievements for the past year on voltage gated sodium channels
- Learn about Glenmark's experience on pain drug discovery
- Develop translational assays to support a small molecule Nav1.7 inhibitor programme

Further information and full speaker line-up is available online at www.pain-therapeutics.co.uk

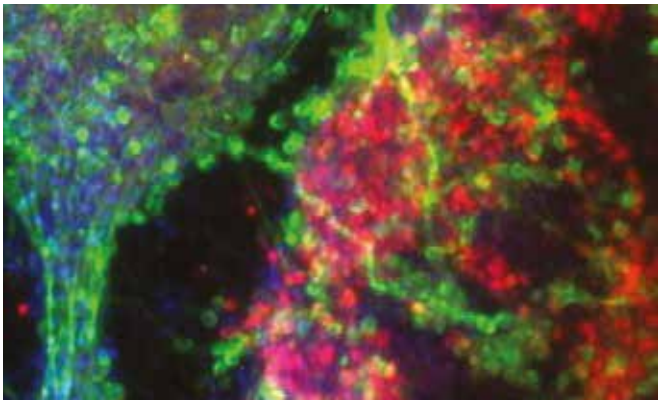
Human Induced Pluripotent Stem Cell Course

Conference details: 7-9 December, 2015, Oxford, UK. ***Report by:*** Dr Imran Noorani, Wellcome Trust Clinical PhD Fellow in Neurosciences, University of Cambridge and Wellcome Trust Sanger Institute, UK. ***First Published online:*** 14th April, 2016.

On December 7 – 9, 2015, the annual Human Induced Pluripotent Stem Cell (iPSC) was held in the Department of Medical Sciences at the University of Oxford, led by Dr Sally Cowley, Head of the James Martin Stem Cell Facility. The course was aimed at scientists and doctors looking to adopt iPSCs as a tool for their own research endeavours, and was an in-depth practical and theoretical course seeking to provide the skills necessary to derive and expand these cell lines as well as to differentiate them into certain lineages.

Since Yamanaka discovered that terminally differentiated adult somatic cells can be reprogrammed into stem cells using just four additional factors, iPSCs have become an increasingly popular and are now an essential tool for medical research. In particular, the main advantage iPSCs provide over other cell lines is that it enables a specific patient's own cells to be studied in vitro, allowing modelling of patient-specific disease – an invaluable tool. The first day of the course provided the historical and theoretical background behind iPSCs before the first practical workshop in the cell culture room, in which delegates observed growing iPSCs in culture and learned how to select single colonies for deriving clonal lines.

The meeting offered many sessions to suit interests of scientists from diverse backgrounds. For example, there was a dedicated session on differentiating iPSCs into pancreatic beta-cells, particularly useful for studying mechanisms of disease of patients with genetically-driven diabetes. However, for neuroscientists perhaps the most exciting sessions



were those on the use of iPSCs for studying neurological disease. The first such session was delivered by Dr Zameel Cader, a neurologist in Oxford specialising in pain disorders. He gave cogent arguments on why iPSCs would be especially useful for studying neurological disorders – the fact that the nervous system has a more limited capacity for self-repair compared with other tissues means that stem cells holds promise for regenerative medicine, and that clinical trials in neurology are more expensive and prone to failure compared with other disease and therefore accurate models of disease are desperately needed (which iPSCs now potentially provide). The talk outlined the steps in differentiating stem cells into sensory neurons, with confirmation of neuronal identity using antibody staining, electrophysiological measurement for mature action potentials and RT-PCR for neuronal markers. Such work promises to help in modelling chronic pain disorders and drug screening.

Continuing with the theme of deriving models of neurological disease, Dr Colin Akerman delivered an insightful session on his research on using iPSCs from patients to derive human cortical neurons in vitro. The most exciting aspect of this work is that both excitatory and inhibitory neurons can be produced using recently established protocol, and moreover that synapses between these neurons form in vitro and are fully functional, validated with detailed electrophysiology. This is important because much work has looked at neuronal degeneration in disease but studying synaptic abnormalities has been more difficult to do. Further novel insights may come from optical techniques for monitoring synaptic transmission, for example with calcium imaging, and for manipulating synaptic transmission using light-activated proteins in these cortical neurons. Closely linked to this session was another delivered by Dr Sarah Newey from the Department of Pharmacology, University of Oxford. Using similar tools as Dr Akerman, her interests are in iPSCs for providing culture models of neurodegenerative disease. She described protocols for taking iPSCs from patients with Alzheimer's disease and differentiating them into cortical progenitors and neurons, and the cell lines made in this way are remarkably reproducible between different laboratories. This approach promises to be useful for drug screening of Alzheimer's disease. A practical session was conducted in which delegates experienced first-hand how to perform antibody staining for cortical progenitors and neurons in order to confirm successful differentiation from iPSCs, and photographs were taken of these neurons under the microscope for delegates to take away with them.

Induced pluripotent stem cells are increasingly being used for a diverse range of research purposes and allow unprecedented study of disease at the level of individual patients. The course was very well planned and conducted, with all attendees having learnt much about the applications of this tool as well as learning the practical skills necessary for establishing and differentiating these cells in their own laboratories.

ACNR partners with Therapy Expo for 2016

Therapy Expo returns on 23-24 November 2016, at Birmingham's NEC, and ACNR are proud to be partners for 2016.

This year's world-class conference programme boasts over 40 hours of accredited CPD education, including a dedicated Neuro Rehabilitation stream covering the prevention, occurrence and treatment of a huge range of injuries and pathologies.

The event offers the opportunity to experience a clinical programme delivered by expert speakers including Jon Graham, Sarah Daniels, Paul Cocker, Mike Stewart, Tom Mercer and Louise Connell, and enhance your career through workshops and specialist sessions. Book your £79 +VAT Early Bird ticket before the price increases to £99 +VAT on the 28th May using the dedicated ACNR registration link www.therapyexpo.co.uk/acnr.

Your conference ticket will also give you access to the exhibition floor where more than 120 companies and associations (including ACNR) will be showcasing ground breaking products and services.

THERAPY EXPO
23rd and 24th November 2016
NEC Birmingham

2016 Highlights:

- Over 40 hours of accredited CPD education
- ALL NEW dedicated Neuro Demo Zone
- Four education streams covering MSK, Sports Injuries & Biomechanics, Neuro Rehabilitation and Acute Care
- An unprecedented opportunity to network with colleagues and peers from all over the country
- Cryotherapy chamber tours
- Specialist CPR & Anaphylaxis training
- Kinesio UK annual conference at Therapy Expo
- In-depth sessions dedicated to each of the conference streams, giving you the opportunity to gain advanced knowledge in multiple specialities

For more information visit www.therapyexpo.co.uk or speak to a member of the team 0207 013 4998.

Preview: 18th National Parkinson's Conference

Conference details: 1st July, 2016; London, UK. ***Preview by:*** Jessica Eden-Smith, Conference Organiser, Mark Allen Healthcare.
First Published online: 20th April, 2016.

Quote ACNR16 for a 15% discount

As our ageing population is causing an increase in those living with neurological conditions, clinicians are continually striving for the best possible care. MA Healthcare are delighted to invite you to our 18th national Parkinson's conference. We bring together the leaders in the field to continue to translate research into a clinical setting. Dr Tom Foltynie explores the potential for disease modifying treatments and Dr Alison Yarnall poses the question 'Is dementia inevitable in Parkinson's?'

Every hour someone in the UK is told that they have Parkinson's. Professor Huw Morris examines diagnosis with tips on distinguishing the different types of Parkinsonism's and Professor David Brooks covers the advances in imaging to aid this process.

In 2017, there will be an update of the Parkinson's NICE guidelines. We hear from two members of the development group on their respective topics. Fiona Lindop presents up-to-date thinking on different types of exercise therapy. Dr Robin Fackrell tackles the challenges in palliative care after the BBC branded around the clock care 'not good enough'. The day will also provide you with a great opportunity to network with colleagues and to earn 6 CPD points.

For more information and the conference programme, please visit www.mahealthcareevents.co.uk/parkinsons2016. On the day, you can follow the conference on Twitter at #parkinsons16. To book your place, please call +44(0)20 7501 6762.
Find more events at www.mahealthcareevents.co.uk/cgi-bin/go.pl/conferences/list.html

Preview:
Neuro Rehab Expo 2016

The Neurological Rehabilitation Expo is at the ExCeL London on the 15th & 16th June 2016, this is the UK's top event for neurologists, physiotherapists, biomechanists, professionals working in acquired brain injury, rehabilitation medicine specialists or any neurological rehabilitation professionals.

This unique event is completely free to attend and provides visitors with seminars, workshops, live demos, interactive features and world class experts. From virtual reality to human-robot interfaces, bionic exoskeletons to neurosensory monitoring and gait rehabilitation to an anti-gravity treadmill, the event brings the very latest developments, leading world-class experts and newest technology under one roof. Visitors will get the opportunity to see, touch, feel and try out first hand some of the newest developments from around the globe.

The Neuro Rehab Expo is also proud to announce Stoke Mandeville Spinal Research as their official charity for 2016, they will be exhibiting at the show and also welcome Kirsten Hart and Ruth Peachment from the National Spinal Injury Centre to the show talking about "Restorative Therapies for Spinal Cord Injuries". ACNR will be exhibiting again for 2016, find us at the show on stand 24.

The show is completely free to attend; visitors just need to register for their ticket via the website www.neurorehabexpo.co.uk. The event also runs alongside COPA (physical rehabilitation), Elite Sports Rehab and Elite Sports Performance. Your free neuro ticket gives you full access across all these adjoining shows, providing a wealth of opportunities you might not have come across before. We look forward to seeing you there!

NEUROLOGICAL REHABILITATION EXPO

To list your event in this diary email brief details to Rachael Hansford at Rachael@acnr.co.uk by 6th July, 2016

May

The Management of Spasticity
25 May, 2016;Raphael Medical Centre, Tonbridge, UK
Workshop to discuss assessment and detail evidence on the utilisation of outcome measures. Cost £95 – www.raphaelmedicalcentre.co.uk

2nd Congress of the European Academy of Neurology (EAN)
28-31 May, 2016; Copenhagen, Denmark
www.eaneurology.org/copenhagen2016

JUNE

Something new in PD – Xadago
7 June, 2016; Liverpool, UK; 8 June, 2016; Newcastle, UK
www.xadago.alphabook.co.uk, T. 01444 412772, E. Lucy@lcwconsulting.co.uk

Parkinson's Advanced MasterClass
7-9 June, 2016; Sheffield, UK – E. info@neurologyacademy.org, @TheNeuroAcademy, T. 0845 338 1726, www.neurologyacademy.org

Obstetric Neurology
8 June, 2016; London, UK – E. pooja.dassan@nhs.net

Red Flags – What to do next?
8 June, 2016; London, UK – Primary Care Neurology Society Workshop with Dr Martin Turner – E. info@p-cns.org.uk

Something new in PD – Xadago
14 June, 2016; Birmingham, UK; 15 June, 2016; London, UK
www.xadago.alphabook.co.uk, T. 01444 412772, E. Lucy@lcwconsulting.co.uk

Dementia Secondary Care MasterClass
15 June, 2016; Manchester, UK – E. info@neurologyacademy.org, @TheNeuroAcademy, T. 0845 338 1726, www.neurologyacademy.org

Neurological Rehabilitation Expo
15-16 June, 2016; London, UK
Free tickets from www.neurorehabexpo.co.uk/index.asp

Something new in PD – Xadago
16 June, 2016; Bristol, UK
www.xadago.alphabook.co.uk, T. 01444 412772, E. Lucy@lcwconsulting.co.uk

6th Essential Stroke Imaging Course
18 June, 2016; Liverpool – Intensive 1 day course.
T. Sam Pickup 0151 709 9125, E.essentialcourses@hotmail.com

Genes, channels and neurological disorders
22 June, 2016; London, UK
Royal Society of Medicine, T. 020 7290 3940, E. cns@rsm.ac.uk

9th International Epilepsy Colloquium
22-24 June, 2016; London, UK – www.activateevents.com/9thiec2016

JULY

Parkinson's 2016
1 July, 2016; London, UK
T. 020 7501 6762, www.mahealthcareevents.co.uk/parkinsons2016

Sleep Study Day: How to treat insomnia
7 July, 2016; Newcastle, UK – E. Laura.dowling@nuth.nhs.uk

Sleep Study Day: Running a sleep service
8 July, 2016; Newcastle, UK – E. Laura.dowling@nuth.nhs.uk

SEPTEMBER

Parkinson's Foundation MasterClass
7-8 September, 2016; Sheffield, UK E. info@neurologyacademy.org @TheNeuroAcademy, T. 0845 338 1726, www.neurologyacademy.org

ECTRIMS
14-17 September, 2016; London, UK
www.ectrims-congress.eu/2016.html, E. ectrims@congrex.com

Royal College Psychiatrists Faculty of Neuropsychiatry Conference
15-16 September, 2016; London, UK – www.rcpsych.ac.uk, T. Virali Shah on 020 3701 2622, E. virali.shah@rcpsych.ac.uk

ILAE British Chapter Specialist Registrar Epilepsy Teaching Weekend
23-24 September, 2017; Oxford, UK
E.members@ilaebritish.org.uk

Multiple Sclerosis MasterClass
26-27 September, 2016; Sheffield, UK
E. info@neurologyacademy.org, @TheNeuroAcademy,
T. 0845 338 1726, www.neurologyacademy.org

Neuro-Oncology: The Essentials 3rd Edition

Editors: Mark Bernstein and Mitchel Berger
Published by: Thieme, 2014
ISBN: 9781604068832
Price: £117
Pages: 594

Reviewed by: Mr James Walkden, Neuro-Oncology Fellow, Department of Neurosugery, The Walton Centre, Liverpool.

The 3rd Edition of this well known book series aims to give a concise overview of the 'essential' topics in neuro-oncology. The book is edited by two prominent North American neurosurgeons and the chapters are authored by leading experts in their field. The book is aimed mainly at neurosurgeons and neuro-oncologists at all stages of training and experience, as a reference resource. This edition of the series has added significantly to the previous versions with detailed chapters on intraoperative management, particularly neuronavigation and endoscopy.

The clear chapter layout makes it easy to gain an overview of a particular topic as required. The book starts with excellent concise chapters on tumour epidemiology and tumour genesis. It systematically builds through tumour imaging ultimately to specific insights on the more complex tumours. The chapters on low grade and high grade glioma dominate, as these represent the major tumours encountered in clinical practice. Other topics covered include the entire range of paediatric and spinal tumours, as well peripheral nerve tumours. The tumour genetics, chemotherapy and radiotherapy chapters are also extremely useful to Neurosurgeons and Neurologists of all grades who would wish to overview these important topics relevant to multidisciplinary management. There is a final detailed chapter covering seminal publications in Neuro-oncology: this is an excellent resource for all physicians.

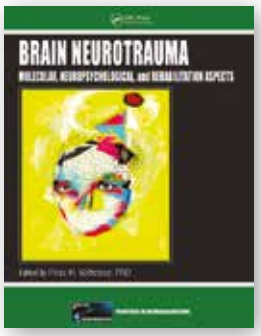
This book adheres to its billing as an overview and resource tool; as such, discussion is kept brief and concise. The addition of an 'Editor's Note' at the end of each chapter, describing the critical points, complements this overview approach very effectively. They are extremely well researched with clear referencing to peer reviewed literature. High quality graphics and intra-operative imaging also effectively add to the discussion of each tumour type. The illustrations in the metabolic, functional and stereotactic radiosurgery chapters in particular are of an exceptional standard.

The chapters pertaining to specific rare tumours are concise; they would not be a definitive guide to management. Discussion of controversies in management is also limited. Topics where the coverage is perhaps too brief are classification systems and genetic profiling in low grade glioma. For example, there is mention of important predictive classifications such as WHO Performance status and the RANO criteria in glioma. These criteria are probably well known by the experienced reader but more detail would be useful for junior residents attending Radiology and Oncology multidisciplinary meetings. The book was also somewhat weak in its exploration of neuro-oncological controversies, such as the management of recurrent high grade glioma.

These are minor issues and the book is a well written and easily readable overview of Neuro-oncology. While clearly relevant to trainees in Neurosurgery or Oncology, the book would earn a place on the bookshelf of any Consultant Neuro-oncological surgeon, as a reference and overview of any neurological tumour likely to be encountered. There is currently no other book of this quality offering such a detailed overview. For those with a subspecialist interest in Neuro-oncology, I would recommend the additional purchase of the excellent 'Controversies in Neuro-Oncology' also published by Thieme ,which complements this book and offers the reader full insight into the more controversial topics not covered by 'the Essentials'.

Brain Neurotrauma: Molecular, Neuropsychological, and Rehabilitation Aspects

(Frontiers in Neuroengineering Series)



Edited by: Firas H Kobeissy
ISBN: 13:978-1-4665-6598-2
Published by: CRC Press
Price: $229.95
Pages: 697

Reviewed by: Dr Ganesh Bavikatte, Consultant Neuro Rehabilitation, The Walton Centre NHS Foundation Trust, Liverpool, UK.

Brain Neurotrauma, edited by Dr Firas H. Kobeissy is a comprehensive textbook of molecular aspects of brain trauma. There are over 119 contributing authors from numerous renowned international centres. The volume is well laid-out and has eight sections, divided into 49 chapters. These cover in extensive detail the basic science, the experimental models and the neurorehabilitative management of patients following brain injury. There is good discussion of the mechanics of brain injury, of experimental brain injuries and brain recovery models, biomarkers and also the after-effects of brain injury. The book also gives insight into various potential treatments and various treatment targets for the future, providing a much needed ray of hope for the reader.

The book is a comprehensive guide to current knowledge of pathophysiology, and the molecular and clinical aspects of brain injury. There is an effort, largely successful, to cover all the aspects of traumatic brain injury causative models, neuromechanics, imaging, biomarkers, neurocognitive and neurobehavioural aspects, and potential targets to enhance recovery following traumatic brain injury. The sections on the after-effects of mild brain injuries and sports injuries were very helpful additions. Neuro-rehabilitation and neuroprotection strategies such as non-invasive stimulation of brain or cranial nerves are especially interesting to me as a neuro-rehabilitation physician, and to my multidisciplinary team colleagues.

Clinicians will be enlightened to read about nanopeptides, roles for stem cells and the effects of comorbid conditions on recovery patterns following brain injury. In these cutting-edge topics, the comprehensive referencing is of course especially useful.

The clinician in search of enlightenment might have been helped along, however, if the authors had made more use of tables, colours and diagrams to illustrate the complex information. On the one hand, the book benefits from having so many contributors of high repute but, almost inevitably, their areas of expertise overlap and so too does the content of their chapters. For readers, wishing a quick read-through, this repetition would be a disadvantage. Conversely, the fact that each chapter is really an essay that can be read on its own will suit many.

The text focuses strongly on veteran injury and is geographically limited to practice in the United States. Much of the content is universal, of course, but some discussion of global issues would have been welcome.

Overall, this book represents a great addition to existing resources and is a good reference source for neuroscientists, neurorehabilitation physicians, neurologists and neurosurgeons with a special interest in traumatic brain injury.

Neurodigest

A neurology news update
See www.neurodigest.co.uk for links

New data intelligence report analyses how people with neurological conditions in Wessex use hospital services and why

A new Neurology Intelligence Report provides insight into how people with various neurological conditions can be better supported to stay well. The report is the work of NHiS in partnership with Wessex Strategic Clinical Network and CLAHRC, and The National Institute for Health Research. It was launched at an event in Southampton on the 19 April 2016 and can be accessed at www.nhis.com/wessex-neurology-report?utm_source=announcement&utm_medium=email-and-share&utm_campaign=Wessex-Report-Launch

News from NICE
Suspecting Neurological Conditions - Recognition and Referral

The final scope and equality impact assessment for this NICE guideline have now been published, along with all the stakeholder comments that were received during consultation and NICE's responses to these comments. See www.nice.org.uk/guidance/indevelopment/gid-cgwave0800/documents http://bit.ly/1WmcIGU

Stroke in Adults Quality Standard update released

The Stroke in adults quality standard has just been updated and is available from www.nice.org.uk/guidance/qs2/chapter/Update-information

Clinical News

Neurological care in England criticised by MPs report

The BBC recently reported that the Department of Health and the NHS are to be held to account in the months and years ahead with regard to provision of neurological care, following the publication of a Public Account Committee report. According to the BBC, the report recommends that NHS England find a way of tackling the problem of variation in services and explain how it will offer everyone with a long-term condition a personalised care plan. It also urges NHS England to make better use of the 650 neurologists in England, as well as other specialist nurses, to improve access to care for patients. Read the report at www.publications.parliament.uk/pa/cm201516/cmselect/cmpubacc/502/50202.htm

Parkinson's Disease and sleep

According a new global study, sleep is the number one factor influencing well-being in people with Parkinson's. Other factors highlighted were exercise, pain, stress and mood. You can read more about this study at http://parkinsonslife.eu/global-parkinsons-study-reveals-sleep-as-biggest-influence-on-wellbeing/

If you are interested in how you can help patients with sleep disorders, you may wish to read about the workshop with OT and sleep specialist, Andrew Green, taking place on the 4th of May. Details are available at www.communitytherapy.org.uk

Improving outcomes for people with neurological conditions

The Neurological Alliance is working with the NHS England Long Term Conditions Support Unit and the Strategic Clinical Network Neurology Collaborative to deliver a coordinated programme of work to improve care and outcomes for people living with neurological conditions. www.neural.org.uk/nhs-england-community-project-for-neurology

Improving neurological function in MS

Recent research with the disease modifying MS drug, alemtuzumab, has shown it improves pre-existing disability in people with relapsing-remitting multiple sclerosis. This is according to the commonly used scale in MS, known as the Expanded Disability Status Scale (EDSS). The results lead the authors to conclude that 'the findings may influence treatment decisions in patients with early, active relapsing-remitting MS displaying neurological deficits'. See www.jns-journal.com/article/S0022-510X(16)30090-9/abstract?rss=yes

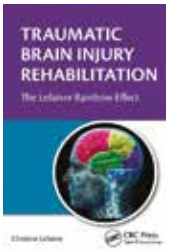
Brighton and Sussex University Hospitals reduces general anaesthetic administration by a third

Royal Sussex County Hospital has helped to reduce the administration of general anaesthetic by a third in patients aged 4-17 by expanding its MR capability with the help of new technology from Siemens Healthcare. The MAGNETOM® Aera 1.5T is part of a three-fold operation to provide enhanced MR access to paediatric patients, relocate the neurology department and ensure a better experience for inpatients, due to its wide bore and comfort-enhancing features.

"The new MAGNETOM Aera is adjacent to The Royal Alexandra Children's Hospital which provides a safer and more comfortable transition for our paediatric patients," states John Wilkinson, Imaging Services Manager at Royal Sussex County Hospital. "Since the installation, Royal Sussex has reduced the administration of general anaesthetic to paediatric patients by a third due to increased compliance and comfort. This is due to a combination of factors including the wide bore system, which makes the process less claustrophobic and an in-bore television, kindly donated by Rockinghorse Children's Charity so paediatric patients can have a more enjoyable and relaxing experience."

The system will also be used to ensure better throughput for neurology patients following Royal Sussex's appointment as a regional centre for neurology.

Ground-breaking treatment for TBI sufferers



Traumatic brain injury is the leading cause of death and disability around the world. Many years of productive life are lost and people suffer years of disability after brain injury. In addition it engenders great economic costs for individuals, families and society. Without effective treatment, many TBI victims lead lives of quiet desperation, isolation, and depression. The Lefaivre Rainbow Effect is ground-breaking treatment for TBI sufferers. Christine Lefaivre's book and courses explore this transformative treatment, which focuses on the cognitive retraining of the brain based on pre-injury lifestyle as well as the organic damage.

"I have worked with Chris using this model, and have seen clients who initially had Glasgow Coma scores of 4-6 recover, over a period of years, to the point where they could live independently, hold employment, and have normal relationships." Bill de Bosch Kemper, Neuropsychologist, Canada.

Traumatic Brain Injury Case Management online courses launched this April, and an examination series in conjunction with the University of British Columbia Continuing Studies will follow: http://rainboweffect.ca/

Christine's textbook is available now in print and ebook formats: Traumatic Brain Injury Rehabilitation: The Lefaivre Rainbow Effect Christine Lefaivre

www.crcpress.com ISBN 9781482228243, priced at £25.99.

Lumie lights to be used in Cambridge University research into Huntington's Disease

Cambridge-based light therapy specialist Lumie is to supply some of its lamps for use in a research study into Huntington's Disease that is to be conducted by the School of Clinical Medicine's Neurology Unit at Cambridge University.

24 of Lumie's most powerful light boxes, Lumie Brazil, are being donated to the research project that will examine the efficacy and tolerability of two non-pharmaceutical interventions to improve the life and sleep quality of people who have Huntington's disease. One of these interventions is bright light therapy, the other being sleep restriction therapy.

Huntington's disease is caused by an inherited faulty gene that damages certain nerve cells in the brain. This brain damage gets progressively worse over time and can affect movement, cognition (perception, awareness, thinking, judgement) and behaviour. Early features can include personality changes, mood swings, fidgety movements, irritability and altered behaviour.

Cambridge-based Lumie is a light therapy specialist whose products promote a healthy sleep/wake cycle by regulating the body clock as well as helping patients to feel more energetic and productive throughout the day. Lumie Brazil offers a much higher light intensity than standard lighting, emitting 10,000 lux at 35cms. To put that in context, on a bright day but not in direct sunlight the level of brightness ranges from 10,000 to 25,000 lux while in direct sunlight that goes up from 32,000 to 100,000 lux. Bright light has been shown to have an immediate impact, increasing levels of alertness, boosting mood and improving performance.

New MR applications to provide greater efficiency in neurology departments

Siemens Healthcare has launched a range of MR applications to help hospitals reduce the time needed for MR imaging within neurology. It is estimated that 20 to 25% of all MR examinations are neurological, with the number expected to grow in 2016. The applications have therefore been designed to help organisations increase patient throughput in order to maintain an efficient workflow.

One of the applications, Simultaneous Multi-Slice (SMS) EPI, employs an innovative technique to acquire imaging slices simultaneously rather than sequentially, reducing 2D acquisition times with acceleration factors up to eight. Simultaneous Multi-Slice (SMS) EPI can bring DTI and BOLD into clinical routine. This can particularly benefit surgical neurology cases through surgical mapping, potentially helping to reduce post-surgical deficits, and ultimately leading to improved efficiency in the utilisation of operating room resources.

A further application, GOBrain, enables clinically validated brain examinations in just five minutes. This can improve patient throughput, and costs per scan can potentially be reduced. Shorter scan times can also be better tolerated by patients, and can help reduce the need of sedations and rescans.

In addition to speed and quality, standardisation across systems is also an important element for hospitals. Siemens Healthcare has introduced the syngo® MR E11 software platform, a uniform application platform for the MAGNETOM® family and the Biograph mMR MR-Pet system. The focus, in addition to expanding the application offering, is achieving consistency across the entire fleet of systems and managing these effectively.

www.siemens.co.uk/healthcare

Xadago – a new treatment for PD

The first new treatment for PD in 10 years will launch in the UK in May. Xadago has had marketing authorisation in Europe since February 2015, having been approved as an add-on to L-dopa alone or in combination with other PD medications in mid-late stage PD patients with motor fluctuations.

The active substance in Xadago, safinamide, is a monoamine oxidase-B (MAO-B) inhibitor. It blocks the enzyme monoamine oxidase type B (which breaks down dopamine), thereby helping to restore dopamine levels in the brain and improving the patient's symptoms.

Xadago, as an add-on treatment to levodopa with or without other medicines for Parkinson's disease, has been compared with placebo in two main studies involving 1,218 patients with late stage Parkinson's Disease who experienced fluctuations. In both studies, 6 months treatment with Xadago increased the time during the day during which patients were 'on' and able to move by 30-60 minutes when compared with placebo. Another study showed maintenance of this effect for 24 months. Xadago is available as tablets (50 and 100 mg).

Find out more at a series of meetings organised by Profile Pharma. See advertisement on page 16 or call 01444 412772 for more details.

Danish design offers a lift for rehabilitation patients

Patients in the UK are learning to walk again and being given new hope from a Danish invention. A new bodyweight-supported rehabilitation invention from Danish mobility company Ergolet offers earlier rehabilitation including gait-training, which improves motor function and strength after serious health problems such as an acquired brain injury.

The Ergo Trainer linear body relief system gives patients an equal body-weight support during training, removes the risk and fear of falls or strain, and props up user confidence along with their weight to let rehabilitation start earlier.

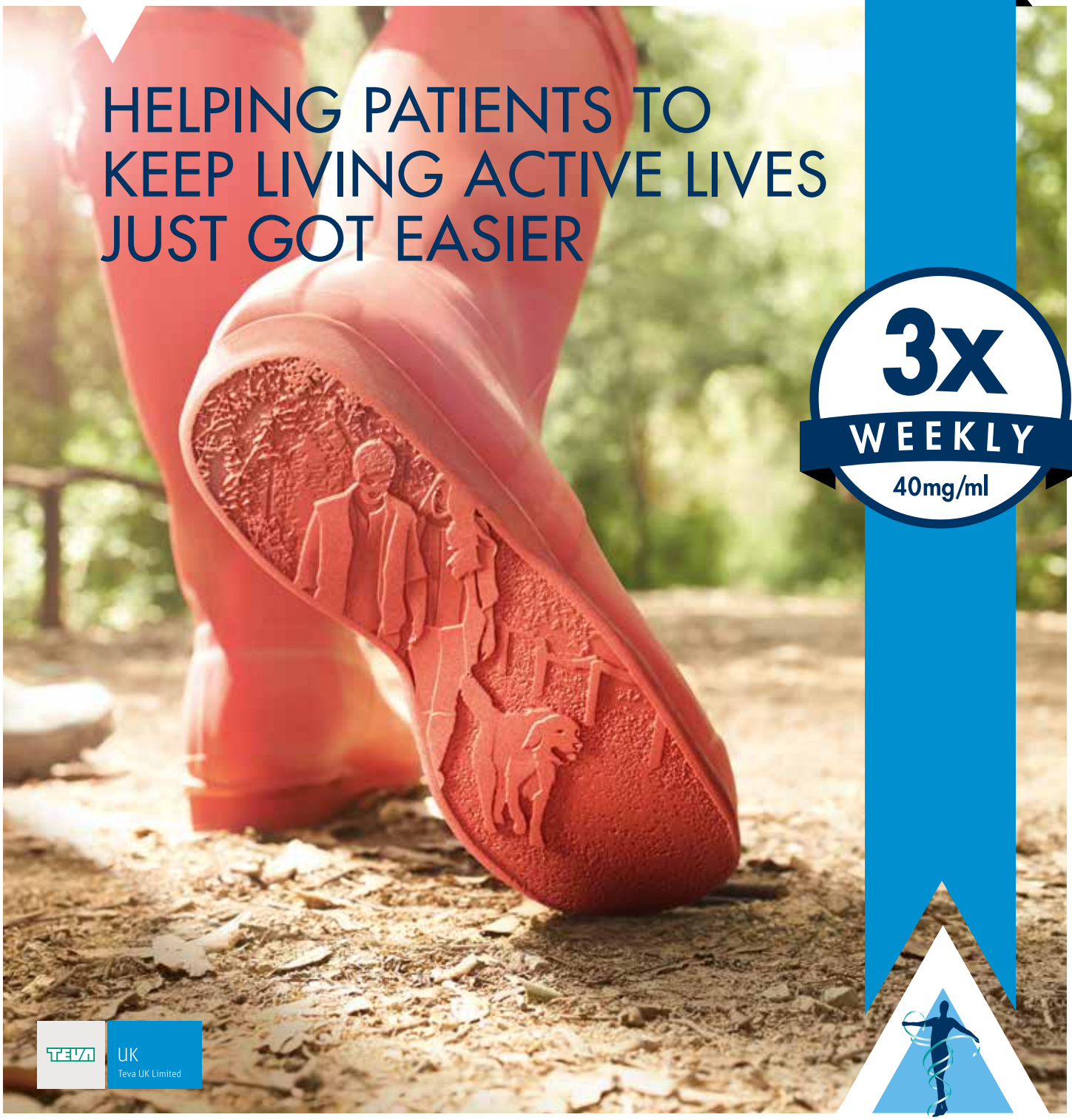
Developed in collaboration with Copenhagen University, its inventors say it offers increased mobility for people recovering from acquired brain injury caused by strokes, accidents and tumours, or learning to use prosthetic limbs.

"We can intensify physical training and show significantly faster, better recovery through an ergonomically designed device which makes the user feel safe and secure, and makes exercise fun and motivating", said UK sales director David Lomas.

"Typically, products come with a built-in treadmill which is very limiting. Ergo Trainer is used with a variety of equipment or for various floor exercise. Clients can even kick a football around".

It was developed in co-operation with the Centre for Rehabilitation of Brain Injury (CRBI), Copenhagen, and used in patient studies there with dramatic results. CRBI's neurorehabilitation specialist Jørgen Jørgensen said stroke patients facing paralysis improved their walking speed by an average of 65% after a 12 week period.

Ergolet will run workshops at Neurological Rehabilitation Expo, on June 15-16 2016 with CRBI study results presented by Jørgen Jørgensen. Book free tickets at www.neurorehabexpo.co.uk



IT'S ABOUT GOOD DAYS, NOT LOST DAYS

Please refer to the Summary of Product Characteristics (SmPC) for full details of Prescribing Information

COPAXONE® (glatiramer acetate) 40mg/ml Solution for Injection, Pre-filled Syringe Abbreviated Prescribing Information

Presentation: Glatiramer acetate 40mg solution for injection in 1ml Pre-filled Syringe. **Indications:** Copaxone is indicated for the treatment of relapsing forms of multiple sclerosis (MS) (see Section 5.1 of the Summary of Product Characteristics (SmPC) for important information on the population for which efficacy has been established). Copaxone is not indicated in primary or secondary progressive MS. **Dosage and administration:** Patients should be instructed in self-injection techniques and should be supervised by a healthcare professional the first time they self-inject and for 30 minutes after. A different site should be chosen for every injection. The recommended dose in adults is 40mg of Copaxone (one pre-filled syringe) subcutaneously three times a week with at least 48 hours apart. It is not known for how long the patient should be treated. A decision concerning long term treatment should be made on an individual basis by the treating physician. *Children and adolescents:* No specific studies. *Elderly:* No specific data. *Impaired renal function:* No specific studies. Monitor renal function during treatment and consider possibility of glomerular deposition of immune complexes. **Contraindications:** Known allergy to glatiramer acetate or mannitol. Pregnancy. **Precautions and warnings:** Subcutaneous use only. Initiation to be supervised by Neurologist or experienced MS physician. One or more of vasodilatation, chest pain, dyspnoea, palpitations or tachycardia may occur within minutes after injection. These generally resolve spontaneously after a short time. If severe, treat symptomatically. Caution in patients with pre-existing cardiac disorders and review such patients regularly. Convulsions and/or anaphylactic or allergic reactions can occur rarely. Rarely, serious hypersensitivity reactions may occur. If severe, treat appropriately and discontinue Copaxone. **Interactions:** No formal evaluation. Increased incidence of injection-site reactions with concurrent corticosteroids. Theoretical potential to affect distribution of protein-bound drugs, therefore concomitant use of these should be monitored. **Pregnancy and lactation:** Contraindicated in pregnancy. Consider contraceptive cover. No data on excretion in human milk. **Effects on ability to drive and use machines:** No studies have been performed. **Adverse reactions:** Serious hypersensitivity reactions have been reported rarely e.g. bronchospasm, anaphylaxis or urticaria. *Very Common:* Infection, influenza, anxiety, depression, headache, vasodilatation, dyspnoea, nausea, rash, arthralgia, back pain, asthenia, chest pain, injection site reactions, pain. *Common:* Bronchitis, gastroenteritis, herpes simplex, otitis media, rhinitis, tooth abscess, vaginal candidiasis, benign neoplasm of skin, neoplasm, lymphadenopathy, hypersensitivity, anorexia, weight increased, nervousness, dysgeusia, hypertonia, migraine, speech disorder, syncope, tremor, diplopia, eye disorder, ear disorder, palpitations, tachycardia, cough, seasonal rhinitis, anorectal disorder, constipation, dental caries, dyspepsia, dysphagia, faecal incontinence, vomiting, liver function test abnormal, ecchymosis, hyperhidrosis, pruritus, skin disorder, urticaria, neck pain, micturition urgency, pollakiuria, urinary retention, chills, face oedema, injection site atrophy, local reaction, oedema peripheral, oedema, pyrexia. Consult the Summary of Product Characteristics in relation to other side effects. **Overdose:** In case of overdose, patients should be monitored and the appropriate symptomatic and supportive therapy instituted. **Price:** Packs of 12 Pre-filled syringes £513.95. **Legal category:** POM. **Marketing Authorisation Number:** PL 10921/0026. **Marketing Authorisation Holder:** Teva Pharmaceuticals Ltd, Ridings Point, Whistler Drive, Castleford, West Yorkshire, WF10 5HX, United Kingdom. **Job Code:** UK/MED/15/0096. **Date of Preparation:** January 2016.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Teva UK Limited on 0207 540 7117 or medinfo@tevauk.com

UK/UKCPX/16/0005a(1)
Date of Preparation: April 2016