ISSN 1473-9348 VOLUME 13 ISSUE 5 SEPTEMBER/OCTOBER 2013

ACNR

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ADVANCES IN CLINICAL NEUROSCIENCE & REHABILITATION

In this issue

PREVIEW: Epilepsy management under the spotlight at this year's World Congress of Neurology meeting

Event details: Monday 23 September (18.30-20.00), Hall B

The Eisai-sponsored symposium at the **XXI World Congress of Neurology in September**, entitled '***Under the Spotlight: Epilepsy management – are we on the right track?***', will take an innovative approach to highlight the key issues in epilepsy management today. Hosted by television health correspondent, **Sue Saville**, and involving an interactive panel discussion of international epilepsy experts, the symposium will address current 'hot topics' in the treatment and management of epilepsy.

Professor Michel Baulac (Hôpital Pitié-Salpêtrière, Paris, France) will focus on the issues involved in the management of individuals with newly diagnosed epilepsy, such as the importance of correctly diagnosing the patient's seizure type and getting the initial treatment correct in order to ensure long-term positive outcomes, highlighting important considerations when selecting and initiating the most appropriate antiepileptic drug (AED) for monotherapy. **Professor Elinor Ben-Menachem (Sahlgrenska University Hospital, Gothenburg, Sweden)** will then cover key challenges involved in the decision-making process for patients who are refractory to monotherapy and require adjunctive treatment with other AEDs, including the crucial importance of individualising treatment for each patient's particular needs. **Dr Manny Bagary (University Hospital Birmingham NHS Trust, UK)** will further expand on the need for a patient-focussed approach to epilepsy management that looks beyond just controlling seizures and addresses the overall quality of life of the patient, including the identification and management of side effects and comorbidities, such as depression and anxiety. **Professor Eugen Trinka (Paracelsus Medical University, Salzburg, Austria)** will then discuss the direction of epilepsy management in the future, including the need for AEDs with unique mechanisms of action and other important issues that are likely to impact the daily clinical practice of delegates.

Covering the spectrum of epilepsy management, the interactive session promises to be stimulating, thought-provoking and informative for delegates, providing practical advice which they can take home and apply to their current daily practices.

Prior to the event, please visit

www.eisaiepilepsysymposia.eu

to fill in a short questionnaire which covers your personal experience in epilepsy management and also some of the issues that will be discussed during the session, you can also pose questions to the faculty. Post-event, this site will host footage of the symposium.

Date of preparation: August 2013
EpiGen-EU0048c

This symposium is sponsored by Eisai Europe Ltd

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SEPTEMBER/OCTOBER 2013

Cover shows the Actigait foot lifter stimulator implant from Otto Bock Healthcare. See page 26 for more information.

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Published by Whitehouse Publishing,
1 The Lynch, Mere, Wiltshire, BA12 6DQ.
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PRINTED BY
Buxton Press T. 01298 21 2000

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Mike Zandi, Editor.

In this issue we have a strong opener with an in depth review article by Edward Roberts, Adolfo Bronstein and Barry Seemungal from Imperial College, on the basic mechanisms of visual and vestibular interactions. Visually-induced dizziness, or visual vertigo is beautifully explained, and the neural basis for the visuo-vestibular interaction is described using neuroimaging and transcranial magnetic stimulation data.

Howard Ring presents the challenging area of epilepsy in those with intellectual disabilities in our epilepsy article. Clinical problems, and the lack of an evidence base for treatment for this group of individuals, whom are generally excluded from clinical trials, are highlighted.

Nadine McCrea in our paediatric article provides a clear and useful approach to diagnosing and managing dystonia in childhood, and Kristian Aquilina presents the second part of his account of the management of posterior fossa tumours in children in our neurosurgery article.

Chris Sampson from Nottingham in our rehabilitation article guides us through the tricky area of quantifying quality of life and making economic healthcare decisions that choose between therapeutic options.

We have a great selection of contributors reviewing and previewing books and conferences in neurology and rehabilitation in this issue – please let us know if you would like to contribute reviews.

Andrew Larner reviews Clifford Rose's last book, we have an interview with Vladimir Hachinksi as part of a preview of the XXI World Congress of Neurology (2013), and a connexin43 related case report from Mazen Sabah and Adam Zeman.

Laura Edwards reviews the Society for Research in Rehabilitation summer meeting, and Tom Foltynie and Alastair Noyce review the recent Movement Disorders Society meeting and let us glimpse at the list of cases presented in the Video Challenge.

We are pleased to welcome Gemma Cummins in the editorial team to develop the journal reviews section of ACNR, and hope you enjoy this issue.

Mike Zandi, Editor.
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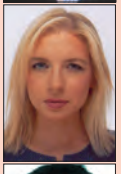

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References:

1. Ries S *et al*. Levetiracetam minitablets improve compliance in patients with epilepsy. Pychopharmakotherapie 2012;**19:**260-264. (English translation with permission).
2. DESITREND® Summary of Product Characteristics, 2012.
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Conflict of interest statement:
The authors declare that there are no financial or commercial conflicts of interest.

Visual-vestibular Interaction:

Basic Science to Clinical Relevance

Summary
The visual and vestibular systems together mediate the reflex and perceptual functions required for efficient postural balance and spatial orientation in the light or the dark. Following an acute unilateral vestibular insult, there is a left-right imbalance in the vestibular input leading to erroneous brainstem vestibular signalling. This asymmetrical vestibular signalling manifests in several ways, e.g. activation of reflex eye movements (vestibular nystagmus) and sensations of vertigo. The net result is a functional impairment in the capacity to locomote and spatially orientate; a high risk situation in a natural environment. The central nervous system can however promote a rapid functional recovery by shifting the brain's relative reliance from vestibular toward visual cues for these functions, i.e. the brain becomes more 'visually dependent' for the sensory monitoring of locomotion and spatial orientation. Given time and the appropriate conditions (e.g. adequate physical activity, avoidance of vestibular sedatives), the fidelity of the brainstem vestibular signal is restored as the brainstem process involved in 'vestibular compensation' removes the left-right imbalance in the vestibular brainstem signal. In patients who make a full symptomatic recovery consequent upon adequate 'vestibular compensation', the reliance on visual signals for locomotion and navigation reduces toward normal levels in tandem with the process of brainstem vestibular compensation. In contrast, some chronically symptomatic patients show a maladaptive persistence of this heightened visual dependency and this is manifest in visually-induced dizziness ("visual vertigo"). Visually-induced dizziness is a major problem in the clinic, with symptoms occurring in visually-busy environments such as shopping malls or supermarkets. We discuss the physiological mechanisms underlying visual-vestibular interaction, how this interaction may be disturbed leading to visually-induced dizziness and finally how understanding the physiological mechanism helps in the development of therapy for these patients.

Introduction

The vestibular system, which provides a signal of head motion to the brain, mediates functions of gaze and postural stabilisation via vestibular-ocular (VOR) and vestibular-spinal reflexes. The vestibular system is also key in generating sensations of self-motion and spatial orientation required for navigation in the environment. The vestibular system influences these reflex and perceptual functions in partnership with other sensory systems, particularly vision. For example, vision calibrates the accuracy of the VOR and, via optic flow and motion parallax generated during self-motion, contributes to our sense of self-motion (or stasis). Occasionally, visual-vestibular interaction can mislead, e.g. the compelling but false sensation of self-motion experienced when looking out of the window of a stationary train as an adjacent train moves past us ('the 'train illusion', Figure 1A). This illusion demonstrates the difficulty the brain has in trying to resolve the complex and ambiguous role of the visual system in signalling both self- and object (environmental) motion.

The occasional failure of the normal brain to accurately estimate measures of self-motion is key to understanding how many patients' symptoms relate to an abnormal visuo-vestibular interaction. Indeed patients with vestibular disorders commonly report a modulation of their dizziness by visual stimuli. In acute vertigo, where typically there are abnormal signs such as a vestibular nystagmus,[1] patients often close their eyes to avoid the distressing illusion of seeing the world spinning. In contrast, in chronic dizziness where there are usually no abnormal signs (an apparent uncoupling of symptoms from signs), patients complain of dizziness in the face of relatively trivial motion in the environment (e.g. crowds in a shopping mall). Since such visual stimuli are ubiquitous in the modern world, visually-induced dizziness (so-called 'visual vertigo') may be crippling for patients' social, occupational and mental well-being. In this overview we explore the basic mechanisms underlying the intimate relationship between visual motion and dizziness, and the relevance of this visual-vestibular interaction for patients' symptoms and their management.

Role of the vestibular system in health

As we navigate through the environment, our visual system is faced with two challenges: (1) the maintenance of a stable and clear image of the world during head movements; (2) the accurate ascribing of visual motion as being due to either self-motion or environmental motion – put simply the brain asks the question: am I moving? or is the object/world moving? To overcome these problems the central nervous system combines visual and vestibular inputs.

Maintaining a clear and stable vision is enabled by a natural 'steady-cam' mechanism called the vestibular-ocular reflex (VOR).[2] The VOR involves a 3-neurone brainstem reflex that begins with the detection of head acceleration by the peripheral

labyrinth. This head motion signal is conveyed by primary vestibular afferents to the vestibular nuclei neurones in the brainstem which in turn project to ocular motor neurones. The VOR thus keeps the eyes steady and 'locked on' to the visual target of interest despite head motion. This mechanism thus maintains visual acuity and a stable visual world by reducing slippage of the visual image across the retina. This 'retinal slip', when it does occur, may provoke the unpleasant sensation of oscillopsia. In general the degree of oscillopsia is coupled to the amount of retinal slip, particularly in the acute state. Retinal slip and oscillopsia symptoms are not however inevitably linked but can be uncoupled in the chronic adapted state.[3-5] The capacity for the brain to render a physical retinal slip unnoticeable is an important concept since it leads to the finding that ocular motor (reflex) parameters of vestibular function (i.e. VOR) relate poorly to perceptual aspects of vestibular function (i.e. dizziness) in the chronic state.[4] Indeed a relatively common but extreme example of such perceptuo-reflex uncoupling is that seen in idiopathic congenital nystagmus where a vigorous nystagmus is not associated with symptoms.[5]

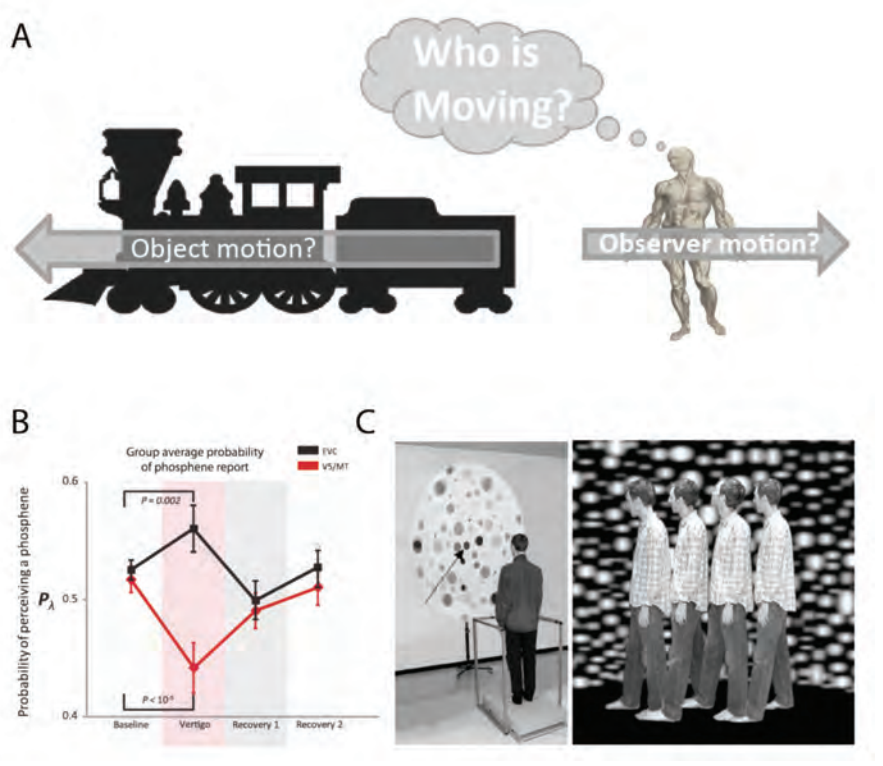

Figure 1. A) The 'train effect'. To differentiate between self versus object motion, visual information alone is sometimes insufficient, therefore the brain can also employ information from the vestibular system to provide an estimate of absolute motion of the head. B) During caloric stimulation the probability of perceiving a phosphene (a marker of visual cortical excitability) was significantly reduced in V5/MT regions, whereas the opposite effect was observed in the EVC (see reference 12). C) The rotating disc (left) affects the perception of the 'true' gravitational vertical in the direction of tilt. The extent to which an individual's perception is influenced by these backgrounds provides a measure of visual dependence. The planetarium (right) is used as a rehabilitation therapy for patients with visual vertigo (modified from reference 51).

The visuo-vestibular interaction

One mechanism proposed to solve the motion ambiguity problem is that of a reciprocal visual-vestibular inhibition (Figure 2). Specifically, if the vestibular system signals 'no motion', then this impedes a visual motion signal from indicating self-motion. Conversely, when there is no vestibular signal, visual input can provoke a sensation of self-motion but only if the visual stimulus occupies a sufficiently large visual area. Cognitive influences are also important since illusory self-motion is more likely to occur if there is a high probability of self-motion, e.g. sitting on a train is a situation where motion is likely, whereas sitting on the sofa has a low probability of motion.

The psychophysical evidence for a visuo-vestibular reciprocal inhibition is supported by behavioural data showing that during self-motion, the threshold for visually detecting object-motion is elevated.[6,7] Similarly visual-vestibular reciprocal inhibition is invoked to explain the observation that vestibular stimulation can disrupt performance on visualisation and mental rotation tasks.[8] Note that although vision is the critical sensory modality for the normal calibration of vestibular signals, the vestibular system can utilise non-visual sensory signals as evidenced by the ability of congenitally blind individuals to orientate themselves using only vestibular cues of motion.[9]

The neural basis for the higher order (perceptual) brain response during visuo-vestibular interaction has been explored using functional imaging,[10] lesion mapping[11] and brain stimulation.[12] Unlike the motor or somatosensory systems, there is no primary vestibular cortex, rather vestibular signals are widely conveyed to the cerebral cortex.[13,14] Conversely vestibular sensitive cortical neurones invariably display reactivity to other sensory inputs such as proprioception or visual motion, i.e. vestibular sensitive neurones are truly multi-modal sensory neurones.[13,15]

Vestibular stimulation e.g. via bithermal caloric irrigation or galvanic stimulation of the vestibular nerve, is associated with increased neuro-imaging signal in a network of brain regions primarily in the Sylvian fissure, insula, retroinsular cortex, fronto-parietal operculum, superior temporal gyrus and cingulate cortex.[16-19] Conversely, signal reduction is observed in visual cortex (the neuro-imaging correlate of visual-vestibular reciprocal inhibition). In contrast optokinetic visual stimulation inducing vection engenders an opposite pattern, i.e. reduced signal in somatosensory and parietal ('vestibular') areas versus increased signal in visual cortex.[20-22]

Since neuroimaging is a correlational technique we recently utilised transcranial magnetic stimulation (TMS) to probe visual cortical excitability during vestibular activation (see Figure 1B and reference 12). We posed two main questions: first, is there a true change in visual cortical excitability during vestibular activation; second, is the visual cortical response uniform or is there a differential response between early visual cortex (includes V1/2) and visual motion cortex (area V5/MT). This latter aspect was prompted by the lack of clarity in the literature with some suggesting a uniform visual cortical involvement,[16,23] versus those proposing a selective involvement[17,24] of visual motion areas. In this experiment, we probed the excitability of visual motion area V5/MT and separately early visual cortex (EVC), i.e. areas V1 and V2, using TMS, during vestibular activation (obtained by caloric stimulation). TMS can be used to probe visual cortical excitability by measuring the relative ease with which one can evoke a phosphene[25] (a perceived flash of light elicited by visual cortex electrical or magnetic stimulation[26]). We found that vestibular stimulation was associated with decreased V5/MT excitability versus increased excitability of early visual cortex (see Figure 1B). Thus, strong stimulation of the vestibular system may reduce sensitivity of visual motion detection areas, but crucially leaves early visual cortex functionally intact (thus not interfering with visual discriminative functioning). This finding provides a possible neurophysiological correlate for the putative reciprocal inhibition between vestibular and visual cortical networks.

Functional imaging has also been used to compare the brain activation of healthy controls during vestibular stimulation to activity in patients following a vestibular lesion. Patients with vestibular neuritis were examined using positron-emission tomography during the acute stage and again three months later.

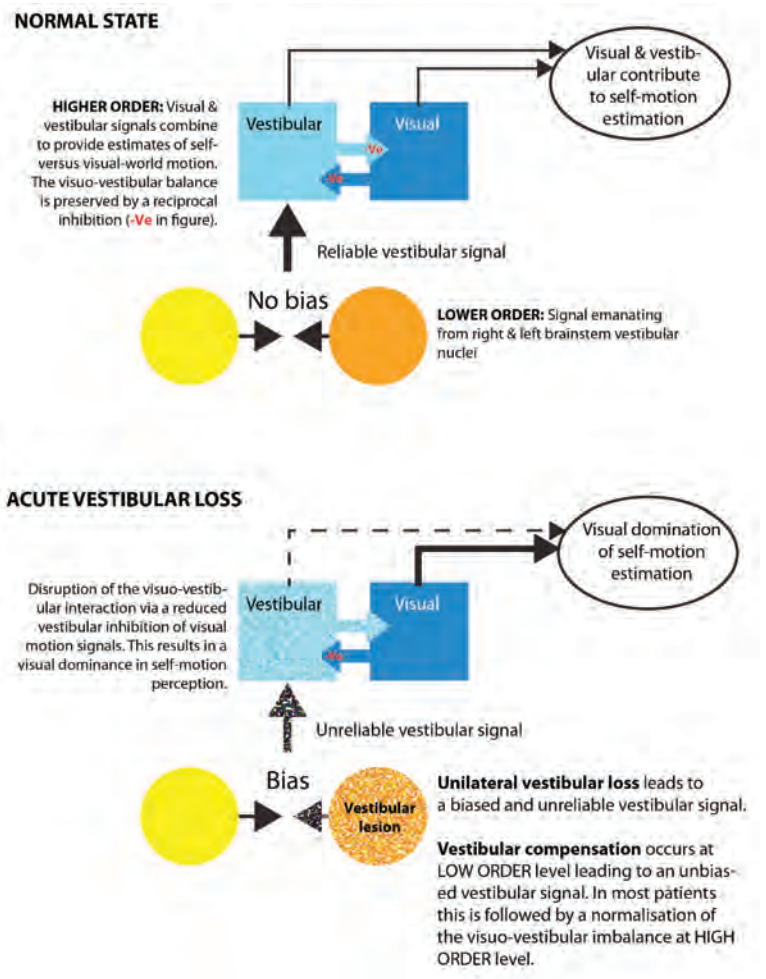

Figure 2. Visuo-vestibular interaction. A proposed schema.
In the normal state visual and vestibular signal combine to provide estimates of self-versus visual-world motion. Following acute vestibular loss, the imbalance of inputs from the vestibular system results in an unreliable vestibular signal. Therefore during this period the brain relies more heavily on visual information.

Increases in regional cerebral glucose metabolism (rCGM) were found in the acute stage relative to the recovery period in multisensory vestibular cortical areas, whereas reduced rCGM was reported in visual and somatosensory areas.[27] These acute stage activation patterns largely mirror those described during vestibular stimulation in healthy volunteers.[28]

The relationship between brain structure and vestibular function has also been investigated using neuroimaging. In a follow-up study, patients with VN were tested at least six months after disease onset. Increased grey matter density was reported in medial vestibular nuclei and right gracile nucleus, and increased white matter in the pontine commissural fibres, whereas reduced grey matter was found in left hippocampus and right superior temporal gyrus. Patients who reported residual canal paresis also demonstrated increased grey matter in MT/V5 regions.[29] A recent study investigated associations between variability in grey matter changes and clinical outcomes in patients with unilateral vestibular failure.[29] Grey matter density in the patients was compared to age-matched controls and revealed signal increases in medial vestibular nuclei and the right gracile nucleus grey matter, and reductions in left posterior hippocampus and the right superior temporal gyrus. Patients who demonstrated a significant residual canal paresis also showed increased grey matter density bilaterally in visual-motion sensitive areas in middle temporal cortex (MT/V5), an area that also receives vestibular input.[30] This may reflect an attempt to compensate for (vestibular) motion sensitive deficits experienced by patients with significant vestibular deficits after vestibular neuritis.[31] Outcomes as measured by the clinical vestibular score and subjective vestibular disability score were positively correlated with grey matter density in insular, retroinsular and MT and STG regions. These studies indicate that both brain functional and structural changes may take place during central vestibular compensation. Similarly, functional[31-33] and imaging[34] changes in visual mechanisms develop in patients with bilateral vestibular failure (e.g. secondary to gentamicin or idiopathic;[35]) probably underpinning adaptation to the oscillopsia experienced by bilateral vestibular patients.

Clinical Relevance – 'Visually-induced dizziness'

The visuo-vestibular interaction is of particular clinical relevance to patients suffering from visually-induced dizziness[36-38] previously known as visual vertigo, 'visuo-vestibular mismatch'[39] or 'space and motion discomfort'.[40] Patients with visually-induced dizziness report dizziness, unsteadiness and disorientation in visually disorienting surroundings but typically not classical rotational vertigo. The distinguishing characteristic of these patients compared to other dizziness patients is their tendency to be over reliant upon vision for postural control and balance, a situation termed 'visual dependency'.[37] Visually-induced dizziness appears to be the end result of repeated exposure to dizziness developing in diagnoses as disparate as vestibular migraine (see consensus statement on diagnosis of vestibular migraine[41]) BPPV or post-vestibular neuritis.

Visually-induced dizziness occurring post-vestibular neuritis should be distinguished from symptoms related to 'poor compensation' of the acquired unilateral peripheral vestibular deficit due to the vestibular neuritis. Poor compensation from a post-vestibular neuritis vestibular deficit can arise due to intermittent vertigo from BPPV, physical inactivity and/or excessive vestibular sedative therapy. A clear identification of the triggers (visual and non-visual) of symptoms post-vestibular neuritis is important since this determines the therapeutic intervention to alleviate these symptoms, e.g. stopping vestibular sedatives, initiating anti-migraine drugs, positional manoeuvres for BPPV, and vestibular physiotherapy, be it Cawthorne Cooksey exercises or optokinetic stimulation for visually-induced dizziness.

The profile of a typical patient with visually-induced dizziness would be a previously asymptomatic individual who suffered an acute vestibular insult such as vestibular neuritis (VN). We also see visually-induced dizziness in any patient with chronic recurrent dizziness, e.g. vestibular migraine (vestibular migraine is now an accepted International Headache Society diagnosis)[41] or benign paroxysmal positional vertigo.

In a patient with post-vestibular neuritis visually-induced dizziness, typically as the patient's overt continuous spinning vertigo abates another form of dizziness gradually increases whereby dizziness occurs in visually-busy situations such as supermarkets or shopping malls (leading to the false conclusion that the patient has a primary agoraphobia). Sometimes the patient does not discriminate between the acute attack of vertigo and subsequent chronic dizziness, and reports an acute onset with failure to improve over subsequent months. These patients may fail to report visual motion exacerbation of symptoms so it is important to always ask about 'supermarkets', 'shopping malls', 'moving trains', 'action films' or 'video games' as triggers of dizziness.

In Figure 2 we outline a hypothetical schema of the brain mechanisms underlying visual-vestibular interaction and visually-induced dizziness. An acute vestibular lesion results in an unreliable vestibular signal leading to impaired visual and postural stability. This unreliable vestibular signal is partially corrected for by the brain shifting its reliance from vestibular to visual motion infor-

mation ('visual dependency'). This acute visual dependence usually remits once the tonic vestibular imbalance resolves (via a process of rapid brainstem plasticity). Occasionally, this visual dependence persists despite an adequate rebalancing of the vestibular signal leading to a maladaptive state of visually-induced dizziness. Why some patients go on to develop long term visual dependency and visually-induced dizziness is not completely understood however investigation of the mechanisms of brain plasticity responsible for these symptoms are on-going.[37,42]

Whatever the neurobiological mechanisms underlying visually-induced dizziness and visual dependency, important aggravators of visually-induced dizziness include psychological symptoms,[43] and migraine. How these aspects affect brain plasticity involved in vestibular compensation for an acute or recurring vestibular insult is unclear.[44,45] Our recent data in individuals adapted to chronic vestibular stimulation suggest however that vestibular cerebellar plasticity plays a critical role in modifying the perceptual response to vestibular stimulation.[46]

Rehabilitation

Rehabilitation works by inducing plastic change in the brain. This plasticity changes the functional characteristics of the brain enabling normal function in the face of a prior insult (e.g. peripheral vestibular loss). Thus initial advice given to patients following an acute vestibular problem is a form of rehabilitation. Vestibular patients are recommended to continue with normal daily activities to ensure they are exposed to visual and vestibular challenges since such sensory stimulation drives the adaptive change required for symptomatic recovery. An important clinical point is that chronic treatment (>3 days) with vestibular sedatives is inimical to the recovery of vestibular patients, presumably by impairing the normal mechanisms of vestibular compensation. In chronic patients rehabilitation regimes should be adjusted to address the nature of the vertigo experienced. There is evidence from experiments in both healthy volunteers and chronically dizzy patients that rehabilitation therapy using optokinetic stimuli is an effective treatment.[47,48] The first RCT study in this field examined the efficacy of simulator-based therapy in addition to customised treatment in a group of chronic unilateral vestibular patients who had responded poorly to conventional vestibular rehabilitation. Interventions included a planetarium and optokinetic disc stimuli (See Figure 2C) in order to examine whether visual dependence could be modulated in the patient group. The authors found significant improvements in visual vertigo symptom scores only in the group receiving the additional optokinetic simulator therapy.

The science underlying the effects of such physiotherapy is scarce. Recent laboratory data using TMS suggests that adapting to random visual motion promotes an acute increase of area V5/MT excitability, thus demonstrating the impact of visual motion stimulation upon visual cortical excitability. The use of a random motion stimulus contrasts with the OKN-type stimuli used in vestibular therapy sessions, however random motion stimulation may be ecologically relevant given patients' symptoms of visual vertigo in situations where the visual motion is 'Brownian' (e.g. shopping malls). Whatever the nature of the visual motion stimulus, the observed modulation of cortical excitability may plausibly mediate the therapeutic effect of current clinical rehabilitation protocols that have been developed empirically.[51]

These studies suggest that rehabilitation training and exposure to visual stimuli may improve the symptoms of chronically dizzy patients by addressing the imbalance in their visuo-vestibular interaction and visual dependency. It is recommended that dizzy patients also pursue behaviours which challenge their visual dependence in addition to any formal rehabilitation they take part in. This is important as 'real-world' phenomena can never be fully replicated in the lab. Particularly helpful sports include those requiring VOR-smooth pursuit integration, e.g. ball sports such as tennis.

Clinical overview

An understanding of visuo-vestibular interaction and the underlying brain mechanisms is key in understanding patients' superficially bizarre complaints ('I feel dizzy when faced with shopping mall crowds or walking down supermarket aisles') and secondly in developing effective treatment for visual vertigo. One potentially problematic group are vestibular migraineurs who frequently also complain of visually-induced dizziness. When treating such patients it is imperative to follow a step-wise approach. The first step is to treat the migraine with effective prophylaxis. We find that standard anti-migrainous drugs work well with propanolol being our first line (second line according to patient profile; including amitriptyline, topiramate, sodium valproate or pizotifen). Often simply treating the vestibular migraine with pharmacotherapy improves the visual symptoms as well. If visually-induced dizziness persists despite good migraine control, we then initiate OKN therapy. If OKN is provided to active migraineurs then symptoms can be aggravated, hence the importance of the first step (in treating the migraine). Once commenced on effective anti-migraine prophylaxis OKN therapy can be provided if symptoms of of visually-induced dizziness persist. Indeed migraineurs show the greatest improvement in response to OKN therapy compared to patients with other chronic peripheral vestibular symptoms.[48] Note however that the clinician should be alert to patients with psychological symptoms who also avoid visually busy environments but for different reasons, e.g. agoraphobia (ref50). Equally many vestibular patients suffer from psychological symptoms as a result of their vestibular symptoms. In cases of doubt a liaison psychiatric opinion should be sought. Needless to say, some patients require a two pronged vestibular and psychological therapy approach. As always in medicine, a diagnosis and appropriate treatment has to be decided on multiple aspects of the clinical history and investigations.

Conclusion

An understanding of the brain mechanisms mediating visual and vestibular interaction has been little studied however multi-modal research involving neuroimaging, lesion mapping and more recently with TMS has enabled a mechanistic explanation for patients' symptoms and the logical development of their treatment. There are many unanswered pertaining to the modulators of visual-vestibular interaction, such as migraine, anxiety and co-existing medical and neurological disorders.

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New Journal Reviews Editor for ACNR

We would like to welcome Gemma Cummins as our new Journal Reviews editor. Gemma is a Specialist Registrar in Neurology at Addenbrooke's Hospital, Cambridge and is currently completing a PhD on movement disorders and cognition at the Van Geest Centre for Brain Repair, Cambridge.

Prof Ebers awarded AAN Prize for MS research

The American Academy of Neurology and the National Multiple Sclerosis Society awarded the 2013 John Dystel Prize for MS Research to George C. Ebers, MD, a researcher with the University of Oxford and Oxford University Hospitals Trust in Oxford, UK. Ebers received the award at the Academy's 65th Annual Meeting in San Diego, earlier this year. The John Dystel Prize recognises a significant contribution to research in the understanding, treatment or prevention of multiple sclerosis (MS). Ebers' research has focused on genetic and environmental influences on MS risks. "We have found that MS risk factors previously considered to be genetic can be changed based on environment, strongly implicating gene-environment interaction. Our studies highlight how climate and diet relate to factors leading to MS, which can be viewed as a largely preventable disease. Vitamin D exposure appears to be the main factor determining geographical risk" said Ebers.

MND Association Lectureship in Translational Neuroscience

Dr Richard Mead, based at the Sheffield Institute for Translational Neuroscience (SITraN) at the University of Sheffield, has been awarded the Kenneth Snowman-MND Association Lectureship in Translational Neuroscience.

The five-year Kenneth Snowman-MND Association lectureship is aimed to embed preclinical expertise in motor neurone disease (MND) models within SITraN as a national resource.

Dr Richard Mead was awarded the lectureship as he has the expertise and knowledge to enable high quality pre-clinical research into MND. Dr Mead has over 14 years experience in both academia and industry with a background in models of MND (mice and fibroblasts or 'skin cells') and multiple sclerosis.

Developing disease models is important for furthering our understanding of MND and allows researchers to screen potential new drugs for a beneficial effect before they can be given to humans, by means of a clinical trial.

As well as a track record of taking compounds into clinical development, Dr Mead hopes to use this knowledge and experience to develop MND specific therapeutic compounds. Dr Mead has already shown effectiveness of two compounds using his pre-clinical screening programme, with one being given 'Orphan drug' designation by the European Medicines Agency (EMA).

For more information see www.mndassociation.org

WFNR Franz Gerstenbrand Award deadline

1st November 2013 is the deadline for entries for the World Federation for Neurorehabilitation (WFNR) Franz Gerstenbrand Award. The Award is open to clinicians, researchers and allied health professionals and recognises and rewards a neurorehabilitation project that has benefitted patients. The annual, single prize of £3000 will be awarded as either a travel bursary to a clinical conference, professional development course or research project.

Named after Professor Franz Gerstenbrand, in recognition of his continuous contributions to neurorehabilitation, the Award is open to WFNR members and non-members worldwide.

Entries can come from any aspect of neurorehabilitation and examples include a patient or clinic management initiative, research project, best practice development or the use of a new technological development. A panel of four or five judges, led by the WFNR President, will review the entries.

For further details and details on how to apply, visit: http://wfnr.co.uk/en/education-and-research/wfnr-award/

New Guidance for Occupational Therapists on Acquired Brain Injury

Anna Bond
is Publications Manager at the College of Occupational Therapists (COT) and is responsible for producing occupational therapy publications, which include titles that focus on interventions in specific conditions, strategic goals and standards, and are developed and written by a range of leading occupational therapists and the COT specialist sections.

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Conflict of interest statement:
Anna Bond has no conflict of interest other than that she edited the book.

Summary
- New guidance for occupational therapists working with adults with acquired brain injury.
- Outlines key recommendations from national guidelines.
- Offers downloadable audit tool and checklist.
- Can be used by other health professionals, managers, commissioners and friends and families of individuals dealing with brain injury.

The College of Occupational Therapists (COT) has published new guidance for occupational therapists working with adults with acquired brain injury. Developed by experts from the Brain Injury Forum of the COT Specialist Section – Neurological Practice, this new book covers specifically 'acquired brain injury' and supports the implementation of two national documents, which aim to improve the delivery of acquired brain injury rehabilitation services: *Rehabilitation following acquired brain injury: national clinical guidelines*[1] *and the National service framework for long-term conditions*.[2]

Background

The effects of brain injury are varied in terms of the severity and causes; no two cases are the same. Lives may be turned completely upside down following the injury, not just for the individual but for those around them. Various functions and/or activities may have to be relearned and, for some, a shift in perspective on life and expectations for the future is required.

The first priority following a brain injury is medical intervention to preserve life and reduce further damage occurring through secondary complications. This, in itself, can be a lengthy process, with many challenges along the way. This may mean that the stay in hospital following a brain injury can be a long one, which can, in turn, lead to further practical issues. The occupational therapist may be involved as part of the multidisciplinary team throughout the hospital admission, from involvement in coma stimulation programmes through acute rehabilitation intervention and discharge planning.

For many people, however, discharge from hospital is just the beginning of a long and challenging journey to rebuild their life. This is where the role of the occupational therapist becomes vital.

What is the occupational therapist's role?

Occupational therapy 'aims to enable and empower people to be competent and confident in their daily lives, and thereby enhance wellbeing and minimise the effects of dysfunction or environmental barriers'.[3] Occupational therapists address such dysfunction 'using a range of interventions that often include environment, teaching clients a new repertoire of skills or helping them to re-establish ones they have lost'.[3] This is particularly important for people recovering from acquired brain injury. A wide range of 'physical and neuropsychological impairments can impact on activities and meaningful occupations, while reducing a person's level of social participation, including their ability to participate in educational and vocational activities'.[4]

Occupational therapists will work with a person, in collaboration with family and friends, to help them make sense of their injury and achieve personal goals through participation in a range of meaningful and purposeful activities.[4]

How will the guidance help?

This new publication has been developed as a practical resource. It outlines the key recommendations from the national guidelines[1,2] in a range of different areas, including: principles and organisation of services, approaches to rehabilitation, carers and families, early discharge and transition to rehabilitation services, inpatient clinical care, rehabilitation setting and transition phases, rehabilitation interventions and continuing care and support. These recommendations have been used to develop a series of key reflections for occupational therapists that can be used on a practical, day-to-day basis to support clinical decision making when working with adults with acquired brain injury.

In addition to this, each section has an audit tool to evaluate current practice against the recommendations, giving the opportunity to identify how this practice can be evidenced. A checklist and action plan is also provided to encourage occupational therapists to ask themselves if they are meeting criteria in all the appropriate areas.

The publication also signposts the reader towards further resources: useful organisations, publications, websites and relevant legislation.

A service user's perspective

Nick sustained a serious head injury following an accident whilst at work in March 2003. The next six months were spent in hospital, during which time, following initial surgery, a long recovery process started. He was then looked after for a further six months by his father at the family home. After an unsuccessful supported return to work he was referred for occupational therapy. Now approaching a decade after the accident he still feels a realistic general improvement every six months; and believes an important element of this is the support and guidance he gets from the occupational therapists and the resulting increased independence it gives him.

"In my experience, the most important factor in recovery is your determination. To sustain this determination and get positive results, it has to be assisted and directed. For me, the input of occupational therapists at various times has been very important. This has come in activities of various types, from gardening to latterly cooking, leaving me with useful skills which I can use everyday and thus increase my self-confidence."

How can the guidance be used?

As well as being a valuable resource for occupational therapists, this publication will also be of interest to other health and social care professionals. It is important, especially within multidisciplinary teams, to be aware of a patient's care throughout the recovery process. This publication will give an insight into the targets and goals occupational therapy services are working towards. It can also be used by the patient, family and carers to learn more about the service and ensure they are receiving the best possible care. ◆

This publication can be purchased from the College of Occupational Therapists website www.COT.org.uk/publications

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Epilepsy in Intellectual Disabilities

Dr Howard Ring

Ring is a clinical academic consultant psychiatrist at the University of Cambridge and the Cambridgeshire and Peterborough Foundation Trust. He trained in neuropsychiatry at the Maudsley Hospital and the Institute of Neurology, Queen Square, London. He has contributed to research, education and clinical services development and delivery in neuropsychiatry and the psychiatry of intellectual disabilities.

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Conflict of interest statement:
Dr Ring has received speaker fees from UCB and Eisai.

Topics addressed in the article

- What is Intellectual Disability (ID) ?
- A brief account of the nature of epilepsy in people with ID.
- Issues around the diagnosis of epilepsy in people with ID.
- Education and communication in the management of epilepsy in people with ID
- Neuropsychiatric comorbidities of epilepsy in people with ID.
- The evidence base informing management of epilepsy in people with ID.

What is Intellectual Disability?

To have an intellectual (learning) disability (ID) is to have a developmental disorder characterised either by never having been able to acquire the educational and functional skills expected for your age, or, early in life suffering a neurological insult that arrested your development such that you could not go on to develop the expected level of functioning. Whatever the cause, those considered as having an ID manifest significantly limited abilities across a wide range of everyday functions including cognitive, language, motor and social activities. In the UK the diagnosis of an ID also requires IQ to be 70 or less. An estimated 828,000 adults in England have an ID and amongst this population epilepsy is common, being the most frequent medical illness experienced.[1]

The nature of epilepsy in people with ID

Across the population of those with ID as a whole, a prevalence of epilepsy of 26% has been reported though this average figure obscures the fact that prevalence of epilepsy increases in line with increasing severity of ID. Amongst those with mild to moderate ID lifetime epilepsy prevalence has been reported at between 6 and 15%. In those with severe ID epilepsy occurs in around 25% whilst in those with profound ID (IQ<20), in whom it has been estimated that there will in the UK be an average annual increase in number of 1.8%, epilepsy is reported in more that 50%. In some specific ID syndromes particularly high rates of epilepsy are reported; for instance in Rett and Angelman syndromes prevalence rates for epilepsy of 80% or more are reported.

Not only is epilepsy more common in those with ID than in the rest of the population: it tends to have a worse prognosis, with lower rates of seizure freedom[4] and high rates of multiple antiepileptic drug use,[5] incurring more side-effects[6] and higher treatment costs.[7] Adults with ID and epilepsy have high rates of morbidity[4,8] and mortality,[9] including sudden unexplained death in epilepsy (SUDEP).[10] Indeed, the Standardised Mortality Ratio (SMR) for SUDEP in adults with intellectual disability and epilepsy is in excess of 30.[10]

There appear to be multiple aetiologies underlying the association between epilepsy and ID and this is currently a very active area of research that in the future may suggest novel treatment approaches. Aetiological processes include not only effects of well-described genetic anomalies such as those leading to Rett and Angelman syndromes, but in an as yet undetermined proportion of people with ID and epilepsy the effects of an unknown number of rare but clinically significant submicroscopic copy-number variants (CNVs).[2] There is also evidence from experimental research to suggest that changes associated with epileptogenesis and seizures in early post-natal life may have effects on developmental processes in the brain including disruption of synaptic plasticity, dendritic development and ion channel maturation that may lead to later impairment in cognitive development.[3]

Diagnosis of epilepsy in people with ID

The diagnosis of epilepsy in people with ID may be complicated by a range of issues including; conflicting eye witness accounts of possible seizure events together with the difficulty that the patient themselves is likely to have in providing a history; the presence, particularly in those with more severe or profound ID, of stereotyped movements or mannerisms that may be mistaken for seizure-related movements; other paroxysmal disturbances of behaviour, for instance related to pain or frustration; and, potentially further compounding the challenges in clarifying the diagnosis; the difficulty that some people with ID may have in tolerating investigations such as EEG and MRI. Evidence suggests that in people with ID there are significant rates both of misdiagnosis of non-epileptic seizures as epilepsy, in up to around a third of cases, and failure to diagnose or to treat episodes that are epileptic in nature.[11] Hence it is important when managing refractory epilepsy in people with ID that the diagnosis is carefully reviewed and at the same that episodes considered to be behavioural in nature are re-considered to check that an epilepsy diagnosis is not being missed.

The role of education and communication in management of epilepsy in people with ID

Unlike most of the population without an ID, many of those who do have ID also rely for

some or all of their day-to-day support on family or on paid care workers. Hence not only can poorly controlled epilepsy impact negatively on quality of life of people with ID and epilepsy – it may also increase demands on families and others who provide support and care. Clinical and research evidence demonstrates that in order to deliver epilepsy management well to people with ID, it is important to appropriately involve this wider circle of individuals. This involvement should include good communication and, importantly, training by appropriate healthcare professionals of the people that support those with ID and epilepsy in the community. This is a critical element of care and one that often does not have a counterpart in epilepsy management, at least of adults, in the rest of the population. Another important consequence of this reliance that adults with ID and epilepsy have on family or paid supporters is that a key element in the therapeutic relationship that clinicians should focus on is their relationship with these supporters. Research has demonstrated that this is important in contributing to the transmission of relevant observations to the clinicians and to the potential uptake of and compliance with suggested antiepileptic therapeutic interventions offered to patients.[12]

Neuropsychiatric comorbidities of epilepsy in people with ID

There is evidence that some psychiatric comorbidities are more common in those with epilepsy who also have an ID and amongst these the conjunction of autism and epilepsy is well recognised, with autism occurring in up to 30% of people with epilepsy,[13] most often in those who also have an ID. In a recent study investigating the details of this relationship it was noted that the frequency of cases positive for epilepsy amongst a group of people with autism was highest in those whose autism was associated with an early age of diagnosis and high rates of repetitive object use and unusual sensory interests.[14] With respect to seizure semiology in autism, all seizure types are seen in people with autism,[15] with those most commonly observed being focal seizures with altered awareness, atypical absence and generalised tonic–clonic seizures. There is no evidence that antiepileptic drug efficacy differs between those with and without autism in addition to epilepsy.

The evidence base informing management of epilepsy in people with ID

Evidence that epilepsy in adults with ID may not be optimally managed comes from a report by the Learning Disability Observatory into Ambulatory care sensitive conditions (ACSCs) (defined as conditions which, given 'effective management' at the primary care level, should not normally result in an admission to hospital) in people with ID. That report[16] noted that convulsions and epilepsy were the most frequent cause of what were considered as potentially avoidable hospital admissions in people with ID, accounting for approximately 6000 admissions a year, equivalent to 40% of all emergency admissions for ACSCs in adults with ID.

Despite the frequency and potential severity of epilepsy in people with ID, many of the clinical trials that have investigated antiepileptic drug use in epilepsy management have excluded those with ID. Hence there is limited research evidence to inform clinical epilepsy management strategies among people with ID beyond that which can be extrapolated from the rest of the epilepsy population. However, a systematic review published in 2009 of the available evidence concluded that AEDs effective in the general epilepsy population are also effective in refractory epilepsy in people with ID, though conclusions on relative efficacy between medications could not be drawn.[17]

In order to inform treatment choices in the absence of a wider evidence base, pragmatic consensus clinical guidelines have been developed,[18] which supplement existing guidelines for epilepsy care in the non-intellectual disability population. They draw attention to a range of issues including; the associated communication difficulties experienced by people with ID and the possible consequences of these for detecting antiepileptic drug treatment-related adverse effects; the fact that presence of ID is not necessarily a contraindication to neurosurgery for epilepsy; and the relatively high rates of other comorbidities experienced by people with ID and epilepsy. ◆

Across the population of those with ID as a whole, a prevalence of epilepsy of 26% has been reported though this average figure obscures the fact that prevalence of epilepsy increases in line with increasing severity of ID

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Oculo-Dento-Digital Dysplasia (ODDD)

Summary

- ODDD is a complex genetic disorder which illustrates the effects of a single mutation on multiple tissues: a multidisciplinary approach to management is necessary.
- The associated radiological changes on magnetic resonance images (MRI) of the brain are distinctive but may easily be misinterpreted or go unrecognised.
- Early recognition of ODDD allows the prevention and treatment of clinical manifestations and complications.

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Conflict of interest statement:
The author declares that there are no financial or commercial conflicts of interest.

Patient has given consent for use of the photos.

Oculo-dento-digital dysplasia (ODDD), also known as oculodentoosseous dysplasia (ODOD), is a rare genetic disorder affecting multiple tissues. It is characterised by multiple, variable craniofacial, limb, ocular and dental anomalies which are often associated with neurological disorder. Some features are evident at birth while others become evident with age.

The disorder results from mutations in the GJA1 gene, located on chromosome 6, which encodes for the gap junction protein, connexin43 (Cx43). It is inherited as an autosomal dominant trait in the majority of cases. Less commonly, sporadic forms occur which may be related to advanced paternal age. Autosomal recessive inheritance has been reported rarely, but this remains to be confirmed. There are more than 60 known mutations, mostly missense in type. Fewer than 1000 patients with ODDD have been reported in the literature, and the prevalence of the disorder is uncertain.

The Story

A 50 year-old right handed woman, who works part time in a bakery, was referred because of progressive disturbance of gait of six years duration. This had started as a limp on the left leg, noticed after recovering from septic shock associated with bursitis of the left knee. Her gait disturbance was initially attributed to this dramatic episode, but further assessment revealed a potentially relevant background history.

She was born with bilateral partial syndactyly of the toes and fingers and complete syndactyly of the 4th and 5th fingers of the left hand. This was later surgically corrected. The proximal phalanx of the little finger of the right hand was absent (Figure 1). Her little fingers and toes remained very small. At the time of birth, her mother and father were aged 31 and 30 years respectively. Neither her parents nor her older brother have any developmental anomalies.

As a child, she developed a squint which was surgically corrected. Between the ages of 14-16, she suffered from epilepsy treated with Phenobarbital. The enamel of her teeth was deficient and she had lost four permanent teeth by the age of 24. She was prone to frequent diarrhoea, urinary frequency, nocturia, urgency, and precipitancy with occasional urinary incontinence. She had primary infertility, due to malformation of the Fallopian tubes. She was never sporty.

Examination revealed microphthalmia, a low bridge of nose with low insertion of columella (figure 2, 3) and small teeth, in addition to the sketetal abnormalities described above. She had thickened skin over the palms and soles. She had a mild convergent squint, manifest on the left and latent on the right. There was spasticity of all four limbs with mild bilateral weakness of finger abduction, hip flexion, and knee flexion, very brisk tendon reflexes with a few beats of clonus at the ankles, and bilaterally extensor plantar responses. Coordination and superficial and deep sensations were intact. Her gait was spastic (stiff and hyperextended).

Brain MRI was initially reported to be normal, but on specialist review (initially at our neuroradiology meeting) there were subtle T2 hyperintensities in the subcortical white matter and T2 hypointensity of the basal ganglia (figure 4). MRI images of the spine were normal.

The diagnosis was suspected clinically. A sequencing analysis of the GJA1 gene undertaken at John Hopkins DNA diagnostic laboratory in the United States, revealed a heterozygous mutation, c.460 A>G (Thr154Ala) in the GJA1 gene (6q22-q23), confirming the diagnosis of oculo-dento-digital dysplasia.

Discussion

The patient suffers from the sporadic form of ODDD. The disorder affects several tissues, including the eyes, nose, teeth, fingers, toes, the skin of the palms and soles, fallopian tubes and nervous system. The Fallopian anomaly has not been described in ODDD previously.

The most common anomalies in ODDD are ophthalmic, nasal, dental and digital. Seventy eight percent of affected families display features in more than two of these categories.[1] The characteristic facial appearance is evident in 92% of the families.[1] Eye findings are present in 68% and include short palpebral fissure (the anatomic name for the separation between the upper and lower eyelids), epicanthal folds (skin of the upper eyelid covering the inner corner of the eye), hyper- or hypotelorism (increased or decreased distance between the eyes), microphthalmia with microcornea and iris abnormalities. Gaze palsies and squint may also occur. Some patients develop cataracts, glaucoma and blindness secondary to

Figure 1: Small little fingers, scar from separation of 4th and 5th finger syndactyly, with absence of proximal phalanx of the little finger in the right hand.

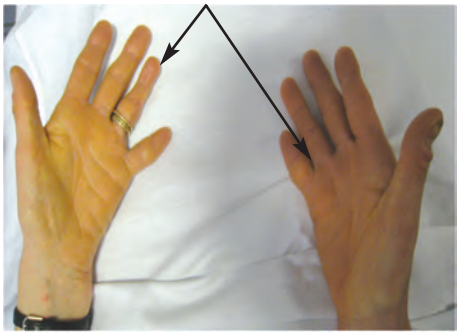
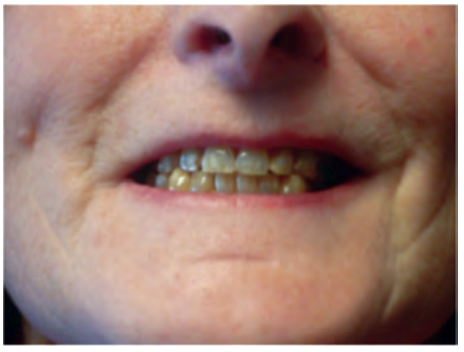


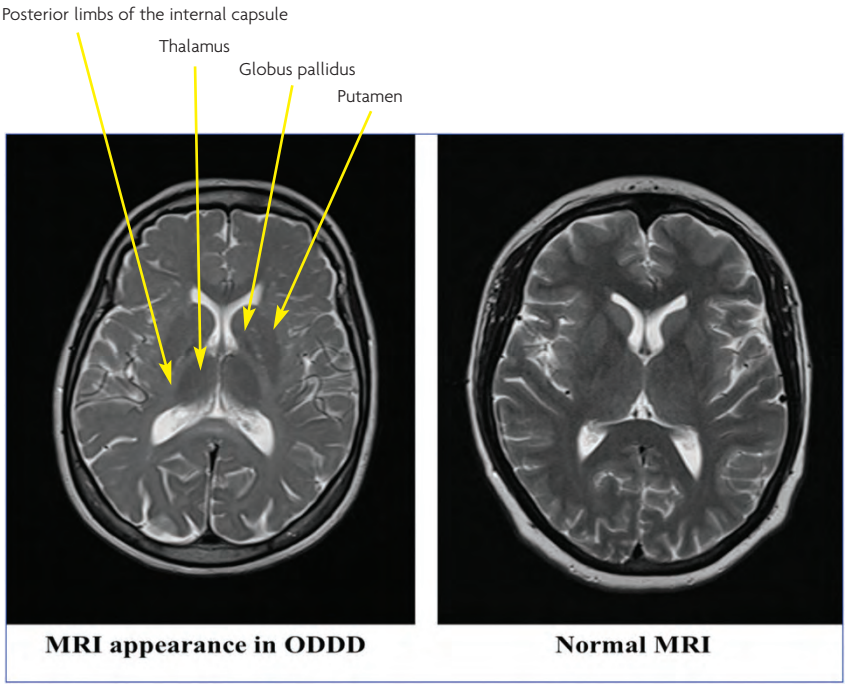
Figure 2: Strabismus, hypotelorism and microphthalmia.

Figure 3: Microdontia and enamel hypoplasia.



glaucoma.[1,2] Nasal features are also prominent in ODDD and may include, a thin nose, usually with hypoplastic alae nasi (the expanded outer wall of cartilage on each side of the nose), small anteverted nares (upturned nostrils), and prominent columella nasi (the fleshy lower margin of the nasal septum). Abnormal primary and permanent dentition with microdontia, partial anodontia, enamel hypoplasia, multiple caries and early tooth loss are evident in 70% of the affected families.[1] Digital malformations occur very commonly and are seen in 80% of the affected families.[1] Bilateral complete syndactyly of the fourth and fifth fingers (type III syndactyly) is characteristic. The third finger may also be involved. Syndactyly of the third and fourth toes may be present. Hypoplasia of the middle or distal phalanges or aplasia of one or more digits or toes may be seen. There may be an associated camptodactyly (permanent flexion) or clinodactyly (abnormally positioning) of the fifth finger.

Figures 4 and 5.



Neurological problems are less common and are said to occur in 30% of affected families.[1] The clinical expression varies widely within and between affected families, as does the age of onset. Neurological involvement is usually evident by the second decade of life but may occur much later. Slowly progressive spastic paraparesis is the most common feature and is associated with characteristic brain MRI changes, described below. Other variable manifestations include neurogenic bladder and bowel disturbance, ataxia, dysarthria, seizures, and mild mental retardation. Neuro-ophthalmological findings include ptosis, nystagmus, gaze palsies, squint and visual impairment that is probably related to glaucoma or amblyopia.[2] No neuropathological post-mortem findings have been reported yet in these patients.[2]

Less common features include hypotrichosis (poor hair growth in 26%), brittle nails, microcephaly, and cleft palate. A few affected individuals have palmoplantar keratoderma (abnormal thickening of the palms and soles), dysplastic ears, conductive hearing loss, and cardiac anomalies, including arrhythmias or congenital malformations (ventricular septal defect).

The typical MRI changes are bilateral hyperintensity in the white matter in T2-weighted images involving the periventricular parieto-occipital region, and extending into the posterior limbs of the internal capsules and along the corticospinal tracts. It has been suggested that these changes are associated with the clinical neurological manifestations of ODDD, and their severity may be reflected in the phenotype.[2] Other MRI findings include signal hypointensity of the globus pallidus, thalamus and cortex, which may be due to premature iron deposition.[2] The Spinal cord images may be normal or show mild atrophy.

Although ODDD mutations have a high penetrance, they exhibit great intra- and inter- familial phenotypic variability that is not related to the mode of inheritance or the mutation type, but to variable expression of the GJA1 gene.[1] GJA1 encodes connexin 43, which is one of 21 connexin proteins that participate in the formation and maintenance of intercellular channels.[1] Each of these proteins affects different functional properties of the channel, including pore conductance, size selectivity, charge selectivity, voltage gating, and chemical gating, influencing the exchange of small ions and signaling molecules between cells.

Early recognition of the syndrome is important for the prevention and treatment of the clinical manifestations. Management is multidisciplinary. Clinicians should be alert to the possibility of ophthalmic, audiological, neurological, and dental complications in particular. Drugs that may precipitate glaucoma should be avoided. Plastic or orthopedic surgery is indicated for severe limb malformations. Genetic counseling should be offered and prenatal mutational analysis may be considered. ◆

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Childhood Dystonia

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Conflict of interest statement:
The author declares that there are no financial or commercial conflicts of interest.

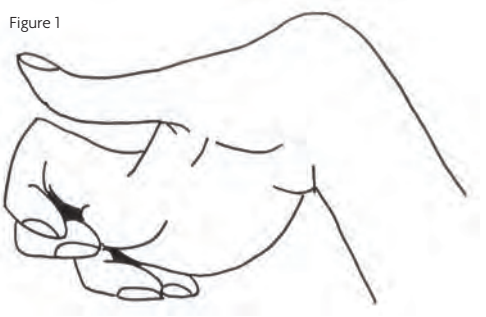
Summary
- Dystonia means involuntary muscle contractions causing repetitive movements and twisted postures
- The commonest clinical picture in children is dystonic cerebral palsy following hypoxic brain injury
- A trial of levodopa is warranted in cases without a clear secondary cause
- Management is often challenging, and must be holistic

Dystonia is a movement disorder in which involuntary muscle contractions cause repetitive movements and twisted postures. Dystonia causes significant morbidity in sufferers, and may even be fatal in severe cases. It may be a primary, genetic disorder, or secondary to a large number of other disorders. In children, these are mainly neurometabolic and degenerative. A thorough history, examination, and targeted use of investigations can provide the diagnosis in a subset of children, and help identify those in whom esoteric tests are warranted. Management is usually challenging, with a lack of robust evidence for treatment strategies in children. This article summarises an approach to the child with dystonia, and provides a framework for management.

Defining dystonia

Dystonia is defined as "a movement disorder in which involuntary sustained or intermittent muscle contractions cause twisting and repetitive movements, abnormal postures, or both".[1] The postures produced by co-contraction of agonist and antagonist muscle groups include hyperextension of the back and neck, torticollis, foot inversion, upward extension of the great toe, and 'spooning' of the hands (Figure 1).[2] Dystonia is often more prominent when voluntary movement is attempted, or in certain postures. Muscle tone may be normal at rest, enabling the clinician to differentiate dystonia from hypertonia. Dystonia may be generalised (or multi-focal), or localised to specific regions of the body, such as in torticollis.[1] In childhood, the commonest clinical picture is one of cerebral palsy with elements of spasticity and dystonia together.[3] However primary dystonia and dystonia secondary to other causes also occur.[1]

Figure 1



Aetiology

Primary dystonia occurs as an isolated presentation and has a genetic (or presumed genetic) aetiology (Table 1). Inheritance is often autosomal dominant; a careful family history may reveal previously undiagnosed relatives with milder phenotypes. Dystonia occurring secondary to another disease process affecting the basal ganglia is the more common finding in children (Table 2). Psychogenic pseudo-dystonia is an important differential diagnosis.

Clinical approach

The aims of the clinical assessment will be to confirm the presence of dystonia, and assess associated co-morbidities, functional impact, aetiology, perpetuating factors and complications.

History

A summary of key elements of the history is provided in Table 3.

Examination

The key aims of the examination are to characterise the dystonia and the degree of functional impairment, document associated motor disorders, review growth parameters and home video footage.

Firstly, inspect from a distance: note the use of orthoses, plot the height, weight and head circumference on a growth chart, looking specifically for malnutrition or microcephaly. Next observe more closely: assess if the dystonia is isolated, or if there is additional chorea, athetosis, or spasticity. Ask the child to walk if they can, preferably with shoes and clothes on at first, and then off. Video is very useful as gait can be very difficult to evaluate as children move swiftly around. Use functional techniques to bring out movement disorders: holding their fingers "as near to the nose as possible without touching it" (tremor), heel- toe walking and turning (ataxia), walking on the heels looking for inserted movements of hands and feet (Fogg sign). If you can see dystonia, note whether it is generalised, focal or segmental, and postural or fixed.

Next move them to the couch (even if wheelchair bound): assess the character of the dystonia and any additional movement disorders. Examine the cranial nerves with emphasis on fundi, eye movements, dysarthria, dysphagia (offer water if they drink orally), and tongue thrusting. Examine the limbs for evidence of other movement problems, e.g. dysmetria, intention tremor, spasticity, or neuropathy. Assess function through handwriting, drawing spirals, and performing tasks such as pouring water into a cup. It is also useful to video this, looking for posture and movement during a simple activity. Home videos can provide excellent insights, and should be reviewed.

Grading severity

Severity of the current episode of dystonia should be determined. Features of increasing severity of dystonia include being unable to sleep, sit or lie

Table 1: Childhood-onset primary dystonia[4]

Gene	Disease	Inheritance	Gene product &	location
DYT1	Idiopathic torsion dystonia	AD	Torsin A	9q34
DYT3	X-linked dystonia-parkinsonism	XL	TAF 1	Xq13-1
DYT4	Whispering dysphonia	AD	TUBB4a	19p13.12-13
DYT5a	AD Segawa syndrome (Dopa responsive dystonia)	AD	GCH1	14q22.1-q22.2
DYT5b	AR Segawa syndrome (TH deficiency)	AR	TH	11p15.5
DYT6	Adolescent/adult-onset Idiopathic torsion dystonia (mixed)	AD	THAP1	8p21-q22
DYT11	Myoclonus-dystonia syndrome	AD	SGCE	7q21.3
DYT12	Rapid onset dystonia-parkinsonism	AD	ATP1A3	19q12-q13.2

Table 2: Causes of secondary dystonia[5]

Cerebral Palsy following hypoxic brain injury (commonest cause)	
Metabolic	
Biotinidase deficiency	Mitochondrial diseases
Creatine deficiency	Mucopolysaccharidoses
Galactosaemia	Neuronal ceroid lipofuscinoses
Glutaric acidura type 1	Neurotransmitter disorders
GM1 and GM2 gangliosidosis	Niemann-Pick C
Hartnup disease	Proprionic acidaemia
Homocystinuria	Sulphite oxidase deficiency
Hypoparathyroidism	Tyrosinosis
Krabbe disease	Vitamin E deficiency
Lesch-Nyhan	Wilson disease
Metachromatic leukodystrophy	
Methyl-malonic acidaemia	
Metabolic	
Ataxia telangiectasia	Neuroaxonal dystrophy
Ataxia with oculomotor apraxia type 1, 2	Panthothenate kinase 2-associated
Infantile bilateral striatal necrosis	neurodegeneration (PKAN2)
Juvenile Huntington's	Pelizaeus-Merzbacher disease
Neuroacanthocystosis	Spinocerebellar ataxias
Drugs/Toxins	
Phenothiazines	
Haloperidol	
Metoclopramide	
Other	
Alternating hemiplegia of childhood	Porencephaly
Basal ganglia infarction	Sandifer syndrome
Basal ganglia neoplasm	Striatal necrosis
HIV infection	Vascular malformations
Kernicterus	

Table 3: History

Birth history

Pregnancy complications, Gestation, Mode of delivery, Cord gas results, Neonatal resuscitation, Encephalopathic features

Early life

Feeding, Seizures, Hospital admissions, Medical diagnoses

Development

Milestones achieved, Delay, Regression, School

Family history

Family tree, Consanguinity, Movement disorders, Neurological disorders, Stillbirths or early deaths

Dystonia

Age of onset, Progression, Focality, Diurnal variation, Functional impact, activities of daily living

Dystonia exacerbating factors

Gastro-oesophageal reflux, Constipation, Dental caries, Orthopaedic problems, including dislocated hips, fractures, Other causes of pain, Infection, Drug addition or withdrawal, Boredom, Emotional abuse/frustration/fear

Dystonia complications

Swallowing problems, Failure to thrive, Anxiety, depression, Aspiration pneumonia, Status dystonicus (potentially fatal exacerbation with multisystem dysfunction)

Co-morbidity

Spasticity, Oculogyric crises. Chorea. Other neurological problems

comfortably, and being systemically unwell. Children who show signs of systemic illness require urgent assessment and treatment for status dystonicus. Several formal grading scores are available.[6]

Investigation

Investigation and treatment are interlinked, as a therapeutic trial of levodopa is often used as a diagnostic tool. This should be considered in any child with dystonia without an obvious secondary cause. Those with Segawa disease (dopa-responsive dystonia) typically show a dramatic improvement within a few days.[3,4,7]

Other investigations will be guided by the clinical findings and response to levodopa (when used), and should be directed at the possible underlying causes (Tables 1 and 2).

Management strategies

There is a lack of robust evidence to inform pharmacotherapy for dystonia, therefore strict recommendations of first, second and third line medications are not practical.[4] Therapeutic strategies tend to vary with individual clinician preference and experience. As well as dystonia-specific therapy, identifying and treating precipitating factors is paramount (Table 3). Spasticity is a common co-morbidity, and it can be difficult to differentiate between spasticity and dystonia in some children. In these cases a pragmatic approach to symptom control should be taken.[4] Medications should be reviewed periodically, addressing whether the drug has had a positive effect on quality of life and the side effects. If there is no improvement with second line medication, consider discussion with colleagues at a complex case review or referring to a quaternary movement disorders clinic. As well as medication, supportive management in a multidisciplinary team including physiotherapy, occupational therapy, speech therapy and psychosocial support is essential.[3] Management is summarised in the algorithm (Figure 2, adapted from[3]).

Status dystonicus

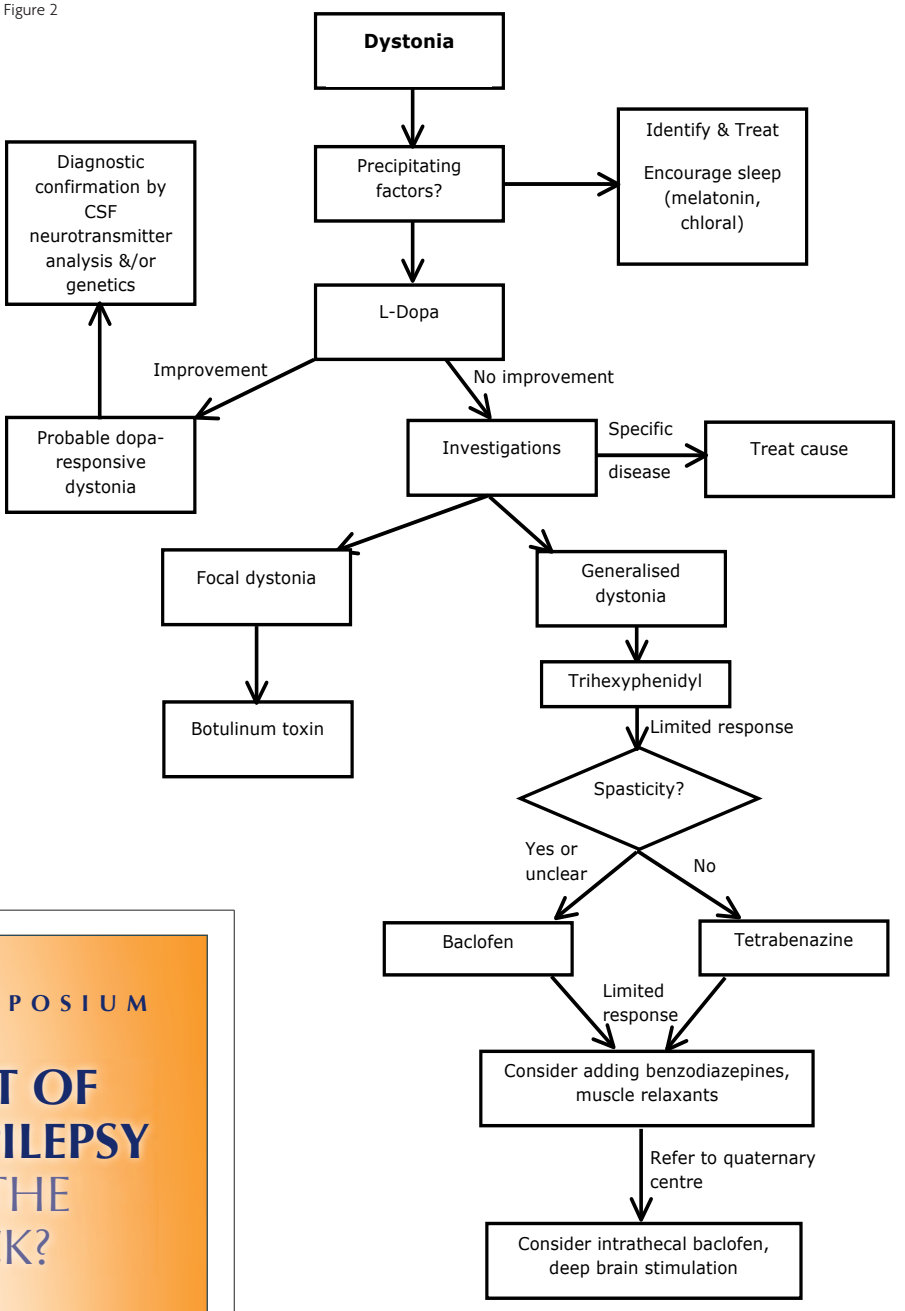
Status dystonicus is a potentially fatal episode of severe generalised dystonia. Complications include bulbar and respiratory compromise, and metabolic disorders such as rhabdomyolysis leading to acute renal

failure.[8] It usually occurs in children with known chronic dystonic disorders, but may occur in previously well children with acute illness affecting the basal ganglia or central nervous system. Children with status dystonicus should be managed in a hospital setting, and will often need intensive care. It is important to address precipitating factors (Table 3) and treat complications.[3] Supportive care such as invasive ventilation and haemofiltration for rhabdomyolysis may be needed. Therapy should be aggressive, with a slow weaning process. Treatment options include benzodiazepines, clonidine, propofol, and deep sedation with barbiturates. Surgical management, such as deep brain stimulation, will be required in up to one third of cases.[9] Once the dystonia severity has lessened, a slow wean of therapy can begin.

Conclusion

Childhood dystonia is a challenging condition. A multitude of external and internal factors often play a part in influencing dystonia, no matter what the underlying cause. A pragmatic, multidisciplinary approach is vital. ◆

Figure 2



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The Surgical Management of Posterior Fossa Tumours in Children

In Part I of this feature, Mr Aquilina described the presenting symptoms and signs of posterior fossa tumours in childhood and outlined the key clinico-pathological features of these tumours. In this second article, the management of these challenging cases is reviewed. This usually commences with appropriately timed investigations followed by surgery. The investigation and management of post-operative complications is also discussed.

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Surgical management

Pre-operative preparation of a child with a posterior fossa tumour

High dose dexamethasone is commenced on presentation. This often leads to improvement in symptoms. However, symptomatic hydrocephalus (headache, vomiting, papilloedema and reduced level of consciousness) requires urgent surgical treatment. Traditionally, an external ventricular drain is inserted with a view to removing it after definitive tumour resection and resolution of the obstruction to CSF flow. Endoscopic third ventriculostomy is currently preferred in most centres, as it reduces the risk of infection associated with external drains and minimises the small risk of upward transtentorial herniation with large posterior fossa tumours.

A full craniospinal pre- and post-contrast MRI scan must be completed before surgery to ensure complete tumour staging before surgical contamination of the CSF by blood products.

Surgical technique

Midline posterior fossa tumours are resected via a midline suboccipital approach. The patient is positioned prone with the head elevated and flexed. The squamous occipital bone is exposed through a midline longitudinal incision from the external occipital protuberance to the level of the posterior arch of C1. C2 is not exposed; it is important to maintain the muscular and ligamentous attachments to this vertebra, as subsequent radiotherapy and surgery may result in progressive cervical instability. The C1 posterior arch is exposed but preserved.

A posterior fossa craniotomy is preferable to craniectomy. This reduces post-operative pain and allows better restoration of CSF flow around the foramen magnum post-operatively.[1] The craniotomy is extended through the foramen magnum. The dura is opened in a 'Y' shaped fashion, remembering that in most young children an occipital sinus, descending in the midline from the torcula, may require ligation. Once the dura is reflected, the microscope is brought into the field and the arachnoid at the craniocervical junction is opened.

At this stage, tumour may be evident between the cerebellar tonsils. Ependymomas sometimes present a 'tongue' of tumour extending into the spinal canal; this can often be removed by gentle traction at the cisterna magna without resection of the C1 posterior arch. Fourth ventricular tumours are traditionally approached through the vermis. The longitudinal incision in the vermis should be as short as possible. Damage to the inferior vermis has been associated with an increased risk of cerebellar mutism; division of the superior vermis risks injury to the decussation of the superior cerebellar peduncles, which lies immediately deep to it.[2]

The telovelar approach avoids direct vermian incision. Dissection begins on one side, medial to the tonsil, between the tonsil and the uvula. This exposes the tumour superficially and the distal fourth ventricular floor deeply.[3] The inferior medullary velum is stretched over a large tumour and often not identifiable. The telovelar approach allows exposure of the entire fourth ventricle up to the aqueduct and the foramina of Luschka laterally, allowing identification of the tumour boundary and gradual resection of the tumour bulk. As the aqueduct is unblocked rapid egress of CSF is often visible (Figure 1). The aqueduct should at this stage be covered by a cottonoid to prevent any blood or tumour falling into the third ventricle. Any tumour involving the floor of the fourth ventricle is reduced as much as possible to the level of the surrounding floor with the ultrasonic aspirator on minimal settings. Disruption of the floor is unforgiving and leads to severe neurological deficit.

As tumour resection is completed, the walls of the cavity are carefully re-examined to ensure that no tumour has been left behind. The capsule of a pilocytic astrocytoma should also be resected if it enhances on post-contrast MRI. Haemostasis is obtained without the use of oxidised methylcellulose or other haemostatic agents; these tend to enhance on MRI and may be interpreted as residual tumour. The dura is closed in watertight fashion, usually with a patch of suturable dural substitute.

Ependymomas often extend into the cerebellopontine angle, necessitating a lateral extension to

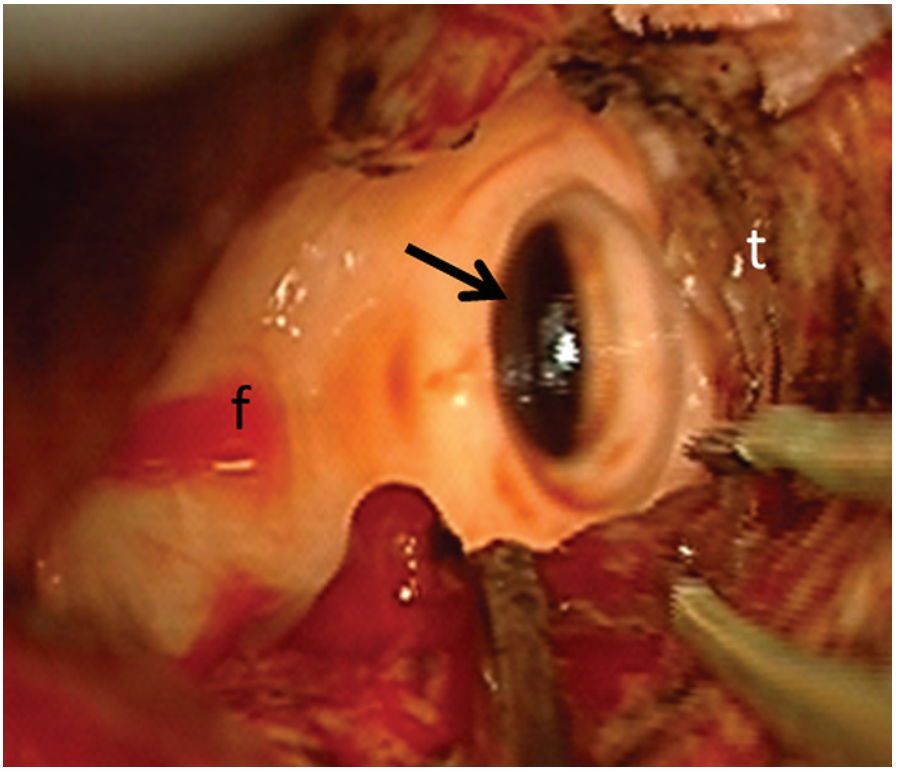

Figure 1: Intra-operative photomicrograph obtained during resection of a posterior fossa medulloblastoma –'t' represents residual tumour around the cavity; the fourth ventricular floor 'f' is exposed and free of tumour; the arrow points to the dilated caudal end of the aqueduct after decompression.

the usual midline suboccipital craniotomy. This allows use of both the fourth ventricular and retrosigmoid corridors during the primary procedure, maximising the opportunity to obtain gross total resection. These tumours infiltrate around the cranial nerves, the brainstem and the arteries of the posterior fossa. Gentle dissection, using microsuction at low setting in combination with a microdissector, proceeding in a lateral to medial direction along the cranial nerves, is necessary. These nerves, as well as perforating arteries from the basilar artery, are fragile and elongated. Patient dissection allows complete tumour resection in most cases without lower cranial nerve palsy or brainstem infarction.[4]

Image guidance is not usually required for midline or cerebellar posterior fossa tumours. However tumours that extend into the cerebellopontine angle or infiltrate the brainstem distort normal anatomical landmarks. Maximal safe resection is then likely to be improved with the use of neuronavigation as well as real-time per-operative imaging such as advanced ultrasound or interventional MRI.

Post-operative issues

Cerebellar mutism

Cerebellar mutism is an important complication arising after resection of midline posterior fossa tumours in children. In a review of two large clinical trials, mutism occurred in 24% of 450 children.[5] Onset occurs from one to six days after surgery. A reduction in speech output, progressing to mutism, is associated with ataxia, hypotonia, irritability and emotional lability. Although it tends to improve spontaneously over two to six months, a significant proportion continues to have speech, language and cognitive deficits, as well as ataxia, one year post-operatively.[5] Risk increases with medulloblastoma, brain stem invasion, and large tumours causing distortion of the brainstem, as well as in younger children.[6]

The precise anatomical substrate is unclear but probably involves the neuronal tracts running from the dentate nucleus through the ventro-lateral thalamus to the supplementary motor cortex.[6] A recent study involving pre- and post-operative diffusion tensor imaging showed that signal abnormalities in the midbrain and superior cerebellar peduncles were more common in patients developing mutism.[7] Bilateral proximal dentate-thalamocortical injury appeared to predispose to the condition. Changes were also evident in both fornices as well as in the white matter of the left superior frontal gyrus and right angular gyrus, suggesting a possible anatomical substrate for the behavioural abnormalities.[7]

Hydrocephalus

Over 80% of children with posterior fossa tumours demonstrate hydrocephalus on imaging studies at presentation.[8] Postoperatively, a mean of 30% of children still have hydrocephalus, presumably related to scarring at the aqueduct or fourth ventricular outlet foramina or distortion of the fourth ventricle. These children may require endoscopic third ventriculostomy or insertion of a ventriculoperitoneal shunt. In a recent study, the risk of persistent post-operative hydrocephalus was shown to be increased in children under two, and in children with papilloedema, intracranial metastases and hydrocephalus on presentation.[8]

Airway and swallowing difficulties

Children with brainstem tumours or ependymomas involving the cerebellopontine angle may develop vocal cord dysfunction post-operatively, rendering them at risk of aspiration and respiratory complications. A recent study has underlined the importance of a dedicated team approach for these children, with controlled extubation on the day following surgery, once the patient is fully awake.[9] The vocal cords are directly inspected by a laryngologist. In the event of bilateral vocal cord paralysis, the child is re-intubated and re-evaluated after several days. Late failure is likely to result in tracheostomy. After successful extubation, a modified barium swallow is carried out to exclude swallowing disorders.

Conclusion

As a result of clinical trials, a deeper understanding of tumour biology and progressive improvements in imaging and microsurgical techniques, the survival and outcome for children with posterior fossa tumours have improved considerably over the last 20 years. The current challenge is not just to continue to improve survival but also to reduce the impact of treatment and improve long-term quality of life, protect cognition and growth, minimise complications and reduce the risk of second malignancies in the long term. ◆

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Generic Preference Based Measures:

how economists measure health benefit

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Conflict of interest statement:
The author declares that there are no financial or commercial conflicts of interest.

Summary

- Decision makers must choose between interventions for different health conditions with myriad outcomes
- The value of health can be derived from people's preferences
- Generic preference-based measures have been validated for use in a number of neurological conditions
- There is much scope for neurologists and rehabilitation specialists to support the development and refinement of preference-based measures

Resources are always scarce, but the possible uses of these resources are limitless. This simple observation underlies much of what economists do. It leads to competing demands from different parties and requires individuals and organisations to make choices about their use of scarce resources. The primary purpose of economics is to help us understand how decisions about the distribution of scarce resources are made, and to identify optimal decisions. It shouldn't take too much of an intellectual leap to see how adopting an economist's perspective might contribute to the improvement of patient care and health outcomes.

The process of evaluating health care interventions is well-established, with the randomised controlled trial maintaining its place as the gold standard method. A crucial decision that must be made in figuring out if an intervention works is which indicator should be used. The purpose of the intervention might be to reduce mortality, improve functioning or prevent falls. It could be all three. If the intervention produces an improvement in these indicators it is probably of value – but of what value? How do we value this intervention? And why might we want to?

Opportunity cost

The NHS must operate within a budget, as society's ability to fund healthcare (not to mention its willingness) is limited. In some countries this limitation applies to the individual. It is not possible for an individual to receive whatever treatment they want whenever they want it. It is necessary to prioritise. This means that decisions and trade-offs must be made. Consider a choice between two interventions of equivalent cost; one prevents 10 deaths, the other prevents 1000 falls. Which is of the greatest value?

Economists value things in terms of opportunity cost; the value of something is defined by the value of the next best alternative. It might be that the next best alternative to an intervention that prevents 10 deaths is an intervention that prevents 1000 falls. In this case the opportunity cost of the intervention that prevents 10 deaths is the value associated with preventing 1000 falls, or vice versa. This is how economists think of cost – the pounds and pence associated with providing an intervention are incidental. In health care it isn't always clear what the next best alternative might be, though there is likely to be a long list of contenders. What this means is that we need a consistent way of estimating the opportunity cost of an intervention, in order to identify its value.

Utility theory

Not only must trade-offs be made between different treatments for the same disease, but also across clinical areas. This is where utility theory comes in. Utility is a complex and widely debated concept, but here we can assume it to be the satisfaction of an individual's desires. This is because health economists generally support the idea that the amount of utility an individual gains from something can be observed in their choices. It is assumed that, given the choice between two possible health care interventions, an individual will choose the one that maximises their utility.

Economists have therefore contributed to the development of measures that can be used as outcomes across disease areas and patient groups. These measures attempt to capture the extent to which a person's health affects their underlying utility level; characterised as health-related quality of life.

EQ-5D-3L

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

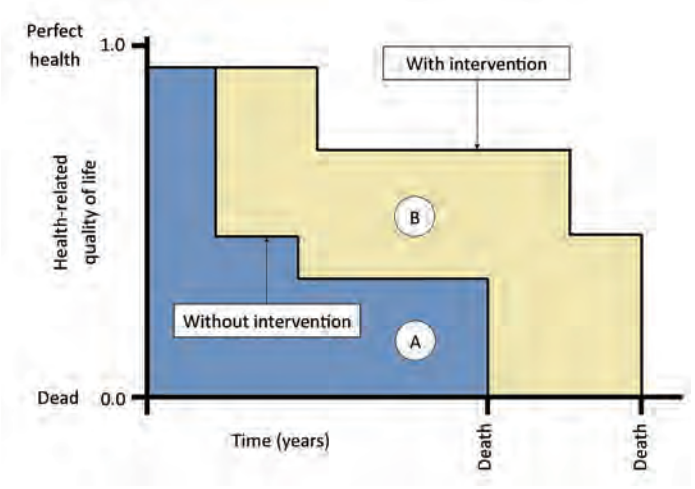
Mobility
I have no problems in walking about ☐
I have some problems in walking about ☐
I am confined to bed ☐

Self-Care
I have no problems with self-care ☐
I have some problems washing or dressing myself ☐
I am unable to wash or dress myself ☐

Usual Activities (*e.g. work, study, housework, family or leisure activities*)
I have no problems with performing my usual activities ☐
I have some problems with performing my usual activities ☐
I am unable to perform my usual activities ☐

Pain/Discomfort
I have no pain or discomfort ☐
I have moderate pain or discomfort ☐
I have extreme pain or discomfort ☐

Anxiety/Depression
I am not anxious or depressed ☐
I am moderately anxious or depressed ☐
I am extremely anxious or depressed ☐



The area beneath the 'without intervention' curve (area A) represents the number of QALYs associated with the control group. The area beneath the 'with intervention' curve (area A plus area B) represents the number of QALYs associated with the treatment group. Area B represents the QALY gain associated with the intervention.

The QALY

But health care has the dual aim of improving life and extending life; of reducing both morbidity and mortality. This represents another trade-off. The quality-adjusted life year (QALY) has been developed to capture both of these goals. The trade-off between the two is again guided by preferences. The QALY works by attaching a value to a year of life in a given health state; based on an individual's health-related quality of life. When QALYs are used as the outcome measure in an economic evaluation we call it a cost-utility analysis.

And finally we arrive at an introduction to the concept mentioned in the title; generic preference-based measures. This is the easy part. Generic preference-based measures capture the 'Q' in the QALY. A number of generic preference-based measures have been developed over the past 25 years. The most well-known of these include the EQ-5D,[1] Health Utilities Index[2] and SF-6D.[3] These are simple questionnaires that attempt to capture an individual's general level of health, consisting of items that have been chosen to reflect aspects of health that people consider important. Collecting individual responses to these questionnaires is the first of two steps. The second is a valuation process. This process is required to reflect individual's preferences – the importance of which is set out above. It is this valuation that enables us to compare very different health problems on the same scale. The most common method, in the UK at least, is to use societal valuations. In this case it is the general public valuing the health states rather than patients. Based on these values the generic preference-based measures produce an index value on a scale from 0 to 1, where 1 represents perfect health and 0 represents a health state equivalent to being dead. It is possible for health states to be negative; that is, worse than being dead. A year spent with a health state of 1 equates to 1 QALY, which equates to 2 years in a health state of 0.5, which equates to 10 years in a health state of 0.1.

In addition to generic measures, it is also possible to use condition-specific preference-based measures. These are designed to detect the extent to which an individual's disease-related quality of life affects their utility. The extent to which these measures are comparable with generic measures is debated.

QALYs in neuroscience and rehabilitation

The QALY is now a widely adopted outcome measure in most areas of health, including rehabilitation and neurology. It is the preferred measure of benefit in the NICE reference case, and generic preference-based measures (PBMs) such as the EQ-5D are the preferred health state descriptors. While generic PBMs might not always be the most appropriate choice of indicator, they have been validated and used in a wide range of clinical areas. For Parkinson's disease, the EQ-5D has been shown to be feasible and valid; correlating well with the PDQ-39.[4] Similarly, the EQ-5D reflects the presence of neuropathic pain,[5] while the EQ-5D, SF-6D and Health Utilities Index have all been found to be responsive in stroke.[6]

Limited work has been done to decide which measure is best in any given situation. Even within a given field, such as neurology, different measures may be more appropriate in different circumstances. Researchers and clinicians should be familiar with different measures to know which is most appropriate, though it is likely that they will need to rely on common sense rather than quantitative or qualitative evidence.

It is sometimes argued that generic measures do not identify the issues that matter to patients.[7] A review of the use of quality of life measures for palliative care of people severely affected by multiple sclerosis found that the EQ-5D did not correlate as expected with condition-specific measures.[8] In cases such as this it might be more appropriate to use, or indeed develop, condition-specific PBMs. In relation to this it is also possible to 'map' onto measures such as the EQ-5D from condition-specific measures. This means that an EQ-5D value can be derived from a validated condition-specific measure. In stroke, for example, preference-based versions of the Barthel Index[9] and Modified Rankin Scale[10] have been developed and used. Measures such as the MSWS-12[11] and MSIS-29[12] have been mapped to the EQ-5D for use in multiple sclerosis, and the HIT-6 and MSQ questionnaires for migraine.[13]

The future

It's crucial that trials of new treatments in neurology and rehabilitation include preference-based measures in order that we can understand their value to patients. It has also been argued that such measures should be collected on a routine basis. Since April 2009, the Patient Reported Outcome Measures (PROMs) programme has collected EQ-5D from NHS patients receiving surgery for hip replacements, knee replacements, hernia and varicose veins. Other services, such as the Improving Access to Psychological Therapies (IAPT) programme, administer similar sets of questionnaires. Rehabilitation services could gain much from doing the same. The routine collection of measures like the EQ-5D will enable researchers to further develop health state valuation methods in the field; whether this be through validating preference-based measures, mapping from condition-specific to generic measures or developing new measures where appropriate. There is also scope for a full systematic review of the use of generic and condition-specific PBMs across all neurological conditions in order to understand when measures should and shouldn't be used and to identify gaps in understanding. Such work is necessary to ensure that interventions are valued appropriately and that decisions can be made to optimise health outcomes. ◆

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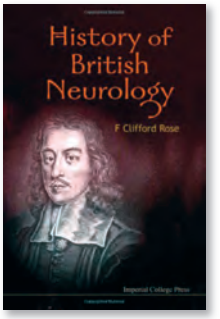
History of British Neurology

The approach to neurological history adopted in this handsome volume is to present a number of brief biographies, usually no more than a page in length, of neurologists and practitioners in allied neuroscientific disciplines who have made "significant neurological contributions" (2). Particularly renowned individuals, such as Thomas Willis, Hughlings Jackson, William Gowers, Henry Head, and Charles Sherrington, merit longer entries. In addition to a summary of their contributions, a brief flavour of personality is also sometimes added to the portrait. Since "history" encompasses institutions as well as individuals, it comes as little surprise that the development of Queen Square is also discussed. The sections are largely arranged chronologically, but there are also chapters devoted to neuropathology, neurophysiology, and other neurosciences. Citations are largely to the secondary literature, but there are a few primary references.

The approach is unrelentingly "whiggish", according to the usage coined by the historian Herbert Butterfield (1900-1979), i.e. that history may be read as a progression towards liberalism and enlightenment. This is apt in some ways, since British neurology has unequivocally made major advances since Willis. However, it probably exacerbates the inevitable gender bias: only one woman, Dorothy Russell (269-270), makes the cut. All other females who appear are either patients (Anne Green: 22-23; Anne Conway, 44) or the discredited assistant to a male protagonist (Kathleen Chevassut, 168, 201). The specified parameter "British" sometimes breaks down: although one can accept Brown-Séquard (152-155) as born in a British colony (Mauritius). And, I suppose, Ireland did not have home rule at the time of Graves (101) and Bentley Todd (102). But no amount of special pleading can explain Hans Berger (295), however great his contribution (EEG). If "contribution" is a prerequisite, Monro *tertius* (61-62) is also a dubious inclusion.

Many neurologists take an interest in the history of their specialty, perhaps most particularly in the lives and discoveries of their predecessors in the discipline, and hence will take a delight in this book. Since numbers of neurologists in the UK have traditionally been few, most practitioners can trace back a "neurological family tree", as it were, to distinguished figures overall a fairly small number of degrees of separation. Clifford Rose himself does this, with his first hand accounts of Charles Symonds (199-200) and Henry Miller (209), amongst others. It is not difficult to think of particular individuals who might also have been included in such a volume as this, and to my way of thinking, Neuropsychology seems a particular omission.

Reviewing this book shortly after the author's death (1 November 2012), it is appropriate to say that it will stand as a monument to one of Clifford Rose's longstanding interests and endeavours, and will be enjoyed by many readers. However, without wishing to seem unduly critical, it would be remiss of any reviewer not to mention the lapses in chronology which are by no means infrequent, and do detract from the overall enjoyment of reading, likewise the inadequacy of the index.



Author: F C Rose
Published by: Imperial College Press, 2012
Price: £73.00
ISBN: 9781848166684

Reviewed by: AJ Larner, Cognitive Function Clinic, WCNN, Liverpool, UK.

Color Atlas of Cerebral Revascularization

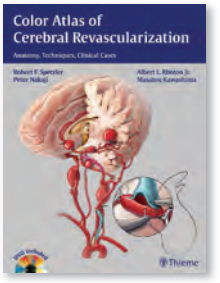
Anatomy, Techniques, Clinical Cases

This formidable text represents a distillation of neurosurgical anastomotic technique to ameliorate (or prophylactically prevent) cerebral ischaemia, encompassing various types of vascular pathology. While describing a discipline that is being progressively supplanted by endovascular methods, the volume accentuates the need for surgical expertise in very particular situations. The distinguished authors have collected contemporary examples of their practice, the majority from the Barrow Institute in Phoenix, and have complemented their text with detailed photographs, line drawings and anatomical dissections. In this way each specific revascularisation takes place before the reader's eyes in a sequential but simple fashion, highlighting correspondence with named structures at critical moments of the operation. As an additional and welcome adjunct, there is an excellent DVD focusing upon key cases, and this is invaluable for understanding the real-time theatre pressures that will always exist.

The book makes no attempt to revisit the complexities of diagnoses, indications for, and outcome measures relating to each procedure, and anyone expecting a breakdown of longer term complications (e.g. cerebral hyperperfusion syndrome, etc.) will be disappointed. Nevertheless, by means of brief vignettes of patients' condition before their operation, the reader gradually gains a better grasp of alternative strategies that may be relevant in his or her practice. However this is a work principally concerned with techniques and technical advances. A significant proportion of the illustrated examples are clearly very demanding, while still being pragmatic in the correct setting. Accordingly it is likely that this book will really appeal to established vascular surgeons wishing to develop their repertoire (rather than junior trainees), although there is much that all could learn from the detail offered.

There are 16 chapters addressing the different bypass procedures, pertinent to both low-flow and high-flow revascularisation, with suitable emphasis upon the more common techniques. While the superficial temporal artery to middle cerebral artery section is very comprehensive (including double-barrel grafts and a large group of different aetiologies), there is also a separate chapter devoted to Bonnet bypass, and even facial – vertebral artery bypass. Everything from saphenous vein bridging grafts to complex skull base tumour resection with high-flow bypass is covered, and one can appreciate the common characteristics of the treatments despite quite varied pathologies. What soon becomes obvious is that, although standard microsurgical methodology will be familiar to most neurosurgeons, the sheer imaginative scope for alternative grafting that has arisen in the authors' unit(s) is inspiring. Furthermore, they are not afraid to demonstrate their means of dealing with inevitable complications (such as vessel tears), and this realistic interpretation of emergency options is indeed refreshing.

UK neurosurgeons might look enviously upon the ease of intraoperative angiography within this case selection. While some specific types of instrumentation (e.g. the patented microsuction system, etc.) may be regarded as unnecessary, it is worth remembering that such approaches have evolved over years in an outcome-proven institute to maximise the chances of technical success; they should not be underestimated! Overall the authors and their support staff are to be congratulated on an excellent piece of work; I suspect that the majority of my Vascular Neurosurgery colleagues will rapidly add it to their library.



Editors: RF Spetzler, AL Rhoton, P Nakaji, M Kawashima
Published by: Thieme 2013
Price: £183.80
ISBN: 9781848166684

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Latest implantable and external neurostimulation technology for drop foot correction and gait rehabilitation

This article was submitted by Otto Bock Healthcare and they have sponsored its publication in ACNR. Dr Michael Jauch is clinical partner to Otto Bock Healthcare UK for Functional Electrostimulation. Dr Jauch graduated in Germany. He undertook postgraduate training in orthopaedics in Germany and the UK as well as training in orthopaedic and neurological rehabilitation in Germany. His Postgraduate work in experimental orthopaedics was undertaken at Imperial College, London. Since 2011 he has operated an FES clinic at BMI Blackheath Hospital, London.

The ability to negotiate the environment independently is fundamental to all aspects of daily life and almost all aspects of social participation are dependent upon adequate mobility. The insufficiency in dorsiflexion during gait results in difficulties in walking, such as slowness, tripping and tiredness [1-3], leading to a reduction in mobility and independence as well as increased risk of falls." NICE [4].

For many patients who suffer from central or upper motor neuron lesions, e.g. stroke, multiple scleroris or head injury, walking becomes a challenging task. In many cases, the damage to the central nervous system results in paralysis and a drop foot.

This article concerns CNS lesions. Lesions to peripheral nerves are an exclusion criteria for the application of Functional Electrical Stimulation (FES).

Walking speed has been shown to be a clinically relevant outcome. Some researchers even considered it to be the 'almost perfect' measure of community ambulation [5]. Reduced gait speed was shown to be related to the increased risk of future hospitalisation, future lower extremity limitation and even mortality.

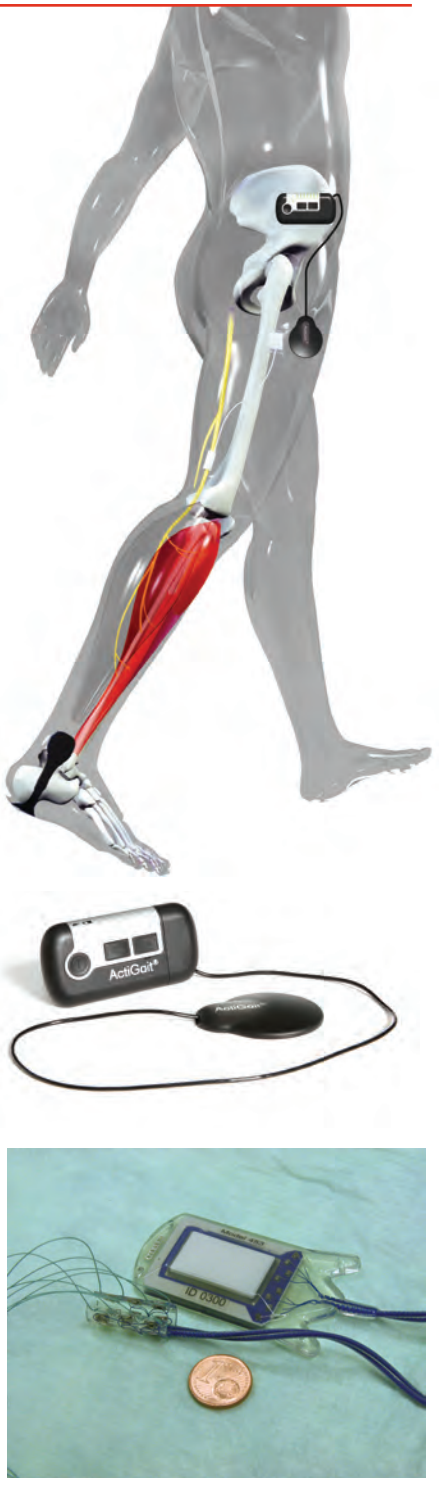
National Guidance

Since the introduction of FES as a drop foot treatment, a number of studies have demonstrated that FES significantly improved walking speed and patient's quality of life [6-8]. These health and quality of life benefits, particularly improved independence, are in line with the goals of the Department of Health Reablement initiatives.

NICE published interventional procedural guidance on FES in 2009 [3] stating that the current evidence on the safety and efficacy (in terms of improving gait) of FES for drop foot of central neurological origin appears adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit. For implantable devices, an interdisciplinary healthcare team should be involved in deciding which patients should have the procedure [3].

Other guidance includes the government's National Stroke Strategy. It acknowledges FES as a new technology with which service providers need to keep pace [9].

The National Service Framework for long term conditions includes a quality requirement (QR7) advocating appropriate assistive technology / equipment [10].



In a 2010 report, the effectiveness and cost-effectiveness of surface FES as treatment for drop foot was examined. The conservative model on the use of surface FES to treat drop foot after stroke shows that it is likely to be cost effective compared to no treatment. This report suggests that it is reasonable to assume that the QALY gain may be higher for implantable systems [11].

The National clinical guideline for stroke (ICSWP) 2012 of the Royal College of Physicians [12] differentiates between Therapeutic Electrical Stimulation (TES) which long-term use aims to improve recovery of function vs Functional Electrical Stimulation for immediate functional improvement. It concludes that so far the findings of RCTs and papers about therapeutic electrical stimulation are contradictory regarding impairment and activity and that there are so far no cost-effectiveness studies in this area. It therefore recommends to use TES only in the context of clinical trials. However, FES can be used where arrangements for clinical governance, audit and consent are in place.

Treatment options

Ankle-Foot Orthosis (AFO)

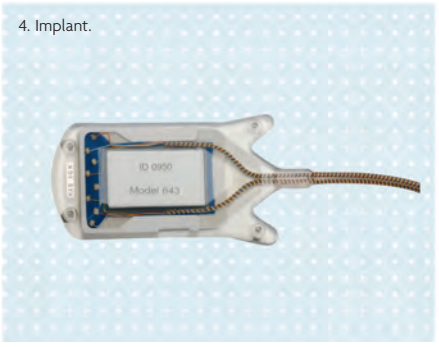
Conventional treatment options for drop foot are primarily physiotherapy and the use of an AFO. AFOs aim to support the foot and ankle, but as it is a passive device, it will not activate the users' own muscles to enhance walking. Additionally, medical therapy (such as baclofen and botulinum toxin) or surgery for refractory cases (tendon transfer, arthrodesis) may sometimes be used [3,13].

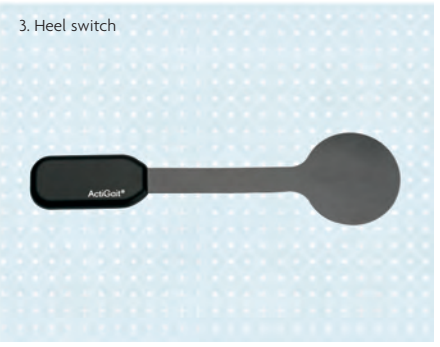
Surface FES

Surface electrodes are applied over the common peroneal nerve in the area of the head of the fibula and a battery-powered stimulator which is controlled by a foot switch or sensor provides timed stimulation of nerve/muscle from heel lift to heel strike, providing the necessary foot lift during the swing phase of the gait cycle.

Clinical studies evaluating the effectiveness of drop foot stimulation suggest that it provides many benefits to patients, such as an improved confidence in walking, increased walking speed and endurance, less effort during walking and reduced spasticity. Additional benefits are related to a potential reduction in the risk of falling [14-18].

The FES systems available nowadays have developed considerably since their introduction in 1961, but still some technical side effects are observed, such as the lack of selectivity of muscle recruitment to electrode placement, as well as pain, tissue irritation and possible skin damage associated with the passage of current through the skin [17]. Taylor et al. identified problems with locating the electrodes for effective





stimulation as the most common non-physiological reason for discontinuing the use of the surface stimulator [18]. Electrode positioning becomes even more of an issue for patients with upper limb impairment.

Surface stimulators currently available are:

Pace by Odstock: A wired system containing a pocket sized control unit, self adhesive skin electrodes and a wired foot switch.

WalkAide by Trulife: A self-contained system which contains surface electrodes, control unit and an inertial gait sensor within one cuff to be worn immediately below the knee.

L300 by Bioness: A cuff based system worn below the knee. A control unit and foot switch are worn separately from the cuff and communicate wirelessly.

MyGait by Otto Bock Healthcare: the newest surface stimulator launched in 2013. A cuff-based unit with the stimulator worn in the cuff linked wirelessly to a foot switch and a patient remote control. The novelty of this stimulator is that it provides two channels of stimulation to combine two different muscle groups where indicated.

Implantable FES

A newer alternative to surface stimulators are implantable devices (the StimuStep from Finetech Medical and the ActiGait from Otto Bock), which overcome most of the problems encountered with surface stimulators and thus are more desirable for the following reasons:

- Electrodes are surgically implanted, and hence no surface electrodes required
- Optimal electrode position achieved and controlled during surgical implantation
- No need for technically challenging electrode placement by patient lengthening daily set-up [13]
- No soft tissue or skin reactions
- No discomfort / pain due to constant electrical sensation through the skin. Improved ease of use and cosmetic appearance.

New Developments

The main new development for surface stimulation is the launch of the MyGait, the first two channel wireless surface stimulator, in early 2013. Clinical follow-up studies will be carried out in time. First results from pre-launch field studies (based on 17 patients) showed that 12 out of 17 patients preferred MyGait over their previous or other fitting, 57% of patients felt MyGait to be an improvement over their previous system. [19]

Indications for MyGait are stroke, cranio- cerebral injury, multiple sclerosis, Incomplete spinal cord injury and infantile cerebral palsy.

Implanted stimulators are still a new development in themselves. Both StimuStep and ActiGait have been implanted in a number of European countries in recent years. ActiGait was launched in the UK in late 2011 in our clinic. Main indication for implanted devices is drop foot secondary to stroke. There are suggestions of benefit for other upper motor neuron conditions, but still with lack of scientific support and regulatory issues.

StimuStep

An implanted system with electrodes (2 channels) imbedded into the epineurium of the common peroneal nerve's deep and superficial branches. The implant receiver under the skin receives power and control signals from the control unit, which is triggered by a footswitch. The control unit is worn on a belt below the knee and needs to be positioned on top of the below skin receiver unit . Communication between the external control unit and the footswitch is wired.

ActiGait

The system consists of a heel switch (3 in diagram above) which communicates wirelessly with a control unit (1), which is worn on a magnetic clip anywhere discreet as chosen by the patient. This unit allows the patient to adjust the intensity of the stimulation. An electromagnetic signal is painlessly sent through the skin at the upper thigh via a lightweight antenna (2) to the implant (4), which converts that signal into electric current for the 4 channel electrode cuff positioned around the Common Peroneal Nerve. The four channels can be programmed to allow for selective nerve bundle stimulation and balanced dorsiflexion / eversion.

Review ActiGait vs StimuStep

A clinical follow-up (a mixed population of 46 cases since 2006 of which 42 were reviewed for the study) of StimuStep was presented by Taylor [20,21]. The StimuStep users were selected from existing surface FES users. Reasons for selection of the implant were skin irritation, patients' difficulties with electrode placement or anticipated long term use. Indications were stroke (18 cases), MS (17 cases, 1 bilateral), traumatic head injury (3), incomplete spinal cord injury (2), brain tumour (1), Parkinson's (1), transverse myelitis (2) and cerebral palsy (1). 4 patients were not followed up due to : 2 non-functioning implants, 1 explantation because of infection and 1 for poor response because of abnormal nerve anatomy. The main benefits to patients reported were improvements in walking speed (18%) and a three-minute walking distance (23%).

Complications were reported as 6 electrode failures, 9 cases of nerve dysfunction (likely due to epineural electrode positioning and direct pressure on the receiver). Electrical sensation only improved 1 point out of 10 in comparison to surface stimulation with two cases even more uncomfortable level of sensation than surface stimulation. Five cases of skin reaction were reported. The patient still needs to wear a cuff directly on the skin which has a large contact area and some contact pressure. Despite implanted device patients still experienced issues with electrode and control box position. 11 of the first 16 cases also had reliability problems with the stimulation channel to the superficial branch of the nerve.

ActiGait was the subject of a safety and performance study conducted in three centres in Denmark [1], which established safety using nerve conduction velocity and performance improvements in walking speed (20%) and distance walked in four minutes (14%). Long-term improvements were detected in walking speed and distance when stimulated, and the orthotic effect of stimulation showed statistically significant improvement. Furthermore, qualitative responses highlighted improvement in confidence with less fear of falling, promoting the long-term potential to provide a positive effect on personal well-being, safety and performance [1,8]. Similar patient benefits were reported in a more recent study [22] showing a 24.5% increase in walking speed, and 17% increase in walking distance in the six-minute walking test. In addition to walking speed and endurance, the kinematic and biomechanical changes were investigated in five subjects by Ernst et al [23]. The study demonstrated a restored ankle joint movement towards a more physiological pattern as seen in normal gait.

The ActiGait implant complication rate was followed up by the manufacturer's internal quality control [24]. Since the introduction of the newest revision of the device in February 2011, 115 implantations were reviewed (mixed population, indication stroke). All reported complications had been operator-caused (surgical procedure / general surgical risk), none have been caused by the implant. The complications reported were 4

cases of infection and 4 cases of temporary nerve damage (3 of which are functional with ActiGait in situ at the time of writing). Surgical reasons were established as causes for those nerve damages. Since the last revision of the surgical procedure 60 implantations have been carried out with no nerve damages, no implant failures nor incidents with external components. For licensing reasons the main indication for ActiGait is stroke. However, first implantations have been carried out for alternative indications in our practice, such as head injury and multiple scleroris with very good individual outcomes in the improvement of quality of life. Further work will be undertaken in implantations for other indications.

It appears that by direct comparison the benefits of both implants are compatible. However, comparing the reported complications, ActiGait has despite higher case numbers a lower complications rate, none of which are caused by the device itself.

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To list your event in this diary, email brief details to Rachael Hansford at Rachael@acnr.co.uk by 6th October, 2013

September

NSpine 2013: The UK's Most Comprehensive Spine Course
5-7 September 2013; Nottingham, UK
T. 0800 0 43 20 60, E. info@nspine.co.uk
www.nspine.co.uk

BioDynamics 2013 – Where Biology, Medicine and Mathematics meet
11-13 September, 2013; Bristol, UK
T. +44 (0) 20 8977 7997,
E. biodynamics@conferencecollective.co.uk

35th Edinburgh Clinical Neurology Course
16-17 September, 2013; Edinburgh, UK
Further information from:
http://www.dcn.ed.ac.uk/dcn/research/training.asp or E. Judi.Clarke@ed.ac.uk

Ion Channels in Health and Disease: To celebrate the 50th anniversary of the award of the Nobel Prize to Alan Hodgkin and Andrew Huxley
16-17 September, 2013; Cambridge, UK
Cambridge Neuroscience
E. dg248@cam.ac.uk,
www.neuroscience.cam.ac.uk

The Children's Trust's Open Day for Professionals
19 September, 2013: Tadworth, UK
Book free online at
www.thechildrenstrust.org.uk/opendays.
E. opendays@thechildrenstrust.org.uk.
T. 01737 365890.

Specialist Rehabilitation Medicine Course
19th and 20th September, 2013; Derby, UK
Karen Kirkland, Course Administrator,
T. 01332 724842,
E. karen.kirkland@nottingham.ac.uk

XXI World Congress of Neurology
21-26 September, 2012; Vienna, Austria
T. +41 22 9080488, E. Dnuriel@kenes.com
www.2.kenes.com/wcn

Management of Epilepsy, Satellite Symposium at the EPNS
26 September, 2013; Brussels, Belgium, 12.30-1.30
For more information
E. Patrick_Standen@eisai.net

October

3rd World Parkinson Congress
1-4 October, 2013; Montreal, Canada
T. (+001) 800.457.6676
E. info@worldpdcongress.org
www.worldpdcongress.org

Improving Patient Pathways in Parkinson's Disease meeting
10 October, 2013; London, UK
Supported by Genus Pharmaceuticals.
Register for free at www.parkinsons-ha.co.uk
or www.apo-go.co.uk/hcp/events/PRM-2013

Diffusion as a Probe of Neural Tissue Microstructure – ISMRM Workshop
14–18 October, 2013; Podstrana, Croatia
www.ISMRM.org
T. +1 510 841 1899

November

Improving Patient Pathways in Parkinson's Disease meeting
5 November, 2013; Newcastle, UK
Supported by Genus Pharmaceuticals.
Register for free at www.parkinsons-ha.co.uk
or www.apo-go.co.uk/hcp/events/PRM-2013

Nurses' Training Day: Chiari Malformation and Syringomyelia Thursday 7th November 2013
7 November, 2013; Sheffield, UK
T. 01964 535 448 or 07976 400 881,
E. info@britishsyringomyelia-chiarisociety.org

12th Clinical Trials in CNS
18 & 19 November, 2013; London, UK
See www.clinicaltrialscns.com or
T. Jonathan Collins, 020 7827 6734,
E. jcollins@smi-online.co.uk
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Improving Patient Pathways in Parkinson's Disease meeting
21 November, 2013; Birmingham, UK
Supported by Genus Pharmaceuticals.
Register for free at www.parkinsons-ha.co.uk
or www.apo-go.co.uk/hcp/events/PRM-2013

The United Kingdom Acquired Brain Injury Forum 5th Annual Conference
21 November, 2013; London, UK
T. 0845 6080788
E. info@ukabif.org.uk
www.ukabif.org.uk

West of England Seminars in Advanced Neurology (WESAN)
21-22 November, 2013; Exeter, UK
Programme and booking online at
www.aquaconferencemanagement.co.uk/wesan/2013-programme
E. barbara@aquavenuesolutions.com

RAatE 2013
25 November, 2013; Coventry, UK
www.raate.org.uk

MS Masterclass 2013
28-29 November, 2013; Bristol, UK
Information from Professor Neil Scolding,
E. N.J.Scolding@bristol.ac.uk

December

The Encephalitis Society Professional Seminar
2 December, 2013; London, UK
Free entry for our Professional Members, for more information
E. admin@encephalitis.info
T. 01653 692585.

Multiple Sclerosis 2013
2 December, 2013; London, UK
Call Jackie on 020 7501 6762,
www.mahealthcareevents.co.uk

24th International Symposium on ALS/MND
6-8 December, Atahotel Quark Milan, Italy
E. symposium@mndassociation.org
T. 01604 250505

BNPA December Teaching weekend
13-15 December, 2013: Oxford, UK
T. 020 8878 0573,
E. admin@bnpa.org.uk or jashmenall@yahoo.com

2014

February

Dementias 2014
13-14 February, 2014; London, UK
Call Jackie on 020 7501 6762,
www.mahealthcareevents.co.uk

March

NEUROLOGY 2014: Leading edge neurology for the practising clinician
27-28 March, 2014; London, UK
www.ucl.ac.uk/ion/education/courses/other/neurology or
E. Jean Reynolds, jean.reynolds@ucl.ac.uk
T. 020 344 84460

April

8th World Congress of Neurorehabilitation (WCNR 2014)
8-12 April, 2014; Istanbul, Turkey
For more information see www.wcnr2014.org
or E. traceymole@wfnr.co.uk

July

ISMRM Workshop on: Function MRI: Emerging Techniques & New Interpretations
July, 2014; Charleston, SC, USA
www.ISMRM.org
T. +1 510 841 1899

PREVIEW

WCN 2013 – Neurology in the Age of Globalisation

Conference details: 21-26 September 2013, Vienna, Austria.

Under the theme of "Neurology in the Age of Globalisation", the XXI World Congress of Neurology (WCN 2013) will provide neurologists from Europe and around the world an unparalleled opportunity to exchange knowledge and information. WCN 2013 is being organised by the World Federation of Neurology, in conjunction with the European Federation of Neurological Societies (EFNS) and the Austrian Society of Neurology (ÖGN), making this a truly global event.

Building on the success of previous congresses, WCN 2013 will provide an exceptional forum for participants to interact with the best and brightest neurology professionals on the scene today. With over 400 renowned speakers, over 2500 abstracts submitted, 92 scientific sessions, 60 teaching courses, 10 plenary lectures, 10 sponsored symposia, various debates and 1 stimulating Tournament of the Minds competition, WCN 2013 promises to be unforgettable.

The scientific programme features world-class speakers who will share their latest research, expertise and insights. A variety of sessions and teaching courses will be held on topics such as epilepsy, stroke, movement disorders, pain, dementia, neuro-rehabilitation, headache and more. Furthermore, WCN 2013 has been approved to provide up to 30 CME credits to its participants. ◆

For further details, visit the official Congress website:
www.wcn-neurology.com

INTERVIEW

Prof Vladimir Hachinksi, President of the World Federation of Neurology, discusses new activities of the organisation and highlights of the XXI World Congress of Neurology.

Tell us why you entered the field of neurology?
Although I was always intrigued by the brain, my becoming a neurologist was what I like to call a happy accident. During my time in Montreal, I was assigned to a radiology-based investigation unit. However, the radiologists were on strike at the time and I was thus re-assigned to neurology. I knew from that point on that a career in neurology would be my future.

What is the mission of the World Federation of Neurology and the priorities of the current administration?
Under the current administration, the World Federation of Neurology has expanded its scope "to foster quality neurology and brain health worldwide". In order to affect such a change in emphasis, we formed a World Brain Alliance, as brain health is key to health. The Alliance is founded on 3 premises. First, brain health is key to health. Second, brain health begins with the mother and child and their education. Third, our brains are our future. In a knowledge-based society, we must develop a higher degree of intellectual competence in order to make the most of life lived in the digital age.

What are some of the scientific highlights expected at the XXI World Congress of Neurology? how is the WFN vision incorporated into the scientific programme?
The theme of the XXI World Congress of Neurology is 'Neurology in the Age of Globalization'. The scientific programme will build on this theme through stimulating sessions and in-depth cooperation of various brain specialty organisations. As a result of the World Brain Alliance and the close cooperation of its members, this year we will introduce – for the first time – co-sponsored sessions with several brain specialty organisations. Another highlight will be the Presidential Symposium, which will focus on global neurology and brain health. Prof. Eduard Auff, President of WCN, will address the theme of neurology in our increasingly globalised world. I will contribute to the session with some thoughts about the World Brain Alliance and how we can further promote brain health worldwide.

Can you tell us about the speakers and specific expertise to be presented?
I would like to highlight special speaker, Nobel Prize winner Prof Eric Kandel, who is acclaimed for his work on memory. Prof Kandel's The Age of Insight elegantly argues that the proliferation of philosophy and science in Vienna in the 19th century had a profound influence on shifting the prevailing paradigm, from describing disease to an examination of the brain. As a matter of fact, Prof Eric Kandel was born in Vienna and it is an absolute privilege to have him as one of WCN's main speakers.

Are there any breakthroughs or new insights in the field of neurology that will be revealed at the XXI World Congress of Neurology?
I would say that WCN is the first congress ever to address brain health as a priority. We will discuss the growing role of brain physicians and scientists to this fascinating specialty. We also expect a great deal of progress to be made simply by sharing what we already know across the different specialties.

Discuss the significance of EFNS, OGN AND WCN being held together in 2013.
This is a wonderful example of collaboration. The Austrian Society of Neurology and the European Federation of Neurological Societies are partnering with us in place of their usual annual meetings, which is a very good example of how the neurological world is coming together. I would like to highlight the main protagonists who have facilitated this development: Prof. Auff, President of the Congress and Prof. Richard Hughes, President of EFNS.

Tell us more about the Tournament of the Minds and how it contributes to an enriched congress experience for participants.
The format is like Jeopardy and it is great fun! With different teams competing, Tournament of the Minds allows people from around the world to interact and teach one another by sharing their unique experiences. It is worth noting that in North America and Europe, neurologists tend to specialise and sub-specialise, becoming experts in a particular area. However, in most other regions, neurologists tend to practice general neurology. As a result, their clinical experience tends to be richer and more diverse.

How will medical specialists from around the world benefit from attending the XXI World Congress of Neurology?
All attendees will benefit by gaining access to state of the art knowledge in all of the relevant areas of neurology as well as detailed insights into the new role of neurologists as guardians of the brain. However, the congress is geared not only towards neurologists, but to anyone who is interested in the brain. True to the global character of WFN, the congress scientific programme will feature speakers from different parts of the world who are recognised for their ability to clearly convey important information.

Acquired Brain Injury UK National Conference Brain and Mind – Mind the Gap

Conference details: : 25 June 2013, Stoke on Trent, UK. ***Report by:*** Dr George El-Nimr, Consultant Neuropsychiatrist, Clinical Lead for Neuropsychiatry / Old Age Psychiatry Services and Clinical Tutor.

Take home messages:

- ABI is a family affair.
- The introduction of national specialised commissioning, dedicated clinical reference groups and a specialist rehabilitation tariff, has placed ABI services in the spotlight.
- Post ABI neuropsychiatric conditions are often under recognised.
- Organic Personality Disorder is a severe complication of ABI.
- There is limited evidence on management of aggression in ABI.
- Childhood onset neuropsychiatric conditions can be related to early life ABI.
- Mild traumatic brain injury continues to be a source of debate.
- Litigation can facilitate rehabilitation.

Over recent years, there has been considerable recognition of Acquired Brain Injury (ABI) and its significant impact on patients, families and society as a whole. While commissioners of services will have ABI on their agenda, there is still a considerable heterogeneity as to which patients will have access to which service.

Our first National ABI Conference was aimed at "bridging the gap" in relation to service developments, clinical management and the interface between ABI and the law. Most importantly, however, it aspired to enhance the notion of always aiming to provide holistic, patient-centred, individually tailored care that will maximise our patients' quality of life and their integration within society.

The programme of the day flowed well with a great mix of keynote and seminar sessions. All presentations and videos from the day were made available for delegates after the event.

The day started with a welcome address from Ms Fiona Myers, Chief Executive of North Staffordshire Combined Healthcare NHS Trust. She highlighted the need for integrated working amongst various organisations. She also addressed the unique interaction of physical and mental health issues in patients with ABI that would obviously have a considerable impact on management and service planning.

Dr George El-Nimr, Consultant Neuropsychiatrist and Clinical Lead for Neuropsychiatry and Old Age Psychiatry Services gave an overview in relation to ABI clinical presentations and management. He emphasised the need to evaluate existing evidence and identify gaps in available research. Recent evidence was presented in relation to specific aspects of ABI services.

Following on from this overview, the impact of ABI on the family was covered by Ms Ava Easton, Chief Executive of the Encephalitis Society. Ms Easton emphasised the fact that ABI is actually a family affair. Relevant video footage and quotes were presented.

This was followed by an outstanding presentation from a local patient who talked about his own experience with ABI and how the reaction of society can make a huge difference to the patient's well being. Similarly, our patient talked about the need for standardised services that should be available to all ABI sufferers.

A session chaired by Professor Saumitra Deb of Imperial College, London focused on ABI services. Two talks were delivered in addition to a question and answer session. The first talk was delivered by Dr Alex Ball, Consultant and Clinical Lead for Rehabilitation Medicine. Dr Ball is currently the West Midlands Director of Trauma Rehabilitation. In her talk, she presented various national drivers for change in such services. The introduction of a Specialist Rehabilitation Tariff from April 2013 was particularly highlighted.

The second talk was delivered by Dr Niruj Agrawal, Consultant Neuropsychiatrist at St George's Hospital, London who gave a talk on Neuropsychiatric services for ABI patients. Dr Agrawal focused on Traumatic Brain Injuries (TBI). The importance of having Neuropsychiatric input both into the acute and chronic phases were emphasised.

After lunch, Dr Andrew Worthington, Consultant in Neuropsychology and Rehabilitation, gave a talk on the therapeutic value of cognitive testing. Dr Worthington discussed the uses and abuses of formal assessment.

Later in the programme, conference delegates were offered the chance to attend two of four parallel seminars addressing specific clinical and medico-legal issues.

Dr Rafey Faruqui, Chair of the Section of Neuropsychiatry at the Royal College of Psychiatrists, explored issues related to prognosis as well as complex physical and mental health comorbidities in the aftermath of early life brain injuries. The talk raised a number of public health related questions.

Another seminar delivered by Dr Mike Dilley, Consultant Neuropsychiatrist, presented the available evidence in relation to pharmacological interventions that would best manage aggression and agitation in ABI.

The issue of clinicians as expert witness was addressed by Richard Crabtree & Mark McGhee of Fentons Solicitors. The seminar presented some of the practicalities clinicians have to bear in mind when providing reports and testimony to courts and tribunals. This seminar covered issues around civil proceedings and the Court of Protection jurisdiction.

Philip Edwards & Hilary Wetherell of Irwin Mitchell Solicitors indicated in their session that, used effectively, litigation can support and facilitate rehabilitation. It was argued that utilising the lawyers as part of the multidisciplinary team can assist in achieving favourable outcomes.

The late afternoon session focused on ABI and the law in more general terms. A talk delivered by Dr Seb Potter, Consultant Clinical Neuropsychologist, addressed clinical and medico-legal dilemmas related to the diagnosis of mild TBI.

Dr Kieran O'Driscoll highlighted the overlapping features with Dissocial Personality Disorder. The presentation explored the anatomical basis and behavioural similarities for these disorders and the implications for the Criminal Justice System.

Feedback from the day was extremely positive and very encouraging for the planned second national ABI conference. ◆

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11th national neuroscience conference

Multiple Sclerosis 2013

America Square Conference Centre, London

2nd December 2013

Highlights will include:

- Emerging areas of research into the causes of MS Professor Gavin Giovannoni
- Brain imaging Professor David Miller
- Current and emerging therapies Professor John Zajieck
- Update on MS clinical trials Dr Jeremy Chataway
- Managing relapsing remitting MS Professor David Bates

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HOSPITAL MEDICINE

16th national conference

Dementias 2014

Royal College of General Practitioners (RCGP), Euston Road, London

13th & 14th February 2014

Highlights will include:

- Dementia in Europe Dr Karim Saad
- Imaging in dementia Professor John O'Brien
- A rapid diagnostic system Professor Derek Hill
- Complexity in dementia Professor Sube Banerjee
- End of life care Professor Louise Robinson

For more information and to book your place:

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PRM PARKINSON'S REVIEW MEETING 2013

LONDON
10TH OCTOBER 2013
NEWCASTLE
5TH NOVEMBER 2013
BIRMINGHAM
21ST NOVEMBER 2013

AREAS FOR DISCUSSION INCLUDE:

Current challenges in the management of Parkinson's Disease;
A Parkinson's Disease patient experience;
Supporting the Parkinson's Disease patient;
Commissioning a Parkinson's Disease service;
Guidelines and protocols;
Coding the Parkinson's Disease pathway;
Setting up an APO-go service;
Homecare to support patient outcomes.

TARGET AUDIENCE

Consultant Neurologists, Registrars, Commissioners involved in the funding pathway, GPs with a specialist interest in Parkinson's Disease, Specialist Pharmacists, Specialist Nurses, CCG Commissioning Leads, CSU Pharmacists and Managers.

THE HEALTH AGENDA
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APO-0813-1859 Date of Preparation: August 2013.

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This meeting is one in a series of three, taking place in Autumn 2013 and combines the Parkinson's Review Meeting with The Health Agenda - a series of multidisciplinary meetings focused on improving patient pathways in specialist care.

There will be a fantastic lineup of speakers at each meeting. Confirmed speakers at the London event include:

Professor Kailash Bhatia (Chair), Professor of Clinical Neurology, National Hospital for Neurology

Thomas Foltynie, Consultant Neurologist, National Hospital for Neurology

Professor K Ray Chaudhuri, Professor of Movement Disorders, Kings College

Seema Buckley, Chief Pharmacist

Alexa Coombes, Neurology Business Manager

Allan Karr, National Homecare Medicine Committee

Please go to the registration website parkinsons-ha.co.uk for further details on the agenda at each of the meetings.

PREVIEW 8th World Congress of Neurorehabilitation

Conference details: 8-12 April 2014, Istanbul, Turkey.

WFNR World Federation for NeuroRehabilitation

WCNR 2014 will be held in conjunction with the Turkish Society of Physical Medicine and Rehabilitation Specialists and aims to bring together scientists and rehabilitation professionals from all around the world.

The WFNR was established in 1996 with over 4000 members worldwide. It is a multidisciplinary organisation; membership and World Congress programmes reflect the interests and expertise of a range of professionals including rehabilitation physicians, physiatrists, physical and occupational therapists, psychologists, rehabilitation engineers, basic neuroscientists and many others. There are 32 National Societies in various countries affiliated to the WFNR and over 25 Special Interest Groups formed for topics as diverse as mild brain injury, robotics and telerehabilitation.

The Congress will comprise half-day workshops, 'Meet the Professor' breakfast sessions and a scientific programme entitled 'Towards New Horizons in NeuroRehabilitation'. The programme will mix basic neuroscience and clinical practice covering international research, discovery and innovation in all the major areas of neurorehabilitation including traumatic brain injury (TBI), multiple sclerosis, stroke, spasticity management and neuro-oncology. In addition there will be WFNR Special Interest Group meetings.

A wide range of eminent speakers will be presenting at the Congress. The 3rd Michael P Barnes Lecture, established in recognition of the visionary leadership and dedication of the founding WFNR President, will be delivered by the eminent Professor Leonardo G Cohen, Chief of the Human Cortical Physiology Section of the USA Bethesda-based National Institute of Neurological Disorders and Stroke. Professor Cohen's experience as a Neurologist has focused on research in neuroplasticity and neurorehabilitation after stroke. Dr Emilio Bizzi, a Professor at the Massachusetts Institute of Technology and an Investigator at the McGovern Institute for Brain Research will be discussing whether motor control concepts have been helpful for neurorehabilitation. Professor Robyn Tate a Clinical Psychologist and Neuropsychologist at Sydney University has extensive clinical experience in rehabilitation after TBI and will be reviewing outcome measures. The clinical effectiveness and cost-effectiveness of cognitive rehabilitation will be discussed by Professor Barbara Wilson, Visiting Scientist at the Medical Research Council's Cognition and Brain Sciences Unit in Cambridge, UK.

The Social Programme will focus on Istanbul's proud culture and national heritage. Delegates will discover the attractions of the timeless city, enjoy the delicious tastes of Turkish and Ottoman cuisine, and experience traditional Turkish hospitality. Those who wish to spend additional time in Turkey can choose to attend the superb pre-or post-congress tours to various magnificent places along the Mediterranean or in Anatolia.

Professor Ayşe A. Küçükdeveci, President of the Local Organising Committee said: "We believe that WCNR 2014 will be a major event remaining long in the memory of all participants". ◆

For more information on the Congress see www.wcnr2014.org

Managing epilepsy: improving outcomes – healthcare professionals conference

Conference details: 5 July, 2013 London, UK. ***Report by:*** Dr Greg Rogers, GP with a special interest in epilepsy in NHS Eastern and Coastal Kent and the Royal College of GPs Clinical Champion for epilepsy.

Epilepsy Society and London South Bank University jointly presented its first ever healthcare professionals conference designed to help shape epilepsy services and ensure the best outcomes for people with epilepsy. The event delivered expert talks and successful strategies for patient involvement, and facilitated the interactive sharing of models of best practice.

Held at London South Bank University, Deborah Wheeler, Regional Head of Quality Assurance (South), NHS England gave the first keynote address. Her lecture 'compassion in practice – the national vision for nursing' was most apt in light of the fact that the conference was held on the 65th birthday of the NHS. She spoke as a mother and as a healthcare professional about how the NHS should be about people. She said the six Cs; Care, Compassion, Competence, Communication, Courage and Commitment should be the vision for future healthcare.

Epilepsy Society's medical director, Professor Ley Sander, set the epilepsy scene, he said the time is right for a major conceptual breakthrough in research into and treatment of the condition.

Pioneering genetic research alongside our greater understanding of the co-existence or co-morbidity of epilepsy with other disorders, should lead to a more holistic approach to diagnosis and treatment of the condition.

Professor Sander said that for too long clinicians and scientists had missed the somatic co-morbidity of epilepsy alongside psychiatric co-morbidities.

Supporting individuals in their treatment choices and promoting medicine adherence was the plenary given by Anthony Linklater, Epilepsy Specialist Nurse at the National Hospital for Neurology and Neurosurgery.

He said the shift of power of balance to the patient was needed, with person centred care and whole person care being at the forefront.

Speaking about medication he said talking it long term is very difficult, AEDs can be especially difficult with hard to follow directions for use. Consequences of non adherence include worse seizure control, increased risk of seizures resulting in unnecessary and expensive use of NHS services and more disruption impacting on the individual's life. Clinicians tend to overestimate adherence, but patients using medication reminders had fewer seizures resulting in less admissions to A&E.

Dr Alison Leary, Reader in Advanced Nursing Practice at LSBU spoke about the value of nurse specialists in long term conditions. She spoke about her work modelling complex systems, specialising in pattern recognition and data mining including workforce modelling in healthcare and economic cost-benefit analysis.

Delegates also had the opportunity to attend two of four breakout sessions which covered 'Commissioning effective epilepsy services: sharing best practice', given by Julie Richardson, Deputy Director of Services, Epilepsy Society; 'Emergency medication in the community: sharing experiences and best practice', given by Jennifer Nightingale, Epilepsy Specialist Nurse at Epilepsy Society; 'Epilepsy-specific social work issues', given by Sally Garrett Smith, Social Worker at Epilepsy Society; and 'Motivational interviewing and the challenges of the 10 minute appointment', given by Professor Jane Wills at London South Bank University.

This first joint conference by Epilepsy Society and LSBU was both interesting and thought-provoking, and delegates gave positive feedback with 100 percent saying they would attend again. In short: an excellent day with excellent speakers. ◆

www.epilepsysociety.org.uk/professionals-conference

PREVIEW 12th Clinical Trials in CNS

Conference details: 18 & 19 November 2013, London, UK.

With an ever increasing average life expectancy neurodegenerative diseases are increasingly becoming more prevalent in society; this results in an increased need for new and improved therapies for treating these neurodegenerative conditions. From Alzheimers to Parkinsons disease the target and mechanism by which a disease manifests is unique and presents challenges in how to approach such treatments not to mention ethical and legal issues behind treatment and trial design.

Clinical Trials in CNS is a two day content packed agenda featuring new approaches taken in this field towards a number of neurodegenerative disorders, from clinical trial modelling and simulation to the role of biomarkers. The agenda presents a detailed look into many aspects of drug discovery and delivery of CNS therapeutics. This innovative conference will give delegates an opportunity to gain insights through case studies and interactive discussion into the best practices to design late stage clinical trials, the importance of understanding the pathophysiology and biology of disease processes with use of biomarkers and imaging techniques. The event also provides an overview of how to overcome challenges of delivery within the CNS.

Keynote Speakers

SMi are pleased to introduce Johannes Streffer, Director of Experimental Medicine Europe, Neurologist, Johnson & Johnson, who will give a presentation on Translational Medicine Models in Neurodegenerative diseases looking at continuous CSF measurements: Indwelling CSF catheters for monitoring CNS effects.

The conference will also feature presentation on early detection of Alzheimer's Disease in Mid-life lead by Craig Ritchie, Clinical Senior Lecturer, Imperial College London, highlighting pathological changes in mid-life which lead to dementia in older people and outline UK-based infrastructure initiatives to support translational medicine innovations in dementia research around mid-life and early dementia.

Visit www.clinicaltrialscns.com for the full speaker line-up, which includes presentations from: NIH/NINDS, Janssen Scientific Affairs, LLC; The Cure Parkinsons Trust, UCB Pharma, Eli Lilly and many more.

Attendees can also attend a half day workshop held on 20th November which will be on: Defining Clinical Relevance. Led by QCTR, the workshop will examine how to develop a better awareness of the limitations of primary outcome measures in neurological diseases and how to select and make a case to regulatory authorities for a single efficacy outcome measure. ◆

Visit www.clinicaltrialscns.com for more information or Contact Jonathan Collins on +44 (0)20 7827 6734 or email: jcollins@smi-online.co.uk

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Movement Disorders Society Conference

Conference details: 16-20 June 2013, Sydney, Australia ***Report by:*** Dr Thomas Foltynie, Consultant Neurologist, National Hospital for Neurology & Neurosurgery, & UCL Institute of Neurology, and Dr Alastair Noyce, Parkinson's UK Doctoral Research Fellow, UCL Institute of Neurology.

As far as conference locations go, Darling Harbour in Sydney Australia, is straight out of the top drawer. Even in the 'dead of winter', clear skies and an average temperature of 18 degrees, might tempt the most dedicated delegate away to admire the many wonderful sights on offer. That is, if the schedule itself were not equally enticing. We were welcomed on Sunday evening with a memorable performance by the aboriginal dance group Descendance. This special show, which included traditional welcome and kangaroo dances, was brought to us by one of Australia's best-known aboriginal dance groups. After the formal welcome messages by the committee, we were further treated to a drinks and canapés reception, complete with up close and personal encounters with koalas, wombats and snakes.

The Movement Disorders Society meeting kicked off formally on Monday with a session on experimental therapeutics involving presentations by two pioneering neurosurgeons – Professor Stephane Palfi on cell and gene therapy approaches for Parkinson's disease (PD), and Professor Tom Freeman on cell repair approaches for Huntington's disease (HD). This was followed by Dr Tom Foltynie's updates on a variety of experimental approaches for PD currently undergoing trials – both symptomatic (Neuroderm's subcutaneous L-dopa, Atomoxetine for PD dementia, Varenicline for gait freezing, Pitolisant for excessive daytime somnolence) as well as potential disease modifying approaches (namely Creatine, Inosine and Isradipine, as well as the two licensed diabetes drugs – Pioglitazone and Exenatide).

The Deep Brain Stimulation (DBS) update featured Dr Elena Moro who highlighted the uncertainties surrounding the future of the pedunculopontine nucleus (PPN) as a DBS target. Dr Jill Ostrem showed that DBS of the subthalamic nucleus (STN) is perhaps equally as good as the globus pallidus interna (GPi) target for dystonia patients, perhaps also without the risk of akinesia as a side effect. Lastly, Professor Jean-Luc Houeto updated us on DBS for Tourette's syndrome and Obsessive Compulsive Disorder (OCD). It was a cautionary note to see violent dyskinesias provoked by STN DBS in a patient with OCD, reminiscent of the hemiballismus provoked by STN infarction.

In the next session, Professor Beom Jeon delivered a comprehensive presentation on our knowledge of the influence of genotype on PD phenotype together with a touching thank-you to Australians for their assistance to Korea during the Korean war. Professor Carl Clarke presented the PD MED data suggesting that L-dopa may perhaps be an appropriate first treatment for all PD patients (although acknowledging that young onset patients are largely under-represented in the trial) and Janis Miyasaki highlighted the importance of the palliative care approach in advanced PD patients.

One particular highlight on the Monday, was the update on Dystonia. Professor Albanese described the process through which a panel of experts have sought to improve our approach to classifying dystonia (soon to be published in Movement Disorders), now including Axis 1 describing clinical characteristics, and Axis 2 referring to the underlying anatomy and aetiology. Professor Bhatia then reminded us of the range of paroxysmal movement disorders, recent genetic discoveries and the overlap between movement disorders and rare epileptic seizure presentations e.g. faciobrachial seizures associated with VGKC antibodies.

The Tuesday morning plenary sessions offered excellent talks on therapeutics in Parkinson's, atypical Parkinsonism and hyperkinetic/ataxic movement disorders. The new clinico-pathologically-themed 'Challenge the Experts' afternoon parallel session saw renowned neurologists pitting their wits in the differential diagnosis of cases that included Fahr's disease, pallido-luysian atrophy and progressive supranuclear palsy/chronic traumatic encephalopathy overlap. An equally excellent panel of pathologists was present to discuss the pathological findings in great detail.

Wednesday morning brought the annual presidential award lectures. Recipient Philip Thomson gave an interesting Stanley Fahn lecture with the title 'The Signs of a Neurologist', and Peter Jenner from King's College London then gave an excellent C. David Marsden lecture entitled 'Parkinson's disease: the Windmills of your Mind'. Alison Yarnall, from Newcastle, spoke beautifully on mild cognitive impairment in Parkinson's; she won the junior award alongside two Korean candidates.

The newly named 'Video Challenge' took place on the Wednesday evening. This event was formerly known as the 'Video Olympics', until a formal challenge from the official Olympic Committee two years ago, and the name was revised to the 'Video Games'. However this was felt to be insensitive to the plight of the patients in the cases, and the 'Games' element has now been dropped. There was a new look panel as well. Traditionally the Video Challenge saw two panels of four international experts go head-to-head in the diagnosis of difficult cases. This year there was a single panel of five experts including Professor Bhatia from Queen Square. The cases were as follows:

Case 1 – Episodic oculogyria – aromatic amino acid decarboxylase deficiency (AADC)
Case 2 – Dystonia and mineralization of the basal ganglia – Neuronal Ceroid-Lipofuscinoses (NCL)
Case 3 – Primary progressive aphasia and extra-pyramidal disorder – CSF1R gene mutation leading to Hereditary diffuse leukoencephalopathy with Spheroids.
Case 4 – Exercise induced ataxia with areflexia – Leukoencephalopathy of brainstem and spinal cord involvement and increased lactate (DARS2 mutation)
Case 5 – Progressive hyperkinetic movement disorder & chorioretinitis – subacute sclerosing panencephalitis (SSPE)
Case 6 – Progressive dystonia & cognitive impairment, strong family history – Gerstmann–Sträussler–Scheinker disease
Case 7 – Myoclonus and dystonia – Klinefelter's syndrome
Case 8 – Generalised myoclonus (Ramsay Hunt picture) & ataxia – mutations in SCA6 and MRE11 (Ataxia telangiectasia like syndrome)
Case 9 – Progressive pyramidal dysfunction, strong family history – SPAX1 mutation
Case 10 – Acute alien limb in hypertensive patient – intracerebral haemorrhage
Case 11 – Parkinsonism, dysmorphic facies – 22q11.2 deletion syndrome
Case 12 – Acute haemolysis, movement disorder and X-linked inheritance – phosphoglycerate kinase deficiency
Cases 5, 1 and 6 won the bronze, silver and gold medals respectively.

The Blue ribbon highlights session took place on the final morning of the Congress. The members of the panel presented the best abstracts from the week. Abstract categories included: basic science (including models and biomarker exploration), clinical aspects of movement disorders (neurobehavioural problems, developing at-risk cohorts, deep brain stimulation, mobile technologies, dopaminergic therapeutic strategies and PD in Africa). Further parallel sessions on Thursday afternoon brought the conclusion of an excellent meeting in an equally excellent city. Roll on MDS Congress 18 in Stockholm! ◆

Report of EFNS/ENS/World Stroke Organisation Regional Teaching Course

Conference details: 10-13 July, 2013, Dakar, Senegal. ***Report by:*** Professor Peter Sandercock, Professor of Medical Neurology Director, Edinburgh Neuroscience.

This was a three-day regional teaching course for young neurologists on stroke and movement disorders. It was attended by 53 participants from 23 African countries. 17 of the participants were supported by a scholarship from the EFNS RTC fund. These individuals were selected by the course organisers from a larger number of neurological trainees who had been put forward by their Head of Department as potential course participants. The remaining 36 were self-funding. Thus these selected participants represented some of the very best trainees from across Africa. The underlying principle was that neurological trainees should receive their training in Africa, and that training would be given jointly by Faculty members from Africa and from the European Federation of Neurological Societies (EFNS) and the World Stroke Organisation (WSO). The participants and teachers were fairly evenly split between Francophone and Anglophone, so the teaching used both languages (slides in English with spoken French translation and vice versa); a very interactive format!

The programme involved one day on stroke and one day on movement disorders, structured as lectures in the morning and in the afternoon small group workshops for case-discussions. The final part of the programme was a half - day dedicated to two workshops: 'meet the professors' and 'how to publish a paper'. The faculty for the stroke day supported by WSO was Thierry Akinodou (Benin), Kamadore Toure (Senegal), Jose Ferro (Portugal) and Peter Sandercock (UK). The faculty for the movement disorders day, supported by the AAN and the MDS was James Bower (Mayo, USA), Dr Joaquim Ferreira (Portugal), Chafiq Hicham (Morocco), Raj Kalaria (UK), Rufus Akinyemi (Nigeria).

The meeting was organised to a very high standard, and the quality of the lectures was extremely high. However, the most striking aspects of the course were the quality of the questions, the lively discussion, and the very active participation of the trainees in both French and English.

The host of the meeting, Professor Amadou Gallo Diop, from Dakar, emphasised that the guiding principle concerning training for African Neurologists was that the training should take place in Africa. This course

really highlighted the value of that approach; the trainees were encouraged to discuss the clinical problems they faced in their daily practice, not only with their peers, but also with Faculty drawn both from Africa and from the rest of the world. This led to very practical, well balanced discussions about the approach to clinical cases, but also how to conduct clinical research in African health care systems. I had the impression that the delegates would have found it much harder to engage so actively had they been attending a teaching course taking place during an international conference in Europe.

In conclusion, this type of course is clearly a very effective model of supporting career development and education for African Neurologists, and I very much hope that the new European Academy of Neurology will build on the success of the EFNS RTC programme in the future. ◆

PREVIEW Improving Patient Pathways in Parkinson's Disease Meeting

Conference details: London 10th October 2013; Newcastle 5th November 2013; Birmingham 21st November 2013.

This meeting is one in a series of three, taking place in Autumn 2013 and combining the Parkinson's Review Meeting with The Health Agenda - a series of multidisciplinary meetings focused on improving patient pathways in specialist care.

There will be a fantastic lineup of speakers at each meeting. Confirmed speakers at the London event include: Professor Kailash Bhatia (Chair), Professor of Clinical Neurology, National Hospital for Neurology and Thomas Foltynie, Consultant Neurologist, National Hospital for Neurology; Professor K Ray Chaudhuri, Professor of Movement Disorders, Kings College; Seema Buckley, Chief Pharmacist, Alexa Coombes, Neurology Business Manager; Allan Karr, National Homecare Medicine Committee

The events will cover a range of topics including: Current challenges in the management of Parkinson's Disease; A Parkinson's Disease patient experience; Supporting the Parkinson's Disease patient; Commissioning a Parkinson's Disease service; Guidelines and protocols; Coding the Parkinson's Disease pathway; Setting up an APO-go service; and Homecare to support patient outcomes. ◆

The event is free to attend. For more information and to register please visit the registration website www.parkinsons-ha.co.uk or www.apo-go.co.uk/hcp/events/prm-2013. If you have any questions please contact Lucy Bailey on lucy.bailey@pharma-mix.com or call 01223 234814.

Society for Research in Rehabilitation Summer Meeting

Conference details: 2-3 July, 2013, Nottingham, UK. ***Report by:*** Laura Edwards, ACF in Rehabilitation Medicine, Royal Derby Hospital.

A team from the East Midlands, led by Dr Kate Radford, did a fine job in hosting the SRR summer meeting with a great venue on the University of Nottingham campus, a wonderful programme with a range of topics and speakers, and some undeniably fine cheesecake. The title for the day was 'Research across the rehabilitation spectrum from preventing decline to return to work' and the two symposia focused on separate aspects of this. In the first, Professor Maud Graff gave a fascinating talk on developing community based occupational therapy interventions in dementia patients, discussing the importance of integrating the patients', carers' and occupational therapists' 'stories' to enable the most suitable programmes and optimise outcome, and also discussed some of the difficulties and differences in implementing programmes between different centres, countries and cultures. Professor Rowan Harwood took to the platform next. His discussion of 'No rehab potential', using as a springboard a case presentation of a demented gentleman who was deemed 'not fit for rehab' yet responded to a slow 'unofficial' rehabilitation programme on a DME ward, was thought-provoking and perhaps best described by an audience member as an elegant mix of 'humanity and erudition'.

The audience was then treated to a mix of free research presentations, ranging from an intriguing study of gait variability in older women with bladder instability, apparently waiting for subjects to reach a 'strong desire to void' meant that the gait analysis area had to be sited en route to the bathroom!, to a demonstration of the sometimes thankless task given to Cochrane reviewers, as a literature search of nearly 2000 papers boiled down to just one useable study!

The SRR Business meeting welcomed 20 new members and discussed recent developments, including responses to the NICE Stroke Rehab Guidelines, raising the profile of the SRR and the exciting prospect of a new website – coming soon, hopefully!

Lunch and poster tours were equally enjoyable, for slightly different reasons. The breadth of completed and ongoing work in the posters was exciting, including topics as diverse as mindfulness and yoga, functional MRI in TBI and correlations between spasticity and upper limb function following stroke.

Professor Marion Walker had the challenge of addressing a post-prandial auditorium and started by reminding us of Philip Nichols' BMJ article – 'Those who are constitutionally fat die more quickly than those who are thin' and inducing some guilty shuffling from myself, at least. Her talk on 'Progress in rehabilitation research: what have we learnt from the RCT? Where to from here?' was a wonderful overview of some of the developments and challenges seen in stroke research over the past few years, with a look towards challenges for the future.

Professor Jan Ekholm took up the baton for the second symposium, discussing 'Vocational rehabilitation: the role of health, the evidence and the future?' with an overview of the key interactions between health, work and society. The relationship between Swedish vocational rehabilitationists and the government is clearly much closer than in the UK and potential reasons and solutions (more and less light-hearted) were discussed.

The final free research session included the results of a postal survey of occupational therapists' roles in returning to work and a study on gait and turning in stroke patients. Overall, it appears that switching to a one-day format for the meeting was a great success. There was plenty of stimulating debate and some outstanding presentations. Congratulations to the organising committee and all presenters. ◆

The next planned SRR meeting will be held in London on February 4 2014.

President and meeting host Dr Kate Radford with Professor Marion Walker MBE who presented the Philip Nichols lecture at the meeting.

Top: Prof Maud Graff from the Netherlands.
Bottom: Professor Emeritus Jan Ekholm from Sweden.

The TRACK to clinical trials in Huntington's disease

Huntington's disease (HD) is an autosomal dominant neurodegenerative disorder classically described as a triad of motor, cognitive and psychiatric features. Given the monogenic nature of this disease and the availability of suitable animal models, finding potential therapies or even a cure should be theoretically feasible particularly since a number of treatments have shown preclinical promise. However, a major challenge facing such clinical trials is the longitudinal assessment of disease progression. Defining tests that are sensitive enough to detect a longitudinal decline over a short period of time in this slowly progressive disease is of utmost importance as it is likely that initial therapies developed for HD will aim to slow down the pathological process and hence hinder decline rather than restoring pathology.

The aim of TRACK-HD, a multicentre longitudinal observational natural history study, is to identify a battery of potential outcome measures to be used in future therapeutic trials. Over the past few years, they have followed up a group of 366 participants divided into groups of premanifest gene carriers (preHD), early manifest HD patients, and controls. In a recent paper in Lancet Neurology, Tabrizi and colleagues reported findings from the 298 participants that completed the 36 month follow up period of the TRACK-HD study. The study was specifically extended beyond 24 months due to the paucity of findings in the preHD cohort. However, by the 36 months visit they were able to demonstrate longitudinal changes in several imaging, quantitative motor and cognitive measures in the preHD group that were close to manifesting disease. In contrast, despite striatal and white matter loss, very little change could be seen clinically in the preHD group estimated to be far from disease onset. In addition, the authors also noted a variety of changes in early HD in accordance with the 12 and 24 month report of the TRACK-HD study. Several baseline imaging and cognitive measures could also predict disease progression in preHD, and functional decline in manifest disease.

HD is unique in the respect that a population which will almost certainly develop disease can be identified prior to the onset of clinically meaningful symptoms. This has led to the ambitious goal of developing a preventative therapy for this disease. However, despite the longitudinal changes in the preHD group estimated to be close to onset in this study, such trials will certainly face many practicality challenges in the preHD population, including identification of a "close to onset" group, lengthy follow up and large sample sizes. Such trials may be more feasible in manifest HD where TRACK-HD has shown that disease progression can be detected reliably at 24 months, with some measurements showing changes as early as 12 months, which will prove useful in planning future clinical trials in HD. ***– FB***

Tabrizi SJ, Scahill RI, Owen G, et al.
Predictors of phenotypic progression and disease onset in premanifest and early-stage Huntington's disease in the TRACK-HD study: analysis of 36-month observational data.
Lancet Neurol. 2013;12:637-49.

Tabrizi SJ, Reilmann R, Roos RA, et al.
Potential endpoints for clinical trials in premanifest and early Huntington's disease in the TRACK-HD study: analysis of 24 month observational data. Lancet Neurol. 2012;11:42-53.

Tabrizi SJ, Scahill RI, Durr A, et al.
Biological and clinical changes in premanifest and early stage Huntington's disease in the TRACK-HD study: the 12-month longitudinal analysis. The Lancet Neurology. 2011;10:31-42.

Consider Earlier Surgical Intervention in people with intractable Frontal Lobe Epilepsy

Frontal lobe epilepsy (FLE) is the second most common type of focal-onset epilepsy treated surgically. Seizure outcomes reported from cohort studies are generally inferior to those reported from temporal lobe surgery, and in particular compared with outcomes from those with mesial temporal lobe epilepsy.

A recent paper from the Cleveland clinic examined potential prognostic factors following frontal lobe surgery. Simasathien and colleagues reviewed 158 people who underwent FLE surgery between 1995 and 2010 with the primary outcome being complete seizure freedom at last follow-up. The mean age at surgery was 20.4 years (SD 1.2) with a mean age of epilepsy onset of 8.4 years (SD 0.7) and mean epilepsy duration of 12.0 years (SD 0.9). The mean duration of follow-up post-operatively was 4.3 years. The predominant underlying pathology identified was malformations of cortical development (MCD) in almost 60% of cases overall. Non-lesional resections (normal MRI) were performed in 38 patients (24%).

Overall, half of the people who underwent surgery for FLE were seizure free at last follow-up. The probability of being seizure free was 66% (95% CI 62-68) at 1 year post-operatively, 52% (95% CI 48-56) at 2 years and 44% (95% CI 39-49) at five years and beyond. The majority (70%) of seizure recurrences occurred in the absence of any provoking factors.

Three factors were identified that predicted (unprovoked) seizure recurrence on univariate analysis: longer epilepsy duration (> 10 years), left (as opposed to right) sided surgery, and the occurrence of seizures in the first postoperative week. All 3 factors remained statistically significant on multivariate analysis with a risk ratio of 1.82 for left sided surgery, 2.61 for epilepsy duration ≥5 years, and a risk ratio of 3.35 for acute postoperative seizures.

The novel finding in this study is the importance of epilepsy duration in determining postoperative seizure prognosis. Sub-analysis of seizure outcome in various pathologies underlies the importance of seizure duration: 68% of people with MCD and epilepsy duration < 5 years were seizure free at last follow-up compared to 40% with duration of ≥5 years with 100% vs 37% seizure free rates in people with FL tumour resection.

This study highlights the importance of early consideration and referral for evaluation of surgery in people with established intractable FLE. It may be that the poorer outcome associated with FLE surgery compared to TLE surgery may be in part explained that TLE surgery, is typically considered earlier in people with refractory TLE (given it's longer surgical pedigree and also the increased number of procedures performed in a typical epilepsy centre) compared to people with refractory FLE. ***– AN***

Simasathien T, Vadera S, Najm I et al.
Improved Outcomes with Earlier Surgery for Intractable Frontal Lobe Epilepsy.
Ann Neurol 2013;73:646-54.

IST-3: Live not longer, but better?

The third International Stroke Trial (IST-3) was designed to test alteplase administered to a wide range of patients, including those aged over 80, and up to six hours after stroke onset. Most previous trials assessing IV alteplase versus control within 6 hours of ischaemic stroke were limited to reported outcomes at 90 days, with none reporting outcomes beyond one year. The Lancet Neurology recently published useful long term clinical data regarding patient outcomes in this cohort at eighteen months post thrombolysis.

3035 patients were originally randomised to receive either alteplase or standard care alone. At 18 months, outcomes from 2,348 patients were analysed, revealing there was no significant difference in mortality between treated patients and controls (35%). The number of patients alive and independent, as assessed by an Oxford Handicap Scale (OHS) score of 0 to 2, had not been significantly improved at the 6-month time point in the trial, published last year. At 18 months however, this endpoint was significant. Furthermore, there were statistically significant and clinically relevant improvements in the health related quality of life of treated survivors as assessed by the Euro QoL instrument, with them having better functional outcomes, and requiring less help with ADL's. Mobility, self-care, ability to perform usual activities, and pain and discomfort were all improved. However, this did not translate into a difference in the proportion of patients living at home as opposed to in care facilities post stroke.

Limitations in study design conceded by authors were that the patients weren't blinded as to whether they had received thrombolysis

or not, which could have led to recall bias when they reported outcomes on quality of life. A high proportion of the health-related quality of life forms were completed by a proxy in the trial due to the severity of stroke in some patients, although we know from other studies that proxies tend to assign worse health status than do patients.

The IST3 trial corroborates evidence from several other previous trials that stroke thrombolysis with IV alteplase within 6h of acute stroke onset does not significantly improve the number of patients who are alive and living independently following treatment at 6 months when compared with controls. The primary end-point of the trial was therefore negative. Caution is of course needed when a secondary exploratory analysis is used to claim efficacy.

On a more positive note, we now have evidence that thrombolysis can lead to a sustained and meaningful improvement in the quality of life of patients, including the elderly. There are also potentially significant economic gains to be made from using a treatment that keeps patients independent (albeit not necessarily in their own homes) at 18 months. As the authors point out, in 2002 the estimated cost of long-term care of an independent stroke survivor was £876 per year as compared to the £11, 292 price of care for a dependent survivor. Although thrombolysis did not improve survival at 18 months in this large cohort, the fact it can make a difference to the lives of individual patients at extended follow-up, as well as lessening societal costs, is encouraging. ***– GC***

**The IST-3 collaborative group.
Effect of thrombolysis with alteplase within 6 h of acute ischaemic stroke on long-term outcomes (the third International Stroke Trial [IST-3]): 18-month follow-up of a randomised controlled trial.
The Lancet Neurology 2013;12:768–76.**

**The IST-3 collaborative group.
The benefits and harms of intravenous thrombolysis with recombinant tissue plasminogen activator within 6 h of acute ischaemic stroke (the third international stroke trial [IST-3]): a randomised controlled trial.
Lancet 2012;379:2352–63.**

Can Sudoku save your marbles?

Iris Murdoch is one of many towering intellects who sadly succumbed to the ravages of dementia in their later years. Yet the mass media is replete with headlines exhorting us to "use or lose it" claiming that everything from crossword puzzles to Nintendo games can stave off "The Big D". With no disease modifying medications available to treat dementia, the idea of being able to modify our lifestyle factors in this way to prevent it, seems like an enticing yet somewhat implausible one.

Wilson et al sought to determine whether childhood (6–12 years), young adulthood (age 18), middle age (age 40), and late-life (current) engagement in cognitively stimulating activities delays late-life cognitive decline and if it is not linked to common neuropathologic measures of amyloid, tangles, cerebral infarcts and lewy bodies. Utilising neuropathologic assessments on 294 individuals followed clinically every year on average 5.8 years before death, they were able to test the cognitive reserve hypothesis. Interestingly, their results supported the cognitive reserve hypothesis as people with current and early-life engagement in cognitively stimulating activities showed slower decline in cognition, despite the presence of underlying pathology. This raises the intriguing question of how cognitive reserve actually exerts an effect, if not through ameliorating the burden of pathology. ***– GC***

**Wilson RS, Boyle PA, Yu L et al.
Life-span cognitive activity, neuropathologic burden, and cognitive aging.
Neurology. 2013 Jul 23; 81:314-21.**

Is ALS a prion-like disorder?

Neurodegenerative diseases are characterised by pathological protein inclusions. The age-old question remains as to whether these inclusions are mechanistically involved in disease or not. In the case of ALS, the hallmark protein in 95% of cases is TDP-43. There has been much interest in the possibility that a prion-like process could explain the pathogenicity of this promiscuous RNA/DNA binding protein. A self-templating, prion-like process is attractive given that patients with ALS initially develop symptoms/signs at a single locus, and that the disease appears to 'spread' to contiguous anatomical regions. Such spread might also explain the clinico-pathological overlap with FTLD-TDP: the primary motor cortex is of course part of the frontal lobe. Indeed, recent evidence has implicated axons as potential conduits for the spread of TDP-43 pathology (Brettschneider et al 2013). Furthermore, TDP-43 does have modest sequence similarity to the prion protein (Guo et al 2011), and a growing list of proteins linked to ALS appear to be prion-like (Kim et al 2013). However, this data does not show that TDP-43 inclusions actually beget TDP-43 inclusions. Establishing whether this is the case or not could have massive implications for the kind of drugs we decide to develop for ALS.

It is interesting, therefore, to see the biochemical studies conducted by Nonaka et al (2013). They actually took human ALS and FTLD brain tissue, mashed it up and purified an insoluble fraction, which they then introduced into cultured cells in vitro. What they found was that if the cultured cells were already forced to express large amounts of TDP-43 using genetic constructs, the addition of the ALS brain solution caused TDP-43 aggregation within those cells. If the brain solution was first treated to remove TDP-43, it no longer caused TDP-43 aggregation. This result, together with further cellular studies suggests that TDP-43 aggregates can 'seed' further TDP-43 aggregation. Similar experiments with brain extracts from Pick's disease and DLB did not cause TDP-43 aggregation, demonstrating a specific effect of ALS brains in causing TDP-43 aggregation.

What is far less convincing is their 'self-templating' conclusion. They argue that the pattern of protein aggregation in their cell cultures is determined by the protein fingerprint seen in the brain samples they add. However, they do not really convince us that TDP-43 'self templates' in the way that true prion protein strains do (have a quick look at their cartoon in figure 3C and come to your own conclusion). The fact remains that ALS is not a true prion disease (even 'prion-like' is a term that still remains unclear) and TDP-43 proteinopathy has not been found to be infectious between humans. This last point is important as some have suggested that ALS patients should not be allowed to do one last good deed and donate their organs after death for fear of spreading disease (Holmes and Diamond 2013)! We still need to better understand how TDP-43 causes disease, and protein toxicity alone is unlikely to be the answer. ***– JS***

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UK/CPX/13/0009 July 2013