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ADVANCES IN CLINICAL NEUROSCIENCE & REHABILITATION

In this issue

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Combined Healthcare
NHS Trust

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COVER Can I Get a Tourettes Assessment Please' by 12-year-old Bella. As shown in the Tourettes Action Creativity Awards (TACA) Exhibition. For more information visit: tourettes-action.org.uk

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I am delighted to introduce another ACNR issue as 2024 begins. We are very grateful to everyone who contributed to ACNR in 2023 and look forward to receiving and collaborating with multiple many new and old colleagues in 2024.

Last year, leading into this one, our profession has faced many challenges - with industrial action leading UK doctors to deeply examine how we are valued, and what we value. It is never an easy choice of career, but it is always fascinating and rewarding in many ways. I hope the best outcome for all is reached.

Thinking of better outcomes for all, equality has been an emerging theme in research – in this issue you can find 'Democratising access to dementia research' examined by Ruth Dobson, Rimona Weil and Niran Rehill.

Dr Vera Barbosa, Dr Samaneh Moghddacy and Dr David O Regan review the management of sleep disorders in patients with intellectual disability.

I am pleased to announce a new section editor for a series of articles on Myasthenia Gravis, Dr Stuart Viegas, with our first article authored by Dr Jennifer Spillane, who looks at 'A new era of treatment options'. Dr Viegas has joined a number of new section editors, and we will be publishing our editorial family tree in our next issue.

Again, we have articles from two special authors who are the backbone of ACNR, and really, who make ACNR unique with their regular historical and interesting articles about the history of medicine or unusual clinical findings in neurology - that is Dr Andrew Larner (Saccadomania this issue) and Dr JMS Pearce (Piriformis syndrome) who are both endlessly fascinating in terms of their contribution to our journal and my own clinical knowledge, and who we cannot thank enough.

This issue contains a review of the British NeuroPsychiatry Association (BPNA) March 2023 meeting, looking forward to their next one coming up on the 14th and 15th of March 2024. Other meetings reviewed include the Lewy Body UK meeting, which will take place again on Friday 7th of June 2024 in Newcastle upon Tyne. Dr Edward Newman and Dr Neil Ramsey review the 23rd International Congress of Parkinson's Disease and Movement disorders which took place in Copenhagen. This will be in Philadelphia this year.

The Epilepsy Specialist Nurse Association meeting was on the 11th and 12th September 2023. They made special mention of the Dr John Paul Leach after-dinner speech filled with fun and laughter. Congratulations to Yvonne Leavy, Clinical Nurse Specialist in Epilepsy NHS Lothian for the award recognising her outstanding contribution to epilepsy nursing.

Among others, there is a book review by Dr Ronan McGinty of Dr Professor Simon Shorvon's book- The Idea of Epilepsy, which is 'an engaging history of epilepsy'.

See pages 24-25 for a comprehensive calendar of courses and conferences coming up in 2024. The events calendar on our website is continuously updated, and you can add details of events free of charge at acnr.co.uk/submit-an-event.

Wishing everyone a happy and healthy new year.

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Sleep disorders in Intellectual Disability; a brief narrative review

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Abstract

Adults with intellectual disability are more likely to experience sleep disorders and disordered sleep, which not only adversely affects their mental and physical health, but also the health and wellbeing of their carers. Despite this, there are neither recommended assessment nor treatment guidelines for this population. In this brief narrative review, we summarise what is known about diagnosing and managing sleep disorders in adults with intellectual disability, share our clinical experience, and highlight the need for further research.

Introduction

Sleep disorders are more common in adults with intellectual disability (ID), with higher prevalence rates (up to 100%) when compared to those in the general population [1]. Despite this, the importance of sleep in ID is often overlooked, especially clinically, where sleep disorder(s) may be viewed as being part of the disability (i.e. diagnostic overshadowing), and/or too challenging to investigate and treat [2-4].

In addition to adversely affecting physical and mental health, sleep disorders in adults with ID may also drive challenging behaviours, increase carer burden, and as a result, increase health and social care utilisation [5-7].

Despite the increased prevalence and adverse sequelae of sleep disorders in adults with ID, there is a paucity of research and guidance regarding optimal assessment, diagnostic and management approaches [2,8-11].

In this brief narrative review, we discuss the current evidence base, as well as our experience, in assessing, diagnosing, and managing common sleep disorders in this population.

Epidemiology

Adults with intellectual disabilities represent a special population with notable health inequalities, such as increased multi-morbidity, and up to an 18-year reduced life expectancy [12]. Both sleep disorders and disordered sleep are very common in adults with ID, and as for the general population, represent a potentially important modifiable health risk factor [13,14]. Owing to the heterogeneity and quality of epidemiological studies in adults with ID, prevalence rates of disordered sleep vary widely. A recent systematic review of twenty studies (> 8, 000 participants) identified prevalence rates of disordered sleep (across a range of sleep parameters) ranging from 6.1 to 74.2%, whilst studies examining sleep-related breathing disorders (> 2,500 participants) identified prevalence rates ranging from 0.5 to 100% [1].

Assessment

We would encourage any clinician involved in the care of an adult with ID to inquire about their sleep. Whilst this may sound simplistic, it is frequently overlooked e.g. sleep is not included in the NHS Learning Disabilities Annual Health Check [15].

When an individual and/or their carer identifies a sleep concern, adopting a person-centred approach can help elucidate the biological, psychological, behavioural, and social factors which may be implicated. For example, in our clinic, we use a 7-step approach to help guide our assessment (Table 1).

Adults with ID are a heterogenous group, and so it is important to bear in mind that specific sleep disorders can cluster around genetic syndromes or disorders, as well as comorbid neurodevelopmental disorders [2,15]. For example, adults with Down's Syndrome have an increased risk of Obstructive Sleep Apnoea (OSA), likely due to the characteristic features of this syndrome e.g. cranio-facial abnormalities, hypotonia, and obesity (as a result, it is recommended that everyone with Down's Syndrome is screened for OSA.); whilst adults with Smith-Magenis Syndrome have a higher risk of circadian sleep-wake disorders, classically presenting with an inversion of their sleep-wake cycle, secondary to melatonin dysregulation [16-19].

Diagnosis

Unlike the general population, adult ID-specific sleep diagnostic guidelines are lacking. Subjective sleep information may be more commonly provided by families/carers, who may have differing opinions on the level of sleep disturbance, or they may simply accept poor sleep as part of the person's underlying condition [20]. As a result, sleep disorders are more likely to be reported when they lead to nocturnal and daytime dysfunction, including behavioural disturbance i.e. rarely are sleep symptoms reported because of their impact on the person's subjective quality of life [21].

Screening questionnaires can be used to assess sleep disorder severity and monitor treatment response, but they are rarely validated in adults with ID, and again, tend to rely more on carer's reports. A pictorial version of the Epworth Sleepiness Scale (for example) has attempted to overcome this challenge, albeit with variable success [22]; whilst the STOP-Bang questionnaire has been successfully validated for adults with Down's syndrome who have a moderate to severe Obstructive Sleep Apnoea (OSA) [16]. The STOP-Bang questionnaire is one of the most widely accepted and easy to use OSA screening tools; it consists of four self-reportable (STOP: snoring, tiredness, observed apnoea, and high blood pressure) and four demographic (Bang: body mass index, age, neck circumference, and gender) items [23]. Individuals with a STOP-Bang score of 0 to 2 can be classified as low risk for moderate to severe OSA, whereas those with a score of 5 to 8 can be classified as high risk for moderate to severe OSA. Individuals whose STOP-Bang scores are in the midrange (i.e. 3 or 4), require further clinical evaluation to determine the likelihood of OSA [23].

Sleep diaries (usually completed by carers) and/or actigraphy (ideally worn for a minimum

Table 1 Sleep Assessment – a 7-step approach guide

Sleep Assessment Domains	Explanation and intervention examples
Homeostatic	i.e. optimise the individual's internal sleep drive by optimising their sleep/wake schedule. For example, a common problem in this area is 'putting' the adult with ID to bed far too early (i.e. when their sleep drive is not optimised), which may be with the intention of giving their carers respite, and/or because this fits in with care staff shift changes.
Circadian	i.e. optimise exposure to appropriate biological clock cues; for example: by ensuring access to appropriately timed natural daylight, to structured daytime activity (including exercise), and to blackout blinds at night.
Physical Health	i.e. optimise the management of any physical health disorder which may disturb sleep. Common examples include gastro-oesophageal reflux, constipation, pain, enuresis, epilepsy, OSA, RLS and other organic sleep disorders.
Mental Health	i.e. optimise the management of any mental health disorder which may negatively impact sleep, such as: depression, anxiety, and psychosis.
ID-Associated conditions	i.e. optimise the management of associated conditions which may negatively impact sleep, such as neurodevelopmental disorders (ASD and/or ADHD).
Environmental	i.e. optimise the sleep environment, by considering the potential impact of: noise levels, bedroom temperatures, and the impact of nocturnal care staff checks, as well as other residents.
Medication	i.e. review current medications to consider their potential sleep impact. For example, mirtazapine can drive restless legs, as can beta-blockers (which can also cause nightmares); and benzodiazepines can worsen sleep disordered breathing.

Abbreviation: ID, intellectual disability; ASD, Autism Spectrum Disorder; ADHD, Attention Deficit Hyperactivity Disorder; OSA, Obstructive Sleep Apnoea; RLS, Restless Legs Syndrome. Table adapted from [2]

of two weeks) can be used to record 24-hour sleep/wake timings (helpful in diagnosing insomnia and/or circadian sleep-wake rhythm disorders for example). If a sleep diary is completed by a carer (as opposed to the individual with ID), there may be reporting errors, such as a lower estimate of wake-after-sleep-onset time (a measure of sleep maintenance) [24] .This potential confounder should be considered when undertaking sleep scheduling, where a gentler approach, such as sleep compression may be utilised [25]. Home or inpatient sleep investigations e.g. pulse oximetry, home video telemetry or inpatient polysomnography can be used to investigate for physical sleep disorders, such as sleep disordered breathing or movement disorders, and epilepsy etc. If undertaking an inpatient sleep investigation, having access to an individual room, as well as the capacity to involve family/ carers can be very helpful. Moreover, additional time may be required for equipment (e.g. electrode) acclimatisation, and sometimes creative thinking is required e.g. if an actiwatch is not tolerated, then (if clinically necessary), we often advise sewing the device into the individual's daily clothing.

There will of course be times when an adult with ID cannot tolerate any clinically relevant sleep investigation, and in this scenario, a pragmatic trial of treatment may be required.

In conjunction with intellectual disability expert colleagues, we have previously proposed one approach for the screening, assessment, and management of sleep disorders in adults with ID (Figure 1)

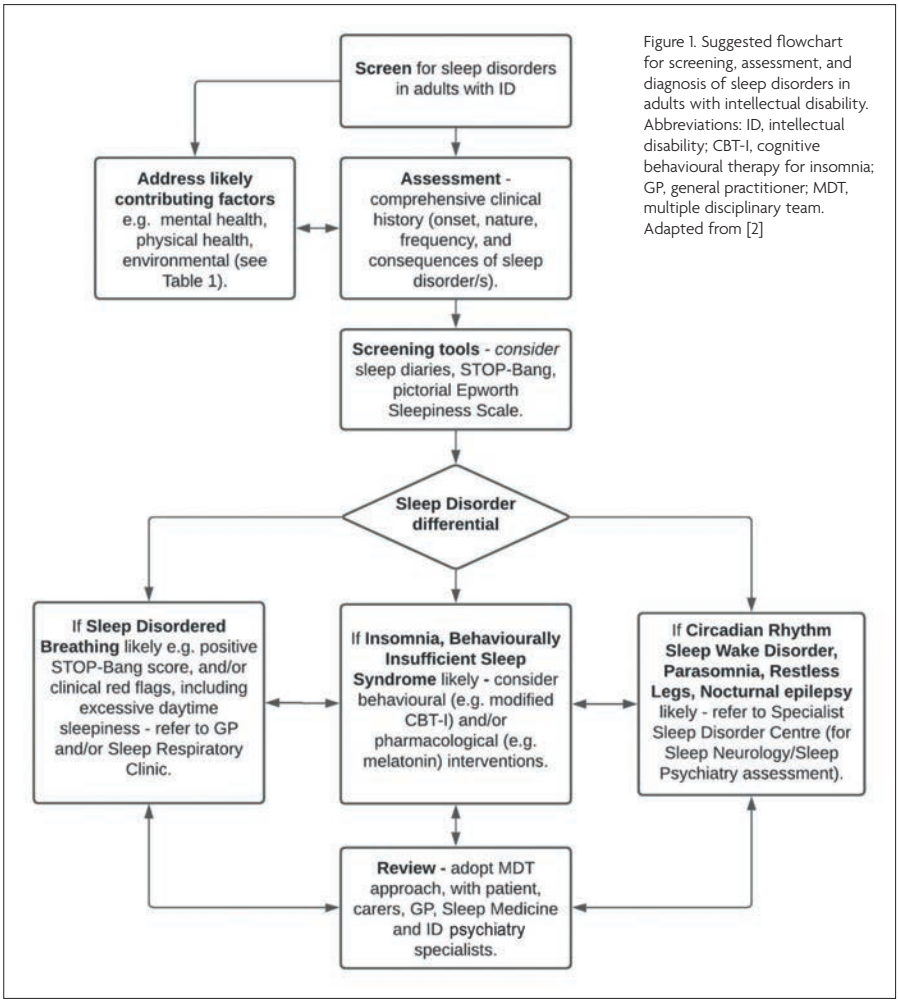

Figure 1. Suggested flowchart for screening, assessment, and diagnosis of sleep disorders in adults with intellectual disability. Abbreviations: ID, intellectual disability; CBT-I, cognitive behavioural therapy for insomnia; GP, general practitioner; MDT, multiple disciplinary team. Adapted from [2]

Table 2: Modified CBT-I for Individuals with intellectual disabilities

Technique	Aim	Method	General Advice
Anchoring the day	To optimise the homeostatic sleep drive.	Setting a latest fixed rising time that is maintained 7 days a week, no matter how tired or little the individual has slept.	This is easier to achieve with the aid of carers, and if there is something to get up for i.e. structured daytime activity. We recommend setting an alarm so that the anchor time is kept constant.
Daylight exposure	To optimise the circadian rhythm	We recommend a minimum of 20 minutes natural daylight exposure within 2 hours of rising.	This is easier to achieve if there is structured daytime activity, and regular breakfast times (which also helps regulate the biological clock).
Stimulus Control	To re-establish the connection in the mind that the bed and bedroom are places for sleep as opposed to places for wakeful activities. (This technique is based on classical conditioning).	Ideally, the bed and bedroom are used for: sleep, sex and getting dressed only. Any other activity should be undertaken outside of the bed and bedroom.	If the individual only has access to one room, then try to make the bed and bedroom look different in the day and in the night e.g. using a different bed cover for the day, and/or placing a plant in the room, and taking it away at night. The more cues we can give the brain to let it know whether the room is in day or night mode will strengthen this technique.
Buffer Zone	To reduce arousal pre-bed.	This is a period of at least 90 minutes before bed, where the brain and body are moved to a state of relaxation ready for sleep.	We advise beginning the buffer zone with a bath (if safe to do so; a shower can be trialled too), and afterwards keeping the room dimly let, and encouraging relaxing (non-stimulating) activities until it is time for bed.
Sleep Scheduling	To optimise the internal sleep drive (in conjunction with anchoring the day), and to reduce hyperarousal.	In this technique the total sleep time is closely matched to the total time in bed (judged by keeping sleep diaries, and/or actigraphy).	This often requires carer education, as individuals with intellectual disabilities often have bedtimes that are too early for them. The technique should be used with caution and under expert behavioural sleep medicine supervision, in individuals with co-morbidities which could be made worse by temporary sleep loss e.g., epilepsy, or bipolar affective disorder,
Other	To promote optimisation of zeitgebers i.e., those signals which feed into the biological clock.	Structured daytime activity. Regular mealtimes. Discourage eating during the night if the individual cannot sleep or giving extra attention at this time. Engagement in regular exercise (ideally, getting out of breath).	All of the techniques outlined in this table require patience and perseverance in order to be effective. Initially, sleep may worsen as usual routines are being changed, which can increase anxiety. To circumnavigate this risk, trialling one technique at a time may be advisable for some individuals.

Adapted from [2]

Management

The management of sleep disorders in adults with ID frequently requires a multi-disciplinary team (MDT) approach, and may require professional input from primary care, social care, sleep medicine and intellectual disabilities psychiatry. Such an approach reflects the heterogeneity of the underlying causes of ID and their associated co-morbidities. Every attempt should be made to optimise the factors outlined in Table 1, as focusing on one area alone is unlikely to be successful (Vignettes 1 & 2).

Physical treatments

Continuous positive airway pressure (CPAP) has been shown to be effective in adults with Down's syndrome and OSA, in improving sleep, excessive daytime somnolence, mood, behavioural disturbance, general health and cognitive function [22]. Moreover, it has been demonstrated to be well-tolerated [22]. For individuals who struggle to accept CPAP, exposure therapy may be beneficial, and in this scenario, collaborative working between sleep medicine specialists and others (e.g., mental health nurses, families, carers) can be helpful. Where positive airway pressure is unsuccessful or not tolerated, consideration could be given to hypoglossal nerve stimulation [26]; and where obesity plays a maintaining role in OSA, medical management e.g. with glucagon receptor-1 agonists, could be pursued [27].

Behavioural treatments

Cognitive Behavioural Therapy for Insomnia (CBT-I) is the first line recommended treatment for chronic insomnia in the general population [28], and there is some evidence that it may also be helpful in adults with ID [21]. In particular sleep scheduling has been successfully utilised, both on its own and as part of a multi-modal CBT-I treatment. In this technique the average total sleep time (obtained from sleep diaries and/or actigraphy) is closely matched to the average total time in bed. This helps to optimise the homeostatic (internal) sleep drive, reduces hyperarousal, and helps to consolidate sleep. The technique is likely to require family/carer education and flexibility, as often adults with ID have an imposed bedtime which may be too early for them [2]. In this scenario, working with social and healthcare providers to increase care package provision may be required. The technique should ideally be undertaken under the guidance of a behavioural sleep medicine specialist, as any unintended sleep deprivation may worsen both physical (e.g. epilepsy) and mental (e.g. bipolar affective) disorders [2,29]. Additional

CBT-I techniques are outlined in Table 2.

Even relatively simple modifications to scheduled daytime activities and sleeping environments can bring about significant sleep improvements e.g. adults with ID attain less daily exercise, and have an unhealthier diet when compared to the general population; two important factors which increase the risk of sleep-disordered breathing [21]. The loss of daytime colleges and placements during the Covid-19 lockdowns had (in our experience) a devastating effect on sleep in adults with ID.

Pharmacological treatments

There is again a paucity of evidence regarding the pharmacological management of sleep disorders in adults with ID, with the management of non-insomnia disorders tending to follow the same treatment algorithms as those for the general population. Unsurprisingly, the medication which has attracted most attention is melatonin, with one meta-analysis concluding that it reduces sleep onset latency, and improves sleep maintenance and total sleep time in adults with ID [30]. Melatonin is associated with few adverse events, and is relatively safe in the short-term, though there are no long-term studies regarding its use in adults with ID [5,30]. As for other hypnotics, if melatonin is unsuccessful there is usually little if anything to be gained from endlessly increasing the dose, and switching to a different class of hypnotics should be considered [31].

Vignette 1

A 36-year-old man with severe intellectual disability (non-verbal) and adult Attention Deficit Hyperactivity Disorder was referred by his intellectual disabilities psychiatrist for the investigation and management of treatment-resistant insomnia. He had additional co-morbidities of anxiety and type II diabetes, and was prescribed: metformin (500mg three times daily), propranolol (40mg twice daily; indication: anxiety) and methylphenidate extended release (60 mg once daily). The psychiatrist had trialled reducing methylphenidate and subsequently introduced modified release melatonin without success. Additional trials of promethazine (to 50mg) and mirtazapine (to 15mg) resulted in sleep deterioration. The patient typically retired to bed at 10pm, and carers described a markedly delayed sleep onset latency, during which time, he repeatedly left his bed and paced. On closer questioning, they described an inability to sit still, beginning each evening (around 8PM), even when they played his favourite television programme or music. Once asleep, there were no obvious difficulties with sleep maintenance, and his rising time was fixed for 9AM to coincide with structured daytime activities. During the day he was noted to be irritable, with worsening hyperactivity (which had not responded to higher stimulant doses). He had no history of anti-social snoring nor seizures, and he would not tolerate home nor inpatient sleep investigations. Based on the history, a clinical diagnosis of Restless Legs Syndrome (RLS) was made. RLS is the commonest mimic of insomnia, and in adults with ID, can present very similarly to this patient [32]. Moreover, medications with anti-histamine function, such as promethazine and mirtazapine can exacerbate RLS (and hence why his sleep deteriorated when these were trialled) [33]. It is also commonly co-morbid in adults with ADHD (~44%) [34] and type II diabetes [35]. The GP arranged for baseline blood tests, including a ferritin level and HbA1c. The ferritin level was <100mcg/L (the recommended lower limit for patients with RLS), which we addressed with Ferinject, when oral iron supplementation resulted in constipation. We withdrew his propranolol (beta-blockers can worsen RLS) [33], and as he remained symptomatic, slowly commenced Pregabalin, up-titrating to 150mg once nightly. He responded well to this, with an abolition of his evening restlessness, a normalised sleep onset latency, and there were notable improvements to his next day mood and function.

Vignette 2

A 21-year-old woman with Cornelia de Lange Syndrome (CdLS), and severe intellectual disability (non-verbal) was referred for the evaluation of sleep-disrupting nocturnal coughing, following an unremarkable respiratory medicine assessment. She had co-morbidities of constipation, for which she was prescribed lactulose, and had a past history of recurrent aspiration pneumonia, requiring a recent inpatient admission. Her parents reported intermittent coughing throughout the night, which at times was associated with emesis, and it disturbed her sleep maintenance. Daytime hyperactivity was notably worse following nocturnal coughing. Her GP had trialled a proton pump inhibitor (PPI) without success. Clinical assessment was not suggestive of a co-morbid sleep disorder, and home pulse oximetry was unremarkable. Despite the failure of a PPI, given her presentation and background of CdLS, we had a high index of clinical suspicion for gastro-oesophageal reflux disease (GORD). Stool analysis confirmed Heliobacter pylori (H. pylori), which when treated, resolved the nocturnal cough, improved sleep maintenance, and daytime hyperactivity reduced. 66% of individuals with CdLS experience GORD, and there is a strong correlation between the degree of oesophageal damage and the behavioural phenotype, with hyperactivity being the most common (up to 85%) [36, 37]. Moreover, worsening of behavioural symptoms is often used as a major sign of oesophageal damage in CdLS [38]. Nocturnal cough is a common sleep disrupter, which may cause neuropsychiatric disorders, and it negatively impacts on health-related quality of life (for review, see [39]).

Conclusion

Sleep disorders are common in adults with ID, and are important determinants of physical and mental health, as well as daytime function. Despite this, they are frequently overlooked, and not considered as primary diagnoses.

There are many challenges when assessing, diagnosing, and treating sleep disorders in adults with ID, particularly when there is an overreliance on informant rather than subjective information. This is complicated by a lack of robust evidence regarding optimal adult ID sleep disorder management, as well as an often-significant reliance on care-giver/system ability and willingness to implement management strategies.

However, as our vignettes highlight, the benefits of successfully addressing sleep disorders in adults with ID far outweigh these challenges.

Further research on sleep disorders in adults with ID is clearly required, including validated tools to aid primary and secondary care clinician screening, assessment and management. Only then will sleep medicine be able to retire Robert Sternberg's quote – "if a child is labelled as having a learning disability, it has very concrete consequences for the kinds of services, …that child will get" [40].

The Cover Story...

Our front cover once again features artwork from the Tourettes Action Creativity Awards (TACA) Exhibition which was launched by the National charity Tourettes Action. The striking image, entitled 'Can I Get a Tourettes Assessment Please' is the work of 12-year-old Bella.

The Tourettes Action Creativity Awards is an online event which celebrates the creativity of young people in the UK living with Tourette Syndrome (TS). The awards give young people with TS a chance to showcase their artistic talents. Artists, animators, stand-up comedians, musicians, short filmmakers, composers, dancers, poets and more are invited to produce an original piece of work, providing an opportunity to feature in the #TACA winners online gallery.

For more information visit tourettes-action.org.uk

References

1. Shanahan P, Ahmad S, Smith K, Palod S, Fife-Schaw C. The prevalence of sleep disorders in adults with learning disabilities: A systematic review. British Journal of Learning Disabilities. 2022:1-24. https://doi.org/10.1111/bld.12480
2. Korb L, et al. Sleep: the neglected life factor in adults with intellectual disabilities. BJPsych Bull, 2021: 1-7.
3. Esbensen AJ, Schwichtenberg AJ. Sleep in Neurodevelopmental Disorders. Int Rev Res Dev Disabil. 2016;51:153-191. https://doi.org/10.1016/bs.irrdd.2016.07.005
4. van de Wouw E, Evenhuis HM, Echteld MA. Prevalence, associated factors and treatment of sleep problems in adults with intellectual disability: a systematic review. Res Dev Disabil. 2012;33(4):1310-32. https://doi.org/10.1016/j.ridd.2012.03.003
5. Wilson S, et al. British Association for Psychopharmacology consensus statement on evidence-based treatment of insomnia, parasomnias and circadian rhyt update. J Psychopharmacol. 2019;33(8):923-947. https://doi.org/10.1177/0269881119855343
6. Carr EG, et al. Using mood ratings and mood induction in assessment and intervention for severe problem behavior. Am J Ment Retard. 2003;108(1):32-55.https://doi.org/10.1352/0895-8017(2003)108<0032:UMRAMI>2.0.CO;2
7. Symons FJ, Davis ML, Thompson T. Self-injurious behavior and sleep disturbance in adults with developmental disabilities. Res Dev Disabil. 2000;1(2):115-23.https://doi.org/10.1016/S0891-4222(00)00028-7
8. Medic G, M, Wille M, Hemels ME. Short and long-term health consequences of sleep disruption. Nat Sci Sleep. 2017;9:151-161.https://doi.org/10.2147/NSS.S134864
9. Brylewski J, Wiggs L. Sleep problems and daytime challenging behaviour in a community-based sample of adults with intellectual disability. J Intellect Disabil Res. 1999;43(Pt 6):504-12. https://doi.org/10.1046/j.1365-2788.1999.00234.x
10. McCurry SM, Song Y, Martin JL. Sleep in caregivers:what we know and what we need to learn. Curr Opin Psychiatry. 2015;28(6):497-503.https://doi.org/10.1097/YCO.0000000000000205
11. Knapp M, et al. Intellectual disability, challenging behaviour and cost in care accommodation: what are the links? Health Soc Care Community. 2005;13(4):297-306. https://doi.org/10.1111/j.1365-2524.2005.00539.x
12. Thornton J. People with learning disabilities have lower life expectancy and cancer screening rates. BMJ. 2019;364:l404. https://doi.org/10.1136/bmj.l404
13. Sateia MJ. International Classification of Sleep Disorders-Third Edition. Chest. 2014;146(5):1387-1394. https://doi.org/10.1378/chest.14-0970
14. Firth J, et al. A meta-review of "lifestyle psychiatry": the role of exercise, smoking, diet and sleep in the prevention and treatment of mental disorders. World Psychiatry. 2020;19(3):360-380. https://doi.org/10.1002/wps.20773
15. NHS. Available from: https://www.nhs.uk/conditions/learning-disabilities/annual-health-checks/.
16. Carvalho AA, et al. STOP-Bang questionnaire should be used in all adults with Down Syndrome to screen for moderate to severe obstructive sleep apnea. PLoS One, 2020;15(5):e0232596. https://doi.org/10.1371/journal.pone.0232596
17. Cornacchia M, et al. The Prevalence of OSA Among an Adult Population With Down Syndrome Referred to a Medical Clinic. Am J Intellect Dev Disabil. 2019;124(1):4-10. https://doi.org/10.1352/1944-7558-124.1.4
18. Trois MS, et al. Obstructive sleep apnea in adults with Down syndrome. J Clin Sleep Med. 2009;5(4):317-23. https://doi.org/10.5664/jcsm.27541
19. Boudrea E.A, et al. Review of disrupted sleep patterns in Smith-Magenis syndrome and normal melatonin secretion in a patient with an atypical interstitial 17p11.2 deletion. Am J Med Genet A. 2009;149A(7):1382-91. https://doi.org/10.1002/ajmg.a.32846
20. Surtees ADR, et al. Sleep duration and sleep quality in people with and without intellectual disability: A meta-analysis. Sleep Med Rev. 2018;40:135-150.https://doi.org/10.1016/j.smrv.2017.11.003
21. McPherson P, Kaushal M, Kothapalli V. The Treatment of Dually Diagnosed Individuals with Sleep Disturbances and Intellectual Disabilities. Handbook of Dual Diagnosis, ed. J.Matson. 2020 Springer. https://doi.org/10.1007/978-3-030-46835-4_36
22. Hill EA, et al. Utility of the pictorial Epworth sleepiness scale in the adult down syndrome population. Sleep Med. 2020;66:165-167. https://doi.org/10.1016/j.sleep.2019.10.003
23. Pivetta B, et al. Use and Performance of the STOP-Bang Questionnaire for Obstructive Sleep Apnea Screening Across Geographic Regions: A Systematic Review and Meta-Analysis. JAMA Netw Open. 2021;4(3):e211009. https://doi.org/10.1001/jamanetworkopen.2021.1009
24. O'Sullivan RBS, Hamilton A, et al. Concordance of objective and subjective measures of sleep in children with neurodevelopmental conditions: A systematic review and meta-analysis. Sleep Medicine Reviews. 2023;71. https://doi.org/10.1016/j.smrv.2023.101814
25. Rosen A, D.O.P., et all, A comparison of sleep restriction and sleep compression on objective measures of sleep: A sub-sample from a large randomised controlled trial. Journal of Sleep Research, 2023. 32(4): p. e13826. https://doi.org/10.1111/jsr.13826
26. Li C, Boon M, Ishman SL, Suurna MV. Hypoglossal nerve stimulation in three adults with down syndrome and severe obstructive sleep apnea. The Laryngoscope. 2019;129:E402-E406. https://doi.org/10.1002/lary.27723
27. Sultana R et al. The Case for Early Use of Glucagon-like Peptide-1 Receptor Agonists in Obstructive Sleep Apnea Patients with Comorbid Diabetes and Metabolic Syndrome. Life (Basel) 2022;12(8) https://doi.org/10.3390/life12081222
28. NICE. Available from: https://cks.nice.org.uk/topics/insomnia/.
29. Pigeon WR. Treatment of adult insomnia with cognitive-behavioral therapy. J Clin Psychol. 2010;66(11):1148-60. https://doi.org/10.1002/jclp.20737
30. Braam, W., et al., Exogenous melatonin for sleep problems in individuals with intellectual disability: a meta-analysis. Dev Med Child Neurol. 2009;51(5):340-9. https://doi.org/10.1111/j.1469-8749.2008.03244.x
31. Wilson SAK, Baldwin D, Dijk DJ, Espie A, Espie C, Gringras P, Krystal A, Nutt D, Selsick H, Sharpley A. British Association for Psychopharmacology consensus statement on evidence-based treatment of insomnia, parasomnias and circadian rhythm disorders: An update. J Psychopharmacol. 2019;33(8):923-947. https://doi.org/10.1177/0269881119855343
32. RCPsych. Available from: https://www.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/college-reports/college-report-cr230--attention-deficit-hyperactivity-disorder-(adhd)-in-adults-with-intellectual-disability.pdf.
33. O'Regan, D, Anderson KN. Restless legs syndrome and periodic limb movements of sleep. Br J Hosp Med (Lond). 2020;81(1):1-8. https://doi.org/10.12968/hmed.2019.0319
34. Cortese S, et al. Restless legs syndrome and attention-deficit/hyperactivity disorder: a review of the literature. Sleep. 2005;28(8):1007-13. https://doi.org/10.1093/sleep/28.8.1007
35. Skomro RP, et al. Sleep complaints and restless legs syndrome in adult type 2 diabetics. Sleep Med. 2001;2(5): 417-22. https://doi.org/10.1016/S1389-9457(01)00110-1
36. Luzzani S, et al. Gastroesophageal reflux and Cornelia de Lange syndrome:typical and atypical symptoms. Am J Med Genet A. 2003;119A(3):283-7. https://doi.org/10.1002/ajmg.a.20191
37. Jean O'Hara, Nick Bouras JM. Intellectual disability and ill-health. In Intellectual Disability and Ill Health: A Review of the Evidence (pp. I-Ii). 2010.
38. Hall SS, et al. Health and sleep problems in Cornelia de Lange Syndrome: a case control study. J Intellect Disabil Res. 2008;52(Pt 5):458-68. https://doi.org/10.1111/j.1365-2788.2008.01047.x
39. Singh DP, Jamil RT, Mahajan K. Nocturnal Cough, in StatPearls. 2023: Treasure Island (FL).
40. Quotes. Available from: https://quotefancy.com/quote/1428622/Robert-Sternberg-So-for-example-if-a-child-is-labeled-as-having-a-learning-disability-it

Rachael Hansford, Publisher

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Time Shelter: Reminiscence therapy for dementia

Author: Georgi Gospodinov (author), Angela Rodel (translator).
Published by: Weidenfeld Nicolson (UK), Liveright (US).
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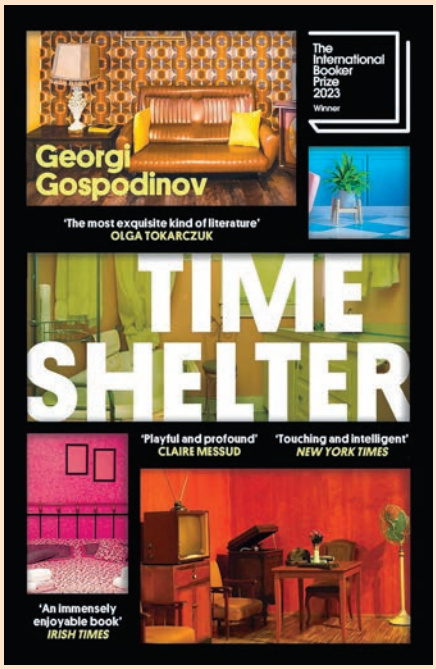

In his novel the Time Shelter, the Bulgarian writer Georgi Gospodinov touches upon the unforeseen consequences of recreating the past for treating people with Alzheimer's disease. This book won the International Booker Prize, the most prestigious award for fiction translated into English, for the year 2023. Leïla Slimani, Chairperson of the judging panel, said that "Time Shelter" made the judges question "the way in which our memory is the cement of our identity."

The protagonist of the novel, Gaustine, established a Time Shelter for people with dementia. Each floor was an exact replica of a past decade. Everything from wallpaper to toilet roll was replicated from the decade. The radios played music and songs from that time, newspapers carried the same news, printed in the same style and same quality of paper as in the past. The staff wore dresses and uniforms mirroring the fashion of that time. The eighties floor had a 'Berlin wall' between the east and west wings, with staff in military uniform patrolling the borders. The enterprise was so successful that the people without dementia started frequenting it. The craving for nostalgia seeped out of the clinic and into society. The novel chronicles the march of Europe towards a dystopia of the past, with all its prejudices, divisions, and unfortunately predictable consequences.

Gospodinov's characters include those who are marooned in islands of memory, professionals trying to help them and entrepreneurs and politicians looking to profiteer from nostalgia. The retired secret service agent who helped his former victim by sharing reminiscences, the mothers-in law who reacquainted themselves every single day, the long distance runner who wanted to save John Lennon from his impending murder, and the man who forgot his past, but not his fantasies are all part of Gaustine's Time Shelter. The staff concerned about the impact of recalled memories on people with dementia, the businessperson who made it rich by staging real life re-enactment of the past and the politicians across the spectrum of ideologies looking to turn unrestrained nostalgia into votes, are all a part of this rich tapestry woven by Gospodinov. The loss of memory and longing for an idyllic past is a combustible mix. The book chronicles the pernicious effect of mass nostalgia.

Time Shelter reminded me of that timeless neurology classic by Oliver Sacks, 'The man who mistook his wife for a hat.' As with Oliver Sacks' patients, the characters of the Time Shelter will find resonance in memories of people struggling with memory loss. The Time Shelter reminds us that the memory loss in dementia is not an orderly retreat, but a chaotic and confusing process. Gospodinov tackles the dark theme of loss of memory and personal identity using an engaging light-hearted style while treating his characters with dementia with sensitivity and respect.

Gaustine's time shelter is a fictional form of reminiscence therapy, introduced to dementia care in the late 1970s. Reminiscence therapy involves discussion of the past, with the help of props like photographs, music, sound recordings, letters, books, and familiar articles. A Cochrane review concluded that '…. reminiscence therapy can improve outcomes for people with dementia, its effects are inconsistent, often small and can differ considerably across settings and modalities [1]. The effect of recalled memories on Gospodinov's characters are also different. Occasionally, the surroundings did evoke unpleasant memories, as in the tale a holocaust survivor who cringed at the sight of showers. During reminiscence therapy participants could get upset. The Cochrane review concluded that such events are rare. Even though infrequent, these recollections could be distressing and sometimes catastrophic [1]. Trials of reminiscence therapy in dementia should have protocols that address such catastrophic events.

Reference

1. Woods B, O'Philbin L, FarrellEM, Spector AE, Orrell M. Reminiscence therapy for dementia. Cochrane Database of Systematic Reviews 2018, Issue 3. Art. No.: CD001120. https://doi.org/10.1002/14651858.CD001120.pub3

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Voluntary saccadic oscillations resembling opsoclonus (saccadomania)

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Introduction

Saccadic oscillations are instabilities of visual fixation which may take several forms. These are generally involuntary in nature and often pathological with localising value as part of the neurological examination [1]. Saccadic oscillations are often categorised according to whether or not there is an intersaccadic interval, present in square wave jerks and macrosquare wave jerks but absent in ocular flutter and opsoclonus (saccadomania). Such movements may be a consequence of structural, inflammatory, or paraneoplastic disease affecting the brainstem and/or cerebellum, hence require investigation.

Sometimes saccadic oscillations may be under voluntary control in the absence of brainstem or other pathology. For example, "voluntary nystagmus" describes brief (few seconds) bursts of high frequency (ca. 25Hz) low amplitude (ca. 1 degree) conjugate horizontal oscillations of back-to-back saccades, often induced by a vergence effort (i.e. these are saccades, not nystagmus, as there is no slow phase). Voluntary nystagmus, also known as voluntary flutter or psychogenic flutter, may in fact be a common, but easily overlooked, phenomenon [2,3]. In contrast, only occasional reports of voluntary saccadic oscillations resembling opsoclonus have appeared.

A further example of voluntary multidirectional saccadic oscillations of high amplitude and low frequency, resembling opsoclonus rather than voluntary nystagmus, is presented.

Case Description

The subject came to neurological attention purely by chance (social acquaintance) and hence only a clinical assessment could be made.

From his primary school years he had been able voluntarily to jiggle his eyes ("googly eyes") but thought nothing of it until a school friend commented, having thought these movements were simply normal and that everyone could make them. However, no family members were known to be able to make similar eye movements. He intuited no particular method or technique to make the movements, and did not feel they were effortful, although he had never tested for how long they could be sustained. He required glasses from his early years but the eye movements were never noted at eye examinations. They were associated with oscillopsia. There was no history of prior brain injury or infection.

Video recording clearly showed large amplitude low frequency multidirectional saccadic oscillations resembling opsoclonus. As the movements were not confined to the horizontal plane, a diagnosis of ocular flutter was not appropriate. In the absence of technical equipment (electro-oculography) it could not be said whether or not there was an intersaccadic interval. (You can view the recording by visiting the ACNR website: acnr.co.uk/case-report/voluntary-saccadic-oscillations-resembling-opsoclonus-saccadomania/).

Discussion

In 1994, Yee et al. described two subjects in whom saccadic oscillations resembling ocular flutter and opsoclonus appeared to be under voluntary control. These oscillations had horizontal, vertical and oblique or torsional components. Unlike voluntary nystagmus, these eye movements were capable of being sustained, sometimes for minutes, and were of low frequency (<10Hz) and high amplitude (up to 40 degrees) [4].

The individual reported here evidently had voluntary saccadic oscillations which could be produced on request, occurring in the absence of any underlying neurological or ophthalmological disorder. Although in the absence of technical equipment to assess presence or absence of intersaccadic intervals it cannot definitively be confirmed whether or not these movements are opsoclonus, they certainly resemble such movements in their directionality, amplitude, and frequency. These oscillations are evidently different from the high frequency small amplitude movements characterised as "voluntary nystagmus".

The prevalence of the ability to generate voluntary saccadic oscillations of this type is unknown, but other cases may be found which are not mentioned in the medical literature. For example, a well-known Spanish singer and actress of the 1960s-1980s, Marujita Díaz (1932-2015), was noted for her ability to make such voluntary eye movements (videos may be found on YouTube) which, after her death, were suggested to be nystagmus [5].

In the discussion of their Patient 1, Yee et al. stated that "when saccadic oscillations similar to ocular flutter and opsoclonus are found in patients who do not have other neurologic signs and symptoms, the possibility of a non-organic cause should be considered" [4]. This recom-

mendation may have been prompted by their suspicion that this patient, who had been referred to a neurology unit for clinical assessment following head trauma (a minor car accident resulting in shunt and whiplash), was making the eye movements intentionally. Additionally, they may have been prompted to this view by the previous characterisation of voluntary nystagmus as "psychogenic flutter". When such patients are referred for assessment they require further evaluation (neuroimaging, psychological) as voluntary saccadic oscillations in this setting is a diagnosis of exclusion.

The current case description, in contrast to the patient of Yee et al., suggests that there is not necessarily anything "psychogenic" or "non-organic" about voluntary saccadic oscillations resembling opsoclonus (unless all our voluntary actions be deemed as such!) when observed in some members of the normal population. Hence evaluation for psychopathology is not necessarily indicated in community members who can demonstrate this "skill" for entertainment.

The mechanism of voluntary saccadic oscillation of this type, resembling opsoclonus, is unknown. It might relate to an ability to suppress voluntarily the brainstem omnipause neurones in the pontine nucleus raphe interpositus which inhibit saccades, such that groups of burst neurones in the paramedian pontine reticular formation, normally inhibited by omnipause neurones, are activated, this being one of the mechanisms thought to underpin opsoclonus [6]. Positive feedback in the synaptic connections of burst neurones might also play a role [7]. It does not appear to be a "normal intrinsic capability" as proposed for voluntary nystagmus [2]. What evolutionary advantage, if any, that the ability to generate saccadic oscillations voluntarily provides is not apparent, but as a "party trick" it is certainly diverting and attention grabbing.

References

1. Brazis PW, Masdeu JC, Biller J. Localization in clinical neurology (5th edition). Philadelphia: Lippincott Williams and Wilkins, 2007:233-245.
2. Hotson JR. Convergence-initiated voluntary flutter: a normal intrinsic capability in man. Brain Res 1984;294:299-304. https://doi.org/10.1016/0006-8993(84)91041-2
3. Leigh RJ, Zee DS. The neurology of eye movements (4th edition). New York: Oxford University Press, 2006:526-527.
4. Yee RD, Spiegel PH, Yamada T, Abel LA, Suzuki DA, Zee DS. Voluntary saccadic oscillations, resembling ocular flutter and opsoclonus. J Neuroophthalmol 1994;14:95-101. https://doi.org/10.1097/00041327-199406000-00009
5. https://verne.elpais.com/verne/2015/06/23/articulo/1435065255_114550.html (accessed 05/07/2023).
6. Zee DS, Robinson DA. A hypothetical explanation of saccadic oscillations. Ann Neurol 1979;5:405-414. https://doi.org/10.1002/ana.410050502
7. Ramat S, Leigh RJ, Zee DS, Optican LM. Ocular oscillations generated by coupling of brainstem excitatory and inhibitory saccadic burst neurons. Exp Brain Res. 2005;160:89-106. https://doi.org/10.1007/s00221-004-1989-8.

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Democratising access to dementia research

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Abstract
As the UK population ages, dementia affects an increasing proportion of the population. There is a drive to accelerate dementia research, however access to research is not equitably distributed. We examine access to dementia research and discuss some enabling factors and barriers. High recruitment is frequently driven by a person (or people) dedicated to improving research participation. Barriers are commonly structural, rather than lack of willingness or knowledge. A recurring issue was lack of time and/or resources. Leveraging existing infrastructure, such as streamlined and efficient governance frameworks, is a clear part of the solution. Research teams need to ensure inclusion/exclusion criteria serve the target population, and that any intervention is accessible to a range of patients. An injection of resources is crucial to support the recruitment process on the ground.

Background:
The current environment

As the UK population ages, cognitive impairment and dementia affect an increasing proportion of the population. Over 900,000 people live with dementia in the UK; this is expected to increase to >1 million by 2030 [1]. The economic cost of dementia is estimated to triple by 2040 [2]. In response, there has been a drive to accelerate dementia research [3], however, in common with NHS service provision, access is not equitably distributed [4].

Patients living in areas with high socioeconomic deprivation and those from minoritised ethnic groups are less likely to be able to access dementia research. This means that current dementia research, which directs clinical practice, is only really applicable to people of White ethnicity and higher socioeconomic status. However, people living in areas of socioeconomic deprivation have a markedly higher risk of dying with dementia [5] and ethnicity substantially contributes to dementia risk [6] alongside other factors in the recent Lancet commission report [7]. A frequent lack of focus on inclusion of underserved groups has led to a scotoma in knowledge around dementia [8]; the impact of potential interventions on people from underserved groups remains unknown. Understanding the causes, presentations, drivers and modifiers of dementia, along with understanding the impact of interventions in all people with dementia is crucial.

Alongside this, there are key benefits to being treated in a service with an embedded research culture and as well as actively taking part in research. Access to clinical trials of potential disease modifying therapies is the tip of the

Table 1: Recruitment to NIHR portfolio studies by CMHT

	Financial Year															
Name of Trust, population	**2014-15**		**2015-16**		**2016-17**		**2017-18**		**2018-19**		**2019-20**		**2020-21**		**2021-22***	
	S	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**
NELFT (c 4.3 million)	3	19	9	246	12	799	13	396	82	279	10	82	51	98	51	62
EPUT (c 2.5 million)	3	19	_	_	_	_	9	150	6	48	7	110	3	10	5	191
ELFT (c 1.4 million)	3	121	4	125	_	_	_	_	1	<5	_	_	2	11	1	15
BEH (c 1.2 million)	4	52	4	20	2	28	4	36	7	44	5	36	4	24	3	28
C&I (c 0.5 million)	6	1694	6	387	7	955	9	672	14	248	9	192	5	54	4	96

* to end March 2022 S=number of studies; R=absolute number of patients recruited.

Table 1: Recruitment to NIHR portfolio studies by CMHT. CMHTs are ordered by size, from largest to smallest population size. The COVID-19 pandemic placed restrictions on study recruitment from the start of financial year 2020-21. NIHR, National Institute for Health and Care Research, CMHT, community mental health trust; NELFT, North East London NHS Foundation Trust; EPUT, Essex Partnership University NHS Foundation Trust; ELFT, East London NHS Foundation Trust; BEH, Barnet, Enfield and Haringey Mental Health Trust; C&I, Camden and Islington NHS Foundation Trust.

iceberg. The opportunity to participate in research is an important aspect of care for people living with dementia and provides an opportunity to take control of their condition and a sense of empowerment.

University College London Partners (UCLP) is a partnership that aims to accelerate research and inject innovation into NHS clinical practice. It brings together eight universities, including UCL and Queen Mary University London (QMUL), with NHS Trusts across the South East to a population of 6 million across 26 boroughs. It encompasses a large geographic area from inner city London to coastal Essex, covering five community mental health Trusts (CMHTs) providing memory and dementia services. Mental health Trusts within UCLP deliver services across a range of clinical commissioning groups, serving highly contrasting populations. These include some of the most deprived regions of the country, such as Tower Hamlets, City and Hackney, and Newham, ranked 13th, 15th and 24th in the UK for deprivation. While London has the youngest population nationally, Trusts towards the east of UCLP serve some of the oldest populations around London: Southend-on-Sea, Castlepoint and Rochford, all have a median age above the national average of 40.3 years at 41.8 years, 46.9 years and 46.2 years respectively [9]. Some Trusts serve populations with particularly high proportions from Black, Asian and Mixed ethnicities (see Office for National Statistics Census Maps). It is important to note that NIHR systems used to record and report research participants do not routinely capture ethnicity or deprivation. There is a move to mandate reporting of these data in the foreseeable future. However data flows, security and reporting mechanisms for this sensitive data at provider level are still being established.

Access to dementia research across UCLP

We sought to understand recruitment to dementia research studies and trials across Trusts within UCLP. Recruitment data demonstrated wide variation in recruitment to NIHR portfolio registered clinical studies (Table 1). These differences become starker when considered in the context of population size, with some of the most successful recruiting Trusts serving the smallest populations. This variation has persisted for a number of years. Although recruitment across all Trusts decreased during the COVID-19 pandemic, high performing Trusts are already showing signs of recovery.

These data include only NIHR portfolio studies; however, these make up the majority of studies within most Trusts. They are not limited to clinical trials (CTIMPS). Fully interventional studies make up around 25% of the total recruited in each Trust; with no substantial variation in proportion of interventional vs non-interventional recruitment between Trusts.

Understanding the underlying drivers of variation

In order to address this variation and achieve equitable research access, potential reasons for differential participation across Trusts must be understood. In order to scope potential solutions, we undertook focused discussions with clinicians, research managers and service leaders at different levels of seniority at a range of services within UCLP Trusts. We focused on professional groups in order to understand variation in research delivery, as this is an early determinant of unequal access to, and hence participation in, research. As this was a scoping exercise focused on understanding potential barriers and solutions, these discussions were not formally analysed, rather they were used to inform the opinions laid out in this paper.

It is vital to note that addressing barriers to research recruitment requires partnership with underserved communities throughout the research lifecycle, from inception to delivery

> *The opportunity to participate in research is an important aspect of care for people living with dementia and provides an opportunity to take control of their condition and a sense of empowerment.*

and interpretation, in order to design relevant interventions that overcome community-specific barriers. There is no "one size fits all", and interventions need to be targeted at particular services, or even groups within services in order to be successful.

Enabling factors

In Trusts with high levels of recruitment, there was frequently a person (or people) dedicated to improving research participation. This was either someone directly involved in research programmes, or a person employed for the specific purpose of improving research recruitment. This person was present in clinical environments within the Trust, and usually attended regular clinical meetings.

Successful sites were able to leverage "easy to recruit" studies in order to boost recruitment numbers, and potentially drive resources to sites ("success builds success"). Such studies are often observational, with minimal burden on clinical teams, and generally involve minimal follow-up or intervention. Where visits were required as part of the research process, they would be at times/places convenient to service users. Key infrastructure included "on the ground" factors such as research studies being discussed as a routine and regular part of clinical practice.

Deeper enabling infrastructure elements were a streamlined governance structure across multiple sites. Noclor, a research support service for mental health, community health and primary care, provides a streamlined research governance and facilitation structure across multiple CMHTs. Within East London NHS Foundation Trust (ELFT) a single governance structure allows studies to receive approval across all services within the Trust without the need for site-level agreements. A potential downside is that studies could be adopted without PI engagement, however the clear benefits afforded by the more efficient governance were widely appreciated. We also noted the potential for a virtuous cycle of grant funding and associated metrics flowing to sites as they become more successful.

Barriers

Barriers were in the main structural, rather than lack of willingness or knowledge. A recurring issue was lack of time and/or resources. In several Trusts, clinical workload meant insufficient time to allow recruitment to studies to be prioritised in any meaningful way. This was coupled with a lack of infrastructure to support recruitment, such as dedicated research staff and/or clinical academics.

At some sites, resource limitation within clinical services, such as inadequate access to imaging for NICE-required standards of dementia diagnosis, meant only a limited number of patients could meet inclusion criteria. Furthermore, the risk of dementia increases with age, and where studies have an upper age limit within inclusion criteria, this can exclude substantial proportions of patients, and subsequently limits applicability of results. Frailty, which is strongly associated with dementia, can limit ability to take part in research studies requiring in person visits. It was also reported that recruitment materials for some studies were inappropriate. Lack of availability of information sheets in languages other than English meant that large numbers of patients were excluded based on language and literacy.

Some more general barriers were an artificial division between mental health and dementia research and a relative lack of institutional experience in the research process leading to time-consuming processes in getting research studies set up. Notably, across different Trusts and levels of service delivery, lack of training or understanding of research was not perceived to be a barrier to research engagement and recruitment.

How can research involvement be improved across Trusts?

Any intervention needs to address the issues highlighted above, rather than further stretching or dividing services. Service benefits from research take time to accrue, thus enabling interventions need to have rapid impact to produce tangible benefit for people living with dementia and their clinicians. Leveraging existing infrastructure is a clear part of the solution alongside learning from high-performing sites, so that excellence can be emulated.

Better engagement of under-represented groups can also be achieved through infrastructures such as the NIHR Clinical Research Networks (changed to NIHR Research Delivery Networks from April 2024) which coordinate high-quality research through support to research sites. A particular aim of the new NIHR Regional Research Delivery Network is to bring research to under-served regions and communities.

Importantly, more general uptake in dementia research participation will lead to increased recruitment amongst under-served groups. However, to specifically improve equity of access for underserved groups, there is a need for targeted strategies, as highlighted in the recent NIHR-INCLUDE roadmap [8]. These need to be considered by funders and reviewers, in addition to researchers and delivery teams within Trusts. Research teams need to ensure their inclusion/exclusion criteria serve the target population; and that any intervention is accessible to the range of patients in their population. Funders and reviewers should ensure that study outcomes are of relevance to the population being studied; and most important for improving democratisation to research: delivery teams need to identify the under-served groups within their delivery areas (or Trust) as well as the specific barriers to including these groups. It is vital to specifically involve patients from under-served groups in planning potential solutions to widen their participation.

Conclusion

In order to trigger a step-change in study participation, and thus patient recruitment, an injection of resources is required, most likely in the form of delivery teams. These teams would ideally be supported via the CRN or other external infrastructure, to support the recruitment process on the ground. Given positive clinical trials of disease modifying therapies in dementia, there is the potential that services will undergo substantial and rapid change, which may bring opportunity for research delivery. However, the number of people eligible for any disease modifying therapy is likely to be a fraction of those living with dementia, which has the potential to drive further inequity. Should such therapies reach clinical practice, patient selection and treatment pathway will be via regional centres, probably led by or run jointly with neurology. There is a real risk that this further entrenches the division between relatively well-funded neurological research centres that operate in close proximity to major universities and community mental health units that do the majority of dementia diagnosis but are situated in community settings.

Equitable patient involvement in research does not just mean taking part in research. Involvement of representative populations throughout the research process is required to build trust; working in partnership with a

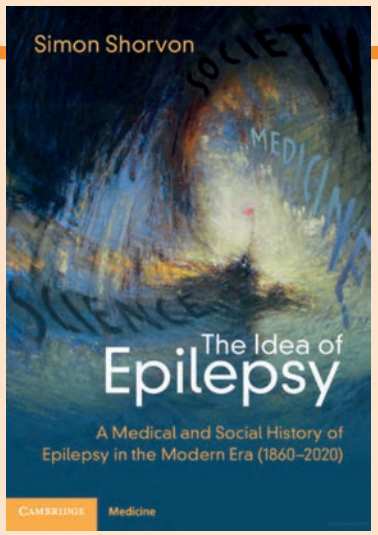
range of patient groups to ensure that research questions and approaches have relevance to all is crucial. Work to improve the cultural competence of researchers designing and setting up studies will ensure that approaches are grounded in meaningful dialogue with individuals and communities. Particular areas of need are around active recruitment to studies together with clinical follow-up, given currently overstretched clinical teams. Ideally, research teams would undergo training at well-performing sites, sharing established knowledge and patterns of effective recruitment strategies. Alongside this, support for new academic posts, research-active clinicians such as psychiatrists and associated healthcare professionals able to drive research and act as study principal investigators, as well as the environments and infrastructure to nurture them will provide an on-going source of potential research instigators.

Approaches such as this will lead to not only higher recruitment across geographical locations, and diverse populations, but will also translate into improved clinical outcomes, especially in under-served groups through more closely embedding research into clinical practice. It will allow clinicians and researchers working to improve access to research for all patients, and facilitate the study of dementia in people from all backgrounds.

References

1. Prevalence. Dementia Statistics Hub https://www.dementiastatistics.org/statistics-about-dementia/prevalence-2/ (2022).
2. England, NHS. NHS England » dementia. https://www.england.nhs.uk/mental-health/dementia/.
3. Challenge on dementia 2020:implementation plan. Gov.uk https://www.gov.uk/government/publications/challenge-on-dementia-2020-implementation-plan (2016).
4. Toh C-H. Enabling an equitable spread of research access, involvement, and funding in the UK. Lancet 2019;394:2048-2050. https://doi.org/10.1016/S0140-6736(19)32685-6
5. Jitlal M et al. The Influence of Socioeconomic Deprivation on Dementia Mortality, Age at Death, and Quality of Diagnosis: A Nationwide Death Records Study in England and Wales 2001-2017. J. Alzheimers. Dis. 2021;81:321-328. https://doi.org/10.3233/JAD-210089
6. Bothongo PLK et al. Dementia risk in a diverse population: A single-region nested case-control study in the East End of London. Lancet Reg Health Eur 15, 100321 (2022). https://doi.org/10.1016/j.lanepe.2022.100321
7. Livingston, G. et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. Lancet 2020;396:413-446. https://doi.org/10.1016/S0140-6736(20)30367-6
8. Improving inclusion of under-served groups in clinical research: Guidance from INCLUDE project. https://www.nihr.ac.uk/documents/improving-inclusion-of-under-served-groups-in-clinical-research-guidance-from-include-project/25435.
9. Subnational ageing tool. https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/ageing/articles/subnationalageingtool/2020-07-20 2020,

The Idea of Epilepsy: A Medical and Social History of Epilepsy in the Modern Era (1860–2020)



Author: Simon D Shorvon
Published by: Cambridge University Press
Price: £64.99
Pages: 750
ISBN: 978-1108842617
Reviewed by: Dr Ronan McGinty, ST in Neurology, Liverpool, UK.

Professor Shorvon's treatise on "the why" and "the what" of epilepsy is structured in three main sections – an introduction and prologue, a chronological history of epilepsy, and an epilogue with appendices, bibliography, glossary and index. He chronicles the modern era of epilepsy through the perspectives of science, medicine, society and the individual's experience of having epilepsy.

The meaty mid-section comprises of five chapters, each focusing on a particular epoch (1860-1914, 1914-1945, 1945-1970, 1970-1995 and 1995-2020). In meticulous detail and rich language, Shorvon traces the seismic shifts in the conceptualisation of epilepsy and how those with the condition have been regarded in the past 160 years.

He draws from an extensive bibliography, invoking Oswei Temkin, Blaise Pascal, Nikolaus Pevsner, George Orwell and Sherlock Holmes within the space of the first three pages. David Cobley's accompanying illustrations accentuate the bleakest facets of epilepsy and at times evoke visceral discomfort.

Most in the neurology community are aware of superstition-laced historical views of epilepsy and the appalling stigmatisation of the condition. Even so, it is jolting to read here of contagion, criminality, eugenics, institutionalisation, epilepsy colonies, marriage prohibition, sterilisation and euthanasia.

Shorvon summarises the radical advances in science and medicine that have enabled epilepsy to become better understood and managed, while highlighting some tragic mistakes and harms along the way. He details the evolution of epilepsy surgery and the development of anti-seizure medications and their use. He delves into the iterations of epilepsy classification and terminology, the realisation that there is not a simple mechanism to explain most cases of epilepsy, and the conceit of epilepsy as a network disorder. He takes stock of which developments have endured and which might yet disappear.

There is a vast amount of material presented, such as the first advertisement for phenytoin, an explanation of the quirky numbering system employed by Epilepsia, and the nugget that lamotrigine was initially developed on the erroneous assumption that it had anti-folate activity.

Notwithstanding the comprehensive glossary, some sections may not be readily accessible to lay readers. At times the text becomes saturated in minutiae and the narrative flow slows. The conscious omission of the achievements of living people is, in part, understandable although results in some conspicuous gaps. The author's passion for and knowledge of the field is evident throughout. Overall, this is an engaging history of epilepsy – an entity that is complex and fascinating but which Shorvon suggests might not even exist…

Introduction

Stuart Viegas MBBS (Hons) DPhil FRCP, is Editor of ACNR's myasthenia gravis (MG) series. He is a Consultant Neurologist who leads the Imperial MG and muscle service, UK. He qualified from UCL medical school before training in Wessex and London. He did his research in MG in Oxford under the supervision of Professor Angela Vincent. He is involved in clinical research projects and continues to support MG patients through the Myaware charity.

I was delighted to be asked by ACNR'S editorial team to help bring a series of articles on myasthenia gravis (MG) to the wider neuroscience community. I hope that the experienced authors in the field will help cover a range of topics that its readers will find stimulating and educational, but most importantly clinically relevant.

Compared with many neurological conditions, MG is a relatively rare but important antibody mediated disease. It is one that all neurologists need to be familiar with. Prompt recognition of the cardinal symptoms - the characteristic pattern of fluctuation and variability should trigger urgent assessment and investigation in all suspected cases. Successful treatment with pyridostigmine, often with good symptomatic improvement, is something most patients will remember for many years.

Early identification of patients who will have a challenging or refractory disease course and the need for further treatment remains a challenge. MG is heterogenous - with pure ocular and generalised cases; the latter ranging from minimal manifestations to life-threating complications. Myasthenic crises are a neurological emergency requiring multidisciplinary input and early involvement of our intensive care colleagues. Timely recognition, good supportive care and effective treatment with plasma exchange and/or intravenous immunoglobulin has led to a significant reduction in mortality across all age groups. Seeing patients responding to such treatment is incredibly rewarding for the treating physician and helps consolidate the doctor-patient relationship.

Our increased understanding of the physiological disturbances and immune mediated mechanisms underlying MG has led to the developments of improved antibody assays, neurophysiology techniques and chest imaging that is critical for ensuring accurate diagnosis. Treatment regimes based around pyridostigmine, corticosteroids, steroid sparing drugs, thymectomy and the emergency treatments outlined above have been used for many years.

The ABN guidelines published in 2015 aimed to disseminate the knowledge and experience of specialists in the field to the wider neurology community and were well received. Reflecting the clinical heterogeneity, the response to standard treatment is also highly variable. The antibody subtypes may respond to different therapies and this information, together with age and comorbidities, influences treatment selection.

In contrast with other neuroimmunological disorders such as multiple sclerosis, there has been a paucity of new treatments until the last few years. Novel biological therapies targeting B cells, T cells and complement pathways have since been developed, trialled and now introduced into clinical practice which makes it an exciting time to be working in the field.

Given the changing landscape with respect to MG treatments, we will start the series with Dr Jennifer Spillane and her overview of the new drugs that have arrived, those on the horizon and those still in the research arena. MG, like many autoimmune disorders, often affects young women and its management in pregnancy warrants special attention. In the second article Dr Georgina Burke will discuss pre-conception planning, antenatal and postnatal care which requires close multidisciplinary liaison with our obstetric medicine and anaesthetic colleagues.

Whilst the incidence of MG in young women has remained static for many years, there is an increasing number of older onset cases, often with a male predominance. Older onset patients with their co-morbidities and polypharmacy require a different management approach. Furthermore, the younger onset patients get older and may also have been exposed to long term immunosuppression and corticosteroid use. Associate Professor Isabel Leite will outline the management of this important patient cohort further in the third article.

Finally, all neurologists looking after MG patients should be aware of some important cardiothoracic and oncological issues relating to the thymus and thymic malignancy which will be described further by Mr Dio Stavroulias and Dr Joanne Evans in the concluding article.

Conflict of Interest Statement: Stuart Viegas is married to Ann Donnelly, the Co-Editor of ACNR. This article has been subject to our normal peer review process, being peer reviewed by two expert, external reviewers prior to acceptance by Todd Hardy, Co-Editor of ACNR.

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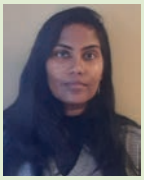

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Myasthenia Gravis – a new era of treatment options

Abstract
Myasthenia Gravis (MG) is an autoimmune disease of the neuromuscular junction that causes fluctuating fatigable neuromuscular weakness. The spectrum of severity ranges from mild intermittent ptosis to respiratory failure requiring ventilatory support.

There are various treatment options. Pyridostigmine is the first line treatment but provides symptomatic relief only. The mainstay of treatment rests on immunosuppression using corticosteroids and non-specific immunosuppressant agents such as azathioprine, mycophenolate mofetil and methotrexate. Intravenous immunoglobulin and plasma exchange are generally reserved for acute severe exacerbations. Thymectomy is also an option for some patients.

Although a large proportion of patients with MG achieve disease control with these treatments, others have refractory disease with ongoing symptoms, frequent exacerbations and dependence on rescue therapies. Other patients are exposed to long term high dose steroids.

Increased understanding of the pathogenesis of MG has led to the development of newer agents with a more specific mechanism of action and a rapid onset of effect. These novel targets include B cells, the complement cascade and the neonatal Fc receptor. Other potential targets include cell surface receptors, chemokines and cytokines.

In this paper we review the evidence for these newer therapies and discuss where they may fit into the treatment paradigm for patients with MG.

Introduction

Myasthenia Gravis (MG) is the archetypical neurological autoimmune disease, characterised by fluctuating fatigable weakness. Although 80% of patients present with ocular symptoms, most will go on to develop generalised disease with a 10-15% lifetime risk of Myasthenic Crisis. The epidemiology of MG is interesting with a bimodal peak-one peak in early adulthood and a second peak in older age.

80% of patients with MG have antibodies to the acetylcholine receptor (AChR). These antibodies are divalent and are of the IgG1 and IgG3 subtypes. They exert their effect by three different mechanisms: cross-linking and internalisation of AChRs, activation of complement leading to formation of the membrane attack complex and subsequent damage to the neuromuscular junction, and functional block of AChRs.

Whilst 15-20% of patients with AChR MG have a thymoma, the thymus in younger patients with AChR antibody positive MG tends to be hyperplastic and infiltrated with inflammatory cells.

Approximately 5-10% of patients with MG have antibodies to Muscle Specific Tyrosine Kinase (MuSK), an important post-synaptic clustering protein. In contrast to AChR antibody positive MG, MuSK antibodies are of the IgG4 subtype, are not divalent and do not activate complement. Antibodies against LRP-4, another post-synaptic protein, are detected in a small number of patients with MG.

The remaining 10% of patients do not have antibodies detectable by conventional assays and are termed seronegative. However about 30% of this cohort will have antibodies to AChRs detected using a more specific cell-based assay [1]. If an antibody is present, it's important to detect it - not only to confirm the diagnosis but also to guide treatment as we enter an era of more targeted specific management.

Current Treatment

The treatment of MG can be thought of as symptomatic, immunosuppressant or immunomodulatory.

Pyridostigmine, an acetylcholinesterase inhibitor is still the first line treatment for most patients with MG. It provides symptomatic relief in a proportion of patients but has no disease modifying effect.

Thymectomy has been used for the management of MG since the 1930s. It is almost always indicated for patients with thymoma, and a randomised controlled trial showed that patients with non-thymomatous MG under the age of 65 had better MG control with lower steroid dose following thymectomy [2]. It is not thought to benefit patients with MuSK antibody-positive MG.

IVIg and plasma exchange are generally reserved for patients with acute deteriorations though a minority of patients remain dependent on these treatments in the longer term.

The management of MG however largely rests on non-specific broad-spectrum immunosuppression using steroids and a range of non-steroidal immunosuppressant agents such as azathioprine, mycophenolate and methotrexate with others, such as ciclosporin and tacrolimus used less frequently. Non-steroidal therapies often have a slow onset of action, and patients can therefore be exposed to high dose steroids for many months before symptoms come under control.

Although symptoms in most MG patients are eventually adequately controlled on the current available therapies, over 10% of patients are refractory [3] and real world studies show that over 40% of patients have unacceptable disease control as measured by a Myasthenia Gravis Activities of Daily Living (MG ADL) score greater than three [4].

There has therefore been a longstanding need for specific, targeted treatments that are more efficacious, with a faster onset of action. Advances in the understanding of the pathogenesis of MG have unveiled a number of new treatment targets which have the potential to herald a new era for the management of patients with MG.

Alternative Approaches

MG is a T cell dependent, B cell mediated auto-immune disease and there are various targets that could be explored to develop treatments for MG.

For the purposes of this review we will focus on the treatments that are either in regular clinical use or are close to clinical use – namely B cell depleting therapy, complement inhibition, and inhibition of IgG recycling by targeting the neonatal Fc receptor.

Anti B cell therapy

Inhibiting the antibody producing B cells is a rational approach to treating antibody mediated autoimmune disease. Rituximab is humanised anti-CD20 monoclonal antibody that depletes memory B cells but not long-lived plasma cells. There have been retrospective observational and single armed reports regarding the use of Rituximab in MG for many years, as well as systematic reviews and meta-analyses that have suggested a positive effect in MG [5]. It was therefore disappointing that a randomised placebo-controlled Phase II trial investigating the steroid-sparing effect of Rituximab was negative in 2021 [6]. Analysing this trial, a number of features stand out: there was a high placebo effect, the steroid dose was low at 20mg, meaning that a change could not be easily detected and a significant proportion of the patients had relatively mild disease. The efficacy of Rituximab in generalised AChR MG therefore remains uncertain. One possibility is that Rituximab is more effective in recent onset MG as was suggested in the recent RINOMAX trial. This blinded placebo-controlled study examined the use of low dose Rituximab in a cohort of patients with newly diagnosed MG and found that Rituximab treatment resulted in a higher proportion reaching minimal manifestations at 16 weeks with less requirement for rescue treatment [7]. Further follow up is required to see the longer-term outcome in this cohort.

Given the disappointing results of Rituximab

particularly in refractory AChR MG, there has been a search for other B Cell depleting agents that may act against long lived plasma cells. A Phase 3 trial is currently underway into Inebilizumab, a humanised monoclonal antibody against CD19 which in contrast to Rituximab depletes a wide range of B cells including plasma cells and plasmablasts (NCT04524273).

In contrast to AChR MG, Rituximab has been shown to be very effective in MuSK MG with a blinded multi centre prospective review showing a statistically significant impact on steroid usage and MG symptoms [8].

Complement inhibition

The classical complement pathway is implicated in the pathogenesis of AChR MG: formation of the membrane attack complex leads to destruction of the neuromuscular end-plate. Targeting complement is therefore a potential treatment to mitigate the pathogenic effects of AChR antibodies in MG.

Eculizumab, a humanised anti-C5 monoclonal antibody was the first complement inhibitor trialled in MG and examined its efficacy in patients with refractory generalised MG – the primary endpoint of improvement in ADL compared to placebo was not met but secondary endpoints of significant improvements in ADL and QMG were and open label extension data were encouraging [9].

Having shown that complement inhibition might be effective in MG – investigators subsequently sought to develop more convenient routes of administration as the requirement for fortnightly IV infusions of Eculizumb have limited its more widespread use.

Ravulizumab is a C5-inhibitor that hasbeen engineered to have an extended half-life and is given as an IV infusion every 8 weeks. The CHAMPION trial met its primary endpoint; Ravulizumab treated patients had improvement in their MG ADL score at 26 weeks compared to standard care [10].

A further complement inhibitor is Zilucoplan, a 15 amino acid cyclic peptide that inhibits the complement cascade by binding to C5a and C5B with high affinity – it is given as a daily subcutaneous injection and its efficacy was established in the RAISE trial which showed a significant improvement MG ADL score at 12 weeks [11].

Both Eculizumab and Ravulizumab are approved by the FDA and the EMA. Eculizumab is approved but not reimbursed in the UK.

Other complement inhibitors are under investigation in Phase 2 or 3 trials including Pozelimab (usually given in combination with Cemdisiran which acts through RNA interference), Gefurlimab and Vemircopan (NCT05070858, NCT05556096, NCT05218096).

The onset of action in all complement inhibitor trials studied so far seems to be rapid. Overall, complement inhibition seems to be well tolerated though the route of administration – either IV or subcutaneous injection - may be a limiting factor for some patients. Complement inhibition is associated with a risk of Neisseria meningitides septicaemia, so all patients must be vaccinated accordingly.

Complement inhibition will be reserved for patients with AChR antibody positive disease – as previously discussed, the complement cascade is not implicated in the pathogenesis of MuSK MG.

Anti FcRN therapies

The neonatal FC receptor (FcRN) is widely distributed in many cells and has an important role in the recycling of IgG, thus prolonging its half-life.

Blocking of the FC receptor interferes with this recycling and reduces the plasma concentration of IgG. By reducing the level of IgG, the effect of the pathogenic AChR antibodies in MG can be reduced, and thus FcRN blocking can be thought of as similar to 'medical plasma exchange'. The serum levels of other immunoglobulins do not seem to be affected by FcRN inhibition,

Various FcRN blocking agents have been investigated or are currently undergoing Phase 3 trials for the treatment of generalised MG.

Efgartigimod is an engineered Fc fragment of human IgG1 that binds to FC receptors with greater affinity than human IgG, thus inhibiting its recycling.

The Phase 3 ADAPT study showed that Efgartigimod was effective in improving MG ADL scores compared to placebo [12]. It was given as a cyclical treatment – a weekly IV infusion for 4 weeks followed by a variable treatment schedule depending on symptom re-emergence.

Efgartigimod is licensed by the MHRA, EMA and FDA and has been available in the UK under an Early Access to Medicine Scheme since May 2022.

A subcutaneous version has just been licensed by the US and different dosing schedules are currently being investigated.

Rozanolixizumab is a high affinity humanised IgG4 monoclonal antibody against FcRn and is administered by weekly subcutaneous injection. The Phase 3 MyCarin study showed a significant improvement in Mg ADL scores, and in contrast to other FcRN treatments is currently approved in the UK and Europe for the treatment of both AChR and MuSK MG [13].

Other FcRN therapies – Batoclimab and Nicolimab are currently undergoing Phase III trials (NCT05403541, NCT04951622).

Anti-FcRN treatments tend to be well tolerated with minor infections and headache being the most reported side effects. In contrast to complement treatment, there is scientific rationale for FcRN use in MuSK positive MG. The onset of action of FcRN treatment is fast. Repeated dosing is necessary with an average inter-treatment interval of 7 weeks though some patients require more frequent treatment.

Other therapeutic targets

Cell-surface receptors, Cytokines & Chemokines

The signalling molecules that help in coordination of the immune response and upregulation of B and T cells are potential targets in MG.

CD40 is a molecule expressed on B cells and is important for differentiation and activation of memory B cells and through its interaction with CD154, is essential for T cell dependent antibody responses. Isacalimab is a monoclonal antibody that targets CD40 and is undergoing a phase II trial in MG currently (NCT0256576).

IL6 has a role in T and B cell signalling pathways and in the differentiation of B cells. Satralizumab has been successful in phase 3 trials for treatment of Neuromyelitis Optica Spectrum Disorder and currently is undergoing investigation for the treatment of MG (NCT04963270). Tocilizumab, which also inhibits IL6 signalling has been found to be beneficial in MG in case reports and a single arm open label study of six patients [14,15].

Bruton's Tyrosine Kinase (BTK) has a role in B cell proliferation and differentiation and is a potential target in MG. Tolebrutinib is an oral BTK inhibitor and has been studied in MS. However, a phase III study was suspended earlier this year because of hepatotoxicity.

Table 1. Newer therapies for MG that are currently available or have been through Phase III trials

Mode of action		Mode of administration	Frequency
Complement inhibition	Eculizumab	IV	2 weekly (following weekly induction dose for 4 weeks)
	Ravulizumab	IV	8 weekly following induction dose
	Zilucoplan	Subcutaneous	Daily
Anti FcRN	Efgartigimod	IV (subcutaneous version recently approved)	4 weekly cycles depending on clinical response
	Rozanolixizumab	Subcutaneous	6 weekly cycles
B cell	Rituximab	IV	6 monthly

B cell activating factor (BAFF) is upregulated in MG – Belimumab, an anti BAFF agent has been studied in Systemic Lupus Erythematosus but a phase 2 trial did not show any clear benefit for its use in MG [16].

Other potential targets include plasma cells with anti CD38 agents such as Daratumumab which is used in Myeloma, and cytokines that target T cell activation such as IL17, IL12 and IL23 but these have not been studied in MG in detail to date.

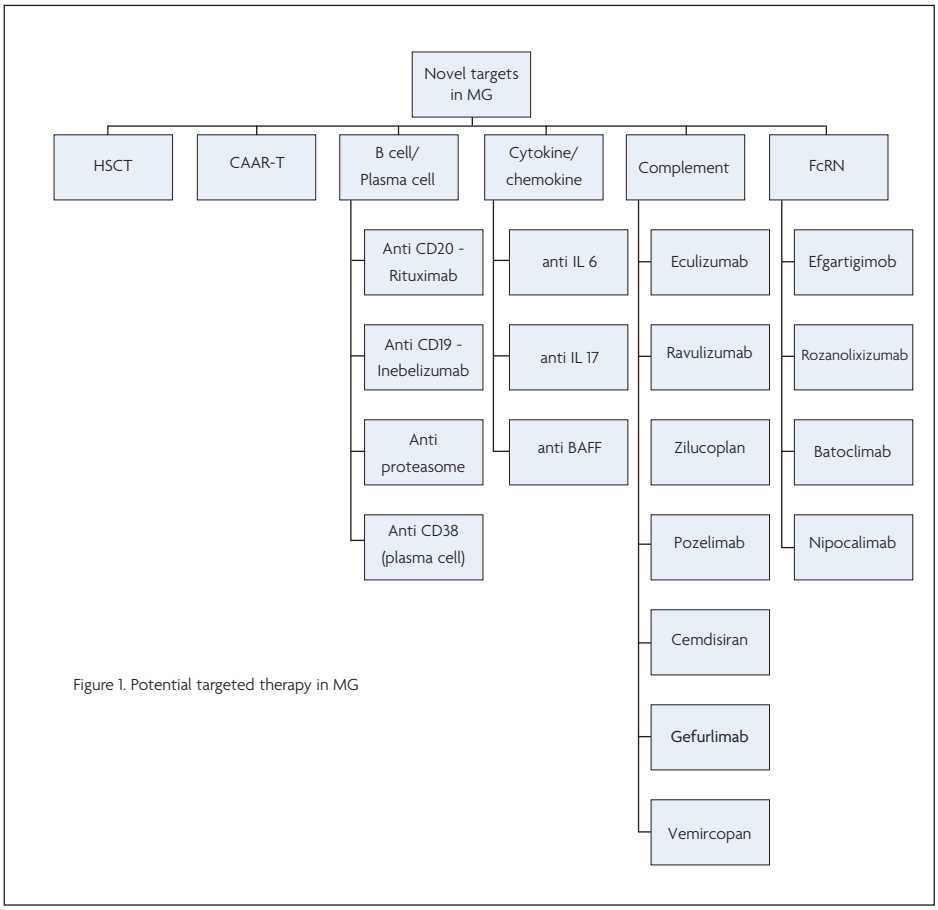

Figure 1. Potential targeted therapy in MG

Alternative strategies

CAR-T cell therapy

Chimeric antigen receptor (CAR) T cell therapy has shown remarkable efficacy in haematological malignancy in recent years.

CAR-T cell therapy could in principle be adapted for autoimmune diseases by using an engineered T cell which could bind to a pathogenic B cell, thus specifically targeting pathogenic cells – so called chimeric autoantibody receptor T Cell therapy.

Haematopoietic Stem cell transplant

'Resetting' of the immune system with haematopoietic stem transplantation has been investigated in several refractory autoimmune diseases. The process involves stimulation of haematopoietic stem cell production, cell harvesting followed by bone marrow ablation and reinfusion of the harvested cells. A retrospective case series reported remarkable benefit with patients having remission of their MG [17]. However, the potential for adverse events means that few patients have undergone this treatment.

Questions and future directions

The landscape of MG treatment is clearly changing. Rather than slow acting non-specific treatments we now have more defined targets for treatments with a faster onset of action. The agents described were mostly not trialled on selected refractory patients, so where these newer therapies should fit into the treatment paradigm amongst the familiar agents remains uncertain. Thus far they have been generally licensed as add on treatments, but how early they should be used and in what severity of MG is unknown. The considerable benefits in terms of efficacy, speed of onset, and reduction in steroid use must be balanced against their cost and the lack of long-term safety data.

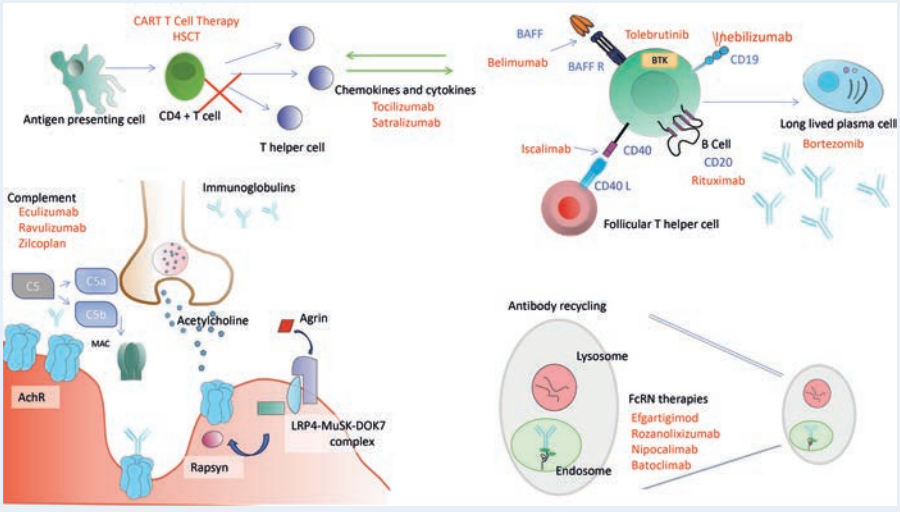

Figure 2. Schematic diagram depicting the site of action of novel Myasthenia Gravis treatments.

Top left - Antigen presenting cells interact with CD4 positive T cells which, under the influence of certain cytokines and other activating factors leads to B cell proliferation. B cells differentiate into antibody producing memory B cells and long lived plasma cells. This pathway can be targeted at different levels. Rituximab (anti CD20) and Inebilizumab (anti CD19) target B cells directly, Isacalimab blocks the CD40 signalling pathway which is important for differentiation and activation of memory B cells. Cytokines such as IL6 are important for B cell differentiation and T cell regulation. Tocilizumab and Satralizumab are anti IL6 monoclonal antibodies. Other targets such as B Cell activating factor (BAFF) or Bruton's Tyrosine Kinase (BK) with agents such as Belimumab and Tolebrutinib affect the B cell pathway indirectly. Bortezomib inhibits long lived plasma cells.

Bottom left - the neuromuscular junction (NMJ) and the clustering pathway of Acetylcholine receptors (AchRs). Agrin is secreted at the nerve terminal into the synaptic cleft. This interacts with the Muscle Specific Kinase (MuSK) – low density lipoprotein receptor-related protein 4 (LRP4) complex which is located on the post synaptic membrane which in turn activated Rapsyn.

Complement activation is an important pathogenic mechanism for IgG1 and IgG3 AChR antibodies. The conversion of C5 to C5a and C5b results in the formation of the membrane attack complex. Complement inhibitors such as Eculizumab, Ravulizumab and Zilcoplan interrupt this pathway.

Bottom left - IgG is recycled in the endosomal-lysosomal system. Binding of IgG to the FcrN protects it from lysosomal degradation. Anti FcRN therapies such as Efgartigimod, Rozanolixizumab, Nipocalimab and Batoclimab bind competitively to the FcRN thus preventing IgG recycling.

References

1. Damato V, Spagni G, Monte G, Woodhall M, Jacobson L, Falso S, Smith T, Iorio R, Waters P, Irani SR, Vincent A, Evoli A. Clinical value of cell-based assays in the characterisation of seronegative myasthenia gravis. J Neurol Neurosurg Psychiatry. 2022 Sep;93(9):995-1000. Epub 2022 Jul 14. PMID: 35835469. https://doi.org/10.1136/jnnp-2022-329284
2. Wolfe GI, Kaminski HJ, Aban IB, Minisman G, Kuo HC, Marx A, Ströbel P, Mazia C, Oger J, Cea JG, Heckmann JM, Evoli A, Nix W, Ciafaloni E, Antonini G, Witoonpanich R, King JO, Beydoun SR, Chalk CH, Barboi AC, Amato AA, Shaibani AI, Katirji B, Lecky BR, Buckley C, Vincent A, Dias-Tosta E, Yoshikawa H, Waddington-Cruz M, Pulley MT, Rivner MH, Kostera-Pruszczyk A, Pascuzzi RM, Jackson CE, Garcia Ramos GS, Verschuuren JJ, Massey JM, Kissel JT, Werneck LC, Benatar M, Barohn RJ, Tandan R, Mozaffar T, Conwit R, Odenkirchen J, Sonett JR, Jaretzki A 3rd, Newsom-Davis J, Cutter GR; MGTX Study Group. Randomized Trial of Thymectomy in Myasthenia Gravis. N Engl J Med. 2016 Aug 11;375(6):511-22. Erratum in: N Engl J Med. 2017 May 25;376(21):2097]. PMID: 27509100; PMCID: PMC5189669.

   https://doi.org/10.1056/NEJMoa1602489
3. Rath J, Brunner I, Tomschik M, Zulehner G, Hilger E, Krenn M, Paul A, Cetin H, Zimprich F. Frequency and clinical features of treatment-refractory myasthenia gravis. J Neurol. 2020 Apr;267(4):1004-1011. Epub 2019 Dec 11. PMID: 31828474; PMCID: PMC7109164. https://doi.org/10.1007/s00415-019-09667-5
4. Petersson M, Feresiadou A, Jons D, Ilinca A, Lundin F, Johansson R, Budzianowska A, Roos AK, Kågström V, Gunnarsson M, Sundström P, Piehl F, Brauner S. Patient-Reported Symptom Severity in a Nationwide Myasthenia Gravis Cohort: Cross-sectional Analysis of the Swedish GEMG Study. Neurology. 2021 Aug 10;97(14):e1382-91. Epub ahead of print. Erratum in: Neurology. 2021 Dec 14;97(24):1141. PMID: 34376512; PMCID: PMC8520390. https://doi.org/10.1212/WNL.0000000000012604
5. Li T, Zhang GQ, Li Y, Dong SA, Wang N, Yi M, Qi Y, Zhai H, Yang L, Shi FD, Yang CS. Efficacy and safety of different dosages of rituximab for refractory generalized AChR myasthenia gravis: A meta-analysis. J Clin Neurosci. 2021 Mar;85:6-12. Epub 2021 Jan 2. PMID: 33581791. https://doi.org/10.1016/j.jocn.2020.11.043
6. Nowak RJ, Coffey CS, Goldstein JM, Dimachkie MM, Benatar M, Kissel JT, Wolfe GI, Burns TM, Freimer ML, Nations S, Granit V, Smith AG, Richman DP, Ciafaloni E, Al-Lozi MT, Sams LA, Quan D, Ubogu E, Pearson B, Sharma A, Yankey JW, Uribe L, Shy M, Amato AA, Conwit R, O'Connor KC, Hafler DA, Cudkowicz ME, Barohn RJ; NeuroNEXT NN103 BeatMG Study Team. Phase 2 Trial of Rituximab in Acetylcholine Receptor Antibody-Positive Generalized Myasthenia Gravis: The BeatMG Study. Neurology. 2021 Dec 2;98(4):e376-89. Epub ahead of print. PMID: 34857535; PMCID: PMC8793103.

   https://doi.org/10.1212/WNL.0000000000013121
7. Piehl F, Eriksson-Dufva A, Budzianowska A, Feresiadou A, Hansson W, Hietala MA, Håkansson I, Johansson R, Jons D, Kmezic I, Lindberg C, Lindh J, Lundin F, Nygren I, Punga AR, Press R, Samuelsson K, Sundström P, Wickberg O, Brauner S, Frisell T. Efficacy and Safety of Rituximab for New-Onset Generalized Myasthenia Gravis: The RINOMAX Randomized Clinical Trial. JAMA Neurol. 2022 Nov 1;79(11):1105-1112. PMID: 36121672; PMCID: PMC9486640 https://doi.org/10.1001/jamaneurol.2022.2887
8. Hehir MK, Hobson-Webb LD, Benatar M, Barnett C, Silvestri NJ, Howard JF Jr, Howard D, Visser A, Crum BA, Nowak R, Beekman R, Kumar A, Ruzhansky K, Chen IA, Pulley MT, LaBoy SM, Fellman MA, Greene SM, Pasnoor M, Burns TM. Rituximab as treatment for anti-MuSK myasthenia gravis: Multicenter blinded prospective review. Neurology. 2017 Sep 5;89(10):1069-1077. Epub 2017 Aug 11. PMID: 28801338. https://doi.org/10.1212/WNL.0000000000004341
9. Howard JF Jr, Utsugisawa K, Benatar M, Murai H, Barohn RJ, Illa I, Jacob S, Vissing J, Burns TM, Kissel JT, Muppidi S, Nowak RJ, O'Brien F, Wang JJ, Mantegazza R; REGAIN Study Group. Safety and efficacy of eculizumab in anti-acetylcholine receptor antibody-positive refractory generalised myasthenia gravis (REGAIN): a phase 3, randomised, double-blind, placebo-controlled, multicentre study. Lancet Neurol. 2017 Dec;16(12):976-986. https://doi.org.10.1016/S1474-4422(17)30369-1. Epub 2017 Oct 20. Erratum in: Lancet Neurol. 2017 Dec;16(12):954. PMID: 29066163.
10. Vu T, Meisel A, Mantegazza R, Annane D, Katsuno M, Aguzzi R, Enayetallah A, Beasley KN, Rampal N, Howard JF Jr, for the CHAMPION MG Study Group. Terminal complement inhibitor ravulizumab in generalized myasthenia gravis. NEJM Evid. 2022.https://doi.org/10.1056/EVIDoa2100066
11. Howard JF Jr, Bresch S, Genge A, Hewamadduma C, Hinton J, Hussain Y, Juntas-Morales R, Kaminski HJ, Maniaol A, Mantegazza R, Masuda M, Sivakumar K, Śmiłowski M, Utsugisawa K, Vu T, Weiss MD, Zajda M, Boroojerdi B, Brock M, de la Borderie G, Duda PW, Lowcock R, Vanderkelen M, Leite MI; RAISE Study Team. Safety and efficacy of zilucoplan in patients with generalised myasthenia gravis (RAISE): a randomised, double-blind, placebo-controlled, phase 3 study. Lancet Neurol. 2023 May;22(5):395-406. PMID: 37059508. https://doi.org/10.1016/S1474-4422(23)00080-7
12. Howard JF Jr, Bril V, Vu T, Karam C, Peric S, Margania T, Murai H, Bilinska M, Shakarishvili R, Smilowski M, Guglietta A, Ulrichts P, Vangeneugden T, Utsugisawa K, Verschuuren J, Mantegazza R; ADAPT Investigator Study Group. Safety, efficacy, and tolerability of efgartigimod in patients with generalised myasthenia gravis (ADAPT): a multicentre, randomised, placebo-controlled, phase 3 trial. Lancet Neurol. 2021 Jul;20(7):526-536. https://doi.org/10.1016/S1474-4422(21)00159-9. Erratum in: Lancet Neurol. 2021 Aug;20(8):e5. PMID: 34146511.
13. Bril V, Drużdż A, Grosskreutz J, Habib AA, Mantegazza R, Sacconi S, Utsugisawa K, Vissing J, Vu T, Boehnlein M, Bozorg A, Gayfieva M, Greve B, Woltering F, Kaminski HJ; MG0003 study team. Safety and efficacy of rozanolixizumab in patients with generalised myasthenia gravis (MycarinG): a randomised, double-blind, placebo-controlled, adaptive phase 3 study. Lancet Neurol. 2023 May;22(5):383-394. PMID: 37059507. https://doi.org/10.1016/S1474-4422(23)00077-7
14. Jonsson DI, Pirskanen R, Piehl F. Beneficial effect of tocilizumab in myasthenia gravis refractory to rituximab. Neuromuscul Disord. 2017 Jun;27(6):565-568. Epub 2017 Mar 16. PMID: 28433474. https://doi.org/10.1016/j.nmd.2017.03.007
15. Jia D, Zhang F, Li H, Shen Y, Jin Z, Shi FD, Zhang C. Responsiveness to Tocilizumab in Anti-Acetylcholine Receptor-Positive Generalized Myasthenia Gravis. Aging Dis. 2023 Jul 6. Epub ahead of print. PMID: 37450932. https://doi.org/10.14336/AD.2023.0528
16. Hewett K, Sanders DB, Grove RA, Broderick CL, Rudo TJ, Bassiri A, Zvartau-Hind M, Bril V; BEL115123 Study Group. Randomized study of adjunctive belimumab in participants with generalized myasthenia gravis. Neurology. 2018 Apr 17;90(16):e1425-e1434. Epub 2018 Mar 21. PMID: 29661905; PMCID: PMC5902787. https://doi.org/10.1212/WNL.0000000000005323
17. Bryant A, Atkins H, Pringle CE, Allan D, Anstee G, Bence-Bruckler I, Hamelin L, Hodgins M, Hopkins H, Huebsch L, McDiarmid S, Sabloff M, Sheppard D, Tay J, Bredeson C. Myasthenia Gravis Treated With Autologous Hematopoietic Stem Cell Transplantation. JAMA Neurol. 2016 Jun 1;73(6):652-8. PMID: 27043206. https://doi.org/10.1001/jamaneurol.2016.0113

Preview: Neurosurgery High Speed Drill Course

Dates: 5 July 2024 (face to face)
Location: St George's, University of London
Course lead: Mr Erlick Pereira, Mrs Fay Greenway
Fee: $50
More details: www.sgul.ac.uk/study/professional-education/short-courses/neurosurgery-high-speed-drill-course

Why join the course?
This one day interactive course aims to build understanding and provide hands-on experience of High Speed Drills. The candidates will learn the basic skills and techniques for high-speed drilling.

Audience
Junior Neurosurgery Trainees (ST1-4) or equivalent level fellows, junior doctors and Physicians Associate graduates with interest in neurosurgery are targeted. Developing drilling skills is an essential operative skill in Neurosurgery (curriculum requirement).

Course outcomes
The course will cover:
- Identifications, set-up and disassemble High Speed Drills
- Differentiate between attachment and cutting accessories and their respective applications
- Short presentations preceding the hands-on training will support the practical work
- Demonstrations of ICP and EVDs insertion.

Lunch and refreshments will be provided.

Certification
Delegates will be issued with a certificate of attendance and CPD will be sought fromthe Society of British Neurological Surgeons (SBNS).

Past students have said...
"Huge amount of material covered clearly. Practical session was fantastic."
"Opportunity to use multiple different drill types under instruction and with helpful comments or tips for improvement. Excellent talks from all speakers."

2023 Parkinson's Excellence Network Awards

Health professionals from across the UK were honoured at the prestigious 2023 Parkinson's Excellence Network Awards.

Since 2015, the Parkinson's Excellence Network has been bringing together health and social care professionals to transform care for the Parkinson's community. The awards recognise the hard work and ingenuity of outstanding individuals, teams and services that make a difference to people with Parkinson's, and the people who love and care for them. Award winners included:

Lifetime Achievement
Liz Scott, a Parkinson's nurse specialist for 28 years, ran outpatient clinics, advised ward colleagues on Parkinson's, and worked as a Nurse Advisor for Parkinson's UK.


Liz Scott - Lifetime Achievement Award winner


L-R Rowan Wathes, Julie Jones, Jane Asher


L-R Robert Gouck, Nick Bryden, Jane Asher, Rory Cellan Jones

People's Choice
(Recognising exceptional support by people with Parkinson's and their loved ones)
Julie Jones, co-lead of the Parkinson's Excellence Network exercise hub, is working to raise the quality of physical activity and exercise provision for people with Parkinson's.

Susan Seymour, North Devon District Hospital, is credited with empowering people with Parkinson's through her physical activity classes and educational sessions.

Innovation in Practice and Excellence Award Winner
Nick Bryden from NHS Ayrshire & Arran. Created a system to alert Parkinson's nurses to their patient's hospital admission and the need for time-critical medication.

Sharing, Learning and Education Winner
Rimona Weil, University College of London, was awarded for her co-development of booklets for patients to access support and information on dementia in Parkinson's, along with a toolkit for healthcare professionals on recognising and managing dementia in specialist clinics.

Community Support Winner
Beccy Oliver, The Exercise Hub, was credited for her nationwide physical activity framework for people with Parkinson's and professionals.

To find out more about the Parkinson's Excellence Network Awards or the Parkinson's Excellence Network, please visit: parkinsons.org.uk/excellencenetwork or follow the Network on X @ParkinsonsEN.

Professor Paul Matthews announced as new Institute Director at The Rosalind Franklin Institute

Congratulations to Professor Paul Matthews on his new appointment as Director of the Rosalind Franklin Institute. The Rosalind Franklin Institute is a national research institute developing new technologies to tackle important health research challenges.

Funded by UK Research and Innovation through the Engineering and Physical Sciences Research Council (EPSRC), the Franklin aims to bring about a revolution in imaging which will allow us to see entire cells and tissues in new ways.

Professor Paul Matthews will be stepping down as Centre Director of the UK DRI at Imperial on 7 April 2024 before he takes up his new post.

9th WFNR Franz Gerstenbrand Award 2024 - Now Open for Entries

The 9th WFNR Franz Gerstenbrand Award, worth $3000 to the winner, is open for entries. The Award recognises and rewards neurorehabilitation projects that have benefitted patients. It is open to WFNR members and non-members worldwide and encourages applications from young applicants especially those under 35 years of age. Entries for the Award must demonstrate a difference to patient outcomes in any aspect of neurorehabilitation in the entrants' country. The project may be a patient or clinic management initiative, research study, best practice development or the use of a new technological development.

All health professionals currently working in neurorehabilitation are encouraged to enter the Award. The project must be completed and have already produced results or been published in the last 12 months. Named after Professor Franz Gerstenbrand in recognition of his contribution to neurorehabilitation, the Award is for a travel bursary to a clinical or scientific conference, professional development course or research project.

The Award winner will be announced at the 13th World Congress for Neurorehabilitation, 22-25 May 2024 in Vancouver, Canada. wfnr-congress.org

For further information and an application form please visit: wfnr.co.uk/awards/awards. Email a maximum 1000-word summary of the project and the completed application form to traceymole@wfnr.co.uk by the 29th February 2024.

WFNR
World Federation for Neurorehabilitation

The deep gluteal (piriformis) syndrome

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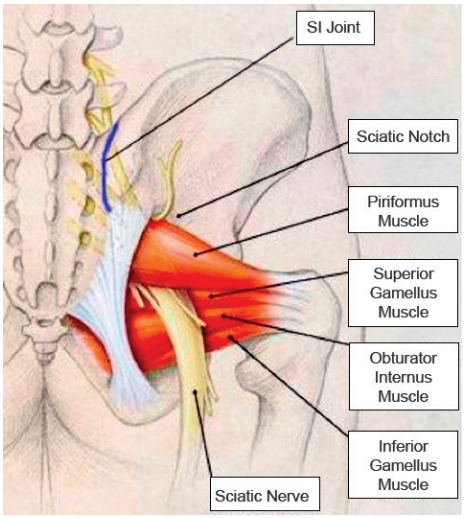


Fig 1. Piriformis and sciatic nerve.

Table 1. Proposed diagnostic features [13]

Deep-seated buttock pain with radiating pain, especially intolerable sitting pain
Tenderness of the piriformis muscle
Positive provocative test: Freiberg's test, Pace test
Positive findings on CT or MRI: asymmetry or enhancement around the sciatic nerve
Pain relief with a local anaesthetic or steroid injection
Piriformis syndrome is diagnosed if 4 or more criteria are present

Abstract
Piriformis* syndrome is a subgroup of the deep gluteal syndrome, an important differential diagnosis of sciatica. Piriformis is a short external rotator muscle of the hip joint passing close to the sciatic nerve as it passes through the great sciatic foramen. The compression causes numbness, ache, or tingling in the buttocks, posterolateral aspect of the leg, and foot. The causes of sciatic nerve entrapment in the deep gluteal syndrome are best shown by endoscopic exploration. The frequency of anatomical variants in normal subjects, however, should caution that such anomalies are not necessarily the cause of symptoms.

Most people have experienced a transient dead numb leg after sitting awkwardly or for too long on a toilet seat or hard chair. This is perhaps a benign variant of the deep gluteal syndrome [1]. It is caused by compression or irritation of the sciatic nerve located within or adjacent to the greater sciatic notch [2]. Piriformis syndrome is a subgroup of the deep gluteal syndrome, first described by Yeoman in 1928 as sciatica caused by arthritis of the sacroiliac joint, the piriformis muscle and the adjacent branches of the sciatic nerve [3].

Other causes of entrapments within the subgluteal space are fibrous and vascular (inferior gluteal artery) bands, obturator internus/gemellus syndrome, and ischio-femoral pathology [4]. Before endoscopic exploration, the validity of this diagnostic label was uncertain since there were then no definite criteria and no specific tests, though many had been proposed (qv). In a paper of 18 studies and 6,062 cadavers the prevalence of piriformis and sciatic nerve anomalies in cadavers was 16.9%; almost identical to 16.2% in the 'surgical cases' [5].

Anatomy

The piriformis muscle is a short external rotator muscle of the hip joint that is stretched with internal rotation of the leg. H. Crooke described it in 1615 as:

> *The fourth extender called Iliacus externus piriformis, the outward hanch peare muscle…because it filleth the outward and lower cauity of the hanch bone with his oblique position, and is like a round peare. (Oxford English Dictionary)*

Its origin is from the anterior surface of the sacrum; it inserts into the greater trochanter via a tendon that is merged with tendons of the obturator internus and gemelli muscles. The sciatic nerve passes out of the pelvis through the great sciatic foramen, usually below the piriformis. (Figure 1)

There are several anatomical variations of the relationship between the piriformis muscle and sciatic nerve, which may conduce to irritation, or entrapment of the nerve [6]. The undivided nerve may pass below or through the piriformis or, it may divide above piriformis into the tibial and lateral popliteal nerves with one portion exiting through piriformis, the other inferior to it.

Clinical features

As a differential diagnosis of sciatica caused by the much more common disk lesions the piriformis syndrome is characterised by buttock numbness or pain that occurs after prolonged sitting [6,7] on a wallet, cycling, or by excessive or repeated exercise [9]. Back pain is not a feature. Most often a mild numbness, ache or tingling in the buttocks, posterolateral aspect of the leg and foot subside after a few minutes in the erect posture or walking.

In less frequent but more severe cases symptoms are persistent. Typical but not diagnostic physical signs are:

- an antalgic posture – sitting on the other 'cheek' with the affected thigh adducted and internally rotated.
- hip flexion, adduction and internal rotation (FAIR) narrow the space between the inferior border of the piriformis, superior gemellus and sacrotuberous ligament which may induce pain.
- pain experienced during forceful internal rotation of the extended thigh (Freiberg sign).
- pain on resisted abduction and external rotation of the hip in a flexed/sitting position (Pace sign). Local tenderness on palpation is variable and pain on straight leg raising is commonly absent.

Investigations

In an MRI study of 783 cases, there were no significant differences in the prevalence of piriformis syndrome, buttock pain, or sciatica between normal and variant sciatic nerve anatomy [10]. The piriformis syndrome is probably overdiagnosed [5,11]. Only if symptoms are persistent or disabling should investigations be used to exclude discogenic lumbosacral root compression, sacroiliac joint dysfunction, spinal, paraspinal, and pelvic masses. In such instances investigations are useful but none are diagnostic. The causes of sciatic nerve entrapment in the deep gluteal region are best shown by endoscopic exploration. The main use of MRI is to exclude lumbosacral spinal aetiologies. MRI may be normal or show hypertrophy/atrophy, fibrosis, or anomalous insertion of the piriformis. MR neurography can show piriformis muscle asymmetry and sciatic nerve hyperintensity at the sciatic notch [12]. Increased H-reflex latency in nerve conduction studies and electromyographic denervation in muscles innervated by the sciatic nerve are variably recorded but unreliable. The study of Han et al [13] after exclusion of other spinal or pelvic pathology proposed diagnostic criteria. (Table 1). The frequency of anatomical variants in normal subjects,

however, should caution that such anomalies are not necessarily the cause of symptoms.

Treatment

Most instances are benign and self-limiting if provocative factors are avoided. A bewildering variety of treatments have been used, many with imperfectly controlled studies, most claiming high success rates. They include: anti-inflammatory drugs, physiotherapy, piriformis stretching [14], injection of local anaesthetics or corticosteroids, and botulinum toxin injections [15]. Periarticular endoscopic decompression of the sciatic nerve [4,16], is less invasive than exploratory surgery and in intractable cases is useful in clarifying the varied causes of the deep gluteal syndrome and in affording means for correcting causal lesions. Thirty-nine of 52 patients had good to excellent outcomes in a review from 2016 [4]. Muscle resection with or without neurolysis of the sciatic nerve should be the last resort but was deemed "satisfactory in 10 of 12 patients who had failed to respond to more conservative treatments." [13]

**Sometimes spelt pyriformis*

References

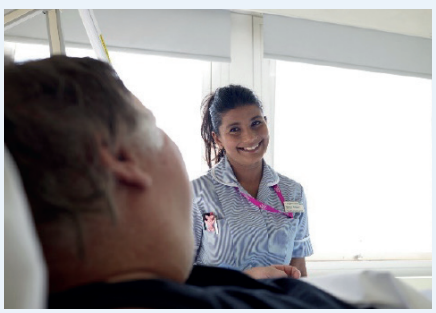
1. Hernando MF, Cerezal L, Pérez-Carro L. et al. Deep gluteal syndrome: anatomy, imaging, and management of sciatic nerve entrapments in the subgluteal space. Skeletal Radiol 2015;44:919-934. https://doi.org/10.1007/s00256-015-2124-6
2. Robinson D R. Piriformis Syndrome in Relation to Sciatic Pain. Am J Surg 1947;73(3):355-8. https://doi.org/10.1016/0002-9610(47)90345-0
3. Yeoman W. The relation of arthritis of the sacro-iliac joint to sciatica, with an analysis of 100 cases. Lancet. 1928;2:1119-22. https://doi.org/10.1016/S0140-6736(00)84887-4
4. Carro LP, Hernando MF, Cerezal L, Navarro IS, Fernandez AA, Castillo AO. Deep gluteal space problems: piriformis syndrome, ischiofemoral impingement and sciatic nerve release. Muscles Ligaments Tendons J. 2016;6(3):384-396. https://doi.org/10.32098/mltj.03.2016.16
5. Smoll NR. Variations of the piriformis and sciatic nerve with clinical consequence: a review. Clin Anat. 2010;23(1):8-17. https://doi.org/10.1002/ca.20893
6. Beaton LE, Anson BJ. The relation of the sciatic nerve and its subdivisions to the piriformis muscle. Anat Record 1937;70:1-5. https://doi.org/10.1002/ar.1090700102
7. Rodrigue T, Hardy RW. Diagnosis and treatment of piriformis syndrome. Neurosurg Clin N Am 2001;12(2):311-319. https://doi.org/10.1016/S1042-3680(18)30056-1
8. Byrd JW. Piriformis syndrome. Oper Tech in Sports Med 2005;13:71-79. https://doi.org/10.1053/j.otsm.2004.09.008
9. Lutz E.G. Credit-card-wallet sciatica. JAMA 1978;240(8):738. https://doi.org/10.1001/jama.1978.03290080028012
10. Bartret AL, Beaulieu CF, Lutz AM. Is it painful to be different? Sciatic nerve anatomical variants on MRI and their relationship to piriformis syndrome. Eur Radiol. 2018;28(11):4681-4686. https://doi.org/10.1007/s00330-018-5447-6
11. Stewart JD. The piriformis syndrome is overdiagnosed. Muscle Nerve 2003;28(5):644-6. https://doi.org/10.1002/mus.10483
12. Filler AG, Haynes J, Jordan SE, et al. Sciatica of nondisc origin and piriformis syndrome: diagnosis by magnetic resonance neurography and interventional magnetic resonance imaging with outcome study of resulting treatment. J Neurosurg Spine 2005;2(2):99-115. https://doi.org/10.3171/spi.2005.2.2.0099
13. Han SK, Kim YS, Kim TH, Kang SH. Surgical Treatment of Piriformis Syndrome. Clin Orthop Surg 2017;9(2):136-144. https://doi.org/10.4055/cios.2017.9.2.136
14. Fishman LM, Dombi GW, Michaelsen C, Ringel S, Rozbruch J, Rosner B, Weber C. Piriformis syndrome: diagnosis, treatment, and outcome-a 10-year study. Arch Phys Med Rehabil 2002;83:295-301.https://doi.org/10.1053/apmr.2002.30622
15. Fishman LM, Wilkins AN, Rosner B. Electrophysiologically identified piriformis syndrome is successfully treated with incobotulinum toxin a and physical therapy. Muscle Nerve 2017;56(2):258-263. https://doi.org/10.1002/mus.25504
16. Park M, Yoon S, Jung S. et al. Clinical results of endoscopic sciatic nerve decompression for deep gluteal syndrome: mean 2-year follow-up. BMC Musculoskelet Disord 2016;17:218. https://doi.org/10.1186/s12891-016-1062-3.

Preview: Recent Advances in Young Onset Dementia

Dates: 24 April 2024 (onsite or virtual)
Location: St George's, University of London
Course lead: Professor Peter Garrard
Fee: From £55

Why join the course?

The course will provide an update on current diagnostic standards, best practice and new developments in clinical practice relating to the young onset dementias. A case-presentation session at the end of the meeting will give delegates an opportunity to have difficult cases or management dilemmas discussed by an expert panel.



Audience

General practitioners; psychiatrists (consultants and trainees); neurologists (consultants and trainees); dementia specialist nurses; dementia support workers.

Learning outcomes

After attending the course, it is aimed that delegates will have an improved understanding of:

- The features that distinguish early stages of neurodegenerative dementia in people under 65 from the worried well or the effects of depression or anxiety.
- The diagnostic processes that lead to the recognition of Alzheimer's disease, the frontotemporal dementias and other, rarer types of dementia in people aged under 65.
- The support that is available to people with young onset dementia after diagnosis.

Certification

Delegates will be issued with a certificate of attendance and CPD will be sought from the Federation of the Royal Colleges of Physicians of the United Kingdom.

Past students have said...

"Brilliantly engaging lecturing style. Excellent breadth of cases. Very well presented and helpful talk. Courses like this always provoke learning or thinking about topics from a different perspective and that is very valuable particularly if you've been practising for a while and might be a bit set in your ways."

"Good combination of talks, representing whole pathway from diagnosis to care home."

More details at: www.sgul.ac.uk/study/professional-education/short-courses/young-onset-dementia

Events Diary

FEBRUARY

Management and Leadership in Neurosurgery
1 February, 2024; Hybrid (onsite/virtual)
www.sgul.ac.uk/study/professional-education/short-courses/management-and-leadership

Neuroanatomy for Imagers
1 February, 2024; In person (London) or Online
www.kcl.ac.uk/short-courses/neuroanatomy-for-imagers-3
E: teachingadmin-imaging@kcl.ac.uk

Circadian Rhythm Disruption and Sleep
5 February - 25 March, 2024
www.scni.ox.ac.uk/study-with-us/oxford-online-programme-in-sleep-medicine/short-courses/circadian-rhythm-disruption-and-sleep
E: sleepmedicine@ndcn.ox.ac.uk

Tourette Syndrome Online Training Course
7 February, 2024; Online
www.essts.org/news/online-ts-school-2024

Dementias 2024
8-9 February, 2024; Cavendish Conference Centre, London
www.dementiasconference.com/dementiasonlineworkshop2023/en/page/dementias-2024

Sleep in Specialist Populations
12 February - 17 March, 2024
www.scni.ox.ac.uk/study-with-us/oxford-online-programme-in-sleep-medicine/short-courses/sleep-in-specialist-populations
E: sleepmedicine@ndcn.ox.ac.uk

EAN Webinar 2: Autonomic Nervous System Disorders
21 February, 2024; Webinar
www.ean.org/learn/elearning/virtual-events/webinars/ean-webinars

MND Webinar: Anticipatory grief – the challenges presented by a progressive condition for people living with and affected by MND
27 February, 2024; Online
www.mndassociation.org/professionals/professional-education-and-development/education-events
E: education@mndassociation.org

The International Newborn Brain Conference
28 February - 02 March, 2024; Cork, Ireland
mcascientificevents.eu/inbc

7th National Neuropsychiatry Conference in North Staffordshire
29 February, 2024; Doubletree Hotel, Stoke on Trent
https://bit.ly/3tAEA3Z
E: NeuroPsychiatryConferenceTeam@combined.nhs.uk

MARCH

Duchenne UK New Horizons Conference
1 - 2 March, 2024; London
www.duchenneuk.org/our-new-horizons-conference

4th ILAE School on Neuropsychology in Epilepsy
3 - 8 March, 2024; Lyon, France
www.ilae.org/congresses/4th-ilae-school-on-neuropsychology-in-epilepsy

AD/PD™ 2024 International Conference on Alzheimer's and Parkinson's Diseases
5 - 9 March, 2024; Lisbon, Portugal and Online
adpd.kenes.com

Queen Square Multidisciplinary Neuro-oncology Teaching Course: Benign and Malignant Tumours
6 March, 2024; CL Queen Square Institute of Neurology
www.ucl.ac.uk/ion/queen-square-multidisciplinary-neuro-oncology-teaching-course

The 34th ANPA Annual Meeting
6 - 9 March, 2024; Houston, Texas, USA
www.anpaonline.org

Stem Cells in Neuroscience
11 - 13 March, 2024; Institute of Neuroanatomy and Developmental Biology, Germany
stemcelltuebingen.com
E: stefan.hauser@dzne.de

Dr Miguel-Mateas on ADHD/Autistic Gut-Brain Axis
12 March, 2024; Westminster, London
buff.ly/46Mw4g3

The BNPA 2024 Annual Meeting
14 - 15 March, 2024; Royal College of Physicians, London
bnpa.org.uk

MS Trust Annual Conference 2024
17 - 19 March, 2024; Leonardo Hotel and Conference Venue, Hinckley Island
mstrust.org.uk/health-professionals/courses-and-training/ms-trust-conference

Teaching Course on Peripheral Neuropathy 2024
21 March, 2024; Liverpool Medical Institute and Online
www.bpns.org.uk/event-details.aspx?Group=events&id=98

18th World Congress on Controversies in Neurology (CONy)
21 - 23 March, 2024
cony.comtecmed.com
E: cophy@comtecint.com

BPNS Spring 2024 Scientific Meeting
22 March, 2024; Liverpool Medical Institute and Online
www.bpns.org.uk/event-details.aspx?Group=events&id=95

Paediatric Polysomnography Course
22 - 23 March, 2024
www.sleepconsultancyltd.co.uk/courses/paediatric-psg/
E: lisa@sleepconsultancyltd.co.uk

APRIL

Insomnia
8 April - 26 May, 2024
www.scni.ox.ac.uk/study-with-us/oxford-online-programme-in-sleep-medicine/short-courses/insomnias
E: sleepmedicine@ndcn.ox.ac.uk

Sleep and Society
08 April - 02 June, 2024
www.scni.ox.ac.uk/study-with-us/oxford-online-programme-in-sleep-medicine/short-courses/sleep-and-society
E: sleepmedicine@ndcn.ox.ac.uk

Data-driven approaches to understanding dementia
8 - 12 April, 2024; EMBL's European Bioinformatics Institute (EMBL-EBI), Wellcome Genome Campus
ukdri.ac.uk/events/data-driven-approaches-to-understanding-dementia

The 9th London-Innsbruck Colloquium on Status Epilepticus and Acute Seizures
8 - 10 April, 2024; Imperial College London and Online
www.statusepilepticus.eu/index.php
E: se2015@cmi.at

MiNT UK CONFERENCE 2024
15 April, 2024; The Royal Society of Medicine, London
themintacademy.co.uk
E: enquiries@themintacademy.co.uk

Neurology 2024: leading edge neurology for the practising clinician
18 - 19 April, 2024; Kennedy Lecture Theatre, UCL
www.ucl.ac.uk/ion/neurology-2024-leading-edge-neurology-practising-clinician
E: ion.educationteam@ucl.ac.uk

8th International Congress of Myology
22 - 25 April, 2024; Paris, France
ern-euro-nmd.eu/event/8th-international-congress-of-myology/

12th Alzheimer's and Parkinson's Drug Development Summit
23 - 25 April, 2024; Boston, United States
alzheimers-parkinsons-summit.com
E: info@hansonwade.com

36th Global Conference of Alzheimer's Disease International
24 - 26 April, 2024; Krakow, Poland
adiconference.org
E: events@alzint.org

Recent Advances in Young Onset Dementia
24 April, 2024; Hybrid (onsite or virtual)
shop.sgul.ac.uk/short-courses/professional-education/neuro/recent-advances-in-young-onset-dementia

BNA Members' Meeting 2024
24 - 25 April, 2024; Online
www.bna.org.uk/mediacentre/events/bna-members-meeting-2024

Deutscher Kongress für Parkinson und Bewegungsstörungen
25 - 27 April, 2024; Rostock, Germany
www.dpg-akbont-kongress.de
E: dpg-akbont2024@cpo-hanser.de

NMN Symposium: Precision Medicine – Diagnostic and Therapeutic Innovations in the Era of Precision Medicine
26 - 27 April, 2024; Billrothhaus, Vienna
www.nmn-society.org

South of England Neurosciences Association Spring
26 April, 2024; Royal Free Hospital, London
sena.org.uk

MND Webinar: "If it affects one of us, it affects us all": the Whole Family approach, effective support for a household living with a diagnosis of MND
30 April, 2024; Online
www.mndassociation.org/professionals/professional-education-and-development/education-events

MAY

The 14th Annual Traumatic Brain Injury Conference
2 - 3 May, 2024; Arlington, United States
go.evvnt.com/1926071-0?pid=10025
E: enquiries@tbiconference.com

Seventeenth Eilat Conference on New Antiepileptic Drugs and Devices
5 - 8 May, 2024; Madrid, Spain
www.eilatxvii.com

18th International Child Neurology Congress
6 - 10 May, 2024; Cape Town, South Africa
www.icnapedia.org/icnc2024

The 16th INS World Congress (INS 2024)
11 - 16 May, 2024; Vancouver, Canada
ins-congress.com

ILAE British Branch 19th SpR Epilepsy Teaching Weekend
11 - 12 May, 2024; Birmingham University Campus
www.epilepsyteachingweekend.com
E: info@epilepsyteachingweekend.com

Edinburgh Sleep Medicine 2024 Course
13 - 17 May, 2024; Edinburgh Carlton, Edinburgh
www.sleepconsultancyltd.co.uk/courses/edinburgh-sleep-medicine
E: lisa@sleepconsultancyltd.co.uk

10th European Stroke Organisation Conference
15 - 17 May, 2024; Basel, Switzerland
eso-stroke.org/esoc2024/

Cognitive Behaviour Therapy for Insomnia
18 - 19 May, 2024
www.sleepconsultancyltd.co.uk/courses/cbt-i/
E: lisa@sleepconsultancyltd.co.uk

World Congress on Parkinson's Disease and Related Disorders
19 - 22 May, 2024; Lisbon, Portugal
www.iaprd-world-congress.com

ABN Annual Meeting
20 - 23 May, 2024; Edinburgh, UK
www.theabn.org

World Congress of Neurorehabilitation
22 - 25 May, 2024; Vancouver, Canada
wfnr-congress.org
E: traceymole@wfnr.co.uk

13th World Congress for NeuroRehabilitation
22 - 25 May, 2024; Vancouver, Canada
https://wfnr-congress.org

EAN Spring School
22 - 26 May, 2024; Frankenfels, Austria
www.ean.org/learn/educational-events/spring-school

Add your own courses and conferences to our online calendar free of charge at https://acnr.co.uk/submit-an-event/

JUNE

Edinburgh Adult PSG Course
7 - 8 June, 2024
www.sleepconsultancyltd.co.uk/courses/adult-psg-course
E: lisa@sleepconsultancyltd.co.uk

Acute Neurology Course
7 June, 2024; St George's, University of London
www.sgul.ac.uk/study/professional-education/short-courses/acute-neurology
E: pec@sgul.ac.uk

16th Conference on Tourette Syndrome & Tic Disorders 2024
12 - 14 June, 2024; Varese, Italy
www.essts.org

3-Day Interacoustics Balance Course
12 - 14 June, 2024; The Principal Hotel, York
www.interacoustics.co.uk/masterclass
E: marketing@interacoustics.co.uk

The Brain Conference: Circuits for Movement
16 - 19 June, 2024; Rungsted Kyst, Denmark
www.fens.org/news-activities/fens-and-societies-calendar/meeting-event/the-brain-conference-circuits-for-movement

NeuroID 2024
19 - 20 June, 2024; The Liverpool Medical Institution
www.liverpool.ac.uk/neuroidcourse/
E: neuroidc@liverpool.ac.uk

2024 Annual PNS Meeting Montréal
22 - 25 June, 2024; Montréal, Canada
pnsociety.com/meetings/future-meetings
E: info@pnsociety.com

FENS Forum 2024
25 - 29 June, 2024; Vienna, Austria
fensforum.org
E: forum2024@fens.org

10th Congress of the European Academy of Neurology
29 June - 2 July, 2024; Helsinki, Finland
www.ean.org/congress2024
E: headoffice@ean.org

21st International Symposium on Pediatric Neuro-Oncology (ISPNO 2024)
29 June - 2 July, 2024; Philadelphia, USA
www.ispno2024.com

JULY

MND Webinar "You matter because you are you, and you matter to the end of your life" – dispelling the myths of hospice care (for people living with and affected by MND)
16 July, 2024; Online
www.mndassociation.org/professionals/professional-education-and-development/education-events
E: education@mndassociation.org

AUGUST

2024 SNO/ASCO CNS Metastases Conference
8 - 10 August, 2024; Denver, Colorado.
www.soc-neuro-onc.org/WEB/Events/2024_SNO_ASCO_CNS_Metastases_Conference/WEB/Event_Content/2024_SNO_ASCO_CNS_Metastases_Conference.aspx?hkey=b-0bc7c24-c14a-400e-b539-16a6e9850402
E: caroline@soc-neuro-onc.org

SEPTEMBER

XX World Congress of Stereotactic and Functional Neurosurgery, Chicago, USA (WSSFN 2024)
2 - 6 September, 2024; Chicago, United States
go.evvnt.com/2005034-0?pid=10025
E: ipopova@kenes.com

15th European Epilepsy Congress
7 - 11 September, 2024
www.ilae.org/congresses/15th-european-epilepsy-congress
E: eec@epilepsycongress.org

CMTA 2024 Patient & Research Summit
7 - 8 September, 2024; Denver, Colorado
www.cmtausa.org

33rd International Congress of Clinical Neurophysiology (ICCN) 2024
10 - 14 September, 2024; Jakarta, Indonesia
iccn-2024.com
E: info@iccn-2024.com

ECTRIMS 2024
18 - 20 September, 2024; Copenhagen, Denmark
ectrims.eu/ectrims2024

37th ECNP Congress
21 - 24 September, 2024; Milan, Italy
www.ecnp.eu/Congress2024/ECNPcongress

International Congress of Parkinson's Disease and Movement Disorders
27 September - 1 October, 2024; Philadelphia, PA, USA
www.mdscongress.org

OCTOBER

Edinburgh Adult PSG Course
4 - 5 October, 2024
www.sleepconsultancyltd.co.uk/courses/adult-psg-course
E: lisa@sleepconsultancyltd.co.uk

Heart Rhythm Congress
6 - 8 October, 2024; Birmingham, UK
www.heartrhythmcongress.org

The Brain Conference: Neuronal Protein Synthesis Mechanisms in Health and Disease
13 - 16 October, 2024; Rungsted Kyst, Denmark
www.fens.org/news-activities/fens-and-societies-calendar/meeting-event/the-brain-conference-neuronal-protein-synthesis-mechanisms-in-health-and-disease

19th Congress of the European Association of Neuro-Oncology (EANO)
17 - 20 October, 2024; Glasgow
www.eano.eu/eano2024
E: eano-meetings@eano.eu

The 16th World Stroke Congress
23 - 26 October, 2024; Abu Dhabi, United Arab Emirates
worldstrokecongress.org
E: wsc@kenes.com

The 18th International Congress on Neuromuscular Diseases
25 - 29 October, 2024; Perth, Australia
icnmd.org/#

The International Neuropsychiatric Association (INA) Conference
27 - 29 October, 2024; Melbourne, Australia
inawebsite.org/news-events

NOVEMBER

The International Association of Neuropsychiatry 2024 Congress
13 - 15 November, 2024; Melbourne, Australia
inawebsite.org/news-events

MND Webinar: A focus on tube feeding in MND: current evidence, managing risks and exploring good practice
26 November, 2024; Online
www.mndassociation.org/professionals/professional-education-and-development/education-events
E: education@mndassociation.org

Preview: The Comorbidities of Epilepsy Course

Dates: 21 June 2024 (onsite/virtual)
Location: St George's, University of London
Course lead: Dr Marco Mula
Fee: From $25
More details:
www.sgul.ac.uk/study/professional-education/shortcourses/comorbidities-of-epilepsy

Why join the course?
Epilepsy is one of the most common, chronic neurological condition in the UK. The course will offer a practical grounding in the most common comorbidities associated with epilepsy. This is an area of growing clinical interest, and relevant to the care of patients with epilepsy. The course aims to provide a basic grounding in the epidemiology, nature, diagnosis and treatment of common comorbidities in patients with epilepsy.

Audience
This course is best suited to those health postgraduates, and health professionals who come into contact with patients with epilepsy. Namely, general neurologists, epileptologists, specialist nurses and psychologists/psychiatrists.

Certification
Delegates will be issued with a certificate of attendance and CPD will be sought from the Federation of the Royal Colleges of Physicians of the United Kingdom.

Past students have said...
"This was a fantastic and informative course and will certainly lead to improvements in my practice. I particularly appreciated the talks on bone health and renal disorders as these had the most bearing on my practice."

"Interactive approach. The course helped to understand an in-depth knowledge of epilepsy."

Review at ACNR online: "This one day course is informative, and is unique in the approach to a common neurological condition. It has relevance to all general neurologists, irrespective of training level, as well as clinical nurse specialists."

BNPA 2023

Conference details: 3-4 March, 2023, Royal College of Physicians, Regents Park, London, UK. ***Report by:*** Laurence Knowles. ***Conflict of interest:*** Laurence Knowles is a BNPA committee neurology trainee representative.

The 36th Annual Conference of the British Neuropsychiatry Association took place on March 2nd and 3rd 2023. It was a pleasure to return to the Royal College of Physicians of London on Regent's Park for the second year running, where we were joined by over 150 Psychiatrists, Neurologists, Psychologists and others with an interest in the interaction between brain and mind, as well as many more virtual delegates from across the globe. A wide range of national and international speakers over two days explored a huge range of topics relating to the meeting's overarching theme of "Our Perception of the World and its Effect on Health", accompanied by a fantastic range of poster presentations and lively in person discussion and networking.

The first session focused on neurodegenerative disease, covering the spectrum from diagnosis and new individual drug treatments to prevention and understanding quality of life. Our first speaker was Professor Peter Garrard of St. George's University of London, who spoke on the utility of "Language as a biomarker in dementia". He reviewed the concept that neurodegenerative dementias may have a presymptomatic signature in spontaneous speech, including some famous examples such as the novelist Iris Murdoch and Ronald Reagan, and that this may hold diagnostic potential. The specific case of the neurodegenerative syndromes which selectively impair language was then discussed, before introducing the new "mini linguistic state examination", a novel bedside linguistic exam which can effectively subclassify variants of primary progressive aphasia. Next, Professor Robert Howard of UCL delivered the BNPA medal lecture entitled "Should we be preparing to give new dementia treatments to our patients?", covering the long history of attempted drug development for Alzheimer's disease since the approval of cholinesterase inhibitors almost twenty years ago, before focusing on the newly approved amyloid antibodies. This talk covered the trial evidence for efficacy of these treatments, which suggests that the benefit is less than the generally accepted minimally clinically important difference, as well as highlighting the need for specifically designed trials to assess claims of disease modification. Dr Naaheed Mukadam of UCL then took us from treatment to prevention, posing the question, 'Can we prevent dementia?'. Taking a global perspective, she reviewed the evidence for modifiable risk factors for dementia throughout the lifecourse and discussed estimates of the total burden of preventable disease, before reviewing the more mixed evidence for specific interventions. Finally, Professor Linda Clare of the University of Exeter concluded the session with a talk on "Understanding quality of life in mild to moderate dementia and what we can do to maintain or enhance it." This talk covered the evidence from the IDEAL study, a large cohort study assessing over 1500 patients with mild to moderate dementia. This has provided a wealth of insight into factors which predict quality of life in dementia, and particularly relevant to the theme of the meeting was the finding that when modelled together, of the multiple domains associated with quality of life the psychological domain dominates, suggesting that other domains influence quality of life through their effect on psychological well being. These insights have led to useful interventions for promoting quality of life in dementia, including the IDEAL "living with dementia map" and toolkit.

Following refreshments we reconvened for the member's platform presentation; three talks from this year's Alwyn Lishman prize winners. Peter Dudley and Jan-Paul Marquez presented their work on "Functional seizures and their misdiagnosis and mimics: A review of video-telemetry referrals and case outcomes in a tertiary epilepsy centre", a large case series of referrals for video telemetry EEG with the thought provoking result that 5% of patients with an initial diagnosis of functional seizures were reclassified as epileptic after monitoring. Nathan Pevy presented his work on "Predicting the cause of transient loss of consciousness using an automated analysis of interactions with a virtual agent", showing how an automated analysis of descriptions of TLOC can improve diagnostic accuracy. Finally, Verónica Cabreira talked on the "Development of a screening checklist to diagnose functional memory symptoms: a Delphi study", introducing a novel 11 point clinical tool for the assessment of patients with potential functional cognitive disorder.

The afternoon session, on the theme "How do we see the world around us; autism, frontotemporal dementia, functional neurological disorder and the effect of perception", was varied and fascinating. It began with two case presentations from Dr Kit Stone and Dr Chris Kipps illustrating the complex interactions between autism, functional neurological disorders (FND) and frontotemporal dementia and how these can present very differently across the lifespan, and giving some clinical context for the subsequent talks.

First was the JNNP lecture by Professor Sue Fletcher-Watson of the University of Edinburgh on "Autism and Neurodiversity: a new paradigm". This was a powerful and incisive talk, contrasting "core deficit" models of autism with a neurodiversity paradigm. She presented data showing (amongst other findings) how the classic social and communication "deficits" associated with autism are far more context dependent than usually understood, and disappear when individuals with autism interact with one another, before building on this data and the work of neurodivergent scholars to address some of the myths around neurodiversity and explore how a neurodiversity paradigm can improve support and services. Richard Cole then discussed the current evidence of links between autistic traits and functional neurological disorders, exploring similarities in neural network alteration, shared constructs such as alexithymia, changes in interoception and sensory over-responsivity, and common predisposing and perpetuating factors. This was followed by Tim Nicholson's overview of sensorimotor features in autism, reviewing both the core features and evidence for a broader range of sensorimotor features beyond these, before discussing potential mechanisms (including analogies with those in functional neurological disorders) and therapeutic implications.

Finally, it was a privilege to hear Professor John Hodges, recipient of

the BNPA Lifetime Achievement award, speak on the links between frontotemporal dementia (FTD) and autism spectrum disorders (ASD). His wide ranging talk covered the history of research into FTD and how differences in social cognition in FTD overlap considerably with those seen in autism, before introducing the idea of the "phenocopy" syndrome of those with FTD-like changes in cognition which do not progress over many years, and how this might represent the effects of environmental or social change on an ASD-like phenotype as well as shared genetic risk factors between FTD and ASD. The session concluded with a lively and engaging panel discussion, continued during the evening's entertainment at the Magic Circle.

The first session of day two had a variety of talks exploring how our preconceptions, perceptions and beliefs shape how we process information and how these processes can go wrong, or conversely be used therapeutically. Professor Sander van der Linden of the University of Cambridge started with a fascinating and topical talk on "Psychological inoculation against misinformation". If we consider that misinformation can spread between individuals in a manner reminiscent of viral contagion, and once spread it is difficult to correct, then the possibility of a "vaccination" to combat misinformation is a logical next step. Professor Van der Linden took us through a variety of lab and field based experiments showing that such "pre bunking" – exposing people to weakened doses of misinformation in a controlled manner – can strengthen resistance to subsequent misinformation and took us through some of the real world implications of this.

Dr Devin Terhune and Professor Mark Edwards of King's College London then gave a joint talk on "Placebo, suggestion and FND – interactions and clues to pathophysiology". Building very nicely on some of the talks from the previous day, they showed us how abnormal beliefs and attention conceptually function as key processes in FND, placebo and nocebo effects, and suggestion effects such as hypnosis. They discussed the mechanisms of these three entities, and explored the degree to which suggestion and placebo might be used as models for FND as well as touching on the long history of the clinical use of placebo and suggestion effects in functional disorders.

Next, Dr Johannes Jungillingens of the University Hospital Knappschaftkrankenhaus unified many of the concepts from the preceding talks with a bravura talk on "A new science of emotion: Implications for functional neurological disorder". Within the framework of constructed emotion theory he built a model of the pathophysiology of functional neurological disorder linking predictive processing with energy dysregulation, miscategorisation of emotions and how life experiences and alexithymia can link to this framework.

Finally, Dr Matthew Burke joined us remotely from Toronto for a talk on "Our evolving understanding of placebo effects: implications for research and practice in neuropsychiatry", showing how placebo effects are no longer a poorly understood entity but rather a biologically based phenomenon which can modulate and interact with neuropsychiatric disorders and highlighting the fundamental implications of this on the design and conduct of research studies in neuropsychiatry and medicine more broadly.

The final session of the conference was a joint one with the American Neuropsychiatric Association, on "Neuropsychiatry in Extreme Situations". Dr Dorothy Wade explored this theme in the context of the intensive care unit (ICU) with a talk entitled "The Psychological Scars of Intensive Care". Survival from critical illness is often linked with adverse psychological and neuropsychiatric outcomes, and Dr Wade gave an overview of current research into how psychological and practical interventions can ameliorate this. Dr Peter Hughes then spoke on the role of "Psychiatry in Humanitarian Emergencies", drawing on his great experience in the delivery of psychiatric care across the globe (most recently in Afghanistan) to discuss the principles of emergency response, building back services hereafter, and situating these principles in the background context of the global burden of mental ill health.

Finally, we were very grateful to be able to welcome Dr Charles Dukes of NASA, who gave a talk on "NASA's Behavioural Health and Performance Services for Long Duration Space Missions". This fascinating talk gave us insight into the unique physiological and psychological stressors associated with long-duration space travel, and how NASA's Behavioural Health and Performance Service is embedded into the entire process from astronaut selection, training, support during missions and aftercare to aim to prevent and mitigate the risk of psychological and psychiatric comorbidity.

Other highlights included two datablitz sessions in the marvellous surroundings of the Dorchester library, with a wide variety of presentations of universally high quality. The prize winners were:

Ashwani Jha – How the emotions of others capture our attention: a human amygdala disruption study.

Merritt Millman – Predisposing, precipitating and perpetuating factors in functional neurological disorder: a pilot study.

Saurabh Sonkusare – Direct neural recordings from human bed nucleus of stria terminalis link alpha activity in empathy and affect evaluation tasks with depression severity.

Next years Annual Meeting will be held on March 14th and 15th, 2024 at the Royal College of Physicians of London.

Lewy Body UK 2023

Conference details: 30 June, 2023, University College London (UCL), Queen Square, London, UK. ***Report by:*** Leigh Townsend, NIHR Academic Clinical Fellow at Newcastle University, UK. ***Conflict of interest:*** None declared.

Lewy Body UK 2023 was hosted by University College London (UCL) at 33 Queen Square on 30th June 2023. This third instalment, organised by Professor John-Paul Taylor (Newcastle University), Dr Rimona Weil (UCL) and Dr Claire O'Callaghan (University of Sydney), welcomed speakers from across the UK and abroad, and covered key domains of cutting-edge research on Lewy body dementia, including advances in molecular pathology, high-resolution neuroimaging, digital phenotyping, artificial intelligence, and clinical drug trials.

The first session, chaired by Professor John Hardy (UCL), was entitled 'Molecular and Pathological Drivers of Parkinson's and Lewy body disorders.' Professor Sonia Gandhi (UCL) spoke about her work to understand the cellular mechanisms of Lewy body disease, describing the use of induced pluripotent stem cells to develop cellular models of alpha-synuclein aggregation, emphasising the role of lipid molecules in the early aggregation process and the immunoreactivity of alpha-synuclein aggregates. Dr Raquel Real (UCL) followed with a talk on the genetic basis of dementia in Parkinson's disease. She described work on genome wide association studies, highlighting the association of ApoE4 and LRP1B with progression and severity of dementia in Parkinson's disease. Dr Laura Parkkinen (University of Oxford) finished this session, speaking on advances in digital technology for quantitative analysis of neuropathological samples, and the insights gleaned on the relative distributions of pathological proteins across brain regions.

The second session, chaired by Dr Rimona Weil, was entitled 'Imaging to shed light on Lewy body disorders'. Dr Claire O'Callaghan (University of Sydney) spoke about the key role of locus coeruleus degeneration in the aetiology and symptomatology, in dementia syndromes, and the novel MRI

imaging techniques which can be leveraged to characterise this degeneration. She described the possible benefits of repurposed and novel noradrenergic therapies and the potential for treatment stratification based on MRI-measured noradrenergic integrity. Dr Christian Lambert (UCL) spoke on the development of MRI techniques incorporating multiple sequences providing structural information about tissue composition in the brain. This quantitative MRI approach is used to achieve in vivo histological estimates and has been shown to offer similar diagnostic fidelity to the DAT scan. Professor Li Su (University of Cambridge) closed this session by describing the MILOS study in which artificial intelligence was used to analyse the findings of a clinical imaging study, providing a physiologically informed model against which the imaging findings could be compared and tested, with greater sensitivity than a typical group-wise comparison.

The third session, chaired by Dr Claire O'Callaghan, was entitled 'Wearables and digital markers.' Professor Michele Hu (University of Oxford) spoke about the utility of wearable and digital monitoring technologies to deliver informative and clinically meaningful measures of motor and cognitive function in Parkinson's and REM sleep behaviour disorder, including for monitoring treatment response and predicting disease progression. Dr Ashwani Jha (UCL) drew on his experiences of designing a smartphone application for measuring and quantifying motor function in Parkinson's disease to give a six-step crash course on app design for a Lewy body researcher or clinician. Finally, Dr Riona McArdle (Newcastle University) spoke on the use of ambulatory monitoring, inside and outside the lab. She described the findings of the GAITDem study, which showed the utility of gait analysis in differentiating between dementia subtypes.

The last session, chaired by Dr Claire O'Callaghan, entitled 'Updates and controversies' heard Professor John O'Brien (University of Cambridge), providing a broad update on the state of clinical drug trials and drug discovery for Lewy body dementia at present. Professor O'Brien then took to the stage again for the debate, as representative for the UK's Old Age Psychiatrists, proposing the motion that 'people with DLB are best managed by Psychiatrists.' Professor Liz Coulthard (University of Bristol) opposed the motion, on behalf of the country's Neurologists, striking a conciliatory tone and calling for cooperation between Neurologists and Psychiatrists, as well as the wider multi-disciplinary team. A few waistcoats were torn, and a tendon hammer broken, but amicable agreement was ultimately reached on the need for interoperability and cooperation between the brain-focused specialties for the good of our patients.

The conference ended with announcement of the winners of the Early Career Researcher prizes for best paper. The winning prize was awarded to Cristina Toomey for her paper entitled 'Mitochondrial dysfunction is a key pathological driver of early stage Parkinson's.' The Runner-up was Leonidas Chouliaras for his paper 'Differential levels of plasma biomarkers of neurodegeneration in Lewy Body dementia, Alzheimer's disease, frontotemporal dementia and progressive supranuclear palsy.'

Finally, the date for Lewy Body UK, 2024 was set for Friday 7th June, 2024 in Newcastle-upon-Tyne. Please do save the date.

Epilepsy Specialist Nurse Association (ESNA) conference

Conference details: 11-12 September, 2023, The William Quarriers Scottish Epilepsy Centre, Glasgow, Scotland. ***Report by:*** Laurie Bibby, BSc Paediatric Nursing and Epilepsy Care. ***Conflict of interest:*** None declared.

The Epilepsy Specialist Nurse Association (ESNA) has celebrated its 30th Anniversary this year. ESNA is the national professional organisation for all nurses supporting people with epilepsy. Its main role is to empower, educate and offer expertise for all professionals working in epilepsy care.

The 30th Anniversary conference was held in Glasgow at the wonderful William Quarriers Scottish Epilepsy Centre. This was held over 2 days with the title 'transformation in epilepsy care'. There have been many developments and changes in epilepsy care over the last 30 years and this gave us the opportunity to reflect on some of these.

Day 1

The first half day of the conference was broadly focused on diagnosis and management of epilepsy in terms of classification and treatment. It reflected on treatment options in terms of newer anti-seizure medications and the updated classifications of the epilepsies.

The conference was opened by Professor Martin Brodie with a keynote speech on the outcomes in newly diagnosed epilepsy.

This lead on to Dr Graeme Sills who is a Senior Lecturer in Pharmacology providing a fantastic insight into experimental and clinical pharmacology. He gave an overview of the pharmacokinetics of some of the 'newer' anti-seizure medications including cannabinoids and highlighted some very interesting points to be considered when discussing this as a treatment option.

Dr Ronit Pressler, Consultant in Clinical Neurophysiology provided an update on the new International League Against Epilepsy (ILAE) classification of seizures and epilepsy. She gave an insightful overview that identified the importance of using correct, up to date terminology. This also highlighted that epilepsy is forever changing and the importance of keeping up to date. She also spoke of the change to diagnose epilepsy after one unprovoked confirmed seizure with a 60% chance of reoccurrence.

Dr Pressler then presented on neonatal seizures and the importance of investigations, clear history, observations, and review was highlighted in the form of case studies. This also highlighted challenges of working with neonates and how this can be faced in practice. It was a fantastic interactive talk.

Day 2

The morning sessions of the second day were focused on the wider issues faced in epilepsy in terms of the global need and working with hard-to-reach patients.

The morning was opened by Tolu Olaniyan, CEO Petrola Global Health and Consulting, who gave a very heartfelt talk around the global need for epilepsy nurses. She spoke passionately about the need for epilepsy nursing care globally and the challenges that are faced in being able to provide these. She spoke about training programmes in epilepsy that are offered globally and the positive impact that these are having on the population. It certainly was a thought provoking presentation that highlighted the many challenges for epilepsy nurse specialists across the world.

Samantha Dorney-Smith, Queens Nurse, spoke of the challenges of homelessness and managing epilepsy and long-term conditions. This talk was extremely thought provoking, particularly for people that work in the inner cities in providing care to hard-to-reach proportions of the population. This generated an interesting discussion with delegates as to how homelessness is met within their services and how they are engaging people in managing their health. It also gave very practical things to think about like appointment letters getting to the patients and how services contact service users. She also touched on professionals' statutory duties in managing these patients.

Tolu then provided another very interesting presentation on the Learning Disabilities and Mortality Review (LeDeR) which was established in 2017 by NHS England and NHS Improvement. She spoke about its role in improving care, reducing inequalities, and preventing early deaths for people with a learning disability. She focused on the LeDeR report 2021, and how deaths of people with a diagnosed learning disability compared to the numbers within the general population. Importantly, it found that people with a learning disability and epilepsy are more likely to die younger. Tolu discussed how important it is that deaths are reported and referred for a LeDeR review as this enables lessons to be learnt and future practice to be informed.

Dr Maria Oto and Joanne Hill gave a presentation on the diagnosis of dissociative seizures and the burden of anti-seizure medication. They highlighted the role of The William Quarriers inpatient beds in assisting with the investigating and diagnosis. They presented case studies of patients who had attended for review, many of whom had been on several high dose anti-seizure medications with significant side effects. These presentations highlighted the importance of correct diagnosis, medication management and review and psychological support, and the impact that these can have on patients if not diagnosed or treated appropriately.

This led onto a presentation by Chris Bennett, Senior Children's Epilepsy Nurse and Margaret Wilson, Paediatric Epilepsy Nurse Consultant. They spoke very passionately about the role of the epilepsy nurse specialist and how this has evolved over the last 25 years. It was a very thought-provoking presentation that highlighted the need for epilepsy nurse specialist/consultants and the importance of the roles that they provide including extended roles such as non-medical prescribing. They spoke of the developing treatments over the years and how these have helped in seizure management. They also spoke about the importance of genetic testing and how this will impact all patients in the future.

The ESNA Executive Board wanted to mark the 30th anniversary with recognition of someone in the field of epilepsy specialist nursing who has shown excellence in their care of people with epilepsy and have had a positive, lasting influence on people. The nominations for this award were: Shelley Anderton, Christine Bennett, Christine Cole, Mel Goodwin, Helen Hodgson, Alison Holmes, Yvonne Leavy, Sheila Shepley and Janine Winterbottom

The winner was announced at the gala dinner by John Paul Leach who gave the after-dinner speech which was filled with fun and laughter. The very worthy winner of the award was Yvonne Leavy, Clinical Nurse Specialist in Epilepsy, NHS Lothian. This award represents her outstanding contribution to epilepsy nursing over her career. Yvonne said on winning the award "This is greatly appreciated, and I hope we can use it as a catalyst to encourage joint work and collaboration across our ESNA family". Well done, Yvonne, a very worthy winner. Congratulations to all the nominees.

Thank you very much to all our speakers who made this conference a great success.

2023 International Congress of Parkinson's Disease and Movement Disorders

Conference details: 27-31 August, 2023, Copenhagen, Denmark. ***Report by:*** Neil Ramsay and Ed Newman, Institute of Neurological Sciences, Queen Elizabeth University Hospital, Glasgow, UK. ***Conflict of interest:*** None declared.

The 2023 Movement Disorder Society congress was hosted in true Scandinavian style in the Danish capital. Whilst delegates may have been distracted by Copenhagen's beautiful waterfront and stunning architecture, the programme was more than enough to keep everyone in the conference centre. Over 5,200 delegates from more than 100 countries shared the latest advances in pathophysiology, diagnosis, and management.

Results from numerous important clinical trials in Parkinson's disease were presented. Follow up data from the UK's PD-MED study compared patients who were initiated on Levodopa versus Levodopa-sparing agents. This confirmed that, despite increased levels of dyskinesia, quality of life remained higher in the patients in the Levodopa group 15 years later. Importantly, in the Levodopa sparing group, the MAO-B inhibitors were not inferior to dopamine agonists [1].

The relationship between the gut and the brain is a hot topic in PD. A study of 74 patients found that after 12 weeks of probiotic therapy, patients showed significant reduction in 'time to on' and NMS scale scores and objective changes in their gut flora compared to placebo. How long might it be before we are routinely prescribing probiotics alongside dopaminergic drugs [2]?

Following on from the exciting recent Exenatide studies, a phase II study of another injectable GLP-1 agonist, Lixisenatide, demonstrated significant improvement in UPDRS-III scores in 156 patients with early onset PD [3].

In the presidential lectures, Dr Caroline Tanner gave an excellent overview of 'prevention' in Parkinson's focusing on early detection, and exposure risk within different US cohorts. Dr

Andy Singleton presented work from the GP2 genetic Parkinson's collaboration highlighting the lack of knowledge about sub-Saharan Africa Parkinson's cohorts with high prevalence of GBA mutations.

The award for the best research article of the year from Movement Disorders went to Zappia et al. for a fascinating study [4] showing a synergistic effect of long duration Levodopa alongside motor learning inducing neuroplasticity and adaptive changes to basal ganglia networks.

Since the pandemic, tic disorders referrals have been on the increase. Pringsheim et al. were presented with the Movement Disorders Clinical Practice article of the year award for their article describing the demographic and phenomenological characteristics of the Calgary tic registry [5]. This highlighted how similar current tic presentations were to historical cohorts and showed slight differences between male and female presentations with the latter having more intense and frequent motor tics. Becker et al presented interesting data which used machine learning to distinguish movements in Tourette's syndrome from healthy controls with accuracy of 83% [6].

The MDS congress enjoys emphasising the importance of clinical skills in its Grand Rounds section where selected clinicians are invited to take a history and examine a few local cases in front of a packed auditorium. Our Danish and Swedish colleagues provided a clinical smörgåsbord of fascinating cases, which prompted discussion and debate. The congress had many interactive video sessions in which clinical phenomenology was carefully explained and taught. Highlights included sessions on functional movement disorders chaired by Alberto Espay, a 'Tics, Tourette's and stereotypies' session chaired by Lis Gitte and Christos Ganos and a hyperkinetic movement disorder session chaired by Mark Stacy.

The congress is famed for its evening Video Challenge with movement disorder legends Tony Lang and Kailash Bhatia sharing master of ceremonies duties across a marathon of 29 complex cases. This session is always educational and highlights interesting genetic, autoimmune, or metabolic presentations with videos submitted from around the world. There was an excellent atmosphere as the audience tried to piece together the clues and arrive at the correct diagnosis.

The final day saw entertaining discussions around controversies in movements disorders. First up was the topic of safety and efficacy of bilateral lesioning for Parkinson's disease. Maria Rodriguez was speaking for and Elena Moro against with her impassioned argument around the lack of data on bilateral lesioning winning over the crowd. Secondly Alastair Noyce argued in favour of genotyping in Parkinson's disease patients with Jonathan Carr speaking against. An honest but forward-looking argument from Professor Noyce narrowly won against Professor Carr's more pragmatic approach in an area with a lack of disease modifying treatments.

In the final session, Giulietta Riboldi and Sanjay Pandey presented research highlights from the past year in both hyperkinetic and hypokinetic movement disorders. They discussed how a new candidate gene for dystonia, ATP5F1B, has been identified with variants in 2 families giving rise to an autosomal dominant early onset phenotype [7]. There has been excitement about emerging treatments for Huntington's disease; data was shown from a recent Phase II trial of Pepinemab, a semaphorin 4D (SEMA4D)-blocking antibody, that failed its primary outcome, but met several secondary outcomes that will provide hope [8]. Furthermore, recent data has shown Velbanizine is both effective and safe for use for chorea in Huntington's disease [9]. Lastly there was interest in the results of a recent phase II trial of Sodium Oxybate which was shown to be efficacious in treating vocal tremor in patients with essential tremor [10].

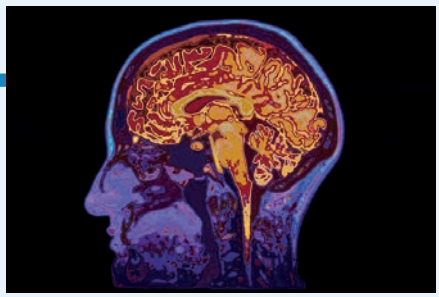
There has been much discussion of seed amplification assays for α-synuclein in PD. More evidence appears to be emerging about the specificity of CSF assays, but there is also excitement around serum sampling, although a cross-sectional study highlighted false negative results in LRRK2 patients [11]. In the area of disease modification for Parkinson's, a recent phase II of Venglustat in GBA1-associated Parkinson's showed a positive safety profile but no benefit against placebo [12]. Lastly there was an important message from a recent paper on the remote assessment of movement disorders highlighting the technical limitations of video conferencing programmes [13].

Overall, there was much for delegates to digest in this packed meeting. It was closed by the incoming President Victor Fung with delegates asked to put the dates in their diary for the 2024 congress in Philadelphia - September 27 - October 1.

References

1. Clarke C. et al. 15-year effects of initiating treatment for Parkinson's disease with dopamine agonists or monoamine oxidase B inhibitors compared with levodopa: final results of PD MED early disease randomisation [abstract]. Mov Disord. 2023;38 (suppl 1).
2. Leta V. et al. Efficacy of a four-strain probiotic on gut dysbiosis, motor and non-motor symptoms in Parkinson`s disease: a multicentre randomised controlled trial [abstract]. Mov Disord. 2023;38 (suppl 1).
3. Meissner WG. et al. Multicenter, randomized, placebo-controlled, double-blind, parallel-group proof-of-concept study of lixisenatide in patients with early Parkinson's disease (PD): the LIXIPARK trial (NCT03439943) [abstract]. Mov Disord. 2023;38 (suppl 1).
4. Sciacca G. et al. Long-Duration Response to Levodopa, Motor Learning, and Neuroplasticity in Early Parkinson's Disease [abstract]. Mov Disord. 2023;38:626–635.
5. Nilles C. et al. Have We Forgotten What Tics Are? A Re-Exploration of Tic Phenomenology in Youth with Primary Tics. Mov Disord Clin Pract. 2023;10:764–773.
6. Becker L. et al. New machine learning approaches in tic detection: Seeking to learn more about the characteristic of tics [abstract]. Mov Disord. 2023;38 (suppl 1).
7. Nasca A. et al. Variants in ATP5F1B are associated with dominantly inherited dystonia. Brain. 2023;146:2730–2738.
8. Feigin A. et al. Pepinemab antibody blockade of SEMA4D in early Huntington's disease: a randomized, placebo-controlled, phase 2 trial. Nat Med. 2023;28:2183–2193.
9. Furr Stimming E. et al. Safety and efficacy of valbenazine for the treatment of chorea associated with Huntington's disease (KINECT-HD): a phase 3, randomised, double-blind, placebo-controlled trial. Lancet Neurol. 2023;22:494–504.
10. O'Flynn, LC. et al. Sodium Oxybate in Alcohol-Responsive Essential Tremor of Voice: An Open-Label Phase II Study. Mov Disord. 2023.
11. Siderowf A. et al. Assessment of heterogeneity among participants in the Parkinson's Progression Markers Initiative cohort using α-synuclein seed amplification: a cross-sectional study. Lancet Neurol. 2023;22:407–417. (
12. Giladi N. et al. Safety and efficacy of venglustat in GBA1-associated Parkinson's disease: an international, multicentre, double-blind, randomised, placebo-controlled, phase 2 trial. Lancet Neurol 2023;22:661–671.
13. Park KW. et al. Potential Pitfalls of Remote and Automated Video Assessments of Movements Disorders. Mov Disord 2023;38:504–506.

Preview: Acute Neurology Course



Dates: 7 June 2024 (face to face)
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Course lead: Dr Kuven Moodley
Fee: From £30
More details: www.sgul.ac.uk/study/professional-education/short-courses/acuteneurology

Why join the course?
The St George's Hospital Acute Neurology Masterclass aims to provide an overview of the management of common and emergency neurological problems presenting to hospital. The acute neurology service at St. George's Hospital is one of the first dedicated services set up in the country.

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Learners will develop a framework on how to diagnose and treat common acute neurological conditions and neurological emergencies, which includes:

- Approach to diagnosis and management of primary and secondary headache disorders presenting to the ED
- Diagnosis and management of stroke and how to distinguish stroke from stroke mimics
- Diagnostic approach to patients presenting with loss of awareness
- Management of neuromuscular emergencies
- Approach to diagnosis of the "dizzy" patient
- Recognition of functional neurological disorders
- How to diagnose and manage CNS infections

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