epilepsy action

issue fifty-seven / Summer 2020 £3.50
(Free to Epilepsy Action professional members)

epilepsy professional

Sleep disruption in children and adolescents with epilepsy

Reducing seizures through managing sleep

Alice Winsor

Virtual clinics – Stevens

Intellectual disability – Tittensor et al

GIVE THEIR brain ITS BEST chance

Time is of the essence for every child with drug-resistant epilepsy.

Every minute that passes brings their next seizure closer.
Every seizure means a bigger impact on their lives.
The earlier we act for children with drug-resistant epilepsy, the more chances there are for a brighter future.

Giving their brain its best chance means considering VNS Therapy sooner rather than later.

LIVANOVA UK LTD
1370 Montpellier Court,
Gloucester Business Park,
Gloucester, GL3 4AH
T: 01452 638500

LIVANOVA BELGIUM NV
Ikaroslaan 83, 1930 Zaventem
Belgium
www.vnstherapy.co.uk

INTENDED USE / INDICATIONS:

Epilepsy (Non-US)—The VNS Therapy System is indicated for use as an adjunctive therapy in reducing the frequency of seizures in patients whose epileptic disorder is dominated by partial seizures (with or without secondary generalization) or generalized seizures that are refractory to seizure medications. AspireSR® and SenTiva™ feature an Automatic Stimulation Mode which is intended for patients who experience seizures that are associated with cardiac rhythm increases known as ictal tachycardia.

Incidence of adverse events following stimulation (>5%) included dysphonia, convulsion,headache, oropharyngeal pain, depression, dysphagia, dyspnea, dyspnea exertional, stress, and vomiting.

Visit http://en.eu.livanova.cyberonics.com/safety-information to view important safety information.

VNS Therapy® by LivaNova

Soleman et al Epilepsy & Behavior 88 (2018) 139–145

CTBOVAd20E1

Welcome to the Summer (or the lockdown) edition of *Epilepsy Professional*. I hope this issue finds you well and adapting to the new normal that the coronavirus pandemic has brought to all our lives.

We are all having to change the way we work to keep ourselves and our patients safe, both from the virus, but also from their epilepsy and comorbidities. Like most of you, I have had to adapt to having much more of my contact with patients on the phone or via video link. We have an article from Liz Stevens, a Community Paediatric Epilepsy Nurse, who has been using video consultations for four years now. She takes us through the pros and cons – timely advice for us all now.

A high proportion of patients with epilepsy have co-morbidities and our approach to their management must take account of these. Tittensor et al describe the joint service they have set up to treat patients with intellectual disabilities and epilepsy; providing a link between the neurology and psychiatry teams with joint clinics. Their report shows an improvement in seizure control in most of their patients.

Sleep disorders are another, oft neglected, comorbidity of the epilepsies and our treatments. Alice Winsor describes the spectrum of sleep disorders in children and adolescents, based on her meta-analysis of the published literature. An important area to improve for patients whose sleep is affected, as poor sleep leads to worse seizure control.

I hope you enjoy this edition. Keep safe and sane during these difficult times.

Dr Seán J Slaght
Consultant neurologist
Executive medical adviser
Epilepsy Professional

contents

22
sleep

Alice Winsor

Alice Winsor investigates the impact of sleep and sleep disorders on seizure and epilepsy, and whether seizure control can be improved with better sleep.

Up and down the country, neurology services have responded to the COVID-19 crisis by taking stock and reforming how their services operate under these new and unprecedented restrictions.

Parents and carers are being reminded about protocols for administering rescue treatments, what constitutes a medical emergency, and equally importantly, what does not. Read our news story on page 6 for more on this. Clinics that have had virtual clinics in place before the pandemic are now having their digital and IT resources thoroughly put through the ringer, largely thanks to the 'enforced' participation of virtual patients. Liz Stevens provides a good account of her experiences with video clinics in Cambridgeshire on page 12.

Hopefully, this means we're on the road to fewer neurology cases presenting at A&E, more patients attending their appointments, reduced transmission of transported bacteria, and a better engagement with the role that digital health can play in the future. Check out Dr Rhys Thomas' opinion on the matter on page 30.

When this pandemic is over, whether months or years from now, we'll need to examine, quantify and understand the impact that COVID-19 has had on the disruption to our health service. And we'll then need to learn how to use all the tools at our disposal to address future issues – otherwise those tens of thousands of deaths (and counting) will be in vain.

I'm sure for many healthcare professionals, the promise of a better NHS is a whole lot better than a round of applause every Thursday evening.

Matt Ng
Editor
If you no longer wish to receive Epilepsy Professional *magazine, email us at editor@epilepsy.org.uk or call us on 0113 210 8800*

Editor/desktop publishing: Matt Ng (mng@epilepsy.org.uk)

Design: Suzanne Horvath (shorvath@epilepsy.org.uk)

Publishers: Epilepsy Action (External affairs department)

Advertising: Louise Cousins – 0113 210 8847 lcousins@epilepsy.org.uk

 ISSN 1750-2233
New Anstey House, Gate Way Drive, Yeadon, Leeds LS19 7XY, UK
tel: 0113 210 8800 | **fax:** 0113 391 0300 | **Epilepsy Action Helpline freephone:** 0808 800 5050
email: epilepsy@epilepsy.org.uk **epilepsy.org.uk**

UK neurology services reorganise in response to COVID-19 pandemic

The COVID-19 pandemic has forced neurological practices around the world to change how they operate in a matter of weeks.

Over the last few months, epilepsy specialists have highlighted their concerns in providing adequate healthcare for their patients. This is at a time when the pandemic has the potential to exacerbate chronic conditions, as well as place additional strains on already overburdened healthcare systems.

In a new study published in *Neurology*, healthcare professionals from around the world have united to develop best practice models for delivering epilepsy services during the pandemic. These systems have looked at how to maintain treatment standards for their patients, as well as to protect them against the risk of contracting the virus in hospital and care settings.

The study focused on developing consensus statements based on two key themes: how clinicians should modify their clinical care pathways for people with epilepsy during the COVID-19 pandemic, and what general advice should be issued to people with epilepsy.

The questions that were posed around these themes included:

- Does SARS-COVID-2 directly cause health issues for persons with epilepsy?
- Are people with epilepsy more predisposed (or vice-versa) to COVID-19 infection?
- How should we/clinicians modify our clinical care for people with epilepsy during the COVID-19 pandemic?
- What are the implications for resources in poor countries?

At present, there is limited evidence that COVID-19 directly causes health issues for those with epilepsy, though the virus can aggravate respiratory impairment, and bring about seizures related to COVID-19 hypoxia or encephalitis.

The study also reports that people with epilepsy are not likely to be at higher risk of contracting the virus and are no more likely to suffer worsened virus symptoms. However, people of concern include those with autoimmune disorders who need immunosuppressive therapies, and who have an increased risk of epilepsy. People also at risk include those with seizures that are triggered by fever or illness, such as Dravet syndrome - here the virus can bring about worsened fevers. The report authors also agreed that strategies need to be in place to reduce transmission rates of the virus in the hospital. It stated that people with epilepsy should have an emergency care plan, which includes lowering the threshold for emergency rescue medication if possible. Families and caregivers should also be informed of when and how rescue medications should be used, as well as clear instructions on when to call on medical assistance for tonic-clonic seizures.

After their revisions, the study team produced consensus recommendations which received a score of seven or higher. These guidelines focused on:

- The administration of as much care as possible at home to keep people with epilepsy out of healthcare facilities, and therefore limit their potential contact with COVID-19 (including strategies for rescue therapy).
- The minimising of risk of seizure exacerbation through adherence, and through ensuring a regular supply of medication.

To see the full study, visit *https://bit.ly/2WXaFjT*

MRI predicts the efficacy of a stem cell therapy for brain injury

US scientists have pioneered the use of MRI to predict the effectiveness of using stem cells to treat brain injuries.

The researchers, from Sanford Burnham Prebys Medical Discovery Institute and Loma Linda University Health, have hailed this the first ever 'biomarker' for regenerative medicine that could help tailor stem cell treatments for neurological conditions such as epilepsy.

The team will now test the findings in clinical trials, where they will evaluate the stem cell therapy in newborn babies who experience brain injury during birth, known as perinatal hypoxic-ischemic brain injury (HII). The study is published in *Cell Reports*.

"In order for stem cell therapies to benefit patients, we need to be thoughtful and scientific about who receives these treatments," says Evan Snyder, professor and director of the Center for Stem Cells and Regenerative Medicine at Sanford Burnham Prebys, and corresponding study author.

"I am hopeful that MRI, which is already used during the course of care for these newborns, will help ensure that infants who experience HII get the best, most appropriate treatment possible. In the future, MRI could help guide the use of stem cells to treat, or in some instances not treat, additional brain disorders such as spinal cord injury and stroke."

In many cases, researchers understand that human neural stem cells are therapeutic because they can protect living cells, as opposed to replacing nerve cells which have already died. Comprehending the health of brain tissue before stem cell treatment is therefore essential to the chances of success.

Tools that help predict the effectiveness of cell therapy could increase the success of trials, which are ongoing in people with epilepsy. They could also prevent people who will not respond to treatment from these invasive procedures from having false hope.

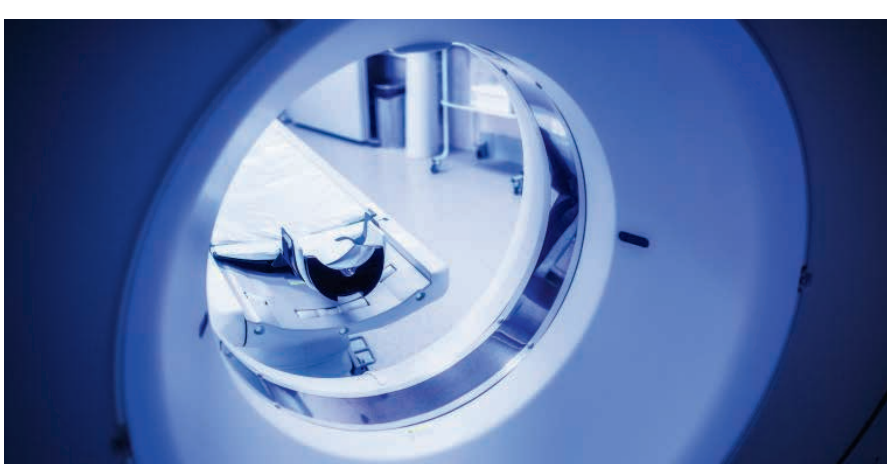
"We know that stem cell therapies hold extraordinary promise, but, like other medicines, they also need to be given at the right time and to the right patients," says Steve Lin, senior science officer at the California Institute for Regenerative Medicine, which partially funded the research. "This study suggests that a readily available technique, MRI--which is already used in many brain injuries to determine the extent of neurological damage--may be a useful tool to determine who will or will not benefit from neural stem treatment."

Snyder's team made the discovery that MRI could be used to determine inclusion and exclusion criteria for this treatment while conducting preclinical studies required prior to starting human clinical trials for babies with HII. HII is caused by a number of complications during birth, including umbilical cord compression, disrupted maternal blood pressure and maternal infection.

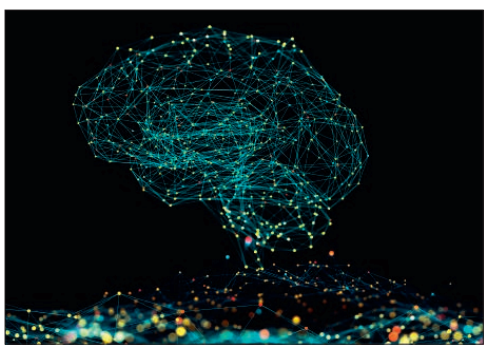
In the study, the scientists used MRI to measure two areas surrounding the regions of HII brain injury in rats: the penumbra, a region that consists of mildly injured, "stunned" neurons; and the core, an area that consists of dead neurons. They found that rats with a larger penumbra and smaller core that received human neural stem cells had better neurological outcomes--including improved memory.

"My hope is that human neural stem cells can help rescue enough injured and vulnerable, though not dead, neural cells," he explains. "This could help prevent the most severely affected infants from developing cerebral palsy, epilepsy, or other neurological disorders that often arise after HII if left untreated."

For the full study visit: *https://bit.ly/36Kfqk8*



AI successfully used to identify different types of brain injuries



An artificial intelligence (AI) algorithm has been developed which can identify different types of brain injuries.

Researchers from the University of Cambridge and Imperial College London have clinically trialled the AI on large numbers of CT scans. They discovered it was able to successfully detect, segment, quantify and differentiate a range of brain lesions.

This could save time during the diagnostic period when resources such as time or expertise are in short supply. In addition, it could help develop more personalised treatments for head injuries and be useful in large research studies. The results are reported in *The Lancet Digital Health*.

"CT is an incredibly important diagnostic tool, but it's rarely used quantitatively," said co-senior author Professor David Menon, from Cambridge's Department of Medicine. "Often, much of the rich information available in a CT scan is missed, and as researchers, we know that the type, volume and location of a lesion on the brain are important to patient outcomes."

Different types of blood in or around the brain can lead to different outcomes for the patient. It's up to radiologists to make best estimates in order to decide on the treatment that will have the best outcome.

"Detailed assessment of a CT scan with annotations can take hours, especially in patients with more severe injuries," said co-author Dr Virginia Newcombe. "We wanted to design and develop a tool that could automatically identify and quantify the different types of brain lesions so that we could use it in research and explore its possible use in a hospital setting."

The researchers developed a machine learning tool based on an artificial neural network. This system was trained on more than 600 CT scans, where it gathered information on lesions of varying sizes and types. This was then validated against an existing set of CT scans. The AI was then able to classify individual parts of each image and tell whether it was normal or not.

This development could prove beneficial in future studies looking at the progression of head injuries, as AI is more readily able to detect subtle changes over time.

"This tool will allow us to answer research questions we couldn't answer before," said Newcombe. "We want to use it on large datasets to understand how much imaging can tell us about the prognosis of patients."

"We hope it will help us identify which lesions get larger and progress, and understand why they progress, so that we can develop more personalised treatment for patients in future," said Menon.

For the full study, visit: *http://dx.doi.org/10.1016/S2589-7500(20)30085-6*

New COVID-19 guidance for valproate

The Medicines and Healthcare products Regulatory Agency (MHRA) has issued updated guidance for the treatment protocol for valproate during the COVID-19 pandemic. Published on the government website *gov.uk,* the temporary advice is for specialists for the management of the Valproate Pregnancy Prevention Programme (PPP). The guidance maintains that valproate has teratogenic effects if used by women during pregnancy, and is therefore contraindicated in these patients unless PPP conditions are fulfilled.

The guidance states: "Initiation of valproate in girls (of any age) and women of childbearing potential requires face-to-face consultation (with appropriate social distancing) except where the patient is shielding due to other health conditions. Where a patient is shielding, a remote consultation should be considered, based on an individual risk assessment carried out by the clinician in charge. The risk assessment should be documented in the notes."

In addition, the guidance says:

- Changes to the usual operation of the PPP may be required, particularly in those needing to self-isolate
- The initiation of valproate requires face-to-face consultation, with appropriate social distancing measures in place
- The required annual review of existing patients should not be delayed. Arrangements can be made for virtual or telephone consultation
- No patient should stop taking valproate without talking to their doctor.

Scientists develop ultrasound neuromodulation technique

Researchers have developed a non-invasive ultrasound neuromodulation technique capable of controlling neuronal excitement, without doing any harm to the brain. Excessive excitement or inadequate inhibition of these neurons is what is known to cause recurrent seizures.

Ultrasound stimulation has recently emerged as a non-invasive method for regulating brain activity. However, its range and effectiveness against a range of neurological conditions such as epilepsy and depression hasn't been made clear.

A team from the Shenzhen Institutes of Advanced Technology (SIAT) of the Chinese Academy of Sciences tested a low-intensity pulsed ultrasound system for non-human and human epileptic tissues.

Their results showed that ultrasound stimulation could have a reducing effect on epileptiform discharges. It may also improve behavioural seizures in a non-human primate epileptic model, with an efficiency of more than 65% in biopsy specimens from epileptic patients in vitro.

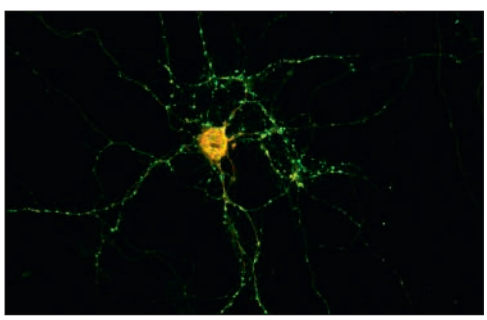
This mechanism could be explained by the altered balance of excitatory-inhibitory (E/I) synaptic inputs from the increased activity of local inhibitory neurons.

The study demonstrated that these low-intensity ultrasound pulses improved electrophysiological activities and behavioural outcomes in primates. They also suppressed epileptiform activities of neurons from human epileptic slices.

This has offered up evidence for a potential clinical use of this technique for epilepsy treatments - though more testing needs to be carried out. The study was published in *Theranostics*.

For the full study visit: *www.thno.org/v10p5514.htm*.

Antibodies in the brain trigger epilepsy



A German study has found a link between antibodies and epilepsy. With this knowledge, scientists at the University of Bonn think they can develop new therapies for some types of epilepsy.

These epilepsies are accompanied by the inflammation of important brain regions. The researchers have identified a mechanism that explains this link, and published their findings in *Annals of Neurology*.

Epilepsy can be a hereditary condition. However, in other cases, it develops in people only as a result of a brain injury, after a stroke or triggered by a tumour. Inflammation of the meninges, or the brain itself can also result in developing epilepsy. Particularly dangerous is inflammation of the hippocampus, a condition known as limbic encephalitis.

Professor Albert Becker oversees the Section for Translational Epilepsy Research at the University Hospital Bonn. He says, "In many cases it is still not clear what causes such inflammation."

Now researchers have found an antibody that is believed to be responsible for encephalitis in some people. Unlike normal antibodies that target molecules that enter the body from the outside, this antibody works against the body's own cells.

The researchers discovered it in the spinal fluid of people with epilepsy who have inflammation of the hippocampus. This antibody targets the protein Drebrin, which ensures the contact points between nerve cells function correctly. When the antibody encounters the Drebrin, it disrupts the communication between nerve cells. At the same time, it alerts the immune system, which then activates an inflammatory mode, which produces even more of the antibodies.

"However, Drebrin is located inside the synapses, whereas this antibody is located in the tissue fluid," says Dr Julika Pitsch. "These two should therefore normally never come into contact with each other."

It was discovered that the antibody uses a back door to enter the cell, piggybacking on to neurotransmitters to gain access into the synapses. In experiments using live cultures, the researchers showed what happened next. When the antibodies entered the synapses, the nerve cells started firing wildly with electrical activity, simulating a seizure.

These discoveries may lead the team on to new treatment approaches. For example, the drug cortisone can suppress the immune system and perhaps prevent the mass production of these antibodies. It might also be possible to intercept and disable them with other drugs. However, scientists say that there is a long way to go before treatments become a reality. For the full study visit: *http://dx.doi.org/10.1002/ana.25720*

Tattoo electrode breakthrough

Ultra-thin conductive polymers that can be printed on tattoo paper have now been adapted for use to measure brain activity. These "tattoo electrodes" were first pioneered in 2015 by European scientists. These were printable polymers that could be stuck to the skin when applied with tattoo paper and could measure heart or muscle activity.

Due to their thickness of around 750 nanometres. the tattoos fare well against uneven skin and are hardly noticeable. In addition, they act as 'dry' electrodes, meaning they operate without a gel interface.

Scientists have now been able to adapt the electrodes to accurately measure brain activity. The composition of the transfer paper has been optimised to acquire a better connection between the electrode and the skin.

Tests have shown measuring EEG using these tattoo electrodes is just as effective as conventional electrodes. Francesco Greco is head of the Laboratory of Applied Materials for Printed and Soft Electronics at Graz University of Technology, "Our tattoos are significantly less expensive than current EEG electrodes and offer more advantages in terms of wearing comfort and long-term measurements," he says.

These new tattoo electrodes are the first dry electrodes suitable for long-term EEG measurements, and are also compatible with magnetoencephalography, another method to measure brain activity. This technique could only be achieved using wet electrodes and gel. Now researchers will be able to capture accurate data over the long-term, as the electrodes do not dry out. The full study is published in *Nature*; visit: *nature.com/articles/s41528-020-0067-z*

epilepsy action

epilepsy.org.uk/yourchild

Your child and epilepsy

Grow your confidence managing epilepsy in your family

Your child and epilepsy is a new online course for parents and carers of children with epilepsy. It's been developed with parents, epilepsy nurses and psychologists.

This course is a helping hand to support families on their epilepsy journey. It's full of advice and stories from parents. It aims to give parents and carers the confidence, skills and knowledge to support their child to manage their epilepsy.

There are eight parts that cover:

- Understanding epilepsy
- Supporting your child with their epilepsy
- Keeping your child safe
- The impact of epilepsy on family life
- Your child's wellbeing
- Learning and behaviour
- Growing up and independence
- Sources of help and support

Free course

The course is free and flexible. It can be accessed at any time on a computer, tablet or smartphone with internet access.

Leaflets about the course to give to families can be requested by emailing **nurseorders@epilepsy.org.uk**

To view the course go to: **epilepsy.org.uk/yourchild**
Get in touch **learning@epilepsy.org.uk**

Epilepsy Action
Information you can trust

Find out more
epilepsy.org.uk/trust

Experience in use of virtual face to face clinics within a children's epilepsy community nursing service

In light of the COVID-19 pandemic, epilepsy specialist nurse Liz Stevens talks about her experiences of implementing virtual clinic at Cambridgeshire Community Services NHS Trust.

Virtual clinics have been in use within our local community children's epilepsy nursing service for over three years. This means that with the current challenges we are facing with clinical contacts during the COVID-19 pandemic, our service and staff are already skilled with this format of service provision. The current risks of infection have required a change in how we deliver epilepsy care. With this in mind, it is a relevant time to share the positive experiences and challenges that virtual clinics have had on children, young people and parents, to inform other services.

Development of virtual face-to-face clinics

Initially, the video link service was identified as a need within the transition pathway to adult care because these patients required additional appointments to regular reviews. This could result in missed education time and parents requesting time away from work, which could be a burden in an area of high social deprivation. Moreover, it was important to consider whether the medium of video link could better reflect the needs of young people when trying to engage them in understanding about their epilepsy.

Options for new technology were explored through a Commissioning for Quality and Innovation (CQUIN) project. This considered IT options, information governance issues and standard operating procedure to involving parents and young people in the process. We found it useful to develop YouTube videos to explain the service with parents and young people taking part in recordings. The choice of platform was explored, a decision to use Cisco Jabber was made, while a standard operating procedure was agreed.

The project was supported by managers and the local Paediatric Consultant Lead for epilepsy. Appointments were held by both the children's Epilepsy Specialist Nurse and Assistant Practitioner within the team. Evidence was found for using video in specialist areas of paediatrics such as diabetes [Fatehi et al, 2015] and acute care [Jury et al, 2013]. However, literature searches made in the early stages of the project did not find any articles about use of virtual face-to-face clinics for paediatric epilepsy care. Further searches identified some use in adult epilepsy care [Haddad et al, 2015], [Ahmed et al, 2010] but minimal literature in paediatrics. As progress was made with the new service, there was a steep learning curve about the approach to parents and young people, processes and possible limitations with this type of care.

User feedback

Ongoing feedback was essential to ensure quality and engagement. Parents and carers reported similar benefits for the video links with easier access and

reduced time for travel and parking. Parents commented "the convenience of it all was great. It can be difficult travelling to appointments and getting time off work" and "saved time rather than waiting in hospitals and saved travel time too".

It had unexpected advantages in engaging with young people. A parent said "my son has confidence issues and yet he was so confident during this appointment. It was a positive experience; he was able to talk more openly". One parent found her teenage son with autism engaged far better through video. Feedback from young people reflected similar advantages regarding reduced waiting time and travel. One young person stated that he liked being at home for the clinic and another that he found it "more private".

Benefits of use

Staff experience of the virtual clinics has been mostly positive. Staff quickly found they had the potential to improve efficiency of the service. This was through carrying out fewer home visits and less time spent arranging and booking clinic rooms. To date, we have found recordings of seizures can be seen relatively clearly over video link provided connectivity is of sufficient quality. It enables parents to demonstrate seizures as they would in a face-to-face clinic. It can promote engagement following new diagnosis or for those managing complex epilepsies.

The video format has been useful to support uncertainties about medication doses, allowing visual confirmation about understanding. This also proved important where English was not the first language. It allows checking of medication labels and has highlighted problems of dosing and strength of supply. On a few occasions, the video links have been useful in offering further discussion when parents have been anxious about starting treatment. They have avoided unnecessary face-to-face appointments and can aid decision making about whether an urgent review is required by medical staff.

On one occasion, a video contact was set up to offer quick assessment of a young child with intractable seizures. This allowed for a discussion with mum, a view of the child having brief but frequent seizures and also a previous recording of a seizure on her phone. While the outcome was for the child to go to hospital for urgent review, the decision was based on robust information. In some cases, their use has increased access and engagement with hard to reach families or those with two or more children with epilepsy.

The procedure for clinics makes clear responsibilities of parents and young people in ensuring the place they make contact from is safe and secure. So far, there have been no safeguarding implications as a result of a video link. On advice from the Information Governance Manager, we routinely request explicit consent to offer an appointment. When seen on the link, often at home, it allows staff to observe the child in their own environment. Video link could, on some occasions, afford a more comprehensive assessment rather than only seeing them in a clinic or hospital setting.

Penny et al [2017] describes the use of video conferencing as being part of a continuum of contact offering better rapport than telephone call alone. It gives greater dimension, while acknowledging the limitations compared to in person face-to-face. They found verbal and visual information available with this delivery improved safety, decision making and avoided errors in communication. We

Video link could afford a more comprehensive assessment rather than only seeing them in a clinic or hospital setting.

have found similar benefits over the last three years and in all aspects of the care. Discussion and information giving are improved via the virtual clinics in comparison to phone call only. Care is needed when discussing more sensitive information such as sudden unexpected death in epilepsy. While this has been required, on very few occasions, it is unclear whether this is an appropriate medium in which to have this type of conversation.

Challenges

As we developed our skills with virtual clinics in various aspects of care, limitations became apparent. It cannot replace face-to-face clinical contact and review. Strategies for co-morbidities can be shared but may still require a home visit or appointment by the medical team for further assessment and similarly, in regards to seizure control. Follow up visits after the initiation of rescue treatment require a face-to-face contact rather than video link. This has been confirmed from recent experience during the pandemic when trying to support parents during restricted visits.

Young people and adults are familiar with using various social platforms and their virtual video links. However, in some cases, we have found patients using similar methods to contact healthcare professionals presented a different concept to them.

It sometimes took one or two sessions for them to become more comfortable. Consideration is required to determine if this type of delivery is appropriate for all patients. The virtual clinic was tried for a few young people with learning disabilities to support transition work but with limited success.

In the early stages of their use, young people and adults did not always contact the clinic as planned. This was possibly because they did not perceive it as a formal appointment. This was addressed by sending a reminder via SMS message. Some parents appeared reluctant with the concept of the video contact or declined. Although this was a minority, it was unclear whether this was due to lack of familiarity with a different model of care, a lack of confidence in IT skills or concerns about information governance. Recent feedback from one parent highlighted their apprehension, saying, "I wasn't sure it would work as I'm not confident in my abilities with technology. But in the end, it was fine."

Use of virtual clinics increased significantly during the lockdown with no-one declining the option. One parent described, "it has been different due to non-face-to-face appointments and needing to have appointments over the phone which is scary. I could see the value of having a video clinic to see clinician and they could see me". Once used, the virtual contact has always been subsequently accepted.

In some cases, there were challenges in setting up these links. However, it was recognised that it would prove useful in the long-term. Therefore, we decided it was appropriate to visit the home on few occasions to offer support and help develop confidence in its use.

There have been audiovisual problems, with audio the most common issue and prompt resolution wherever possible supports confidence in the service. Generally, the issues were around setting links up correctly with simple instruction. It has become important to recognise at what point to abandon the video link when there are difficulties and offer an alternative option. There are now more platforms to consider for the video format. Cisco Jabber is a US software developer with free access for the user but with cost to the provider. There are now free public platforms such as AccuRx and Attend Anywhere which our service has had no experience of to date. Upgrades in PC and IT support, identified as limitations in 2019, remain essential.

Future use within epilepsy care

The literature on health care video links suggests some health professionals can be resistant to this change of service. However, one consultant in the east of England is already offering the service within secondary care. Within the regional epilepsy network group there is keen interest in the potential for research. The IT skills in our team of two were limited but this demonstrated that delivery should not be restricted on this basis. Accountability for practice remains a core principle but the experience and skill mix within the epilepsy nursing team has allowed appropriate allocation in the different aspects of care with no identified problems so far.

They found verbal and visual information available with this delivery improved safety, decision making and avoided errors in communication.

It has been difficult to determine any cost saving for the clinics, but the flexibility of the service to young people and parents as an alternative contact has been evident. Over time, it no longer felt unusual during the virtual clinics to discuss transition skills and concerns with a young person in the comfort of their own room. Or talking about seizure management with parents in their workplace. However,

despite the current increase in uptake of the virtual clinics, it is clearly too soon to assume that these changes will be sustained.

Conclusion

The video format and the experience it has afforded has been a supportive resource as part of the response to our patients during the current pandemic. However, it would be useful to consider the potential for research, particularly in the current climate in determining what added value virtual clinics may offer. This may include a clear vision for their use, information governance, which platform/s are preferred, who is best placed to offer the service, cost effectiveness and possible training required. Despite the challenges, virtual clinics are now embedded in our service and continue to offer increased flexibility and efficiency in providing an effective community children's epilepsy nursing service.

Liz Stevens
Children's Epilepsy Specialist Nurse, Cambridgeshire Community Services NHS Trust

Acknowledgements

Dr Tekki Rao, Paediatric Consultant with specialist interest in epilepsy, Luton & Dunstable Hospital NHS Foundation Trust.
Mary Hunt Assistant Practitioner, Cambridgeshire Community Services NHS Trust.

Benefits versus challenges of virtual clinics

Benefits	Challenges
• Time and cost saving for travel and parking • Flexible • Responsive to need • Efficient format for information giving • Improves engagement • Convenience – at home and from work • Reduces time out of education • Can relieve employment pressures • Allows more robust assessment of seizures than phone call alone • Supports medication changes – safety aspect • Can reduce number of face to face appointments and access for patients with problems tolerating clinic settings	• Cannot replace face to face contact • IT issues • Parents may need to arrange weighing at GP • Parents may lack confidence with use • Not all will have device to use

Further reading

Ahmed, S. Nizam, Wiebe, Samuel, Mann, Carly., Ohinmaa, Arto. Telemedicine and Epilepsy Care-A Canada Wide Survey. *Canadian journal of Neurological Sciences*. Volume 37, Issue 6 pp. 814-818 Nov 2010

Fatehi F., Martin-Khan M., Smith A.C., Gray L.C., Russell A.W. Patient Satisfaction with Video Teleconsultation in a Virtual Diabetes Outreach Clinic. *Diabetes Technology and Therapeutics:* Vol17 (No1);p43-48 Jan 2015

Jury, Susan C., Walker Amanda M., Kronberg Andrew J. The introduction of web based video-consultation in a paediatric acute setting. *Journal of Telemedicine and Telecare*. Nov 10 2013

Haddad, Naim., Grant, Irish., Eswran, Hari Telemedicine for patients with epilepsy: A pilot experience. *Epilepsy & Behavior* Volume 44, p1-4. March 2015

Henry, B W., Ames, LJ., Blocl,DE., Vozenilek, JA. Experienced Practitioners Views on Interpersonal Skills in Telehealth Delivery. *Internet Journal of Allied Health Sciences & Practice;* Vol.16(no.2);p.1-13 Apr 2018

Penny, R.A., Bradford, K.A., Langbecker, D. Registered nurse and midwife experiences of using videoconferencing in practice: A systematic review of qualitative studies. *Journal of Clinical Nursing:* Vol.27 (no. 5/6) Mar 2018

Rasmusson, Karen A., Hartshorn, Jeanette. A Comparison of Epilepsy Patients ina Traditional Ambulatory Clinic and a Telemedicine Clinic. *Epilepsia*. 46(5): 767-770 2005

SMITH A.C., Garner L., Caffrey L.J., McBride C.A. A review of paediatric telehealth for pre and post-operative patients surgical patients. *Journal of Telemedicine and Telecare;* Vol. 20 (no 7); p 400-4 2014.

A structured, multi-disciplinary approach for the management of epilepsy for people with intellectual disabilities

Phil Tittensor et al examine the challenges of managing epilepsy in those with intellectual disabilities in the Midlands

Background

A learning disability or intellectual disability (ID) is broadly defined as a person who possesses a Full Scale Intellectual Quotient (IQ) below 70, encompassing developmental delay and impaired cognition social and adaptive skills [Ring, 2013]. Fisher et al [2014] state that epilepsy is a disease of the brain defined by any of the following: at least two unprovoked (or reflex) seizures occurring greater than 24 hours apart, one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years, or the diagnosis of an epilepsy syndrome.

People with ID are more likely to develop epilepsy than the general population, with a mean incidence ranging from 22-26% and increasing with the severity of the learning disability [Robertson et al, 2015]. These people can have a range of comorbidities that differ depending on the presence and degree of brain damage. Additionally, people with ID and epilepsy have a higher likelihood of communication, psychiatric, behavioural and drug sensitivity problems that make the condition more difficult to treat compared to those with higher IQ [Royal College of Psychiatrists, 2017]. They require expert support from a range of professionals.

People with ID have a significantly shorter life expectancy – 23 years for men and 27 years for women, when compared to the general population [Learning Disabilities Mortality Review – LeDeR, 2019]. According to LeDeR [2019]. 4% of deaths in people with ID were due to epilepsy, compared to less than 1% of the general population. The National Sentinel Audit of Epilepsy Deaths [Hanna et al, 2002] reported that almost half are preventable with optimal treatment. Although nearly 20 years old, this statistic has not significantly changed [Kerr et al. 2020]. In Cornwall, an integrated epilepsy and ID service has significantly reduced mortality figures, with one incident of sudden unexpected death in epilepsy (SUDEP), the most common reason for epilepsy mortality, since the service was commissioned in 2010 [Shankar et al, 2015; Shankar, Jory, 2020]. With a Cornish population of 538,000, Shankar and Jory [2020] state that the number of epilepsy related deaths for people with ID in the county would be expected to be between one and three per annum, demonstrating that a multi-disciplinary approach can make a positive contribution to safety for this vulnerable group of people.

People with ID and epilepsy have a higher likelihood of communication, psychiatric, behavioural and drug sensitivity problems

Aim

People with epilepsy and ID in South Staffordshire, Wolverhampton and parts of the Black Country in the West Midlands have, historically, experienced differences in care, depending upon the catchment area of each of the three NHS Trusts (one acute and two community – appendix 1) providing epilepsy services in the locality. There is considerable geographical overlap between the Trusts, but the services roughly align with three Clinical Commissioning Groups [Wolverhampton, Cannock Chase and South East Staffordshire and the

Seisdon Peninsular] with a combined population of approximately 626,000, approximately 2,700 of whom will be adults with ID and epilepsy (Appendix 2). Some people have been managed by neurology, some by ID services, and some access a joint clinic run by clinicians from both specialties. We have wanted to ensure that there is an equity of service for all people with epilepsy and ID in the area, aiming for the gold standard of a specialist epilepsy team commissioned by the liaison of adult, learning disability and physical health commissioners, with all the necessary components of epilepsy and learning disability care across the lifespan, ensuring a biopsychosocial approach [Kachika and Shankar, 2018]. We believe that this will improve care and enhance safety by providing optimal treatment and management of people with epilepsy and ID.

The joint service follows evidence based practice. Integral to this is research and audit. The discrete departments comprising the joint service are research active. We aim to critically evaluate our service outcomes, participate locally and internationally [EpiNet, 2020] in efforts to identify and understand epilepsy related deaths, and to participate in multi-centre research projects, such as the UK ID and anti-epileptic drugs registry [Shankar et al, 2015].

Many people with severe or profound ID will require the support of professional care staff. Education of carers about epilepsy in the UK is patchy [Shankar et al, 2017], and guidelines provided by the Joint Epilepsy Council of the UK and Ireland (JEC) expired in 2016 [JEC, 2012]. The Epilepsy Nurses Association (ESNA), in conjunction with the International League Against Epilepsy (ILAE) and Royal College of Psychiatrists (RCPsych), published new guidelines recently [ESNA, 2019]. An important role for the joint service is to provide education and guidance for families, care staff and other health professionals, to raise the standards of care for people with epilepsy and ID, thereby improving safety and enhancing quality of life.

Education of carers about epilepsy in the UK is patchy and guidelines provided by the Joint Epilepsy Council expired in 2016

Methods

The Community Learning Disabilities Team (CLDT), and the Department of Neurology in mid and South Staffordshire (services currently provided by the Midlands Partnership NHS Foundation Trust and Royal Wolverhampton NHS Trust respectively), developed a joint epilepsy and intellectual disability service over 10 years ago. Originally conceived to improve the care of patients in an NHS residential facility, the service expanded, and now comprises bimonthly joint epilepsy and ID clinics run by a consultant nurse for the epilepsies and a consultant psychiatrist for people with ID. There is input into the clinic from nursing staff from the CLDT, who monitor patients between clinic visits, assist with medication changes and monitoring of seizures, and provide education and support to people with ID, their families and carers. This includes training in epilepsy awareness and midazolam administration in line with the latest guidelines [ESNA, 2019]. Patients have access to the full range of services offered by the CLDT, alongside the full range of

Table 1
Interview regarding independence during the transitional period.

Change in seizure frequency	All seizure types (N=32)	Tonic Clonic seizures (N=24)
Seizure free	6%	8%
>50% reduction	47%	29%
<50% reduction	6%	8%
No change	19%	42%
Seizures worse	22%	17%

diagnostic facilities offered by the Department of Neurology. There are facilities for further neurological opinion and formal tertiary referral to the regional epilepsy centre. In 2019, we developed a similar service for people from Wolverhampton in collaboration with the Black Country Partnership NHS Trust CLDT.

The service advocates the use of EpsMon [SUDEP Action, 2020], an app to estimate an individual's risk from seizures. This can be used by the family or care team to provide an early warning of deteriorating seizure control (the primary risk factor for SUDEP), enabling them to seek specialist medical advice.

Results

Clinics for the last five years have been analysed. In that time, 33 people have accessed the service. 18 remain under ongoing review. Of those people discharged from the joint service, five have continued to be seen by the learning disability service, three have been discharged to their GP with no ongoing issues requiring specialist input (all patients have the opportunity for carers to self-refer back to the epilepsy service in the event of problems), two have moved out of the area, one discharged to neurology only follow-up and four have died (no deaths were epilepsy-related).

Over the five years, there have been 158 consultations in 25 joint clinics. About a third of patients had mild ID (30%), a third moderate ID (30%), and a third severe or profound ID (40%). All the patients had at least one comorbidity in addition to their ID and epilepsy, the most common being cerebral palsy (29%), autism (19%), genetic syndromes (19%) and other physical conditions (e.g. diabetes, cardiac conditions) (52%). 97% of the patients had involvement from the CLDT, and 87% had documented, up to date, risk assessments and epilepsy care plans in place. 86% of the patients had a documented epilepsy syndrome or classification using the current ILAE system [Fisher et al, 2017]. 95% of patients using the service have documented EEG, but only 43% had inter-cranial imaging (MRI or CT). 45% of patients were taking two anti-epileptic drugs, with 15% on monotherapy. Conversely, 9% were taking four or more anti-epileptic drugs. 70% had never tried one of the newer anti-epileptic drugs*. The seizure outcomes of patients using the joint epilepsy and ID service are summarised in Table 1.

All the patients had at least one comorbidity in addition to their ID and epilepsy, the most common being cerebral palsy

Discussion

The joint epilepsy and ID clinic supports a relatively small but extremely complex group of people. Their epilepsy is highly refractory, with the majority of patients requiring more than one anti-

epileptic drug to manage the condition. All have comorbidities that can impact upon the choice of anti-epileptic drug treatment and epilepsy itself. Despite this, over half of the patients accessing the service have seen a greater than 50% reduction in their seizures, with roughly double the seizure freedom rate that might be expected from a highly refractory cohort [Kwan and Brodie, 2000]. Given that improvements in seizure control is one of the biggest factors influencing SUDEP Hanna et al, 2002], the audit results indicate that patients may have a reduced mortality risk since they accessed the service. There is further evidence for this with the widespread use of risk assessments, epilepsy care plans and the involvement of the CLDT. We are currently exploring methods of identifying all epilepsy related deaths in Wolverhampton and South Staffordshire, in conjunction with the local coroner, in order to better understand the risks locally, as well as the impact of the joint service.

Fewer patients have accessed inter-cranial imaging than might be expected. There are a number of reasons for this, the most common being the difficulties in compliance with the requirements of the examination, particularly in the case of MRI where the patient needs to lie still for around half an hour. There was also a surprisingly low number of patients who had tried one of the newer anti-epileptic drugs, which we defined as those receiving marketing licences in the UK since 2006*. Anecdotally, many professional and family carers have voiced concerns about mood changing side-effects associated with some of the newer drugs, which could account for their relatively low use.

The present service offers support to a highly selective group of patients with difficulties relating to their ID as well as their epilepsy. There would need to be a considerable increase in provision to offer this joint approach to all individuals with ID and epilepsy in our area. However, the service is undergoing rapid expansion, with another epilepsy specialist nurse, and several consultant psychiatrists and specialist nurses for people with ID interested in the approach.

Further service evaluation and audit are planned in order to ensure that we place patients, their families and carers at the heart of the service. This focus on quality will help us to identify the benefits of the joint approach as well as any problems. Continual audit and evaluation will also guide us when considering further development of the service.

While the majority with ID and epilepsy will be well managed in either service, there are a number who need the expertise of both services.

Conclusion

The management of epilepsy in people with intellectual disability is often challenging and complex. Seizure freedom is more difficult to achieve in this population, and in the long-term, specialist support is likely to be needed. While the majority of people with ID and epilepsy will be well managed in either neurology or ID services, there are a number who need the expertise of both services. Given the significant interplay between comorbidities commonly associated with intellectual disability and epilepsy, we believe that best practice is to develop joint clinics and close working relationships between the CLDT and Department of Neurology. Further study is required to examine outcomes for people with intellectual disability served by neurology services alone, intellectual disability services alone and a joint service such as that which is described in this article.

*Zonisamide, Pregablin, Rufinamide, Lacosamide, Eslicarbazepine, Retigabine, Perampanel, Brivaracetam.

Tittensor PA, Rowe J, Youssef C, Manfredonia F: The Royal Wolverhampton NHS Trust
Baker S: Midlands Partnership NHS Foundation Trust
Varghese S: Black Country Health NHS Foundation Trust

Appendix 1. Participating Trusts.
The Royal Wolverhampton NHS Trust
Midlands Partnership NHS Foundation Trust
Black Country Health NHS Foundation Trust

Appendix 2. Local epidemiology.
The three Clinical Commissioning Groups covered by our services (Wolverhampton, Cannock Chase and South East Staffordshire and the Seisdon Peninsular) have a combined population of approximately 626,000. 2.4% of people in the UK have ID [Mental Health Foundation, 2011], so there are approximately 15,000 people with ID in the area. Using Robertson et al's [2015] incidence estimates, the local population of people with epilepsy and ID is about 3,600. 25% will be children, so there are about 2,700 adults with ID and epilepsy in the area.

Further reading

Epilepsy Nurses Association (ESNA) (2019). Best practice guidelines for training professional carers in the administration of buccal (or mucosal) midazolam for the treatment of prolonged and/or clusters of epileptic seizures in the community. *www.esna-online.org* (accessed 22/04/2020).

EpiNet (2020). *http://www.epinet.co.nz/index.cfm?PageID=1* Accessed 01/05/2020.

Fisher RS, Cross JH, French JA, Higurashi N, Hirsch E, Jansen FE, Lagae L, Moshé SL, Peltola J, Roulet Perez E, Scheffer IE, Zuberi SM (2017). Operational classification of seizure types by the International League Against Epilepsy: Position Paper of the ILAE Commission for Classification and Terminology. *Epilepsia*, 58: 522–530. doi:10.1111/epi.13670

Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, Engel Jr J, Forsgren L, French JA, Glynn M, Hesdorffer CD, Lee BI, Mathern GW, Moshe SE, Perucca E, Scheffer IE, Tomson T, Watanabe M, Wiebe S (2014). A practical clinical definition of epilepsy. *Epilepsia*,55(4):475–482,2014 doi:10.1111/epi.12550

Hanna NJ, Black M, Sander JW, Smithson WH, Appleton R, Brown S, Fish DR (2002). *The National Sentinel Clinical Audit of Epilepsy-Related Death: Epilepsy – death in the shadows*. The Stationery Office.

Joint Epilepsy Council of the UK and Ireland (JEC) (2012). Guidelines on the administration of buccal midazolam. JEC, PO Box 186, Leeds, LS20 8WY.

Kachika J, Shankar R (2018). Step Together: Integrating care for people with epilepsy and learning disability. NHS England (unpublished).

Kerr M, Sen A, Hanna J (Eds) (2020). Prevent 21: SUDEP Summit. *Epilepsy and Behaviour*. Vol 103, Part B.

Kwan P, Brodie MJ. (2000). Early Identification of Refractory Epilepsy. *New England Journal of Medicine*. 342 (5): 314–319.

LeDeR (2019). The Learning Disability Mortality Review (LeDeR) Programme, Annual Report 1018. The LeDeR team, Norah Fry Centre for Disability Studies, 8 Priory Road, Bristol BS8 1TZ. *http://www.bristol.ac.uk/media-library/sites/sps/leder/LeDeR_Annual_Report_2018%20published%20May%202019.pdf* accessed 22/04/2020.

Mental Health Foundation (2011). Learning disability statistics. *www.mentalhealth.org.uk*

Ring, H (2013). Epilepsy in Intellectual Disabilities. *Advances in clinical neuroscience and Rehabilitation.* 13: 13-15.

Robertson J, Hatton C, Emerson et al (2015). Prevalence of epilepsy among people with intellectual disabilities: a systematic review. *Seizure*. 29:46 - 62.

Royal College of Psychiatrists (2017). Prescribing anti-epileptic drugs for people with epilepsy and intellectual disability (CR206 Oct 2017). *http://www.rcpsych.ac.uk/usefulresources/publications/collegereports/cr/cr206.aspx* (accessed 25/06/2019).

Shanker R, Jory C (2020). Personal communication.

Shankar R, Jory C, McLean B, Tittensor PA, Walker M (2017). Epilepsy awareness and emergency rescue training: Ignorance is bliss! *Epilepsy and Behaviour* 70 (2017) 212–216.

Shankar R, Doran Z, Sander LJ, McLean B, Hillier R, Cox D et al (2015). A register for collecting and measuring outcomes of licensed anti-epileptic drugs in patients with epilepsy and intellectual disability and or pervasive developmental disorders. Conference paper 2015, 1st congress of the European Academy of Neurology, Berlin.

Shankar R, Newman C, Hanna J, et al (2015)1. Keeping patients with epilepsy safe: a surmountable challenge? *BMJ Open Quality* 2015;4:u208167.w3252. doi: 10.1136/bmjquality.u208167.w3252.

SUDEP Action (2020). EpsMon: epilepsy self-monitoring. Safety in your pocket. *https://sudep.org/epilepsy-self-monitor* (accessed 01/05/2020).

Sleep disruption in children and adolescents with epilepsy

University of Birmingham Researcher Alice Winsor analyses if seizure reduction can be achieved through the improvement of sleep

Introduction

Epilepsy is one of the most frequently occurring neurological diseases in childhood, arising in approximately 1% of children and often presenting very early on in the developmental trajectory [Tsai et al, 2019].

The primary clinical issue in this population is the management of seizures. However, over the years there has been an increased focus on other outcomes beyond seizure control. One of these is sleep health, which has been recognised as playing an integral role in childhood development and in epilepsy.

Sleep difficulties are commonly experienced in children without epilepsy, with a prevalence rate of up to 40% in early childhood [Mindell et al, 2008]. In children with epilepsy, sleep difficulties are even more commonly observed and can ultimately worsen their prognosis. These difficulties are not fully acknowledged and understood despite sleep health being a major determinant of quality of life, not only for the child but within the family.

Underlying mechanisms

Effect of sleep on epilepsy

Sleep consists of two main states, non-rapid eye movement sleep (NREM) and rapid eye movement sleep (REM). These exert opposite influences on the interictal conditions. NREM sleep encourages the spread of interictal epileptiform discharges (IEDs) and promotes the occurrence of seizures. The desynchronised environment in REM sleep restricts the spread of IEDs to the seizure area only [Gibbon, 2019]. Children with epilepsy have also been found to have a high prevalence of co-morbid sleep disorders, such as parasomnias and obstructive sleep apnoea, which are often undetected. Such disorders further disturb sleep, resulting in sleep deprivation and worsening seizure control [Dehghani et al, 2019].

Evidence has shown that even on nights without seizures, sleep architecture remains fragmented indicating that the epilepsy itself can leave individuals vulnerable to sleep disruptions

Effect of epilepsy and seizures on sleep

The interaction between sleep and epilepsy is bidirectional, with multiple factors playing a role. On one hand, epilepsy characteristics have a negative impact on sleep. IEDs have been found to impair the smooth transition through sleep-wake cycles [Maganti et al, 2005]. Similarly, nocturnal seizures often result in arousal from sleep, disrupting sleep continuity, resulting in alterations in sleep architecture and reduced sleep efficiency (proportion of time spent asleep while in bed) [Ong et al, 2010]. Interestingly, evidence has shown that even on nights without seizures, sleep architecture remains fragmented indicating that the epilepsy itself can leave individuals vulnerable to sleep disruptions [Lanigar, 2017].

Effect of anti-epileptic drugs on sleep

Treatments of epilepsy can have both a negative or positive effect on sleep depending on the type of anti-epileptic drugs (AEDs) administered [Shvarts and Chung, 2013]. Some older, first generation AEDs can have negative effects, such as valproate which increases nocturnal arousals and reduces REM sleep. Carbamazepine on the other hand has been found to reduce nocturnal arousals and increase slow wave sleep. Second generation AEDs

also have varying effects. Topiramate and levetiracetam have little to no effect on sleep, whereas lamotrigine can result in reductions in slow wave sleep. The number of AEDs children are treated with has been found to be a predictor of disturbed sleep, whereby polytherapy has worse effects on sleep patterns in comparison to monotherapy [Al-Biltagi, 2014].

Consequences of poor sleep in epilepsy

Sleep difficulties have detrimental consequences in both children with epilepsy and their families. Mothers of children with epilepsy have been found to have reduced sleep quality, which may be attributed to the anxiety associated with nocturnal seizures or to their child's disrupted sleep patterns [Larson et al, 2012]. This in turn has been linked with parent's mental wellbeing. Children with epilepsy who have anxiety surrounding sleep also have higher rates of internalising and externalising problems including depression, anxiety and aggressive behaviour, while daytime sleepiness has been linked to anti-epileptic drugs and impairments in cognition. Furthermore, some children who experience poor quality sleep have higher rates of behavioural problems and attention difficulties [Becker et al, 2004].

Aims

The meta-analysis and systematic review we report here aims to synthesise and collate previous studies investigating sleep parameters in children with epilepsy compared to children without epilepsy, to quantify these differences. It is anticipated that by quantifying what aspects of sleep are affected in children with epilepsy, possible treatment implications may be identified, such as, screening of sleep difficulties as part of routine diagnosis of epilepsy.

This meta-analysis was conducted with the following goals:

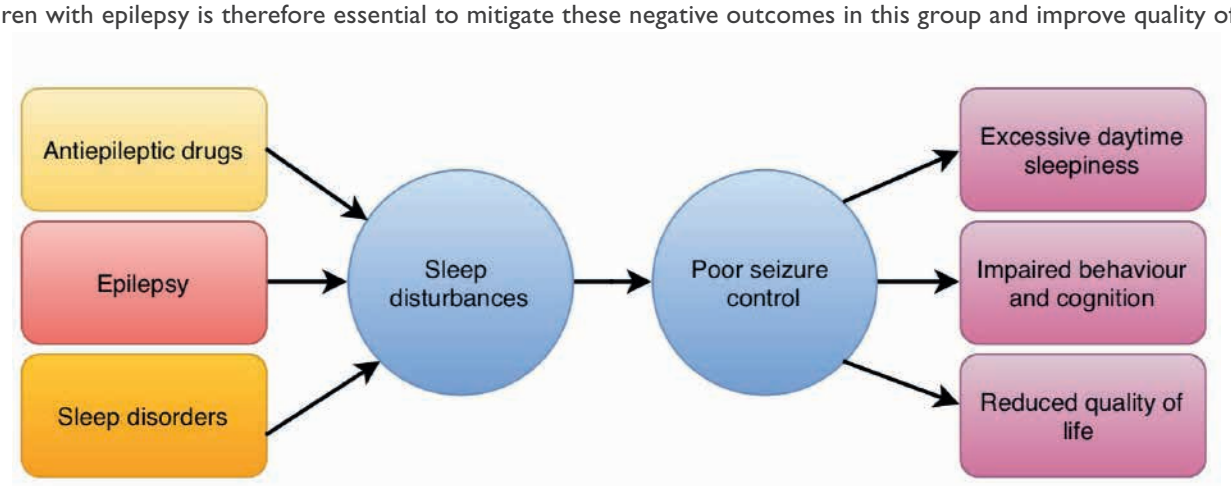
- To assess differences in sleep timing, sleep efficiency, sleep architecture and sleep difficulties in children with epilepsy compared to children without epilepsy
- To assess heterogeneity between studies and provide recommendations to reduce between-study heterogeneity for future research

Methods

A systematic literature search was conducted across the databases Medline, Embase, PsychINFO and PubMed. The initial search resulted in 14,951 papers. Following removal of duplicates, 8,838 papers were screened against strict inclusion criteria. 19 studies met the eligibility criteria and were used in the meta-analysis to assess the differences in sleep parameters between a total of 901 children with epilepsy and 1,470 children without epilepsy, all with a mean age of 10.8 years. Within these studies there

Figure 1

There is a clear relationship between sleep and epilepsy and the detrimental consequences on quality of life because of disturbed sleep. From a child's perspective, their quality of life is determined by their psychological and social health rather than epilepsy characteristics. Accurate quantification of the nature and range of sleep difficulties experienced by children with epilepsy is therefore essential to mitigate these negative outcomes in this group and improve quality of life.



were a broad range of tools used to assess sleep including polysomnography (PSG), video EEG, parent reported questionnaires and actigraphy.

A wide range of sleep parameters were considered within the meta-analysis including sleep timing, sleep difficulties, sleep efficiency and sleep architecture to incorporate a variety of findings and approaches.

Results
See Figure 2

Discussion
This meta-analysis revealed significant differences between children with epilepsy and children without epilepsy across both objective and subjective sleep parameters. This evidence of disturbed sleep in children with epilepsy warrants further investigation and a greater degree of clinical acknowledgement.

Children with epilepsy were found to experience significantly shorter total sleep time (ranging from 151 minutes less to nine minutes more across studies), confirming previous empirical research. This is clinically relevant to the management of children with epilepsy, especially given that insufficient sleep can act as a precipitating factor for the occurrence of IEDs and seizures. Similarly, reduced sleep duration results in daytime sleepiness which has been shown to affect behaviour and learning.

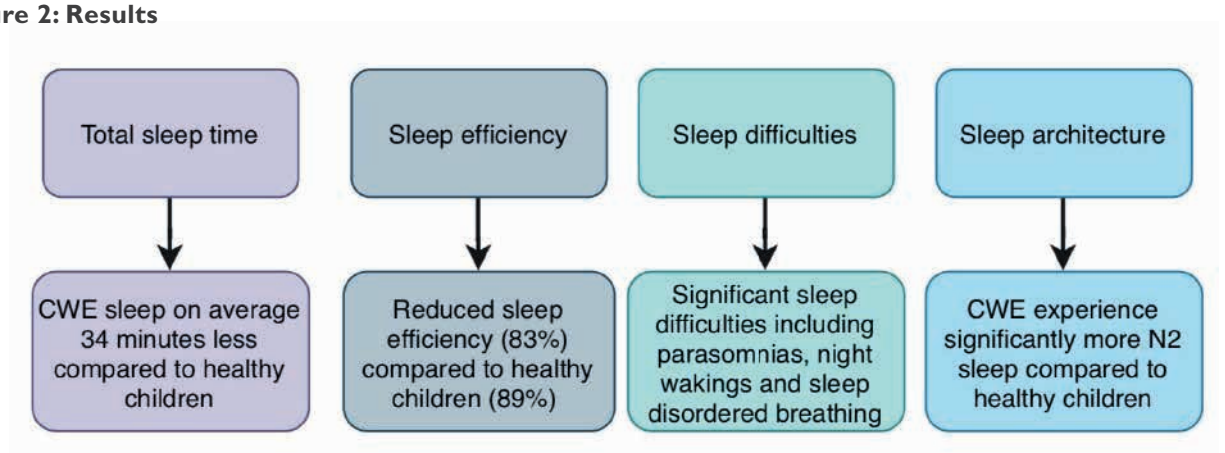
Sleep difficulties often contribute to the development of clinical sleep disorders, and thus pose a clinical issue in their own right.

CWE also had significantly more frequent and worse sleep difficulties. These included night waking, parasomnias and sleep disordered breathing, as assessed via the Child Sleep Health Questionnaire. Sleep disordered breathing has been implicated in cardiovascular system dysfunction, which is suggested to play a role in SUDEP [Sivathamboo et al, 2018]. Similarly, sleep difficulties often contribute to the development of clinical sleep disorders, and thus pose a clinical issue in their own right. They should therefore be addressed early on to mitigate the risk of these difficulties worsening and complicating the epilepsy diagnosis.

Our analysis of sleep architecture revealed a significant increased percentage of NREM stage two (N2) in children with epilepsy compared to children without epilepsy. This increased amount may be related to higher rates of sleep disruption, including sleep disordered breathing which can result in frequent arousals during sleep, increasing the time children spend in their lighter stages of sleep. Finally, children with epilepsy were found to have reduced sleep efficiency, a measure of sleep quality, which is associated with poor seizure control.

Recommendations for future research
There were several methodological constraints within the papers

Figure 2: Results



included in the meta-analysis, which restricted our ability to assess factors which have been shown to be predictors in sleep disturbances. We have outlined a list of considerations for research that may aid in standardisations between studies in the future. Future studies should aim to:

- Investigate different epilepsy syndromes to understand the specific disruptions in sleep across epilepsy types
- Detail the type of AEDs to allow investigation of their impact on sleep
- Investigate the associations between disturbed sleep and indicators of quality of life, behaviour, cognition and mental health
- Develop behavioural or educational interventions to aid in tackling sleep difficulties early in childhood and to reduce the impact of poor sleep on developmental outcomes

Findings from our meta-analysis suggest that screening of sleep difficulties should be an integral part of epilepsy management, to identify children with sleep disturbances and possible underlying sleep disorders.

Implications for clinical practice

Despite the clear evidence of major sleep difficulties in children with epilepsy, these are not fully acknowledged in clinical practice, which may be attributed to the primary goal being to treat seizures, or to the complexity of the disease. Findings from our meta-analysis suggest that screening of sleep difficulties should be an integral part of epilepsy management, to identify children with sleep disturbances and possible underlying sleep disorders. By addressing sleep health in this group, children and their families have the potential benefit of improving the frequency and severity of seizures, as well as quality of life.

Alice Winsor is a doctoral researcher based at the Centre for Human Brain Health in the University of Birmingham, working under the supervision of Dr Andrew Bagshaw and Dr Caroline Richards. She is investigating the impact and mechanisms of sleep disruption in children with rolandic epilepsy.

Further reading

Al-Biltagi, M.A., 2014. Childhood epilepsy and sleep. World *journal of clinical pediatrics,* 3(3), p.45.

Becker, D.A., Fennell, E.B. and Carney, P.R., 2004. Daytime behavior and sleep disturbance in childhood epilepsy. *Epilepsy & Behavior*, 5(5), pp.708-715.

Dehghani, M., Fayyazi, A., Cheraghi, F., Hakimi, H., Mosazadeh, S. and Almasi, S., 2019. The relationship between severity of epilepsy and sleep disorder in epileptic children. *Iranian journal of child neurology,* 13(2), p.77.

Gibbon, F.M., Maccormac, E. and Gringras, P., 2019. Sleep and epilepsy: unfortunate bedfellows. Archives of disease in childhood, 104(2), pp.189-192.

Lanigar, S. and Bandyopadhyay, S., 2017. Sleep and epilepsy: a complex interplay. *Missouri medicine,* 114(6), p.453.

Larson, A.M., Ryther, R.C., Jennesson, M., Geffrey, A.L., Bruno, P.L., Anagnos, C.J., Shoeb, A.H., Thibert, R.L. and Thiele, E.A., 2012. Impact of pediatric epilepsy on sleep patterns and behaviors in children and parents. *Epilepsia*, 53(7), pp.1162-1169.

Maganti, R., Sheth, R.D., Hermann, B.P., Weber, S., Gidal, B.E. and Fine, J., 2005. Sleep architecture in children with idiopathic generalized epilepsy. *Epilepsia*, 46(1), pp.104-109.

Mindell, J.A. and Meltzer, L.J., 2008. Behavioural sleep disorders in children and adolescents. *Ann Acad Med Singapore*, 37(8), pp.722-728.

Ong, L.C., Yang, W.W., Wong, S.W., AlSiddiq, F. and Khu, Y.S., 2010. Sleep habits and disturbances in Malaysian children with epilepsy. *Journal of paediatrics and child health*, 46(3), pp.80-84.

Shvarts, V. and Chung, S., 2013. Epilepsy, antiseizure therapy, and sleep cycle parameters. *Epilepsy research and treatment,* 2013.

Tsai, S.Y., Lee, W.T., Jeng, S.F., Lee, C.C. and Weng, W.C., 2019. Sleep and Behavior Problems in Children with Epilepsy. *Journal of Pediatric Health Care*, 33(2), pp.138-145.

Sivathamboo, S., Perucca, P., Velakoulis, D., Jones, N.C., Goldin, J., Kwan, P. and O'Brien, T.J., 2018. Sleep-disordered breathing in epilepsy: epidemiology, mechanisms, and treatment. *Sleep*, 41(4), p.zsy015.

Highlights

Top picks from *Seizure*

Editor of the journal *Seizure*, Professor Markus Reuber highlights his key papers from the latest editions

In its latest classification of the epilepsies, the International League Against Epilepsy (ILAE) stresses the importance of aetiology – explaining causes. It aspires to go beyond the largely phenomenological (description of what can be observed or measured), electroclinical description of different seizure types and syndromic seizure combinations which characterised previous classification systems [Scheffer et al, 2017]. However, in clinical reality, the aetiology of most patients' epilepsy remains undetermined at present. This is despite all the progress which has been made in genetics and our neurophysiological understanding of the epilepsies over the last few decades. One field in which progress has been particularly impressive is that of auto-antibody-associated epilepsies [Bakpa et al, 2016]. The relatively recent description of these epilepsies has highlighted the possibility that a large proportion of the as yet aetiologically unexplained epilepsies could be immune-mediated – those which result from abnormal activity of the body's immune system.

My Editor's Choice article from issue 75 of *Seizure* is an original research study by Anna Børsheim et al. The study used routinely collected healthcare data from the public Norwegian Prescription Database to add to the evidence of possible links between epilepsy and

autoimmunity [Børsheim et al, 2020].

In order to reach their conclusions, Børsheim et al initially identified all individuals with epilepsy in their country. They cross-referenced everyone who received at least two anti-epileptic prescriptions during the 10-day capture period with all those for whom a reimbursement code for epilepsy had been used. This process yielded almost 80,000 people with (probable) epilepsy (PWE), who were compared to a population of 4.7 million people likely not to have epilepsy. Børsheim et al then identified individuals with a wide range of conditions thought of as immune mediated, such as type 1 diabetes mellitus, multiple sclerosis (MS), myasthenia gravis and hypothyroidism. This was done by searching for all those who had received medications for these disorders (for instance insulin and insulin analogues but no oral antihyperglycaemic drugs). They found evidence of an association between epilepsy and autoimmunity across many of the indicators examined. PWE were almost twice as likely to be treated with insulin or insulin analogs, one and a half time as likely to receive thyroid hormones or pyridostigmine. Medications for MS were used almost five times as often in those with epilepsy as in the general population.

These findings add further weight to previous studies demonstrating an association of epilepsy and autoimmune disorders [Devinsky et al, 2013] on both sides of the blood brain barrier. These involve intra and extracellular immune targets, cellular and humoral autoimmune processes. However, they do not prove the direction of the association. The authors provide a number of arguments why autoimmune disorders may make the development of epilepsy more likely (including immunogenic effects of seizures and side effects of anti-epileptic drugs). There are also a number of mechanisms which could mediate a bidirectional relationship between the epilepsies and the many interacting parts of the immune system. Last but not least, the chances of receiving treatment for epilepsy may be increased in those under medical care with autoimmune disorders and vice versa. Regardless of the direction of the relationship, this association with autoimmune disorders could explain one part of the increased mortality, as well as psychiatric morbidity, associated with epilepsy. At a time when the world's attention is focused on the response of emergency medical services to the COVID-19 pandemic, my Editor's Choice from issue 76 of *Seizure* is a scoping review by Lisa Burrows et al It summarises research exploring interventions aimed at reducing unnecessary emergency department (ED) attendances by individuals with epilepsy [Burrows et al, 2020].

England is a high-income country with a universal public health system providing free access to routine and emergency healthcare and antiseizure medicines. Yet only 50% of patients with epilepsy become free of seizures [Dixon et al, 2015]. Those individuals with uncontrolled epilepsy are not the only ones who are at risk of frequenting EDs with seizures. One study suggested that while three-quarters of ED patients

with suspected seizures had experienced an epileptic seizure, only one-third of patients carried a diagnosis of epilepsy during admission [Dickson et al, 2017]. However, it has been estimated that epileptic seizures lead to 60,000 ED (113 per 100,000), and 40,000 hospital admissions in England per year (76-148 per 100,000). This makes epileptic seizures one of the three most common neurological causes for attendance in emergency departments [Dickson et al, 2018].

This means that a substantial proportion of seizure-associated ED attendances are related to an 'ambulatory care sensitive condition', i.e. conditions where effective community care and case management can help prevent the need for hospital admission.

So they occurred in a context in which optimal out of hospital care may have prevented the need for the involvement of emergency services. Most presentations to EDs turn out to be related to problems which could have been managed outside EDs (such as resolved seizures) [Dickson et al, 2016]. ED management by non-seizure experts often adds little to longer term seizure control. But it is associated with considerable expenditure and a risk of complications, such as hospital acquired infection). Therefore, it is important to explore how care could be improved to avoid unnecessary admissions.

The scoping review by Burrows et al is consequently of great clinical importance. Their overview of recent research is based on 29 pieces of original research which could be subdivided into four themes. These are care pathways, conducting care and treatment reviews, educational interventions and the role of ambulance staff. Although there is clearly more work to do, some of these interventions have been welcome by patients and associated with reduced healthcare expenditure.

The identification of demographic and clinical risk factors for repeated attendance to EDs due to seizures has allowed interventions to be focused on the third of patients who are responsible for two-thirds of all epilepsy related admissions [Noble et al, 2012]. The nature of these factors (including mental health problems, low educational attainment and social problems) means that successful intervention will be particularly challenging. However, the urgent and increasing need to use limited healthcare resources most effectively means that the search for more effective interventions of ambulatory care and reducing epilepsy-related demands on emergency services must continue.

It may seem badly out of step with current lived experience and sentiment to produce a Special Issue on paediatric epilepsy surgery. We are facing a crisis – city streets have emptied, societies are struggling with increasingly stringent social distancing and self-isolation measures, and hospitals are struggling to deal with the stream of acutely ill patients flooding through their doors. So why publish about complex interventions suitable for less than 5% of individuals with epilepsy, and only available to those who live in rich countries? And why at this time?

First I would like to apologise in advance in case my answers seem inappropriate by the time they are read. My colleagues and I have transformed a multidisciplinary neuroscience service into a support service for acute respiratory, intensity and high dependency care. All non-urgent elective neurosurgery has been stopped. Many outpatient appointments are being cancelled or delayed and all face-to-face outpatient contacts have been replaced with telephone or video-phone interactions. However, the emergency staffing rotas we discussed only yesterday are already out of date. And the scenarios we imagined as we made our plans last week already seem strangely naive. Now we anticipate that we will need at least twice as many neurologists to support acute medical services and enable home treatment of neurological emergencies than was deemed necessary only 24 hours earlier. I am therefore acutely aware that anything I write today, as more people and healthcare professionals around the world become direct or indirect victims of COVID-19.

Life will continue after the pandemic. While many of us will come to think of our lives as split into two distinct parts – before and after the pandemic – the modern world will not end. People will continue to suffer from long-term conditions such as epilepsy. We will still want to provide effective treatments and reduce the burden of the disease. And in the case of paediatric epilepsy surgery, we can actually go much further than this. This particular treatment remains our only chance of providing a cure of epilepsy. Even more clearly than adult epilepsy surgery, this treatment can make a profound difference to our patients' whole life trajectories. Even if shortages of funding, material or staffing should force restrictions upon overstretched health care services after the pandemic. For this reason, the resumption of paediatric epilepsy surgery should be given priority over other elective neurosurgical procedures.

My editor's choice from issue 77 of *Seizure* – is an original research paper by Christoph Helmstaedter et al. It is entitled "Cognitive outcome of paediatric epilepsy surgery across ages and different types of surgeries: A monocentric 1-year follow-up study in 306 patients of school age". This paper reminds us that epilepsy is not simply a disease characterised by recurrent seizures. In most cases, epilepsy is also

associated with some degree of cognitive compromise. As demonstrated in the SANAD study, even at the point of diagnosis, patients with epilepsy perform worse than healthy volunteers on a range of cognitive measures. In that study, 53.5% patients but only 20.7% of controls scored >2 standard deviations below the control mean in at least one testing domain [Taylor et al, 2010]. These cognitive deficits are even more important in children than in adults because they can affect subsequent cognitive development [Holmes et al, 2016]. In view of the ability of the brain to recover after epilepsy surgery, successful interventions in children and adolescents often improve cognitive performance. Equivalent improvements are unexpected in older patients even when seizures stop postoperatively [Helmstaedter et al, 2002].

In my Editor's Choice paper, the large paediatric and adolescent epilepsy surgery series described by Helmstaedter et al, 85% of patients were found to have preoperative impairments in at least one domain (i.e. they performed >2 standard deviations below the level of healthy controls), and 71% had behavioural problems. Postoperatively, the status of 21-50% of the patients changed from impaired in at least one domain to unimpaired across all domains. At the individual patient level significant gains in test performance were observed in 16-42% of patients in different domains. The proportion of patients who had become seizure-free through surgery was 81%. At last follow up, patients in the surgically treated group were more likely than the others to have decreased their antiseizure medicine load.

Postoperative seizure freedom, a younger age at evaluation, a later age at epilepsy onset, a lower anti-epileptic drug load, and less baseline damage predicted better cognitive and behavioural outcomes after epilepsy surgery in children and adolescents. In keeping with the finding of previous studies that neuropsychological deficits tended to be less focal or domain specific in the brains of children than adults [Holmes et al, 2016], the specific location of the surgery in the brain had little or no impact on neuropsychological outcomes. Likewise, gender and type of pathology were not found to predict postoperative neuropsychological outcome [Helmstaedter et al, 2020].

This study shows how much good we are able to do with the advanced neurosurgical techniques described in the Special Issue 77 of *Seizure* on paediatric epilepsy surgery. The final reason for publishing this Special Issue while we are all grappling with the COVID-19 pandemic is to remind us that a better time will come. A time when we will be able to dust ourselves down and refocus on providing surgical treatments which can transform the lives of individuals with epilepsy.

Further reading

Bakpa O D, Reuber M, Irani S R. Antibody-associated epilepsies: Clinical features, evidence for immunotherapies and future research questions. *Seizure* 2016;41,26-41.

Børsheim A, Engeland A, Gilhus NE. Epilepsy and autoimmune diseases: comorbidity in a national patient cohort. *Seizure* 2020; 75.

Burrows L, Lennard S, Hudson S, McLean B, Jadav M, Henley W, Sander JW, Shankar R. Interventions reducing unnecessary emergency department attendances for seizures: a scoping review. *Seizure* 2020

Devinsky O, Schein A, Najjar S. Epilepsy associated with systemic autoimmune disorders. *Epilepsy Curr* 2013;13:62–68.

Dickson JM, Dudhill H, Shewan J, Mason S, Grunewald RA, Reuber M. Cross-sectional study of the hospital management of adult patients with a suspected seizure (EPIC2). *BMJ Open.* 2017;7(7),e015696. doi: *10.1136/bmjopen-2016-015696*.

Dickson JM, Jacques R, Reuber M, Hick J, Campbell MJ, Morley R, et al. Emergency hospital care for adults with suspected seizures in the NHS in England 2007-2013: a cross-sectional study. *BMJ Open* 2018;8(10),e023352. doi: *10.1136/bmjopen-2018-023352*

Dickson JM, Taylor LH, Shewan J, Baldwin T, Grünewald RA, Reuber M. A Cross-Sectional Study of the Pre-hospital Management of Adult Patients with a Suspected Seizure (EPIC1). *BMJ Open* 2016;6:e010573. doi:*10.1136/bmjopen-2015-01057*

Dixon P, Kirkham J, Marson A, et al. National Audit of Seizure management in Hospitals (NASH): results of the national audit of epilepsy in the UK. *BMJ Open* 2015;5:e007325.

Helmstaedter C, Beeres K, Elger C, Kuczaty S, Schramm J, Hoppe C. Cognitive outcome of pediatric epilepsy surgery across ages and different types of surgeries: A monocentric 1-year follow-up study in 306 patients of school age. *Seizure* 2020; 77: 86-92.

Helmstaedter C, Reuber M, Elger CE. Interaction of cognitive aging and memory deficits related to epilepsy surgery. *Ann Neurol* 2002;52,89-94.

Holmes GL, Effect of Seizures on the Developing Brain and Cognition. *Semin Pediatr Neurol* 2016; 23: 120–126.

Noble A, Goldstein L, Seed P et al. Characteristics of people with epilepsy who attend emergency departments: Prospective study of metropolitan hospital attendees. *Epilepsia*. 2012;53(10):1820-1828.

Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L, et al. ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. *Epilepsia* 2017;58:512-21.

Taylor J, Kolamunnage-Dona R, Marson AG, Smith PE, Aldenkamp AP, Baker GA, et al. Patients with epilepsy: cognitively compromised before the start of antiepileptic drug treatment? *Epilepsia* 2010;51,48-56.

The times they are a-changing

I am not someone who is regularly lost for words. I think this comes with the territory – epilepsy is such a chatty speciality – and there are whole research groups that focus on what people say and how they say it in the diagnosis of epilepsy. How we communicate with patients and colleagues has been transformed over the last few weeks, and it is likely that things will never be the same again.

Epilepsy is predictably unpredictable. How often do you need to see someone with epilepsy? Annually to discuss risk reduction? When they want to see you? After their last seizure? Or four times a year (in Germany) because you will not get paid for seeing them a fifth time… Working at maximum clinical capacity makes it nigh on impossible to personalise acute support. When the COVID-19 pandemic broke, we were asked to rationalise clinical work, we cancelled non-essential travel and meetings, and we found a previously undiscoverable commodity – time. Now much of this time would or could be used for redeployment to front-line COVID19 work or preparing to be overwhelmed with seizures / status / non-epileptic attacks – but this tsunami did not come.

The second realisation was that the NHS could be reorganised at light speed during times of chaos, where it appeared to be stagnated with a stoic resistance to change at times of peace. We are all now providing some or all of telephone follow-up, video-consults, email advice and guidance and more – and we are seeing the benefits of this. Travel two and a half hours from Whitehaven and I may pad the consult out with a few niceties and small talk to justify the day's disruption. In contrast telephone reviews for people who remain well can be rapid. There's an environmental argument, there are no complaints about the parking situation, people are not running late. I also am sure that I've caught a few people at home on the phone who would otherwise have DNA'd – and had a worthwhile consultation. Many people also seem much more relaxed at home without that trip in to see the 'doctor' or 'nurse'. Why do we think that only the blood pressure doctors see 'white coat hypertension'? Hospital based anxiety is prevalent and negatively impacts on face-to-face consultations. Not that the phone is a panacea. It is hard to act out a seizure on the phone, harder still to evaluate someone's tremor. It is a tough ask to create a rapport down the wires – making discussing non epileptic attack disorder a trickier affair.

Living in a corner of England, camped on Hadrian's Wall, I would apologetically call in to some national meetings – acutely aware that it was hard to contribute fully that way. But now everyone – and I mean everyone has gone Zoom/Skype/FaceTime/MS Teams crazy. Now I am dropping in to virtual consults with psychiatrists in Cumbria and psychologists in Gateshead, with the same ease as the weekly family Zoom quiz (always won by my mum). I've been part of a research collaborative with four people I have never knowingly met in the flesh… and get this – one person I have never seen, even on Zoom – as she refuses to put the camera on because of the impact of COVID-19 on her ability to get her hair cut. These are unprecedented times indeed. We have proven how adaptable we can be, and we can use this experience to deliver real and meaningful change in the future.

I am sure that I've caught a few people at home on the phone who would otherwise have DNA'd – and had a worthwhile consultation

I am reminded of an old joke. "How many psychoanalysts does it take to change a light bulb? Only one, but the light bulb has to really want to change." We have proven that we can introduce significant and rapid change, what more are we capable of?

Dates for the diary

Dates and events may be subject to change – please check on the relevant websites.

2020

5-9 July
14th European Congress on Epileptology (ECE)
POSTPONED TO 2022
Geneva, Switzerland
epilepsycongress.org/ece

28 Aug-1 Sept
34th International Epilepsy Congress
Paris, France
epilepsycongress.org/iec

10-12 September
4th International Video-EEG in Paediatric Epilepsies from Seizures to Syndromes
Madrid, Spain
2020.videoeeg.es

20-26 September
7th Residential International Course on Drug Resistant Epilepsies
Tagliacozzo, Italy
ilae.org/congresses

2-5 October 2020
14th World Congress on Controversies in Neurology
London, UK
emedevents.com

8-10 Oct
4th ILAE British Branch Epilepsy Neuroimaging Course
Chalfont St Peter, UK
https://ilaebritish.org.uk/events/

6 Nov
Irish Epilepsy League Annual Meeting
Dublin, Ireland
ilae.org/congresses

12-13 November
4th Dianalund International Conference on Epilepsy:
Comwell, Korsør, Denmark
ilae.org/congresses

2021

3-5 March
Fetal and Neonatal Neurology Congress
Paris, France
mcascientificevents.eu

Next issue:

Mark Atherton

Case study: biotinidase deficiency in infancy.

Sukhvir Wright

A look at MOG-Ab related epilepsy in childhood.

If you are interested in submitting a research paper for inclusion in *Epilepsy Professional,* please contact the Editor: *editor@epilepsy.org.uk*

optima

XLTEK

Diagnostic EEG

- Lightweight ambulatory EEG for comfortable at home recordings
- Continuous video and EEG monitoring for the I.C.U.
- Longterm video EEG including intracranial recording

natus neurology

To find out more call 020 3058 0850

www.optimamedical.com