epilepsy action

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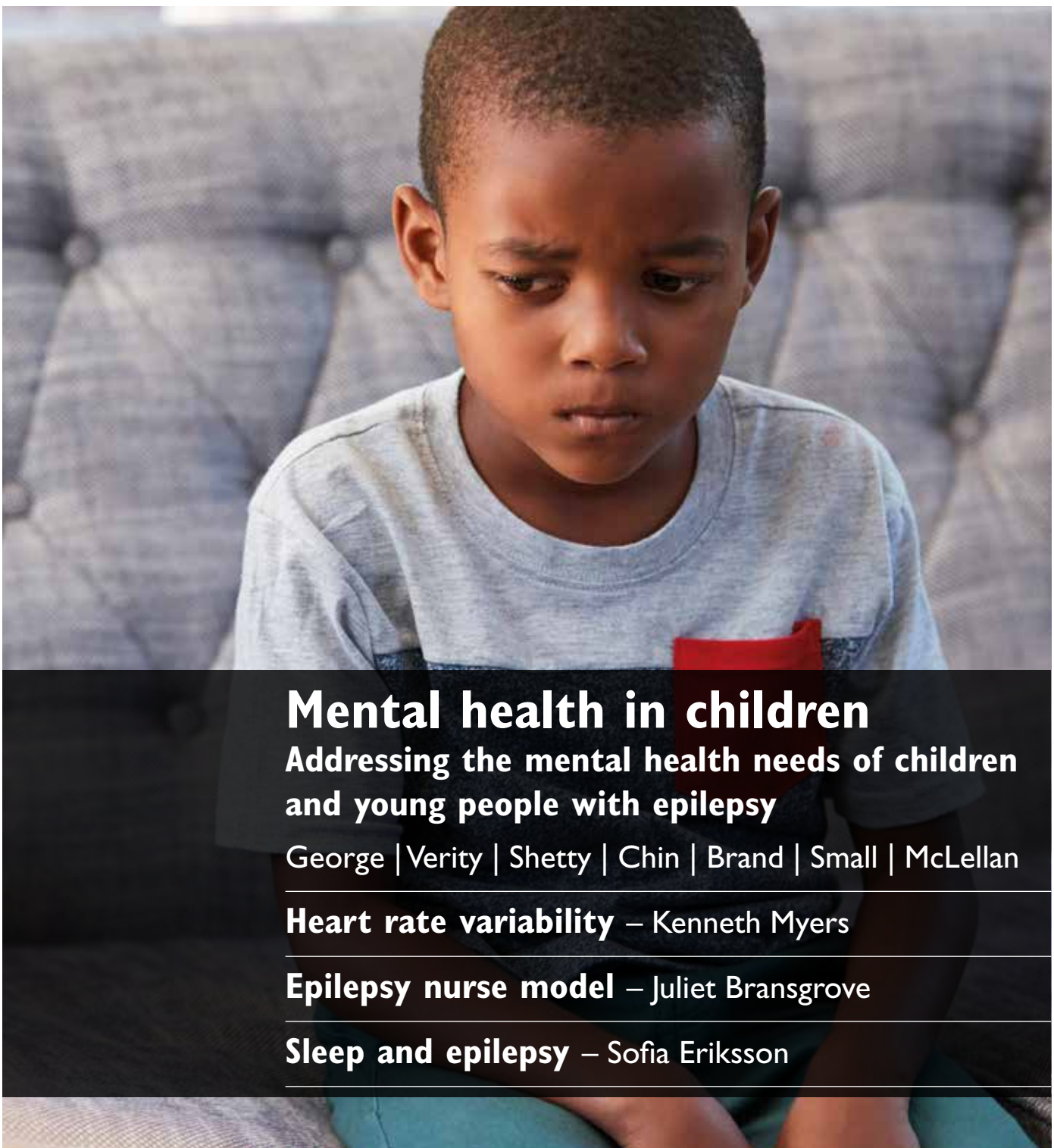
epilepsy professional



Mental health in children

Addressing the mental health needs of children and young people with epilepsy

George | Verity | Shetty | Chin | Brand | Small | McLellan

Heart rate variability – Kenneth Myers

Epilepsy nurse model – Juliet Bransgrove

Sleep and epilepsy – Sofia Eriksson

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Health innovation that matters

There is more to epilepsy than seizures, and more to epilepsy treatment than seizure control. So, it follows that there is more to *Epilepsy Professional* – and you, the epilepsy professionals – than the relentless desire to minimise seizures. Welcome to this bumper edition of *Epilepsy Professional*! In this issue, we have four articles themed around epilepsy care – but not one focussed directly on seizure control.

The first pertains to the most overlooked and yet oh-so-prevalent comorbidity – the mental health of our patients. Catriona George, Kirsten Verity and colleagues focus on the needs of children and young people, providing a topical review in the light of the recent Epilepsy12 findings. Not only is the scale of the problem discussed but they suggest a solution that is underway in Edinburgh – PAVES: Psychology Adding Value: Epilepsy Screening. Over a third of those screened showed signs of a significant concern; this is a rate of seven times the population average. They really show the magnitude of the problem that we are not adequately addressing at present.

Questions about sleep are often how I get people to open up about mood and confidence. People are more comfortable to talk about sleep difficulties when direct questions about low-mood can be obtrusive. Sofia Eriksson tackles the bidirectional relationship between sleep and epilepsy; it is remarkable how disturbed the sleep of our patients can be. This article is a tour-de-force and contains many helpful clinical gems collected at the coalface. I will certainly consider CBT more readily in my patients with insomnia.

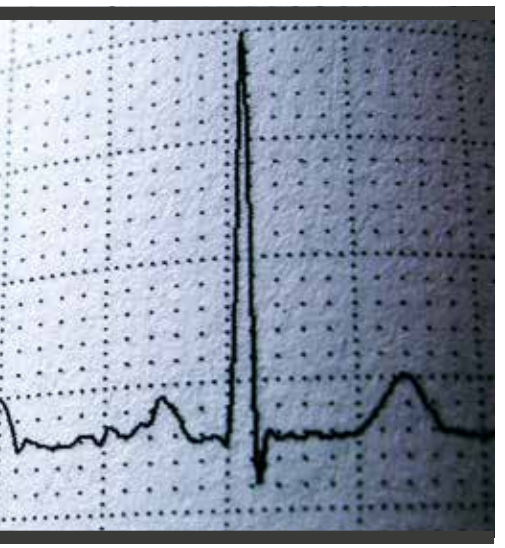
Do you need more epilepsy specialist nursing capacity? I bet you do. The third article addresses how the Norfolk adult epilepsy specialist nursing team more than doubled their numbers to meet the minimum requirements of a large rural area. The article both reads as an inspiring tale of how to persuasively argue for an increase in services, but also as an exemplar of a stratagem that can be successfully reemployed. The targeted use of the correct statistics and 'levers for change', such as the RightCare data, are lessons from which we can all learn. Their aims to reduce drug spend while improving mortality rates sounds like a dream win-win for CCGs; and our patients.

Finally, we have an important and interesting review of the heart-brain-heart axis; one all too often ignored by neurologists who may be tempted to believe that all the vital organs are neck-up. Dr Myers discusses heart rate variability and how to change 20-years of research into a clinical tool. Derangements of heart rate variability are seen more commonly in people with tough to treat epilepsies and it is tempting to consider how they can be utilised to stratify SUDEP risk if validated.

As a jobbing epilepsy doctor, what I love most about *Epilepsy Professional* is that the articles are hand-picked to be about subjects of importance to you – the epilepsy clinician and by extension – to your patients. These curated reviews are written primarily by UK authors and therefore have a credibility – a ring of truth. If you can't learn something new or change your practice after reading one of these reviews, then perhaps you are in the wrong game.

Rhys Thomas
Consultant neurologist
Chief medical adviser
Epilepsy Professional

contents



16
mental health in children

George | Verity | Shetty | Chin | Brand | Small | McLellan

Dr George, Dr Verity *et al* look at how common mental health conditions in children and young people are, why they might be missed in the clinic, and solutions to the problem

It's encouraging to see that mental health is seemingly more readily spoken about, both in general life and in the media. The organisation Mind states that approximately one in four people in the UK will experience a mental health condition each year. But it also says only one in eight adults with a mental health condition are currently receiving treatment.

Our cover article in this issue deals with mental health conditions in children and young people with epilepsy. This group is more likely to be affected by mental health conditions than their peers without epilepsy. Early recognition and treatment is important to reduce the impact mental health conditions can have on things like education and quality of life. Dr George, Dr Verity and the rest of the team suggest a way to assess this and introduce interventions on page 16.

But when it comes to quality of life of patients, there are other aspects to this, too. This issue, we also look at quality of sleep and the quality of care. On page 30, Dr Eriksson discusses the relationship between sleep and epilepsy, and suggests how epilepsy clinicians can assess and address problems linked to sleep. On page 22, Juliet Bransgrove describes the important role epilepsy specialist nurses play in care provision, and the business case that led to the expansion of the ESN roles in her area. Finally, don't miss our article on heart rate variability (HRV) on page 10. Dr Myers describes how HRV changes in people with seizures and discusses its potential as a clinical tool in epilepsy in the future.

We hope you enjoy this issue!

Kami Kountcheva
Editor
Epilepsy Professional
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AEDs not part of government plans to let pharmacists ration medicines in case of no-deal Brexit

The government has said anti-epileptic drugs (AEDs) will not be included in plans to allow pharmacists to ration medicines in the case of a no-deal Brexit, the *Sunday Times* has reported.

In December, the government set out plans to avoid shortages of medicines, which it called a "serious shortage protocol". This would be in the event that no Brexit deal is reached ahead of the UK leaving the EU.

As part of this plan, the government would allow pharmacists to ration medicines in order to avoid extreme shortages. This includes changing prescriptions without having to contact GPs first. Additionally, pharmacists would be able to supply a reduced quantity of a medicine, a different dose, a therapeutic equivalent or a generic equivalent.

Epilepsy Action chief executive Philip Lee said: "We are pleased to hear the government has pledged to exempt epilepsy patients from its contingency plans to deal with post-Brexit medicine supplies as reported in the *Sunday Times*. However, there still remains some uncertainty around access to epilepsy medicines in the event of a no-deal Brexit."

After the "serious shortage protocol" plans were published by *The Times* in December, an open letter was sent to Health Secretary Matt Hancock with concerns about the effects on epilepsy. This was put together on behalf of a number of epilepsy charities and organisations. They included SUDEP Action, Epilepsy Action, Young Epilepsy, the International League Against Epilepsy (ILAE) and Epilepsy Specialist Nurses Association (ESNA), among others.

The letter explained that sudden or unsupported medicine changes, or stopping of medicines, poses a risk for people with epilepsy. The letter also stressed that the best treatment for a person with epilepsy should be worked out between a doctor and patient. "No change to a prescription should be made without checking with the prescribing clinician and the patient," it said.

Epilepsy Action responded to the original "serious shortage protocol" in December. The organisation said: "It is right and proper that the government should prepare for all possible outcomes in the Brexit process, including no-deal. However, the suggestion of giving pharmacists emergency powers to alter prescriptions in the event of a no-deal, without discussing this with prescribing clinicians, is very concerning." Epilepsy Action warned that for people taking multiple AEDs, finding the right combination requires oversight from an experienced clinician. It added that switching between different forms of AEDs can also be a problem for some people.

The Department of Health and Social Care explained that the protocol would be developed in collaboration with doctors. "In the unlikely event of a shortage of any medicine, it is vital that patients continue to receive the high level of treatment they expect."

Mental health after surgery

A new Portuguese study has looked at potential risk factors for mental health conditions newly arising after epilepsy surgery.

Researchers Novais and colleagues recruited 106 people due to undergo surgery for refractory epilepsy from their Refractory Epilepsy Reference Centre. People were evaluated for psychiatric conditions before surgery and every year for three years afterwards. As well as psychiatric data, the researchers also collected demographic and neurological data from the people undergoing surgery.

Two types of surgeries were included – resective surgery and palliative surgery. The latter was deep brain stimulation of the anterior nuclei of the thalamus (ANT-DBS).

The results found that 15% of people developed psychiatric conditions after surgery that were not found beforehand. The predictors of developing these were having a multilobar epileptogenic zone and undergoing ANT-DBS. The latter could be a result of the intervention itself or the structures of the brain requiring this type of treatment being associated with mood and cognition, the researchers explained.

The research, published in *Epilepsy & Behavior*, concluded that people considered at a higher risk of developing mental health conditions after surgery should be submitted for more frequent routine assessments. The study can be found at: *bit.ly/2EJX0mS*

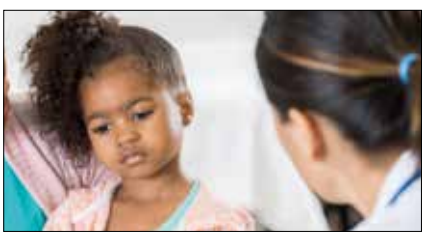
Poor mental health support for children in epilepsy clinics, national audit shows

Almost nine in 10 Health Boards and Trusts in England and Wales do not enable mental health provision within epilepsy clinics. This is despite research showing that children with epilepsy are four times more likely to experience a problem with mental health than their peers.

This is a finding in the new Epilepsy12 National Audit report from the Royal College of Paediatrics and Child Health (RCPCH). The report also found that nearly a quarter of Health Boards and Trusts are failing to provide routine and comprehensive care planning for children with epilepsy.

The report also highlighted areas of improvement. The number of epilepsy specialist nurses (ESNs) across England and Wales has increased significantly since 2014, when the last audit was published. However, the report also found that almost a quarter of Health Boards and Trusts were not able to provide access to ESNs.

Philip Lee, chief executive of Epilepsy Action, said: "It is encouraging to see that clear improvements have been made in some areas of children's epilepsy services.



"Despite this, there are still too many children and young people with epilepsy whose health, wellbeing and safety is being put at risk. There needs to be a strong focus on good care plans and support between appointments to improve epilepsy services and outcomes for young people.

"The report does a good job of highlighting best practice in this area and provides an opportunity for those services that are still lagging behind to step up."

The Epilepsy12 National Audit was introduced to assess epilepsy care for children and young people in England and Wales. Care is measured against national guidelines and standards as set out by the National Institute for Health and Care Excellence (NICE).

The full report is available at: *rcpch.ac.uk/about-epilepsy12-audit*

Carbagen out of stock in the UK

The Department of Health and Social Care (DHSC) has said that Carbagen (carbamazepine) tablets are out of stock until mid to late 2019. This includes both the immediate-release and prolonged-release tablets from the manufacturer Mylan. The company explained that the shortage is due to manufacturing issues. The DHSC has written to healthcare professionals advising them to switch their patients from Carbagen to Tegretol.

Epilepsy Action has advised people with epilepsy concerned about taking a different version of carbamazepine to speak to their GP or epilepsy specialist.

Everolimus available for TSC-related seizures

NHS England has agreed to make everolimus available to treat refractory focal onset seizures caused by tuberous sclerosis complex (TSC). This has come after the organisation initially decided not to commission the medicine in June 2018.

NHS England has said that from 1 April 2019, everolimus can be given as adjunctive therapy to patients two years and older with TSC-related seizures. This is in cases where seizures have not responded to at least two different epilepsy medicines and where surgery is not considered appropriate. This followed recommendations made by the Clinical Priorities Advisory Group that everolimus be made available.

Louise Fish, CEO of the Tuberous Sclerosis Association (TSA) said: "We are thrilled that NHS England has decided to fund this potentially life-changing and life-saving treatment."

Simon Wigglesworth, deputy chief executive at Epilepsy Action, said: "There is good evidence to suggest that everolimus could have a life-changing impact on those people living with tuberous sclerosis, whose seizures do not respond to current epilepsy treatments."

Epilepsy not a priority in NHS Long Term Plan, epilepsy organisation says

Epilepsy organisation Epilepsy Action has said it is disappointed with the lack of priority given to epilepsy in the NHS Long Term Plan.

The Long Term Plan was published on 7 January, detailing how the NHS intends to move healthcare forward over the next 10 years.

In a post, Epilepsy Action highlighted that while epilepsy is mentioned in the plan, it is not made a priority.

The Long Term Plan discusses the creation of clinical networks to improve care for children with epilepsy. These are set to help share best practice and integrate skills across different services.

The organisation welcomed this and the NHS' plans to reduce care inequality. A Public Health England (PHE) report in 2018 showed that people with epilepsy living in deprived areas were at an increased risk of death. This was compared to those living in wealthier areas.

However, Epilepsy Action noted that no mention is made of adult epilepsy services or transition services. The post said: "Epilepsy and neurology services in the NHS are already under pressure. It is very concerning that these services are not given the focus they need."

The PHE report also found that death rates in England in people with epilepsy had risen by more than two-thirds (70%) between 2001-2014. This was also compared to a fall in overall death rates over that period.

The Royal College of Paediatrics and Child Health (RCPCH) also published a report last year, looking at child health across England and Wales. The report showed that death rates in children and young people with epilepsy was higher than that of other western countries between 2001-15. This was despite substantial falls in overall death rates during that time.

Simon Wigglesworth, deputy chief executive at Epilepsy Action, said: "Epilepsy Action is pleased that the NHS Long Term Plan includes proposals to improve the quality of care for children with epilepsy.

"While some aspects of these proposals are promising, there is little detail about how suggested improvements will be made. We would welcome more information and the opportunity to work with the government and NHS to improve health services for people with epilepsy."

Investigations of sudden death in epilepsy differ across countries

A new study in *Acta Neurologica Scandinavica* has found that there are significant differences in the investigation of sudden death in epilepsy across different countries.

Study authors Kinney and colleagues aimed to identify the level of confidence clinicians had in the cause of death. They also wanted to know how often autopsies are undertaken and identify factors that influenced whether autopsies are done.

The researchers surveyed the International League Against Epilepsy (ILAE) chapter chairpersons in each country to find out their perceptions. Out of 144 individual chapter leaders, 77 responded to the survey. The results showed that factors standing in the way of accurate diagnoses being made included family attitudes, as well as legal, coronial, cultural and religious reasons not to carry out autopsies.

The study showed that only 13% of respondents said there was high level of confidence in the accuracy of causes of death. There was a positive correlation between autopsy rates and confidence in the diagnoses of causes of sudden death.

The research concludes that there are significant differences in how sudden death in epilepsy is investigated across different countries. The study authors explain that the factors identified as barriers can be used to create a global public health strategy to help bridge the gap. The full study is available at: *bit.ly/2U9yb9f*.

FDA approves first generic form of vigabatrin

The US Food and Drug Administration (FDA) has approved the first generic version of vigabatrin. It was previously available for prescription in the US under the brand name Sabril.

The generic 500mg vigabatrin tablets are manufactured by the company Teva Pharmaceuticals USA. This medicine is intended as adjunctive therapy for refractory focal seizures in adults and children over 10 years old who have not responded to other treatments.

Teva explained that the medicine can also be prescribed for infantile spasms in babies aged between one month and two years. This is if the benefits outweigh the side-effect risks.

Serious side-effects of this medicine include the risk of suicidal thought or actions and permanent vision loss.

The FDA said the labelling for vigabatrin includes a boxed warning of

the risk of permanent vision loss. More common side-effects of this medicine quoted by the FDA include dizziness, fatigue, somnolence, memory problems, tremors, aggression and joint pain. There are also other vision side-effects, such as involuntary eye movements, as well as blurred and double vision.

Scott Gottlieb, FDA commissioner, said: "Prioritising the approval of generic drugs to compete with medicines that face little or no competition is a key part of our efforts to support access and reduce drug costs to patients."

Sanofi comments on valproate stock levels

Pharmaceutical company Sanofi has confirmed that its valproate medicines (Epilim and Depakote) are available in the UK. However, the company said that normal tablet or granule medicines might be substituted by doctors for liquid or syrup versions, or vice versa. The company warned this may result in a change to the frequency of dosing.

Sanofi added that stock levels may be lower than usual due to a disruption to production at a manufacturing site outside the UK. The company said it has notified the Department of Health and Social Care and is managing the situation.

"This temporary disruption in supply of some valproate-based treatments is not related to Brexit," the company confirmed.

Sanofi added that pack sizes have changed from 100 to 30 tablets at the request of the Medicines and Healthcare products Regulatory Agency (MHRA). It said 100-tablet packs may appear 'unavailable' at pharmacies, but this does not mean the medicines are out of stock. The codes for 30 tablet packs should be used.

Brivaracetam accepted for use in children in Scotland and Wales

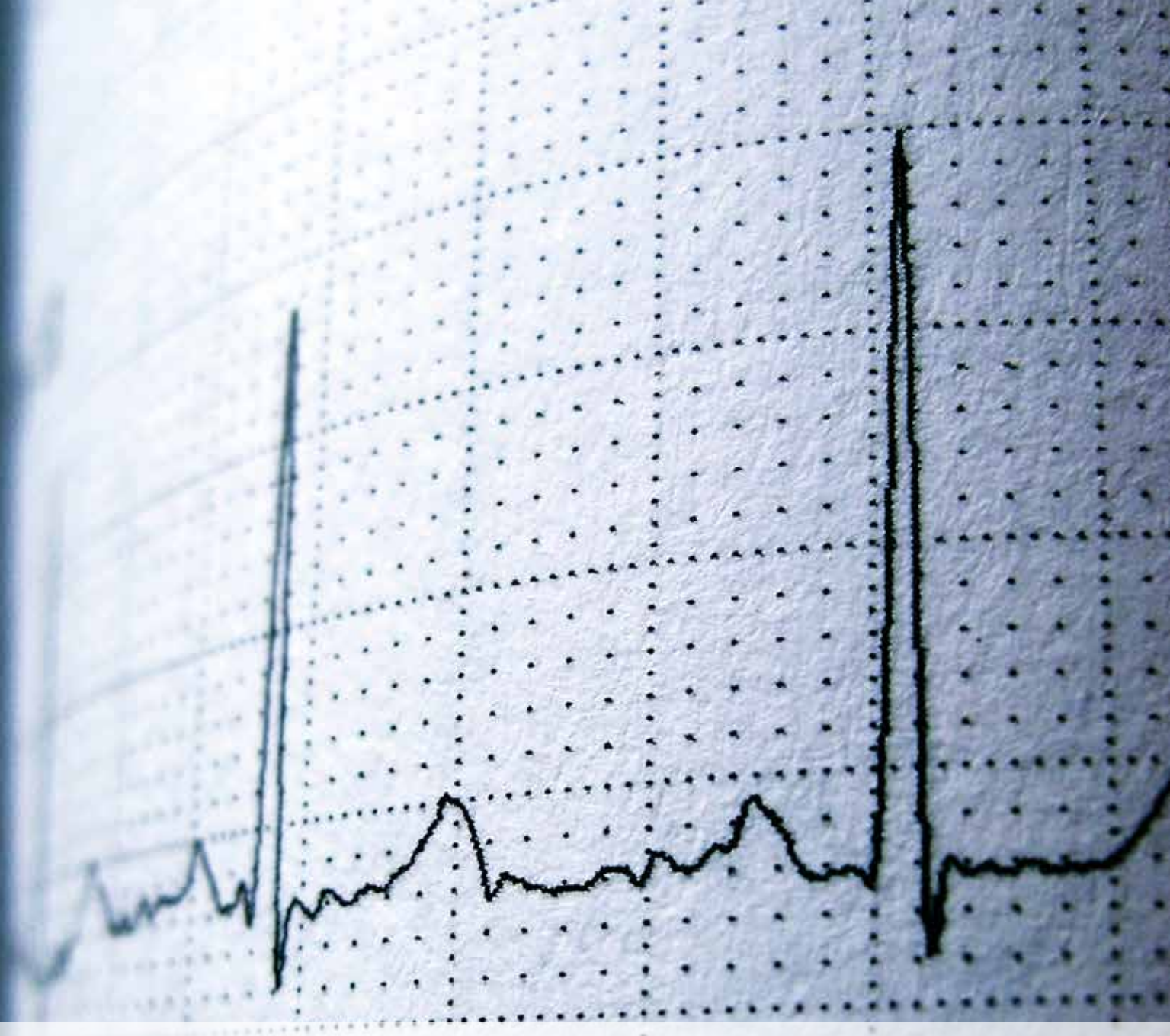
Briviact (brivaracetam) will now be available within NHS Scotland and NHS Wales for children over four years old for focal-onset seizures. It is intended for use as adjunctive therapy.

Brivaracetam is already available for use in children four years and older across Europe, authorised by the European Medicines Agency in July 2018.

The Scottish Medicines Consortium accepted expanding the use of this medicine in Scotland on 10 December 2018. The All Wales Medicines Strategy Group also extended the licence for the medicine in December to include children over four years old in Wales. UCB, the manufacturer of Briviact, said that this decision will give children with uncontrolled epilepsy another option.

The company explained that the safety and effectiveness of brivaracetam has been studied in adults, with additional safety studies carried out in children over four.

The possible side-effects from this medicine in children are similar to those seen in adults. These include drowsiness, dizziness, headaches and tiredness. However, an additional side-effect reported in children was psychomotor hyperactivity.



Heart rate variability

An important tool in the evaluation of autonomic dysfunction in epilepsy

Dr Kenneth Myers describes the changes in HRV in people with seizures and discusses how it could become an important clinical tool in epilepsy in the future

Heart rate variability (HRV) describes the variation, for a given individual, in the time interval between successive heart beats. This measure has physiological relevance as HRV can serve as a surrogate measure of autonomic balance – increased HRV indicates parasympathetic dominance while decreased HRV reflects a shift towards sympathetic control. In normal, healthy individuals, there will be diurnal variation in HRV with low HRV during waking hours and increased HRV at night during sleep. The clinical importance of HRV was originally shown in the late 1970s, in adults with myocardial infarctions; lower HRV was associated with an increased risk of mortality [Wolf et al, 1978]. Subsequently the relationship of lower HRV to mortality was demonstrated in other populations, including the elderly.

The potential importance of HRV for people with epilepsy did not begin to receive significant study until much later, around the early 2000s. There are now over 200 published manuscripts related to HRV in epilepsy. However, there is still much work to do in order to clearly understand autonomic dysfunction in epilepsy, as well as to determine the best way to incorporate HRV measurement into clinical practice. For a detailed critical review of HRV in epilepsy, readers could consult our recently published paper in Epilepsia [Myers et al, 2018].

There is still much work to do in order to clearly understand autonomic dysfunction in epilepsy and incorporate HRV measurement into clinical practice

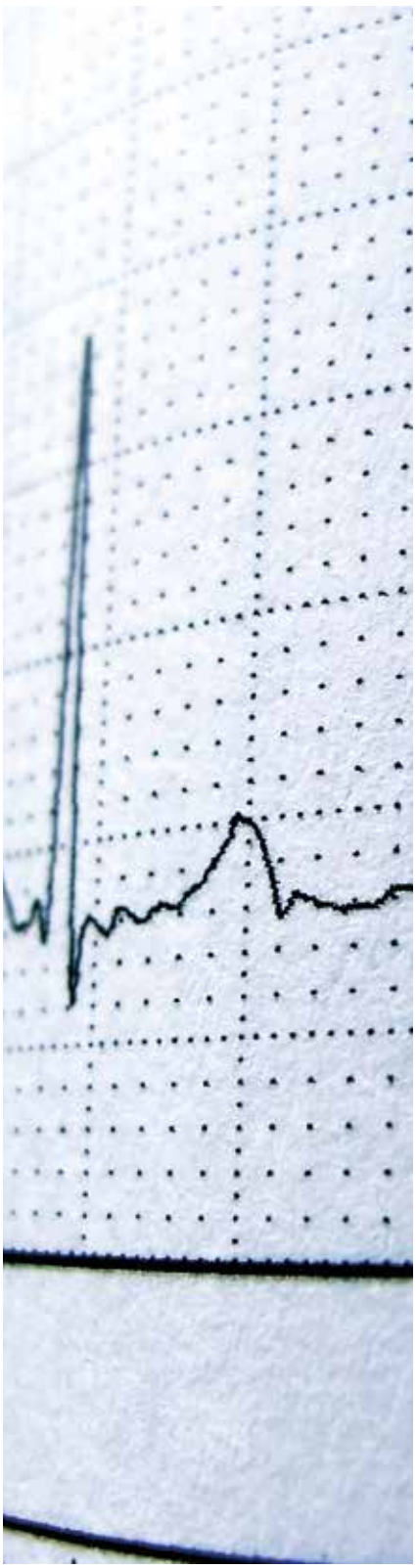
What do we know now?

The studies of epilepsy to this point can be broadly separated into those studying interictal and those studying ictal patterns:

Interictal

Overall, it seems that autonomic dysfunction is probably present to some extent in all epilepsy populations; however certain types of epilepsy appear to be considerably more vulnerable. Temporal lobe epilepsy in adults has received the bulk of the study. It is clear that these individuals have lower interictal HRV overall, with the most severe derangements seen in those with drug-resistant epilepsy or hippocampal sclerosis. These findings are not especially surprising, given that autonomic features are commonly seen as an ictal phenomenon in patients with temporal lobe epilepsy.

However, interictal altered HRV has also been described in other forms of epilepsy, including generalised epilepsy, epileptic spasms, frontal lobe epilepsy and Dravet syndrome. In the latter, HRV derangements may also be very severe. Two separate studies have



indicated that Dravet patients tend to have more abnormal HRV when compared to other patients with other forms of epilepsy [Delogu et al, 2011; Myers et al, 2018].

One important aspect of interictal HRV that is often overlooked in research studies, is the importance of awake versus asleep HRV, and the ratio of the two. This cannot be reliably evaluated in studies using Holter monitors, as it is not possible to determine when the patient is asleep. However, if heart rate data is collected during an EEG recording, it is possible to evaluate sleep:awake patterns. We incorporated this analysis in our recent study of HRV in patients with drug-resistant epilepsy with or without sodium channel gene mutations [Myers et al, 2018]. Some of the patients had suffered sudden unexpected death in epilepsy (SUDEP). We noted extreme derangements in sleep:awake HRV patterns in those patients who had suffered SUDEP, suggesting autonomic dysfunction likely plays a role in at least some cases of SUDEP.

There are some encouraging findings from some research studies, indicating that the altered interictal HRV in people with epilepsy may be a modifiable abnormality. Several studies have shown that certain treatments have the potential to shift HRV patterns to more closely resemble those of normal, healthy individuals [Hattori et al, 2007; Hallioglu et al, 2008]. These findings are particularly exciting in light of the recent SUDEP data, as modifying HRV could be a strategy employed to reduce or possibly even eliminate SUDEP risk.

Peri-Ictal

There has also been considerable study of HRV changes in the peri-ictal period. Overall, the data indicate that there is typically a drop in HRV, indicating a spike in sympathetic activity, correlating with seizures. This pattern has been shown most clearly in generalised tonic-clonic and temporal lobe seizures. In some cases, the decreased HRV was shown to persist for several hours following the clinical event [Toth et al, 2010].

Patterns of HRV were thought to be a potential method that could be used to differentiate different types of epileptic seizures. It was also thought they could differentiate epileptic seizures from psychogenic non-epileptic seizures (PNES). Regarding the latter hypothesis, interestingly, patients with PNES also tend to have lower interictal HRV and may show a similar acute drop in HRV with their clinical events. HRV analysis has not yet shown the capability to confidently distinguish between epileptic and non-epileptic seizures [Ponnusamy et al, 2012; Jeppesen et al, 2016].

How can we move HRV from an area of research to a clinical tool?

Despite more than 20 years of studies of HRV in epilepsy, we are not yet at the point of incorporating HRV into routine clinical decision-making. There are two main reasons for this.

There are some encouraging findings from some research studies indicating that the altered interictal HRV in people with epilepsy may be a modifiable abnormality

Heterogeneous outcome measures

There are many different measures of HRV. Some include time domain

measures of R-R intervals (time between consecutive heart beats). These could be standard deviation of R-R intervals, root mean square of successive differences in R-R intervals (RMSSD), and percentage of R-R intervals greater than 50 milliseconds. Others include frequency domain measures such as high frequency power, low frequency power and the ratio of the two. Additionally, the period of time over which the measures are calculated is important, and this varies from minutes to hours between different research studies. We recently proposed a standardised minimum reporting protocol for HRV, using RMSSD 5-minute periods in wakefulness and sleep. The rationale for this protocol is described in our recent critical review [Myers et al, 2018].

Although there is much preliminary work yet to be done, HRV has the potential to eventually improve the clinical care of people with epilepsy considerabliy

Lack of established age-appropriate reference ranges for patients with epilepsy

In order to classify an individual's HRV pattern as 'normal', 'abnormal', or 'critically abnormal', we first need a large cohort of epilepsy patients, as well as healthy controls, of varying ages. This data needs to be generated based on the standardised minimum reporting protocol discussed above. Once these data are gathered, it will be possible to interpret an individual's HRV measurement within an appropriate context.

How could we eventually incorporate HRV measurement into clinical practice?

Although there is much preliminary work yet to be done, HRV has the potential to eventually improve the clinical care of people with epilepsy considerably. In the future, HRV measures may be calculated concurrently with a patient's clinical EEG study, with the data included on the official report.

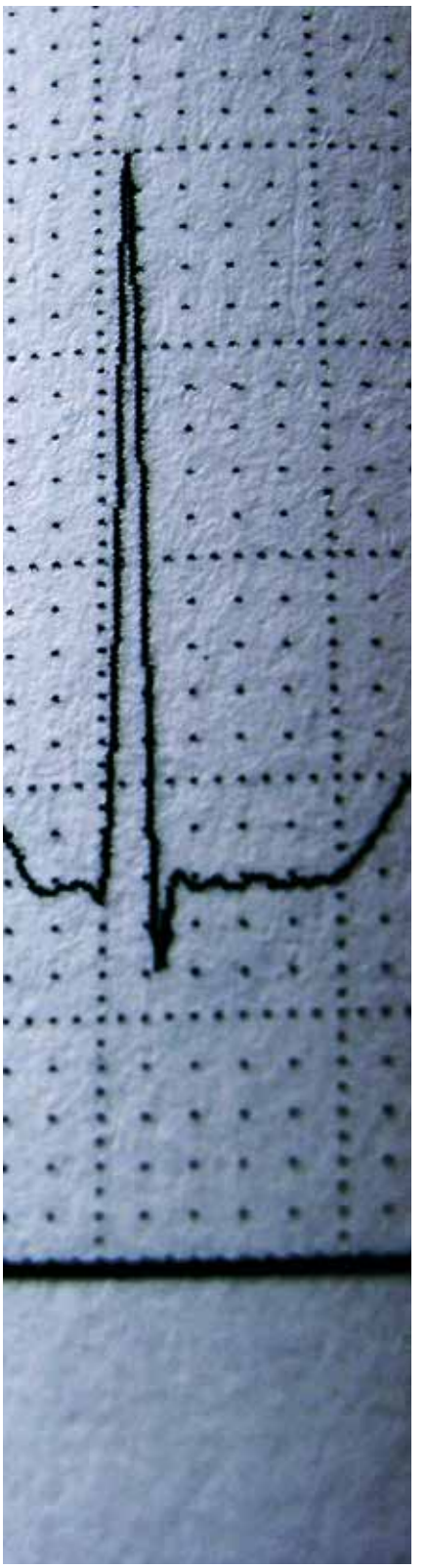
These are some possible avenues in which HRV measurement could be incorporated into epilepsy practice.

SUDEP counselling

If we can define 'normal', 'abnormal', and 'critically abnormal' HRV values, we could eventually apply these to SUDEP counselling in the clinic. At present, these discussions tend to be emotional, yet are often also very vague. Our evaluation of risk is generally based on the individual's type of epilepsy, their seizure types, and the degree to which their seizures are controlled. Eventually, HRV could allow us to give patients a quantitative estimate of SUDEP risk, as well as updates as to how that risk has changed based on recent changes in treatment or lifestyle.

Evaluation of therapeutic effectiveness

We know that HRV derangements are more severe in those patients with drug-resistant epilepsy. Seizure logs will likely always be the gold standard in assessing treatment response. However, HRV may eventually have utility as a measure of epilepsy severity and could be used to assess an individual's response to treatment. Additionally, as mentioned above, HRV could be used to assess if a given treatment has reduced an individual's SUDEP risk.



Choice of therapy

There are now limited data indicating that individuals with more severe HRV derangements pre-surgery had poorer outcomes following resective epilepsy surgery [Persson et al, 2005]. With more study in this area, we might eventually be able to use HRV data to guide therapeutic decisions (eg resective surgery versus vagus nerve stimulator versus medical therapies). We may also eventually learn that patients with certain forms of altered HRV tend to respond better to specific anti-epileptic drugs.

Classifying epilepsy syndromes

As we gather large volumes of HRV data and correlate to epilepsy phenotype, we may find that certain epilepsy syndromes have characteristic patterns of HRV derangement. Eventually, a patient's HRV signature may become a key element and may describe the 'electroclinical' phenotype.

Summary

The considerable HRV epilepsy research conducted over the past 20 years has demonstrated that autonomic dysfunction is present in many if not all patients with epilepsy. It has also shown that this tends to correlate with treatment resistance and risk of SUDEP. There is a potential for HRV measurement to be a valuable clinical tool; however, there is still considerable work to do before HRV can truly go from the bench to the bedside. In order to accomplish this, a greater emphasis must be placed on standardising reporting protocols and generating normative data from healthy populations.

Dr Myers receives research funding support from Citizens United for Research in Epilepsy, dravetCanada, and the Research Institute of the McGill University Health Centre. He is the site principal investigator for a study sponsored by LivaNova (receives no financial remuneration). He has received a travel grant from Zynerba.

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Further reading

Delogu AB, Spinelli A, Battaglia D, Dravet C, De Nisco A, Saracino A, Romagnoli C, Lanza GA, Crea F. Electrical and autonomic cardiac function in patients with Dravet syndrome. *Epilepsia*. 52 Suppl 2(55-8 (2011).

Hallioglu O, Okuyaz C, Mert E, Makharoblidze K. Effects of antiepileptic drug therapy on heart rate variability in children with epilepsy. *Epilepsy Res*. 79(1): 49-54 (2008).

Hattori A, Hayano J, Fujimoto S, Ando N, Mizuno K, Kamei M, Kobayashi S, Ishikawa T, Togari H. Cardiac vagal activation by adrenocorticotropic hormone treatment in infants with West syndrome. *Tohoku J Exp Med*. 211(2): 133-9 (2007).

Jeppesen J, Beniczky S, Johansen P, Sidenius P, Fuglsang-Frederiksen A. Comparing maximum autonomic activity of psychogenic non-epileptic seizures and epileptic seizures using heart rate variability. *Seizure*. 37(13-9 (2016).

Myers KA, Bello-Espinosa LE, Symonds JD, Zuberi SM, Clegg R, Sadleir LG, Buchhalter J, Scheffer IE. Heart rate variability in epilepsy: A potential biomarker of sudden unexpected death in epilepsy risk. *Epilepsia*. (2018).

Myers KA, Sivathamboo S, Perucca P. Heart rate variability measurement in epilepsy: How can we move from research to clinical practice? *Epilepsia*. 59(12): 2169-78 (2018).

Persson H, Kumlien E, Ericson M, Tomson T. Preoperative heart rate variability in relation to surgery outcome in refractory epilepsy. *Neurology*. 65(7): 1021-5 (2005).

Ponnusamy A, Marques JL, Reuber M. Comparison of heart rate variability parameters during complex partial seizures and psychogenic nonepileptic seizures. *Epilepsia*. 53(8): 1314-21 (2012).

Toth V, Hejjel L, Fogarasi A, Gyimesi C, Orsi G, Szucs A, Kovacs N, Komoly S, Ebner A, Janszky J. Periictal heart rate variability analysis suggests long-term postictal autonomic disturbance in epilepsy. *Eur J Neurol*. 17(6): 780-7 (2010).

Wolf MM, Varigos GA, Hunt D, Sloman JG. Sinus arrhythmia in acute myocardial infarction. *Med J Aust*. 2(2): 52-3 (1978).

Highlights

Top picks from *Seizure*

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

Menstruation-related seizure frequency fluctuation is not equally marked in all women with epilepsy. However, across all women with epilepsy, seizures are more likely during phases of the menstrual cycle when progesterone levels are relatively low and oestrogen levels relatively high [Verrotti et al, 2012]. Both oestrogen and progesterone are broken down in complex ways in different compartments of the body. They have numerous metabolites with a wide range of effects, including on gene transcription, GABA receptor functioning and inflammatory pathways.

My editor's choice article from *Seizure issue 63* by Wu and Burnham is a fine narrative review summarising the progesterone story that emerges from studies in animals and humans to date [2018]. It concludes by describing the therapeutic potential of a number of progesterone derivatives as anti-epileptic drugs. They include ganaxolone, a synthetic analog of the endogenous neurosteroid allopregnanolone and a positive allosteric modulator of GABA-A receptors.

Previous therapeutic interventions focusing on progesterone have been limited by relatively modest benefits and a considerable potential to cause side-effects. Time will tell whether the better understanding of these molecules and their effects on the body summarised in Wu and Burnham's review will lead to better treatments. Potentially, progesterone derivatives could provide patients and clinicians with a novel anti-seizure (or even anti-epileptic) mode of action suitable for many people with epilepsy.

SUDEP

Despite steadily accumulating evidence, the involvement of subcortical and brain stem structures in ictal physiological changes (and their interictal consequences) is still not widely appreciated. Too often, the autonomic nervous system is considered an ancient feature of brain development shared by highly developed and much more primitive animals. It is thought as quite separate from the parts and networks that are of interest to epileptologists. However, this understanding of epilepsy cannot really be upheld, as some recent studies have shown [Zhan et al, 2016; Englot et al, 2018].

My editor's choice selection from *Seizure issue 64*, a narrative review by Manolis *et al*, demonstrates that the involvement of the autonomic nervous system in epileptic seizures may be an important factor in sudden unexpected death in epilepsy (SUDEP) [2019]. The close links between ictal cortical discharges and brain networks involved in the control of heart rate, blood pressure and breathing are likely to be highly relevant in this most serious potential consequence of epilepsy. For some time, SUDEP has been acknowledged as the most common cause of death in younger adults with epilepsy [Devinsky et al, 2016]. Recent evidence demonstrates the absence of any post-mortem signs of drowning in many individuals with epilepsy who died in the bath [Cihan et al, 2018]. This suggests that SUDEP may make an even greater contribution than previously thought to the increased levels of mortality observed in those with epilepsy. This comprehensive overview of the seizure-related changes in the brain which affect the functioning of the autonomic nervous system should help to correct the 'corticocentric' view of epilepsy. It demonstrates that a wider understanding of this disorder will be needed if we want to stop more people from dying in the context of epileptic seizures in the future.

Further reading

Cihan E, Hesdorffer DC, Brandsoy M, Li L, Fowler DR, Graham JK, Donner EJ, Devinsky O, Friedman D. Dead in the water: Epilepsy-related drowning or sudden unexpected death in epilepsy? *Epilepsia* 2018;59:1966-72.

Devinsky O, Hesdorffer DC, Thurman DJ, Lhatoo S, Richerson G. Sudden unexpected death in epilepsy: epidemiology, mechanisms, and prevention. *Lancet Neurol* 2016;15:1075-88.

Englot DJ, Gonzalez HFJ, Reynolds BB, Konrad, Jacobs ML, Gore JC, Landman BA, Morgan VL. Relating structural and functional brainstem connectivity to disease measures in epilepsy. *Neurology* 2018; 91: 2018 Jul 3;91(1):e67-e77.

Manolis TA, Manolis AA, Melita H, Manolis AS. Sudden Unexpected Death in Epilepsy: The Neuro-Cardio-Respiratory Connection. *Seizure* 2019 – Jan;64:65-73.

Verrotti A, D'Egidio C, Agostinelli S, Verrotti C, Pavone P. Diagnosis and management of catamenial seizures: a review. *Int J Womens Health* 2012;4:535-41.

Wu YV and Burnham WM. Progesterone, 5a-Dihydropogesterone and Allopregnanolone's Effects on Seizures: A Review of Animal and Clinical Studies. *Seizure* 2018 Dec;63:26-36.

Zhan Q, Buchanan GF, Motelow JE, Andrews J, Vitkovskiy P, Chen WC, Serout F, Gummadavelli A, Kundishora A, Furman M, Li W, Bo X, Richerson GB, Blumenfeld H. Impaired Serotonergic Brainstem Function During and After Seizures. *J Neurosci* 2016;36:2711–2722.

Mental health in children

Addressing the mental health needs of children and young people with epilepsy

Dr Catriona George, Dr Kirsten Verity and the team at the Royal Hospital for Sick Children Edinburgh look at how common mental health conditions in children and young people with epilepsy might be and why they might be missed. They propose a solution to this issue, which has been piloted in Scotland

Currently in the UK, approximately one in 220 people under the age of 18 has diagnosis of epilepsy. Such a diagnosis brings an array of concerns and challenges for young people, families and all those supporting them. It is now increasingly recognised that the impact of epilepsy is far wider reaching than simply the effects of the seizures themselves. This article aims to give an overview of the psychosocial difficulties faced by this population and their impact. It will also provide a description of a new approach employed in Scotland in an attempt to meet their needs.

Children and young people with epilepsy (CYPwE) have been found to be at a significantly higher risk of developing social, emotional, behavioural and learning difficulties. This is even when compared to young people with other chronic health conditions [Davies et al, 2003]. Within this population, reported rates of diagnosable depression are between 12% and 36.5%, and up to 48.5% have been reported to meet criteria for anxiety disorder [Reilly et al, 2011]. Worryingly, these young people are also more likely to experience suicidal ideation as children, a risk which continues into adulthood [Jones et al, 2013; Nilsson et al, 2002].

Intellectual disability (ID) and autism spectrum disorder (ASD) are known to be more prevalent within this population [Reilly et al, 2014; Strasser et al, 2018]. In addition, CYPwE are up to four times more likely to have a diagnosis of ADHD or conduct disorder [Williams et al, 2016; Russ et al, 2012]. This can have significant impact both academically and socially as children progress through school. 'Accelerated forgetting', or impairment in medium to long-term memory function, despite ability to recall information following a short delay, is a phenomenon which has been found to affect some CYPwE [Davidson et al, 2007]. This means that they may be unable to retrieve memorised information from previous weeks, which would clearly disadvantage these young people in the classroom. Even for those CYPwE who do not have ID, ASD or ADHD, they are consistently found to be achieving less well academically when compared to their peers [Wo et al, 2017]. This is a finding which appears to be especially true in adolescence, and which continues to be problematic even when seizure frequency improves.

Cognitive, behavioural and mental health problems have been found to be more prevalent in CYPwE both before seizures emerge and after becoming seizure free

Why are CYPwE particularly vulnerable to these types of problems? Cognitive, behavioural and mental health problems have been found to be more prevalent in this population both before seizures emerge and after becoming seizure free. This would suggest that the link is not entirely due to the effects of seizures. Nor indeed can it be put down to the effects of anti-epileptic drugs (AEDs), which is often put forward as another explanation. The reality is that a complex combination of factors is likely involved in the development of these difficulties. It includes the impact of seizures and medication, alongside other internal, external and social factors. For example, in cases where a brain injury or abnormal brain development is understood to be the cause of epilepsy, it is likely that other aspects of neurodevelopment will also be affected. This can result in cognitive,

behavioural or emotional difficulties. AEDs can be a factor in the development of learning problems, which can, in turn, impact on a young person's self-esteem and therefore their mood. Children's social development can be impacted due to the stigma of their epilepsy or missing out on social opportunities through concern for their safety. This can then have long-term effects on mood, anxiety and self-esteem. In addition, it is important to bear in mind that seizures in children are impacting the developing brain, and so may disrupt normal developmental processes. Sometimes these effects are not immediately obvious, but emerge as the young person moves through childhood. This might be at times of transition or on reaching puberty, whether or not seizures are ongoing at that time.

Impact of psychosocial problems

It is clear that the many factors involved in the development of psychosocial difficulties also serve to maintain and exacerbate these problems. They can have lasting effects on quality of life, if not identified early or if help is not available. CYPwE consistently report reduced quality of life compared to their peers [Moreira et al, 2013; Reilly et al, 2015] which has often been found more strongly related to psychosocial rather than epilepsy-related factors [Baca et al, 2011; Fayad et al, 2015]. Parental mental health is also lower among parents of children with epilepsy [Puka et al, 2018; Reilly et al, 2018]. These effects are often bidirectional, further impacting the psychological wellbeing and quality of life of the child. Perhaps not surprisingly, negative impact has also been reported for siblings of CYPwE [Tsuchie et al, 2006].

In the longer term, these young people will continue to be vulnerable. There is strong evidence indicating that adult mental illness often begins in childhood or adolescence. This is particularly when, as is often the case, it is not identified or treated at this stage [Fryers and Brugha, 2013]. In epilepsy, these comorbidities are more common and can significantly impact social outcomes, such as completion of college or gaining employment [Berg et al, 2016; Chin et al, 2011]. They can lead to increased risk of premature mortality [Fazel et al, 2013], with rates four times as high as the general population reported for suicidality in adulthood [Hamed et al, 2012].

The Children with Epilepsy in Sussex Schools (CHESS) study, published in 2014, carried out in depth assessment of all children with epilepsy in the area. It found that 95% of CYPwE included had problems in at least one area assessed, ie learning, behavioural or emotional difficulties. Of the cohort, 60% met criteria for at least one behaviour disorder (including depression or anxiety), but only a third had previously been diagnosed. This highlights the many CYPwE whose problems remain unrecognised and untreated [Young Epilepsy, 2014].

Problems may be attributed solely to impact of seizures or medication, and so the assumption is made that these cannot be usefully addressed through psychological intervention

There can be various reasons for this under-recognition. Seizure control

and adjustment to diagnosis can initially overshadow mental health or learning problems. Later on, problems may be attributed solely to impact of seizures or medication, and so the assumption is made that these cannot be usefully addressed through psychological intervention. However, there are barriers even when these mental health problems are reported by families or identified by clinicians managing epilepsy. Symptom thresholds for overstretched and under-resourced child and adolescent mental health services (CAMHS) are currently so high that families often have to reach crisis point before they gain access to appropriate interventions.

Possible solution – PAVES

Over the last two years, a project has been developed within NHS Lothian. This aims to respond to these issues by identifying those at risk of developing psychosocial difficulties at an early stage and providing a stepped care intervention pathway to address them. The Psychology Adding Value: Epilepsy Screening (PAVES) project originated through a discussion within the Scottish Paediatric Epilepsy Network. The organisation had been highlighting the problems outlined above and the difficulties with accessing CAMHS services for these young people for some time. This culminated in a successful funding bid to the Edinburgh Children's Hospital Charity, allowing the pathway to be developed and piloted.

The project was set up within routine neurology epilepsy clinics at the Royal Hospital for Sick Children, Edinburgh, beginning in January 2017. It was decided that the project should focus on CYPwE of school age and within mainstream education, as these are the young people most likely to have problems that are not identified. Young people are excluded if they are already open to CAMHS for psychological therapy, as they are already receiving support. All eligible CYPwE and their parents complete questionnaires within the waiting room prior to their routine neurology review. Their scores on the questionnaires then link to a traffic light metaphor, which has been introduced as a means of communicating the level of difficulty identified to families and medical professionals. The traffic light rating also indicates level and type of intervention that might usefully be offered via the intervention pathway.

As a result of this screening programme, we have been able to identify a significant level of psychosocial difficulty in this population (see *Figure 1*). Of those screened between January 2017 and September 2018, 36% were rated as showing 'significant' concerns (red on traffic light). Using the same criterion, less than 5% of the general population would be expected to show this level of concern. A further 11% were identified as at risk of developing problems (amber). It seems likely that both these groups represent the population of CYPwE who would benefit from some level of stepped intervention to improve mental

Figure 1: Ratings of psychosocial difficulties in CYPwE compared with general population. a) Ratings of psychosocial difficulties in young people with epilepsy (N=155). b) Approximate ratings in general population taken from normative data

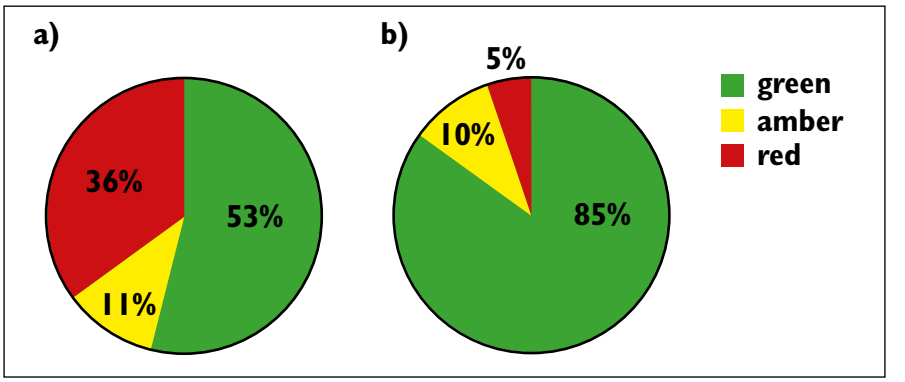
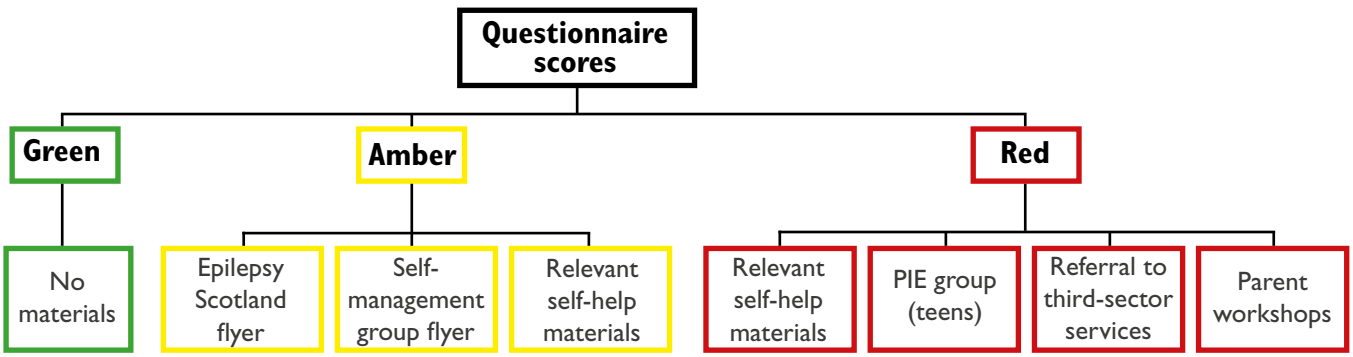


Figure 2: Intervention pathway



health, but who might not otherwise be able to access this.

In order to maximise effectiveness and efficiency, we have developed an early intervention, stepped care pathway to address these concerns (see *Figure 2*) and have piloted several interventions. For those scoring within the red range, we offer two face-to-face interventions:

- Newly developed age-specific parent workshops, delivered over two sessions by a clinical psychologist in collaboration with third sector colleagues (Epilepsy Scotland)
- The Psychosocial Interventions in Epilepsy (PIE) [Dorris et al, 2017] group: a six-session programme for 12-17-year-olds, delivered by a clinical psychologist and specialist epilepsy nurse

An integral part of the PAVES project has been in strengthening our relationship with local third sector organisations. With this we hope to maximise the use of already existing services for these young people and their families. For those within the red range, who will be triaged by psychology, we offer direct referrals for individual or group work within these organisations, making it easier for families to access these. For those within the amber range, we will signpost them to relevant resources, eg Epilepsy Scotland youth group. In addition, we have developed an extensive database of approved, problem-specific self-help resources. They are given to families directly at the point of screening, covering issues ranging from anxiety and self-esteem, to sleep, behaviour management and advice for schools.

Outcomes from the pilot interventions have been promising. Eight young people attended our initial PIE group, with another due to start soon. There was a 94% attendance rate over the six sessions, with 100% of attendees feeling more confident about managing and discussing their epilepsy following the group. All of the attendees furthermore decided to join the local Epilepsy Scotland youth group following PIE, for ongoing peer support. Twenty-two parents have so far attended a parent workshop. Feedback has been positive so far, with parents reporting a better understanding of the wider impact of epilepsy on their child. Other aspects reported as helpful were the information on parenting strategies and the opportunity to share experiences and ideas with other parents. The neurologists within the pilot clinics have also provided positive feedback on the PAVES pathway. They

have highlighted its utility in teasing out the nature of the problems reported in clinic and providing options for low-level intervention.

Following the success of the pilot, we have secured funding to develop an electronic version of the screening tool. The aim that the screening can be widely available in routine neurology clinics without the direct presence of a psychologist. Neurologists can then use the intervention pathway to inform their decisions on how to address the mental health needs of their patients. They can be useful when patients do not meet thresholds, or face a long wait, for CAMHS intervention. Any CYPwE scoring within the red range will also be triaged by psychology. This relatively simple, yet effective method of early identification and intervention can then potentially be developed in other areas across the country. It can then increase capacity nationally to help these families, through maximising use of existing resources and working in a more collaborative way. We have initial plans and funding from Scottish Government to pilot this project in two further areas of Scotland over the coming year as a first step towards this.

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Further reading

Baca CB, Vickrey BG, Caplan R, Vassar SD and Berg AT. 2011. Psychiatric and medical comorbidity and quality of life outcomes in childhood-onset epilepsy. *Pediatrics*, pp.peds-2011.

Berg AT, Baca CB, Rychlik K, Vickrey BG, Caplan R, Testa FM and Levy SR. 2016. Determinants of social outcomes in adults with childhood-onset epilepsy. *Pediatrics*, pp.peds-2015.

Chin RF, Cumberland PM, Pujar SS, Peckham C, Ross EM and Scott RC. 2011. Outcomes of childhood epilepsy at age 33 years: a population-based birth-cohort study. *Epilepsia*, 52(8), pp.1513-1521.

Davidson M, Dorris L, O'Regan M and Zuberi SM. 2007. Memory consolidation and accelerated forgetting in children with idiopathic generalized epilepsy. *Epilepsy & Behavior*, 11(3), pp.394-400.

Davies S, Heyman I and Goodman R. 2003. A population survey of mental health problems in children with epilepsy. *Developmental Medicine and Child Neurology*, 45(5), pp.292-295.

Dorris L, Broome H, Wilson M, Grant C, Young D, Baker G, Balloo S, Bruce S, Campbell J, Concannon B and Conway N. 2017. A randomized controlled trial of a manual-based psychosocial group intervention for young people with epilepsy [PIE]. *Epilepsy & Behavior*, 72, pp.89-98.

Fayed N, Davis AM, Streiner DL, Rosenbaum PL, Cunningham CE, Lach LM, Boyle MH, Ronen GM, Connolly M, Bello-Espinosa L and Rafay MF. 2015. Children's perspective of quality of life in epilepsy. *Neurology*, 84(18), pp.1830-1837.

Fazel S, Wolf A, Långström N, Newton CR and Lichtenstein P. 2013. Premature mortality in epilepsy and the role of psychiatric comorbidity: a total population study. *The Lancet*, 382(9905), pp.1646-1654.

Fryers T and Brugha T. 2013. Childhood determinants of adult psychiatric disorder. *Clinical Practice and Epidemiology in Mental Health: CP & EMH*, 9, p.1.

Hamed SA, Elserogy YB, Abdou MA and Abdellah MM. 2012. Risks of suicidality in adult patients with epilepsy. *World Journal of Psychiatry*, 2(2), p.33.

Jones JE, Siddarth P, Gurbani S, Shields WD and Caplan R. 2013. Screening for suicidal ideation in children with epilepsy. *Epilepsy & Behavior*, 29(3), pp.521-526.

Moreira H, Carona C, Silva N, Frontini R, Bullinger M and Canavarro MC. 2013. Psychological and quality of life outcomes in pediatric populations: a parent-child perspective. *The Journal of Pediatrics*, 163(5), pp.1471-1478.

Nilsson L, Ahlbom A, Farahmand BY, Åsberg M and Tomson T. 2002. Risk factors for suicide in epilepsy: a case control study. *Epilepsia*, 43(6), pp.644-651.

Puka K, Tavares TP, Anderson KK, Ferro MA and Speechley KN. 2018. A systematic review of quality of life in parents of children with epilepsy. *Epilepsy & Behavior*, 82, pp.38-45.

Reilly C, Agnew R and Neville BG. 2011. Depression and anxiety in childhood epilepsy: a review. *Seizure*, 20(8), pp.589-597.

Reilly C, Atkinson P, Das KB, Chin RF, Aylett SE, Burch V, Gillberg C, Scott RC and Neville BG. 2014. Screening for mental health disorders in active childhood epilepsy: population-based data. *Epilepsy Research*, 108(10), pp.1917-1926.

Reilly C, Atkinson P, Das KB, Chin RF, Aylett SE, Burch V, Gillberg C, Scott RC and Neville BG. 2015. Factors associated with quality of life in active childhood epilepsy: a population-based study. *European Journal of Paediatric Neurology*, 19(3), pp.308-313.

Reilly C, Atkinson P, Memon A, Jones C, Dabydeen L, Das KB, Gillberg C, Neville BG and Scott RC. 2018. Symptoms of depression, anxiety, and stress in parents of young children with epilepsy: A case controlled population-based study. *Epilepsy & Behavior*, 80, pp.177-183.

Russ SA, Larson K and Halfon N. 2012. A national profile of childhood epilepsy and seizure disorder. *Pediatrics*, pp.peds-2010.

Strasser L, Downes M, Kung J, Cross JH and De Haan M. 2018. Prevalence and risk factors for autism spectrum disorder in epilepsy: a systematic review and meta-analysis. *Developmental Medicine & Child Neurology*, 60(1), pp.19-29.

Tsuchie SY, Guerreiro MM, Chuang E, Baccin CE and Montenegro MA. 2006. What about us?: Siblings of children with epilepsy. *Seizure*, 15(8), pp.610-614.

Williams AE, Giust JM, Kronenberger WG and Dunn DW. 2016. Epilepsy and attention-deficit hyperactivity disorder: links, risks, and challenges. *Neuropsychiatric Disease and Treatment*, 12, p.287.

Wo SW, Ong LC, Low WY and Lai PSM. 2017. The impact of epilepsy on academic achievement in children with normal intelligence and without major comorbidities: a systematic review. *Epilepsy Research*, 136, pp.35-45.

Young Epilepsy. The identification of educational problems in childhood epilepsy; The Children with Epilepsy in Sussex Schools (CHESS) Study, Young Epilepsy, 2014 *http://www.youngepilepsy.org.uk/dmdocuments/ChessReport-2014.pdf*

Epilepsy nurse model

Expansion of the Norfolk adult community epilepsy specialist nurse (ESN) team

Juliet Bransgrove describes the business case behind expanding the Norfolk epilepsy community service from 1.6 whole time equivalent (WTE) ESNs to 4.5 between 2016 and 2018

I want to share how the Norfolk adult community service epilepsy specialist nurse (ESN) team expanded between March 2016 and November 2018. The team went from 1.6 whole time equivalent (WTE) ESNs (0.8 Band 7 and 0.8 Band 6) to four WTE Band 7s, 0.5 Band 6 and 1 WTE Band 3. It's been quite a journey with plenty of learning to impart to anyone else embarking on a similar voyage.

The recipe for success included having lead consultant neurologists' or neuropsychiatrists' endorsement from Norfolk and Norwich University Hospital (NNUH), Queen Elizabeth Hospital King's Lynn (QEHKL) and West Suffolk Hospital (WSH). It also involved having patient engagement. I was also fortunate to have Norfolk Community Health and Care (NCH&C) Trust's support in letting me work directly with the Clinical Commissioning Groups (CCGs).

Our venture was also rooted in best practice guidelines and plans from the NHS to improve care. The National Institute for Health and Care Excellence (NICE) guidelines on epilepsy [NICE, 2012] state that ESNs should be an integral part of the network of care of individuals with epilepsy. The NHS Long Term Plan [NHS, 2019] set out the NHS's aims for the next 10 years. They include 'bringing together different professionals to coordinate care better' and 'developing more rapid community response teams to prevent unnecessary hospital spells'. This also underpinned the vision for our community ESN service.

The NHS Long Term plan addresses doing things differently. A part of this is encouraging more collaboration between GPs, their teams and community services, to increase the services they can provide jointly. Joined up collaborative approach with patients and their families is a vital factor for our service.

Improving patient services

We serve the population of patients with epilepsy from the age of 16 years across four CCGs – North Norfolk, Norwich, South Norfolk and West Norfolk. This is a community-based service, managing patients in local settings in nurse-led clinics, or through home visits, residential home visits and the telephone. We work closely with the secondary care hospitals and a well-established children's and adult nurse-led transitional service for patients from the age of 16.

Figure 1. Register of patients aged 18 or over receiving drug treatment for epilepsy in North Norfolk, Norwich, South Norfolk and West Norfolk.

CCG	Number of Practices	Epilepsy Register	Prevalence (%) England 0.97%	Learning Disability Register
NHS North Norfolk CCG	18	1,277 30% – 383	0.93	1,281
NHS Norwich CCG	23	1,686 30% – 506	0.87	1,729
NHS South Norfolk CCG	24	1,520 30% – 456	0.83	1,299
NHS West Norfolk CCG	21	1,177 30% – 353	0.82	1,038

National statistics [JEC, 2011] predict that about 70% of patients could be seizure free on appropriate treatment and 30% will have uncontrolled seizures due to medically refractory epilepsy. Therefore, the vulnerable, at-risk epilepsy population among over 18-year-olds across the four Norfolk CCGs (total over 18-year-old epilepsy population is 5,660) is estimated at 1,698. Additionally, 50% of patients with a moderate to severe learning disability have epilepsy [JEC, 2011].

According to the guidance for General Medical Services (GMS) contract 2018/19, 'the contractor establishes and maintains a register of patients aged 18 or over receiving drug treatment for epilepsy' [NHS England et al, 2018]. The register for our service is detailed in *Figure 1*.

For many years, the small but highly experienced team of 1.6 ESNs covered a large rural geography, which eventually led to a breakdown in resilience and sustainability. It was difficult for the team to promote the service as this would have impacted on an already overstretched resource. The care given was of very high quality but, despite many negotiations and the best efforts of the lead ESN, Dee Elleray, the service was unable to expand.

I started in post in April 2016, as the previous Band 7 nurse (Dee Elleray) retired, bringing the team to 1.8 WTE ESNs. On 10 June 2016, I was fortunate to be invited to a meeting with Dr Cochius, neurologist with a special interest in epilepsy, Dr Staufenberg, neuropsychiatrist, and commissioners from North Norfolk CCG at NNUH. There was unanimous agreement that the provision of ESNs across Norfolk was insufficient and unstainable. Our vision was ambitious: to have one WTE Band 7 and one WTE Band 6 for each Norfolk CCG. Ann Touray, commissioning lead from North Norfolk CCG and I were tasked to make the case for an increased establishment of community ESNs. We had a meeting (with biscuits) to get to know each other and understand each other's priorities and drivers. We needed to find those all-important hooks, with competing priorities and a challenging financial climate.

We explored all avenues on how we could make the case, starting with the implementation of national guidance NICE quality standards [NICE, 2012]:

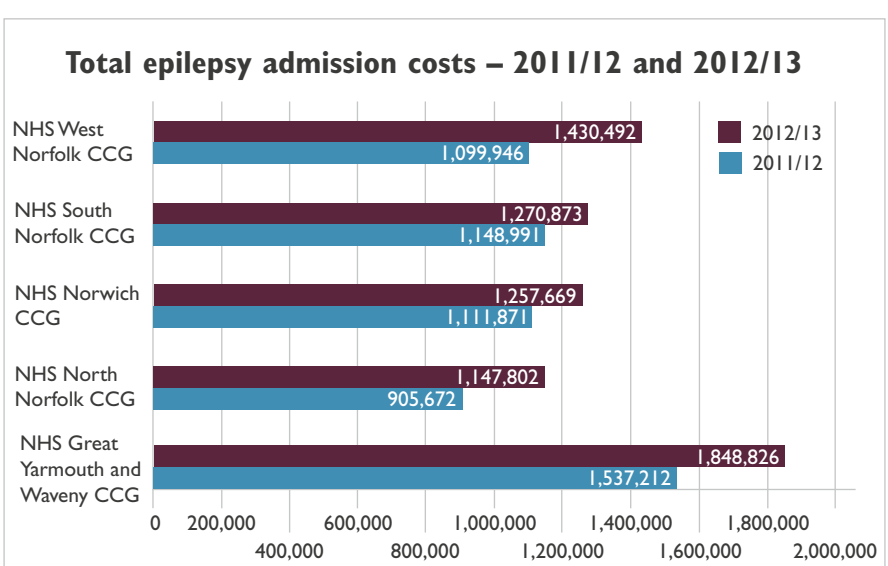
***Statement 4**. Children, young people and adults with epilepsy have an agreed and comprehensive written epilepsy care plan*

***Statement 5**. Children, young people and adults with epilepsy are seen by an epilepsy specialist nurse who they can contact between scheduled reviews*

***Statement 6**. Children, young people and adults with a history of prolonged or repeated seizures have an agreed written emergency care plan*

***Statement 9**. Young people with epilepsy have an agreed transition period during which their continuing epilepsy care is reviewed jointly by paediatric and adult services*

Figure 2. Epilepsy admissions costs with an ESN (2011/12) and without (2012/13).



Evidence on supporting medical teams and financial savings

We had evidence of the effectiveness of the ESNs and the impact their absence had in 2012/13 when both nurses were on long-term leave. *Figure 2* illustrates the rise in non-elective admissions seen across all CCGs in this year.

Another compelling factor was saving GP time.

The General Practice Forward View [NHS England, 2016] said that according to an international survey, British GPs are under far greater pressure than their counterparts. They face rising workloads and patient concerns about convenient access. The document explained that the Primary Care Workforce Commission set out how the talents of the wider workforce can be better deployed to reduce the workload burden on GPs. It suggests this would help meet patients' needs and free GPs up to do what they do best.

We identified that the ESN could achieve this by:

- Implementing and monitoring medication titrations advised by neurologists
- GPs being able to task ESNs directly on SystmOne with patient reviews
- Ensuring clinic letters are communicated clearly and promptly with GPs no later than 14 days after the appointment, aiming for 24 hours
- Accepting self-referral of patients discharged from the service without the need for GPs to write a referral letter
- Referring directly to neurologists or neuropsychiatrists for a neurological opinion, saving the GP making the referral
- Liaising directly with neurologists or neuropsychiatrists by secure email for advice and guidance, including chasing investigations and results
- Being a point of contact for paramedics to refer patients to the ESN team instead of GPs
- Organising concessionary bus pass forms, support for benefits applications and appeals, evidence for continuing healthcare decision meetings, referrals onto social services, learning disability teams etc
- Supporting patients to self-care through high quality care planning with patients and families or carers
- Undertaking medication reviews
- Establishing close working pathways with community pharmacists
- Reducing the associated mortality rates of avoidable deaths through care planning and education of both patients and families or carers about risk and safety issues. This includes mitigating risks of sudden unexpected death in epilepsy (SUDEP)

Other factors that supported our cases included improving demand management by freeing up neurologists' and neuropsychiatrists' time. This allows for more appointments for new patients, thereby reducing the waiting lists for new patients to be seen within the 18-week target. This would realise a financial saving of £116 per follow up appointment.

We used the NHS Rightcare Commissioning for Value Pack [NHS Rightcare, 2016] which demonstrated where the four Norfolk CCGs were an outlier compared to the 10 most similar CCGs, in either:

- Non-elective spend
- Achieving seizure freedom in past 12 months
- Spend on anti-epileptic medication
- Mortality rates

We used guidance on what the ideal caseload for an ESN should be. We referenced the research undertaken by Fiona Irvine [Epilepsy Action, 2010] where she acknowledged that a

recognised caseload for a 1 WTE ESN should be 250 patients.

Initially, only 250 patients out of a possible 1,698 (with refractory, uncontrolled seizures) across the four Norfolk CCGs were registered with the service. Those patients not known to the service were likely:

- To not have appropriate care plans drawn up
- To not have medication reviews
- To be at risk of injury and harm due to safety advice not being given, including at preconception and during pregnancy
- To be at risk of poor self-management through lack of training
- To potentially make unnecessary visits to A&E (with associated ambulance costs)

- To potentially make unnecessary visits to GP practices
- To have higher than expected, inappropriate prescribing of emergency medication (buccal midazolam)

We agreed the key performance indicator for the service would be at least 95% of patients on the ESN caseload to have a seizure care plan. These would have a read code attributed to them on SystmOne to allow for monthly monitoring.

We were lucky to be able to use SystmOne through working for the NCH&C Trust. Through this, the Commissioning Support Unit (CSU) was able to provide data on various aspects. These included the patients referred to the service since 2015, the amount of A&E attendances and admissions, and cost a year prior to and post referral. They could also inform on the number of appointments with neurologist and the cost, again a year pre- and post-referral to the ESN service. Both datasets provided the crucial evidence to forecast the financial savings for the business case.

Outcomes of more ESNs at the service

North Norfolk CCG commissioned 1 WTE Band 7 in February 2017. The task was then to present to a planned care meeting with all the CCGs across Norfolk with endorsement of the Clinical Commissioning Board. This happened in September 2017 and, one by one, three more CCGs came on board. This involved working closely with each CCG, making the business case come to life from a clinical perspective. Once the business cases were accepted from a clinical and quality need for patients, the next step was selling the case in five minutes at a clinical executive meeting.

The respective clinical executive reference groups strongly supported the proposal. Comments made included:

- "This is a patient cohort who would benefit from enhanced specialist support as they are not known well by GPs"
- "This will have a positive impact for patients' quality of life, including reduced hospitalisation"
- "A suggestion would be to see whether we can learn from learning disability mortality reviews"
- "Education for families and patients is key to reducing risks"
- "It will reduce workload for GPs"
- "It does not feel like the enhanced service would need to visit all GP practices as new referrals would be easily identifiable"
- "One proposal would be to recruit to the Band 7 ESN initially and then the Band 6 ESN when caseload demand required it"
- "The service would have a quick route back in for patients when their situation started to destabilise"
- "Transition from paediatrics to adults will be carefully managed"
- "Improved patient outcomes plus supports new model of care, Quality, Innovation, Productivity and Prevention programme (QIPP), demand management, and GP Forward View"
- "This will provide coordinated management with the neurology departments, GPs, practice nurses and pharmacists to implement the MHRA pregnancy prevention programme for women of childbearing potential taking sodium valproate"

The outcomes have been significant. We have grown from seeing patients in six locations to 23 across the geography of the four CCGs. These venues range from NCH&C hospitals and clinics, GP practices, secondary care hospitals and residential homes. Patients can also be seen at home where reasonable adjustments need to be made for patients with a learning disability. This has led to a dramatic decrease in the 'did not attend' rates, from 20% down to 0% in some months, and improved patient satisfaction of the range of appointment settings. The monthly reporting from the CSU is showing a downward trend in admissions, A&E attendances and neurology outpatient appointments and an increase in cost savings.

We have been fortunate to recruit Dee Elleray out of

Feedback following expansion of the ESN roles

Parents of a patient with complex epilepsy
"Thank you again for all the work on my daughter's care plan, involving us and the care team. It really does look well organised and a useable document in our eyes."

Dr Staufenberg, consultant in epilepsy neuropsychiatry
"New format has substantially improved the communication with GP colleagues, community learning disability nurses, social services and residential providers."

Continuing healthcare team
"The seizure care plan really helped with the panel's assessment of excess funding. Thank you for all your help."

Feedback from Dr Cochius, neurologist at NNUH
"There is improved responsiveness to acute deteriorations in epilepsy control or problems relating to medication side-effects. This is done through efficient use of email to communicate, when necessary, with neurology consultants and by passing on therapeutic recommendations to the GP with less delay. ESNs reduce the likelihood of a situation deteriorating to the point that A&E attendance or possibly admission to hospital is required. Paediatric patients and families are well supported in the transition through to the adult service, by well-timed, supportive and informative nurse-led adolescent transitional epilepsy clinics."

Feedback from neurologists at QEHKL
"ESNs are crucial in the writing of care plans for patients with epilepsy. Colleen (Taylor, ESN at the Norfolk community epilepsy service) often writes out plans to change medication and offers a phone service for questions which arise during drug titrations. Colleen saves hospital time by seeing many follow ups and this frees up appointment spaces for other patients to reduce our large waiting list and saves GP time by answering many patient questions herself."

Patient feedback
"To put it succinctly, from our first meeting both my husband and I felt there was a seismic shift in the level of support, information and care you offered. Your epilepsy expertise, explanations of different types of epilepsy, providing a structured care plan including us and arranging an appointment with Dr Cochius, neurologist, has given us both a real sense of safety and accessibility."

"June (Greenway, ESN at the Norfolk community epilepsy service) has been there for me and my family through the tough times and great times. I could just ring June and she would listen. I trust her."

"I feel my mum and I can talk to the epilepsy nurse in between appointments, she has an easy and relaxed approach. I now feel more confident to talk about my epilepsy. I now have a Buddi alarm, which gives me confidence to go out on my own. I have a free bus pass which stops me relying on lifts or being restricted to home. She noticed that my head and body were moving a lot and knew that I was on too much medication She contacted my neurologist and GP so they knew what was happening and reduced my tablets and now the movement has gone and I feel brighter in myself. I received information about the 'Epilepsy and You' course. I have completed that and set a goal to go out on my own, which I have worked towards and now manage to do."

retirement as the 0.5 WTE Band 6 ESN, to focus on the MHRA pregnancy prevention programme.

The caseload for our service has grown from 250 in April 2016 to 1,110 in February 2019. Patients who have been seizure free for 12-18 months have been discharged, with self-referral back to the service if needed.
The seizure care plan has been reviewed and updated following feedback from patients, families and carers. We have been able to achieve our target of 95%.

Pathways have been set up to integrate the service with teams where a patient presents with seizures. There is a greater awareness of the team, leading to the increase in referrals. This has resulted from attending GP practice meetings and promoting the service and how it can support GPs and patients. Joint working with the neurology departments at NNUH, QEHKL and WSH has also been instrumental.

We have been able to work closely with the voluntary sector, specifically the Epilepsy Action coffee and chat group in our area. This was an award-winning group of the year in 2018. The group has helped with reviewing the care plan and service leaflet, making sure it reflects the needs of people with epilepsy. We have 52 funded places for the online self-management 'Epilepsy and You' course, through Epilepsy Action and Coventry University. This uses the Patient Activation Measure to test the activation improvements from undertaking the course.

Photo taken in September 2018. Left to right – Dee Elleray ESN, Dr Cochius neurologist at NNUH, Dr Staufenberg neuropsychiatrist, Juliet Bransgrove ESN North Norfolk, Colleen Taylor ESN West Norfolk and June Greenway ESN Norwich.

Debbie Davey, joined the team as South Norfolk ESN in November 2018.

The team works as one Norfolk service, based from Dereham hospital in the centre of Norfolk. We have one phone number so if one of the team are on leave a patient or family member can always speak to an ESN for advice. The access to SystmOne allows for proactive continuity of care and direct communication with GPs. The NHS Long Term Plan also describes backing the NHS workforce. It said "we will also make the NHS a better place to work, so more staff stay in the NHS and feel able to make better use of their skills and experience for patients".

Our expanded service quickly got a very favourable reputation as a team nurses would want to come and work in. This was demonstrated by the final recruitment for the South Norfolk post attracting five highly qualified candidates, internally and externally, applying for the post.

Now the team is formed, but our work has just begun. We will aim to enhance the pathways we've started, especially working closely with out-of-hours and ambulance services. We have signed off the contract variation with the four CCGs and have a comprehensive monthly reporting on all the outcomes including service development.

Once we have proved the worth of the investment in our new establishment, we will also be looking to commission a community ESN for Great Yarmouth and Waveney CCG. This post will complement the newly appointed adult ESN at the James Paget University hospital.

We are happy to share the business case and have already had enquires from CCGs and neurology departments across the country.

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Further reading

Nice.org.uk. (2012). Epilepsies: diagnosis and management | Guidance and guidelines | NICE. [online] Available at: *https://www.nice.org.uk/guidance/cg137* [Accessed 21 Feb 2019]. guidance 270, p79
NHS. (2019). The NHS Long Term Plan. [online] Available at: *https://www.longtermplan.nhs.uk/wp-content/uploads/2019/01/nhs-long-term-plan.pdf* [Accessed 21 Feb 2019]
Joint Epilepsy Council of the UK and Ireland. (2011). Epilepsy prevalence, incidence and other statistics. [online] Available at: *http://www.epilepsyscotland.org.uk/pdf/Joint_Epilepsy_Council_Prevalence_and_Incidence_September_11_(3).pdf* [Accessed 21 Feb 2019]
NHS England, NHS Employers, BMA. (2018). 2018/19 General Medical Services (GMS) contract Quality and Outcomes Framework (QOF) | Guidance for GMS contract 2018/19. [online] Available at: *https://www.nhsemployers.org/-/media/Employers/Documents/Primary-care-contracts/QOF/2018-19/2018-19-QOF-guidance-for-stakeholders.pdf* [Accessed 21 Feb 2019]
NHS England. (2016). General Practice Forward View. [online] Available at: *https://www.england.nhs.uk/wp-content/uploads/2016/04/gpfv.pdf* [Accessed 21 Feb 2019]
NHS Rightcare. (2016). NHS RightCare » Focus packs for CVD, Neurological, Respiratory, Maternity – April 2016. [online] England.nhs.uk. Available at: *https://www.england.nhs.uk/rightcare/products/ccg-data-packs/focus-packs/focus-packs-for-cvd-neurological-respiratory-maternity-april-2016/* [Accessed 21 Feb 2019].
Epilepsy Action. (2010) Best care: The value of epilepsy specialist nurses | A report on a study by researchers at Liverpool John Moores University on behalf of Epilepsy Action. [online] Available at: *https://www.epilepsy.org.uk/sites/epilepsy/files/images/campaigns/care-the-value-of-epilepsy-specialist-nurses.pdf* [Accessed 21 Feb 2019]

We're stronger together – please keep in touch!

Epilepsy Action works closely with epilepsy specialist nurses (ESNs) across the UK. We can provide literature, resources and information for ESNs to help them support their patients. We would like to keep in touch about ways that we can continue to work together. If you are an epilepsy specialist nurse and you have not received an email from us inviting you to confirm what you would like to hear from us about and how, please let us know. Contact Kath Barker on *kbarker@epilepsy.org.uk*. Thank you.

Stave off the panic

It's hard not to mention the elephant in the room in this opinion piece – Brexit. It doesn't matter if you are a Brexiter, a Remainer, or whether you do or don't understand the backstop, the customs union or article 50. It doesn't matter if you are of the so-called 'snowflake generation', or were too young to vote and will bear the aftermath of all this for years to come. Whatever your position, I think it's fair to say there is a heightened state of anxiety across the nation, in particular with regard to health.

It's hard to prepare for something when we don't quite know the true consequences. To name but a few examples, the housing market is slow, with people reluctant to buy or sell. Uncertainties exist for those living abroad, and for non-British people living and working in UK. Not to mention more basic issues, such as what will happen to our fresh fruit and veg supply. Not to be flippant about such a constitutional crisis, but I do see one huge winner in this process; sky-high profits at the Irish passport office. I can imagine there to be an unrecognisable surge in applications (still waiting for mine to arrive, suspect there's a bit of admin backlog?). I had heard from my mum that her local post-office was completely out of forms…

So, as 29 March looms ever closer, with political parties no closer to a deal, and those elected to serve falling by the wayside, I think we have an important role. We need to try and remain a constant force of calm for our patients and provide reassurances where we can.

One of the big uncertainties for patients is consistency of medication supply. Some are already struggling with this. The exact reason is unclear, although stockpiling of drugs by companies has been cited.

I suggest that there may be various options for clinicians to help people with epilepsy, and chronic disease, navigate this storm. Panicking helps no-one. Not ideal, and a bit awkward, but when 500mg tablets are in short supply, we could combine 200mg and 300mg tablets, trying not to mix and match different pharmaceuticals suppliers. Other therapeutic options are to consider using once daily drugs and those with a longer half-life. Advice has already been issued to GPs, advising against stockpiling and against issuing longer prescriptions, as this obviously has safety implications.

It's encouraging to read that epilepsy leaders are pressing forward with this and that there is a contingency plan from the Department of Health and Social Care. The government has also confirmed that epilepsy medicines will be exempt from its serious shortage protocol. This protocol will give pharmacists power to dispense alternative drugs if those prescribed by GPs are in short supply at any time, including if there is a 'no-deal Brexit' scenario. If there is a shortage of a particular epilepsy medication, clinicians could advise on the most appropriate course of action. Where necessary, the Department of Health would seek to access the medication from an alternative source.

So, it's a political soup, an ever-changing sea, but it's important not to panic. I would encourage clinicians to stick to their normal clinical prescribing practice. I'd also urge people with epilepsy to continue to take their medications as recommended by their doctors and to keep in regular contact with – and take advice from – their clinicians. And I would strongly recommend steering clear of the 'advice' from the tabloid headlines, the disgruntled politicians, social media or fake news (such is our generation…).

Sleep and epilepsy

Managing sleep problems in people with epilepsy

Dr Sofia Eriksson describes the relationship between sleep and epilepsy and offers some practical advice on identifying and tackling sleep problems in people with epilepsy

There is a close relationship between epilepsy and sleep. Sleep deprivation may trigger seizures, and some types of seizures occur from sleep or following awakenings. Sleep complaints are common in the patients we see in our epilepsy clinics – both insomnia and daytime tiredness. This article reviews the interaction between sleep and epilepsy and provides some practical guidance on how to approach sleep problems in patients with epilepsy.

Distribution of seizures and epileptic activity in wakefulness and sleep

The tendency for seizures to occur during a specific time of day has been noted since the Babylonian time. This has been confirmed using implanted neurostimulator systems monitoring seizures and epileptiform activity for months or even years [Baud et al 2018]. Interictal epileptiform discharges (IEDs) are more frequent during non-REM than REM sleep and wakefulness. This might be due to the more synchronised activities, such as sleep spindles, delta waves and slow cortical oscillations, associated with non-REM sleep. Facilitation of IEDs during sleep appears to be unrelated to the type of epilepsy, but the timing of seizures appears to be at least partly influenced by seizure onset zone. Frontal lobe seizures occur predominantly during sleep and temporal lobe seizures are more common during wakefulness. This suggests that although there are common sleep-related activating factors for epileptiform activity, the transition from interictal to ictal state is modulated by other factors that may vary between different parts of the brain. It also seems that it is sleep itself, and not just circadian phase, that promotes some type of seizures, as seizures may occur from daytime as well as night-time sleep [Khan et al 2018].

It seems that it is sleep itself, and not just circadian phase, that promotes some type of seizures, as seizures may occur from daytime as well as night-time sleep

IEDs are also facilitated following sleep deprivation. It has been suggested that this is due to instability of sleep and wakefulness, and frequent fluctuations in vigilance levels. During sleep, seizures also more commonly occur during shifts between sleep stages and less stable sleep. Cortical excitability, measured with transcranial magnetic stimulation (TMS), increases with time awake but is also influenced by circadian phase and is lower in evening than morning hours. This also seems to vary according to the epilepsy syndrome. Bilateral changes tend to be seen in patients with generalised epilepsy and changes only on the side of seizure onset are more comon in those with focal epilepsy. It has been speculated that this is mediated by variability of GABA medicated inhibition [Badawy et al, 2006].

Clarifying the relative influence of sleep, vigilance and circadian factors

would require studies under strictly regulated light/dark and sleep/wakefulness conditions. This would be difficult to do in patients with epilepsy as it might potentially trigger seizures.

Differential diagnosis of paroxysmal nocturnal events

Correctly diagnosing the nature of nocturnal events is often difficult. To aid the differential diagnosis between epilepsy and parasomnias, particularly non-REM parasomnias, a number of scales and scores have been developed, mainly based on clinical characteristics of events. The sensitivity and specificity of these scales has not been established and they are rarely used in everyday clinical practice. There are some clinical features that may help in differentiating nocturnal events, such as timing of events during sleep. Non-REM parasomnias tend to occur in the first third of sleep, unless the person has disrupted sleep architecture, whereas seizures can occur throughout the night as outlined above. The number of events per night can also be useful to differentiate between types of events. Non-REM parasomnias tend to occur 1-3 times a night, while seizures may occur much more frequently. The frequency of non-REM parasomnia events usually varies. They may at times be very infrequent, with weeks or months between events, while at other times may occur every night. Although the frequency of epileptic seizures can also vary, it is usually a bit less variable than the parasomnias. Non-REM parasomnias often start in childhood and many grow out of the disorder in their teens. However, adult onset does not exclude the diagnosis.

Semiology of sleep-related events can play a key role in distinguishing epileptic seizures from sleep disorders. For example, stereotypy, dystonic posturing and bizarre, unnatural movements are more common features in seizures, while waxing and waning, prolonged duration and indistinct offset are more common in parasomnias. With video cameras now readily available on smartphones, it has become easier to get video footage of events. Home videos can provide valuable data and are recommended whenever possible. From a practical perspective, it is often difficult to capture the onset of the events as these tend to occur when the patient and any bed partner are both asleep. Often, footage may be limited to the end of the event or even the postictal phase. Instructions should be given to bed partners or family members about trying to capture as much of the events as they can. This includes capturing the whole body of the person and removing blankets and duvets to provide a better view of movements and any posturing. Seeing more than one event is often very helpful.

Stereotypy, dystonic posturing and bizarre, unnatural movements are more common features in seizures, while waxing and waning, prolonged duration and indistinct offset are more common in parasomnias

The term nocturnal frontal lobe epilepsy (NFLE) was previously commonly used for seizures during sleep. But it is recognised that the seizures are associated with sleep rather than time of day, they may arise from brain areas outside the frontal lobe and often include characteristic

motor aspects. Therefore, it was recently recommended to change the name to sleep-related hypermotor epilepsy (SHE) [Tinuper et al, 2016].

Sleep disorders in people with epilepsy

Causes

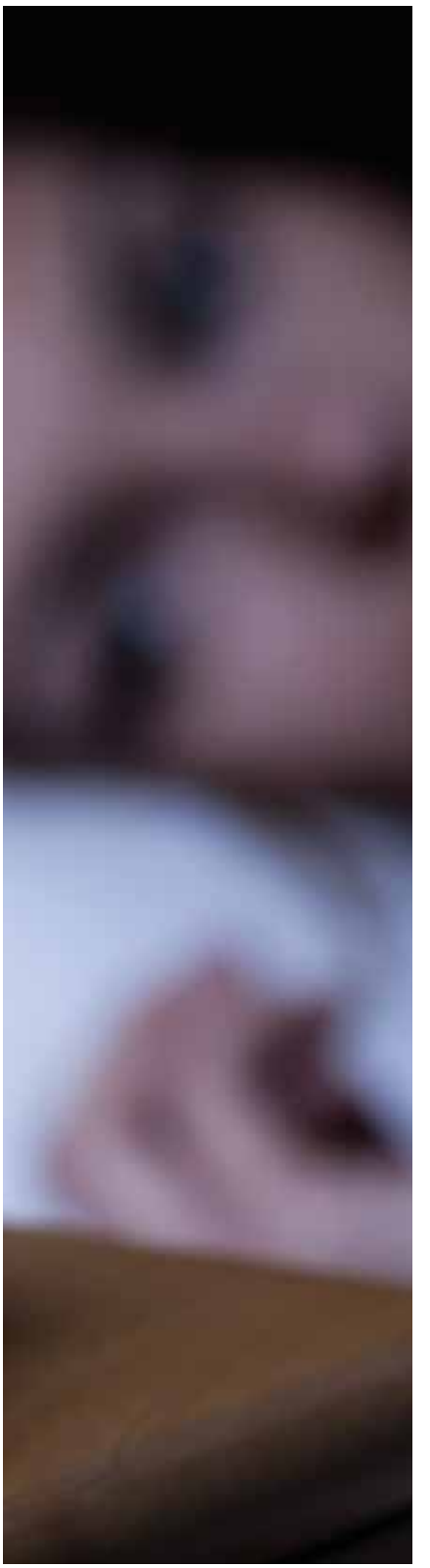
Daytime tiredness is a common complaint when we see our epilepsy patients in clinic. Sedation is one of the most common adverse events of anti-seizure medications and tiredness is often thought to be due to the treatment. There may, however, be a number of other reasons why people with epilepsy are tired than their medication. Some studies have found worse tiredness in people with frequent seizures, which can improve after surgery. Seizures may also affect sleep architecture. Reduced amount of REM sleep has been seen during nights after seizures had occurred. Nocturnal seizures also reduced the amount of deeper stages of sleep and increased the amount of the lightest stage of sleep [Bazil et al, 2000]. Concomitant sleep disorders such as obstructive sleep apnoea (OSA), restless leg syndrome (RLS) and periodic limb movements of sleep (PLMS) may also cause sleep disruption. These may contribute to daytime sleepiness and worsening seizure control [Phillips et al, 2013]. The frequency of sleep disordered breathing (SDB) has been reported in up to 30% of patients undergoing epilepsy surgery investigations but this may vary between different populations. A recent study from Scotland found that the rates of OSA in patients admitted for video-telemetry was similar to those of the general population [Popkirov et al, 2019]. This is in line with the observations from our own video-telemetry unit (unpublished audit data). Insomnia is also common in people with epilepsy and may have a number of different causes, as in people who do not have epilepsy.

Daytime tiredness is a common complaint when we see our epilepsy patients in clinic

How to evaluate

From a practical point of view, assessment of overnight sleep and daytime somnolence is recommended, starting with open questions on general aspects of disturbed or non-restorative sleep and sleepiness. Lifestyle and sleep times should also be assessed. Further, more detailed questions may then follow depending on symptoms highlighted. A history of snoring, possible pauses in breathing or the patient being overweight should raise the clinical suspicion of comorbid SDB and trigger further investigations with overnight sleep studies. Lately, an increasing number of reports of SBD in people treated with vagus nerve stimulator (VNS) has been described. The onset of snoring or sleep disruption after VNS insertion should also trigger further investigations. Similarly, a history of restlessness or kicking at night may raise the suspicion of RLS or PLMS that may require further investigations with sleep studies. All patients with suspected RLS or PLMS should also have their ferritin level checked.

For people complaining of insomnia, it is useful to know if there are difficulties falling asleep or staying asleep, as the causes may be very different. Anxiety, RLS or medication could potentially delay sleep onset, whereas PLMS or OSA



may disrupt sleep and wake people during the night.

Anti-seizure medications can cause daytime tiredness, so medication effects on sleepiness should be assessed. The medication may also worsen OSA by reducing respiratory drive and upper airway tone (eg phenobarbitone and benzodiazepines) or contributing to weight gain (eg sodium valproate, pregabalin and gabapentin). RLS has been reported in some patients treated with topiramate and zonisamide. Insomnia is often reported in patients treated with lamotrigine.

How and when to treat

If it is clear from the history that the anti-seizure medication is causing sleepiness and there is no history to suggest additional causes, changing dosages or dosing regimen should be considered. This could include taking a higher dose of sedating medications in the evening than morning, or taking a lower dose of lamotrigine in the evening if this contributes to insomnia.

As SDB can make epilepsy worse and improvement of seizure control has been seen after successful treatment of OSA, treatment with continuous positive airway pressure (CPAP) is often considered. Treatment should be considered earlier and for less severe symptoms than in people without epilepsy.

Ferritin levels lower than 50-75ug/l can make RLS and PLMS worse and iron supplement can improve symptoms. For people with normal ferritin, choosing anti-seizure medications, such as pregabalin or gabapentin, that are also used to treat RLS and PLMS, may improve both the sleep disorder and seizures.

Cognitive behavioural therapy (CBT) should be considered as first-line treatment choice of chronic insomnia in people with epilepsy, as for people without epilepsy. However, caution should be adopted in using sleep restriction as part of CBT, as it may cause sleep deprivation, potentially triggering seizures.

Conclusion

There is an intricate relationship between sleep and epilepsy, and sleep plays an important role for seizure control. Sleep problems are common in people with epilepsy and it is important to ask about sleep problems or excessive daytime somnolence. This is key for identifying and treating sleep disorders as well as epilepsy. It can help to ensure optimal management and potentially improve quality of life.

Dr Sofia Eriksson
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Further reading

Badawy RA, Curatolo JM, Newton M, Berkovic SF, Macdonell RA. (2006). Sleep deprivation increases cortical excitability in epilepsy: syndrome-specific effects. *Neurology* 67, 1018-1022.

Baud MO, Kleen JK, Mirro EA, Andrechak JC, King-Stephens D, Chang EF, Rao VR. (2018) Multi-day rhythms modulate seizure risk in epilepsy. *Nature Communications*. 9: 1-10.

Bazil CW, Castro LH, Walczak TS. (2000). Reduction of rapid eye movement sleep by diurnal and nocturnal seizures in temporal lobe epilepsy. *Arch Neurol*. 57, 363-368.

Khan S, Nobili L, Khatami R, Loddenkemper T, Cajochen C, Dijk D-J, Eriksson SH. (2018) Circadian rhythm and epilepsy. *Lancet Neurol*. 17(12):1098-1108

Phillips MC, Costello CA, White EJ, Smit M, Carino J, Strawhorn A, Jackson B, Kwan P, French CR, Yerra SR, Tan KM, O'Brien TJ, Goldin J. (2013). Routine polysomnography in an epilepsy monitoring unit. *Epilepsy Res*. 105(3):401-4

Tinuper P, Bisulli F, Cross JH, Hesdorffer D, Kahane P, Nobili L, Provini F, Scheffer IE, Tassi L, Vignatelli L, Bassetti C, Cirignotta F, Derry C, Gambardella A, Guerrini R, Halasz P, Licchetta L, Mahowald M, Manni R, Marini C, Mostacci B, Naldi I, Parrino L, Picard F, Pugliatti M, Ryvlin P, Vigevano F, Zucconi M, Berkovic S, Ottman R. (2016) Definition and diagnostic criteria of sleep-related hypermotor epilepsy. *Neurology*. 86:1834-42.

Dates for the diary

April 2019

4-7
13th World Congress on Controversies in Neurology (CONy)
Madrid, Spain
www.comtecmed.com/cony/2019

6
EEG in Status Epilepticus and on the Intensive Care Unit Teaching Course
London, UK
bit.ly/2ODcMqq

7-9
7th London-Innsbruck Colloquium on Status Epilepticus & Acute Seizures
London, UK
statusepilepticus.eu/index.php

May 2019

9-10
Joint British and Danish ILAE British Advanced Epilepsy Meeting: Channelopathies and Neurosurgery
Copenhagen, Denmark
bit.ly/2ABANoW

June 2019

5
Professional Study Day | Diwrnod astudio proffesiynol
Abergele, UK
epilepsy.org.uk/Abergele-prof

16-20
XV Workshop on Neurobiology of Epilepsy WONOEP 2019
Ayutthaya, Thailand
internationalepilepsycongress.org/wonoep

22-26
33rd International Epilepsy Congress (IEC)
Bangkok, Thailand
internationalepilepsycongress.org

September 2019

6-7
International Congress on Mobile Devices and Seizure Detection in Epilepsy
Lausanne, Switzerland
mhsdepilepsy2019.com/

Stress and epilepsy

Dr Christophe Bernard describes research around the effect of stress on epilepsy and what this relationship might mean for clinicians treating people with epilepsy.

Laser interstitial thermal therapy

Dr Sophia Varadkar discusses laser interstitial thermal therapy (LITT) for epilepsy and describes what the situation with this treatment is in the UK.

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