2018 Paediatric Epilepsy Research Report

Young Epilepsy

Great Ormond Street Hospital for Children NHS Foundation Trust

UCL GREAT ORMOND STREET INSTITUTE OF CHILD HEALTH

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Introduction

I am delighted to present our annual Research Retreat for the period July 2017 to June 2018 for the paediatric epilepsy research unit across Young Epilepsy, UCL GOS - Institute of Child Health and Great Ormond Street Hospital for Children.

2018 marks my tenth year as the Prince of Wales's Chair for Childhood Epilepsy and I am pleased to share with you some of the achievements across the unit within that time in this report. During this year alone, we have initiated 8 new research projects, adding to 19 active projects spanning the clinical, educational and social elements of paediatric epilepsy. We have published 80 peer-reviewed items of primary research and a further 19 books, chapters in books, reviews and commentaries of expert opinion.

In May 2018 we held the 6th Mind The Gap Symposium at UCL GOS - Institute of Child Health and Young Epilepsy. This meeting and resultant Workshop was dedicated to sharing the latest views on the problems associated with childhood epilepsy beyond seizures and to developing guidance for more integrated services. We welcomed expert speakers and delegates from as far afield as the USA and Canada to share best practice and discuss the global challenge of integrating services.

January 2018 saw our 8th International Paediatric Epilepsy Research Retreat for researchers and collaborators across the unit, moderated by Professor Kees Braun of the Rudolf Magnus Brain Centre, Utrecht University, Netherlands. The Retreat is indeed a one-of-a-kind event where early career and seasoned researchers meet to constructively share their research and forge collaborations.

This report features a spotlight on our educational research, which shed light on the true nature and gravity of challenges faced by children with epilepsy in their learning and development. As a

charity, Young Epilepsy seeks to incorporate this body of work into materials for all professionals surrounding a child with epilepsy and to influence educational support for children with epilepsy in UK schools.

Young Epilepsy's vision is to build better futures for young lives with epilepsy. We continue to evidence the need for integrated holistic care, the benefit of early interventions and improving our understanding of the epilepsy's, in order to offer smarter treatments and stronger outcomes for all.

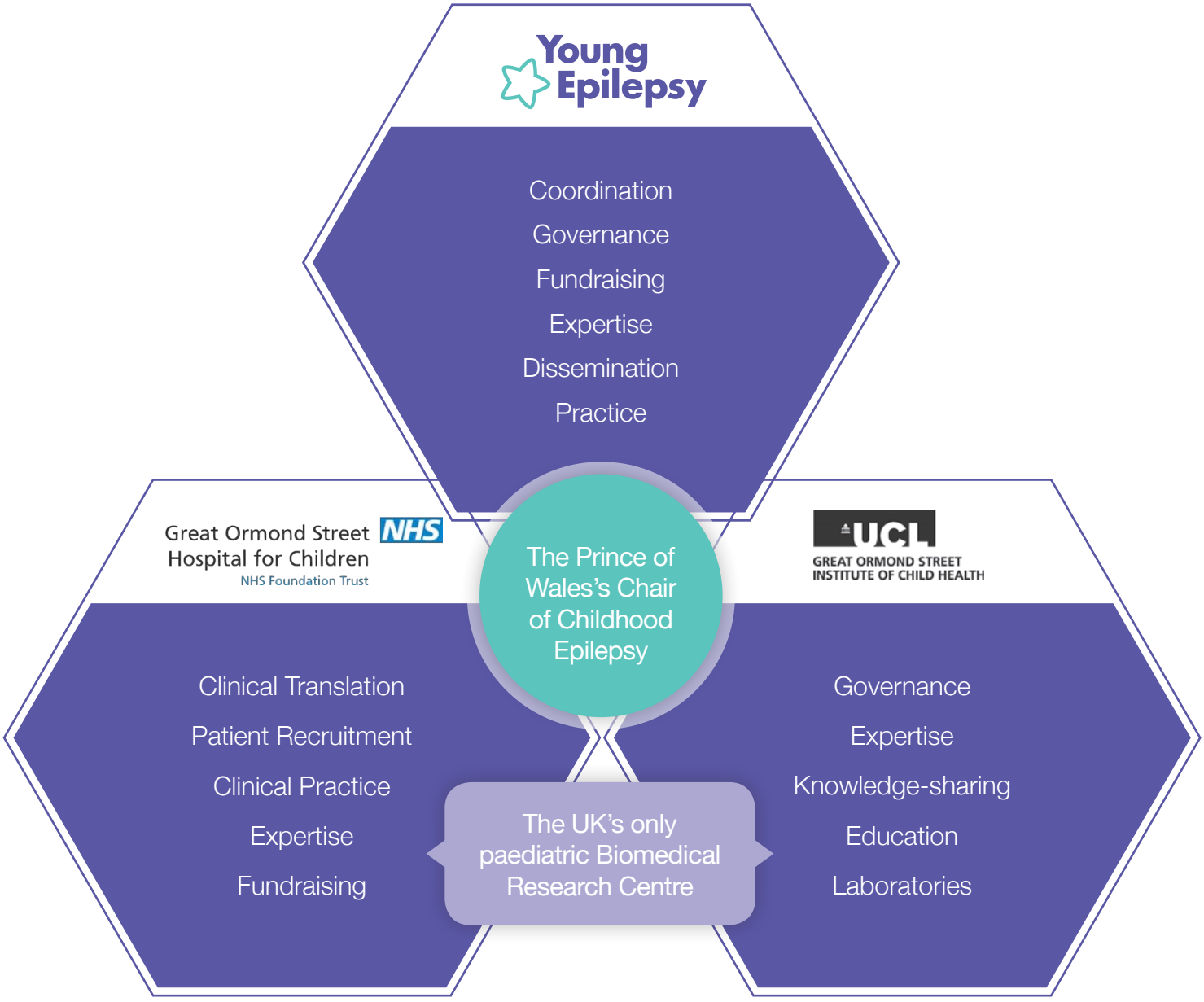
Professor Helen Cross OBE

The Prince of Wales's Chair of Childhood Epilepsy

Who we are

Research Partners

Our research programme operates under the auspices of The Prince of Wales's Chair of Childhood Epilepsy, Professor Helen Cross OBE. It is a collaborative scheme between Young Epilepsy, Great Ormond Street Hospital for Children and UCL GOS - Institute for Child Health.



Who we are

Young Epilepsy is the national charity working exclusively on behalf of children and young people with epilepsy and related conditions. With over 100 years expertise, it provides world class diagnosis, assessment and rehabilitation for children and young people with epilepsy. Young Epilepsy has a specialist school and college, providing day and residential services, for those up to 25 years of age, offering education and healthcare for children and young people with epilepsy, autism and other neurological conditions. Young Epilepsy aims to achieve better futures for young lives with epilepsy and to raise awareness and understanding of epilepsy along with issues associated with the condition. The charity provides support and information for parents, children and young people as well as training for professionals. It campaigns for better access to, and quality of, health and education services.

Great Ormond Street Hospital for Children (GOSH) is an international centre of excellence in child healthcare, at the forefront of paediatric training in the UK. GOSH plays a leading role in training paediatric doctors and training more children's nurses than any other hospital. The hospital is committed to carrying out pioneering research to find treatments and cures for some of the most complex illnesses. Together with UCL GOS - Institute of Child Health, GOSH forms the UK's only Biomedical Research Centre specialising in paediatrics.

University College London Great Ormond Street-Institute of Child Health (ICH) together with its clinical partner GOSH, forms the largest concentration of children's health research in Europe. ICH pursues an integrated, multidisciplinary approach to enhance understanding, diagnosis, therapy and prevention of childhood disease. All specialties, as they relate to children's health, are included so that ICH fulfils the role of a world-leading academic establishment in paediatrics. In keeping with a commitment to disease prevention, ICH is active in teaching and research aimed at developing interventions to promote health both during childhood and in the later years of life.

Research Funding

Central to the research programme is the ability to apply for and manage research grants and donations.

Our collaborative funding strategy has enabled us to build the world's largest paediatric epilepsy research unit and network of multidisciplinary practitioners. We marry academic project grants with the safeguard of smart fundraising, which allows us to keep the expertise within the unit and develop the impact of our work.

Alongside academic grants raised by researchers and academic institutions, we rely on the grace of unrestricted funding from private individuals and Trusts, raised by Young Epilepsy, which allow us to redirect funds where the need is greatest within a project. This flexibility is vital and provides stability when the parameters of projects change. The future of this programme rests on the ability to maintain and build the current infrastructure which allows us to maintain a base of operations to lead, coordinate and provide governance.

We remain ever grateful for the generosity and dedication of the organisations and individuals who support our work.

Thank you!

Action Medical Research

Action Medical Research Clinical Research Training Fellowship

Brain Tumour Charity

Cancer Research UK

Charles Wolfson Foundation

Child Health Research Trust

Children with Cancer UK

Desitin

Epilepsy Research UK

EPSRC Global Challenges Research Fund 2018

EU-Chafea

European Commission

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Great Ormond Street Hospital Children's Charity

GW Pharmaceuticals

Innovate UK

McCarthy's Laboratories

MRC DPFS Award

Neville UK

NIHR

NIHR EME Programme

NIHR GOSH Biomedical Research Centre - Research Infrastructure Support

NIHR GOSH Biomedical Research Centre - Rare Disease Cohorts Grant

NIHR PGfAR Programme

Novartis

Nutricia

Olivia Hodson Cancer Fund

Rogue Resolutions BrainBox Initiative

Rosetree's Trust

Sir Jules Thorn Charitable Trust

Sparks Charity

Swedish Research Council

True Colours Trust

Veriton Pharma

Vitaflo

Who we are

Research Team

The research team contribute to a wide spectrum of activities from basic science to patient care. The team consists of a multidisciplinary range of experts working across Young Epilepsy, UCL GOS - Institute of Child Health and Great Ormond Street Hospital for Children.

Principal Investigators

Professor Helen Cross OBE The Prince of Wales's Chair of Childhood Epilepsy and Head of UCL GOS - ICH Developmental Neurosciences Programme
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Who we are

PhD students

Sam Amin *An investigation into mTOR inhibitors in Tuberous Sclerosis Complex*

John Apps *Molecular characterisation of Childhood Craniopharyngioma and identification and testing of novel drug targets*

Filipa Bastos *Memory outcome after temporal lobectomy*

Victoria Bryant *Sudden Unexpected Death in Childhood; characteristics, autopsy findings and investigation*

Emilia Carlsson *Language, communicative functioning and literacy in school-age children with autism spectrum disorders*

Aswin Chari *Novel network evaluation of intracranial EEG to identify the epileptogenic zone*

Rosie Coleman *Functional and structural plasticity after epilepsy surgery*

Maria Davidsson *Parents and children's experiences of traumatic events, the PACET study*

Bianca De Blasi *Multi-parametric imaging using hybrid PET/MRI to investigate the epileptogenic brain*

Lisa Dinkler *Aetiology of eating disorders in a neuropsychiatric perspective: overlap and trajectories*

Maria Eriksson *Cognitive outcomes after neurosurgical treatment for focal epilepsy: developing a neuroanatomical predictive model for clinical decision making*

Amy Fairchild *Characterisation of high-risk paediatric brain tumours and their aberrant gene networks*

Linda Häger *EEG based biomarkers for ADHD and autism*

Jane Kung *Epilepsy in infancy - relating phenotype to genotype*

Valdemar Landgren *Symptomatic developmental disorders in childhood (ESSENCE): Bio-psychosocial development and follow-up in adults*

Yao-Feng Li *Modelling cell-cell interactions in developmental cortical lesions*

Adeline Ngoh *Clinical and Molecular genetic characterization of Landau Kleffner Syndrome*

David Nobbs *Upper limb movement after hemispherectomy*

Birgit Pimpel *Neurophysiological methods to aid decision making in paediatric epilepsy surgery*

Apostolos Papandreou *Investigation of disease mechanisms and screening for treatments in Beta-Propeller Protein-Associated Neurodegeneration (BPAN)*

Joyeeta Rahman *Novel diagnostic and therapeutic approaches for mitochondrial disorders*

Richard Rosch *Dynamic causal modelling of large-scale networks in human development and their relationship to network abnormalities in paediatric patients with developmental epilepsies*

Darco Sarovic *Neurophysiological markers in autism*

Izabella Smolicz *Cellular heterogeneity underlying childhood brain diseases*

Fatma Taha *Understanding the phenotypic variability and tissue specificity of paediatric mitochondrial diseases*

Siobhan Titre-Johnson *Ketogenic diet in infants with epilepsy*

Aitkaterini Vezyroglou *Deep phenotyping of alternating hemiplegia in childhood*

Lena Wallin *Mental health in 22q11 deletion syndrome from childhood to adult age: a prospective longitudinal study*

Matthew Wilson *The biochemical investigation of vitamin B6 - responsive inborn errors of metabolism*

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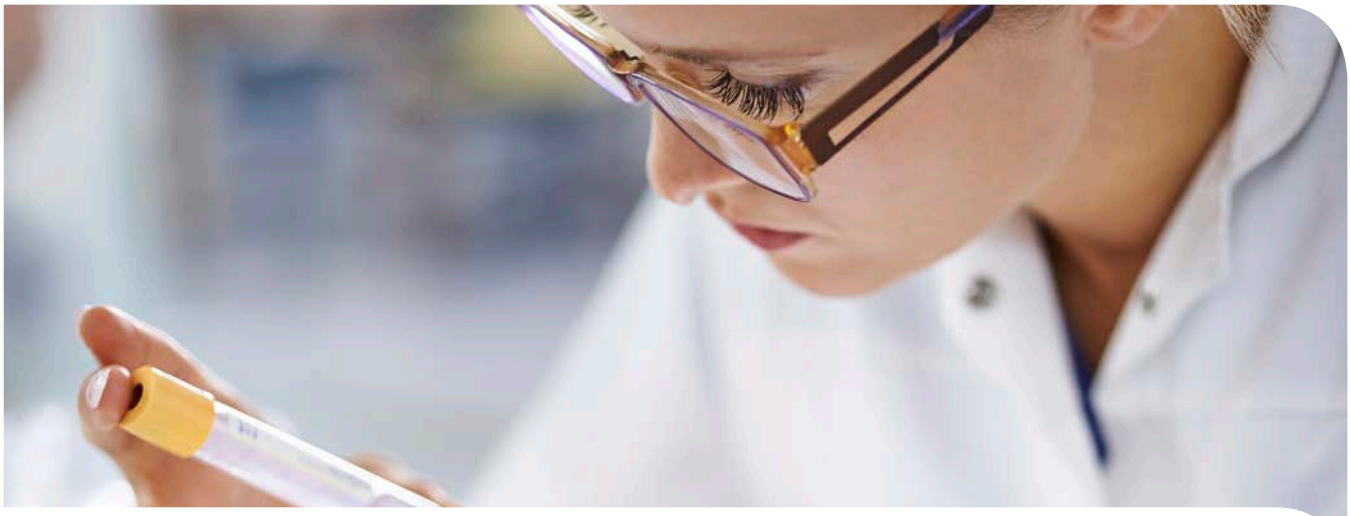

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What we do

Research Strategy

The principal objective of research within the unit is to reduce the overall burden for children with epilepsy and establish successively better long-term outcomes.

Collaboration and integrated working across the unit puts us in a unique position to incorporate data which spans:

- the entire range of complexity and comorbidity in epilepsy
- all stages of diagnosis and care
- the full age range, from neonates to young adults
- multidisciplinary expertise to improve holistic understanding of epilepsy and service design.

We operate under six strategic goals:

GOAL 01

Gain a better understanding of the medical causes of epilepsy

25% projects currently contribute to this goal

The majority of epilepsy treatment is symptomatic. The more we know about the underlying causes of the epilepsies, the more chance there is of developing curative treatments.

- Cohort epidemiological studies to determine incidence, prevalence and outcome
- Population and family studies to gain further insights into new treatments
- Studies to determine the molecular or genetic basis to the epilepsies
- Enhanced structural studies using neuroimaging to increase detection of structural correlates
- Correlative studies in neurophysiology to enhance detection of origin
- Pathological examination of tissue from surgical specimens to enhance our understanding of structural correlates and related epileptogenesis

GOAL 02

Gain a better understanding of how epilepsy affects development and behaviour

22% projects currently contribute to this goal

Epilepsy is associated with myriad comorbidities. Evidence suggests that the effects of these comorbidities have a greater impact than seizures over the course of someone's life. This work will help us to understand how to treat epilepsy holistically.

- Cohort studies to evaluate prevalence, natural history and outcome of comorbidities
- Experimental animal studies to examine the effects of epileptiform discharges on development
- Correlative neurophysiology and neuropsychology studies
- Collaborative outcome studies

GOAL 03

Determine the benefits of early interventions in improving long-term outcomes

30% projects currently contribute to this goal

The longer one has epilepsy, the longer its underlying cause is able to threaten or cause neurological damage. Early intervention is therefore vital in slowing or halting any damage.

- Short and long-term evaluation of outcome following early epilepsy surgery ✓
- Evaluation of new medical treatments ✓
- Evaluation of educational intervention ✓

GOAL 04

Gain a better understanding of barriers to learning and determine the benefits of educational interventions.

6% current projects contribute to this goal

We know that epilepsy can affect the way people learn and therefore may significantly affect someone's academic achievement if not properly understood. We want to know exactly what the challenges are and how best to support children with epilepsy in education.

- Evaluation of measures of progress in children with severe impairments ✓
- Evaluation and development of targeted educational interventions across all educational settings ✓
- Evaluating and enhancing the understanding of professionals working with children with epilepsy ✓

GOAL 05

Make life better for children and families and make support systems more effective

11% projects currently contribute to this goal

Childhood epilepsy can affect the whole family and treatment must involve multiple disciplines and agencies. Support for families must be evidenced and treatment pathways must be made more efficient. Evidencing these needs allows service providers to plan more effective services.

- Interventional behaviour programmes ✓
- Rehabilitation and follow-up studies ✓
- Assessment of service provision ✓
- Evaluation of the impact of epilepsy on family life ✓
- Evaluation of the economic costs involved in epilepsy care ✓

GOAL 06

Develop a network of multidisciplinary professionals to strengthen our research and shape the education of future practitioners

6% projects currently contribute to this goal

To ensure the continuation of excellent research in paediatric epilepsy by nurturing future talent and continually improving knowledge.

- Development of training fellowships ✓
- Projects working towards higher degrees with encouragement for independent working thereafter ✓
- Joint working between ICH, GOSH and Young Epilepsy ✓
- Enhancing research and interoperability across all areas of expertise ✓
- Providing specialist education events and networking opportunities ✓

10

Ten Years On

The Prince of Wales's Chair of Childhood Epilepsy is Europe's first Chair in Childhood Epilepsy. The role was established to bring together multiple domains of knowledge relating to childhood epilepsy and to find solutions to one of the most complex and disabling set of conditions. In 2018 we celebrate our tenth year with Professor Helen Cross OBE at the helm.

In 2001, three organisations - Young Epilepsy (then the National Centre for Young People with Epilepsy, NCYPE), UCL GOS - Institute of Child Health (then UCLICH) and Great Ormond Street Hospital (GOSH) – embarked on a major fundraising appeal which successfully raised £2 million for the first-ever Chair in Childhood Epilepsy under the patronage of His Royal Highness The Prince of Wales.

Professor Cross is the second incumbent of the Chair, succeeding the late Professor Brian Neville on his retirement from the role in 2008.

The overarching focus of research under The Prince of Wales's Chair of Childhood Epilepsy is to improve outcomes in complex childhood epilepsy. We asked Professor Cross to share her view of the key achievements of the unit during her time as Chair, and what is most exciting about the next decade of our research.

Key Achievements 2008 - 2018

- Established vital genetic collaborations through gene discovery and contribution to cohort studies
- Overseen research in new techniques of neuroimaging which has resulted in an increase in the number of children considered for epilepsy surgery
- Overseen several studies determining outcomes from epilepsy surgery and promoted surgery as an intervention both nationally and internationally
- Demonstrated that real improvements can be seen with long-term follow-up, in relation to seizure freedom and weaning from medication following epilepsy surgery. A Collaborative study across Europe, with our participation, demonstrated that an early wean of medication can be successful, which has led to change in practice
- Determined the incidence and impact of epilepsy onset in the first two years of life; and outcomes at three years following presentation. This formed the ground work for a larger epidemiological study (EpiPEG, see page 24) for which aetiologies and developmental outcome will be determined
- Established an evidence base for the use of the ketogenic diet (a high fat, low carbohydrate diet) and widened its use in children with drug resistant epilepsy and obtained funding for further evaluation in infants (KIWE see page 26)
- Demonstrated the extent of educational difficulties and the high rate of cognitive and behavioural problems in school age children with epilepsy and are working towards creating national guidelines for schools in the UK (WINS see page 28)

What we do

Demonstrated key issues amongst parents of very young school children with epilepsy in comparison with parents of children with non-epilepsy related neurodisability. Specifically, we identified significant sleep difficulty, and risk levels for stress, anxiety and depression in mothers of children with epilepsy. This work lends strong evidence to having a child with epilepsy being an indicator for potential maternal mental health issues.

Pilot work in the health economics of epilepsy strongly illustrated the need to explore further the real cost of childhood epilepsy in order to aid service provision and commissioning.

Established a successful European Reference Network (EpiCARE see page 30), a network of centres specialising in care of individuals with rare and complex epilepsies across Europe. EpiCARE is moving toward developing e-tools to aid care, diagnosis and access to expertise without borders.

It seems only fitting that during this year, Professor Cross was awarded the incredibly prestigious Clinical Science Research Award from the American Epilepsy Society. This award is the highest given by the society and recognises professional excellence for those with a distinguished history of pioneering research in epilepsy and anticipated productivity over the next decade - here is to the next ten years!

What to watch – the next 10 years:

- ✔ EpiPEG - We look forward to developing a longitudinal extension of our original epidemiological work. We aim to determine true prevalence of aetiologies, and establish strong natural histories and neurodevelopmental outcomes of relevance to future management.
- ✔ MICE (see page 29) – this project constitutes the first large scale clinical integration of mental health and medical management in paediatric epilepsy in the UK.
- ✔ EpiCARE – we continue to develop the network, working with Lyon, France, as the new coordinating centre with UK input via Professor Cross. We look forward to further collaboration under EpiCARE to move toward clinical trials in rare epilepsies. Using a pan-European cohort of patients will allow for much greater power of research evidence than we can manage with one country's cohort alone.
- ✔ Emerging interest in the development of a registry-based solution to the demand for holistic care in paediatric epilepsies strengthened by collaboration with the Epilepsy12 National Audit, NHS Digital and the third sector.

Education Research at Young Epilepsy

GOAL 04

"My vision is that our work will not only ensure children with epilepsy get the right diagnosis and the best medical intervention, but also go through school with the appropriate support and leave education having reached their true potential."

Professor Helen Cross OBE *The Prince of Wales's Chair of Childhood Epilepsy*

In 2012 we set out to evidence and address the challenges faced by children with epilepsy in UK schools. We began by investigating the barriers to inclusion in education and were presented with a very bleak picture. Led by Dr Virginia Fenton, the *Inclusion Project*[1] illustrated, for the first time, the extent of the exclusion of children with epilepsy from education in mainstream schools. Largely due to 'innocent ignorance' of, and stigma towards, epilepsy, we found exclusion perpetuated by education professionals at every level. We also began to understand and document the enormous onus on families to firstly recognise problems with their child's learning or support, and then to campaign for better support themselves.

Clearly there was a problem. We now needed to document and quantify what made academic inclusion and success such a challenge. To answer this question, Professor Brian Neville, Professor Rod Scott and Dr Colin Reilly embarked on our landmark education research study, the *Children with Epilepsy in Sussex Schools Study* (CHESS). When published in 2014[2,3], we could finally evidence the breadth and depth of the problems which children with epilepsy in the UK face in their school careers:

- 95% of children with epilepsy were struggling in at least one of the assessed areas critical to learning
- 58% had problems with memory and 42% had problems with processing speed
- 60% met the criteria for an undiagnosed additional disorder such as autism, ADHD or Developmental Coordination Disorder.

Despite these numbers, these children, their families and their schools had extremely limited access to support services. This evidence was so sobering that we took the results to parliament to champion a manifesto for change which filtered into epilepsy being formally recognised in the 2014 Children and Families Act. As a charity we strengthened our training for schools and began to target clinicians with this information, to ensure that all professionals were aware of the additional risks and indicators for crisis in epilepsy.

From here, we sought to understand the challenges outside of school; to explore the impact that having a child with epilepsy has on the neurobehaviour of a family. The *Sussex Early Epilepsy and Neurobehaviour Study* (SEEN)[4], again led by Professor Neville, Professor Gillberg and Dr Reilly, confirmed the high level of additional needs faced by children with epilepsy[5] but, critically, shed first light on the extent of problems at home[6,7]. Three-quarters of mothers, and half of the fathers, were at risk of sleep problems, anxiety, depression or stress. Mothers of children with epilepsy were at significantly greater risk of mental health problems than mothers of children with non-epileptic neurological disorders - giving the first evidence that epilepsy itself was an indicator for parental metal health problems.

What we do

The principal goal of this work is to translate the findings into practice across education and healthcare. Dr Reilly is currently leading the *What I Need in School Study* (WINS); the culmination of our current education research. WINS seeks to understand the most practical way to translate our research by garnering the views and experiences of school age children with epilepsy, their parents and teachers on the impact of epilepsy in school and on optimal educational support.

We will record these challenges and identify the best interventions, as expressed by young people themselves. We will do the same with their families to ensure that parental concerns too, have a voice. Teacher knowledge and understanding of epilepsy will be assessed[8] with an emphasis on effective practices and training needs. Additionally, we will pilot the validity of Young Epilepsy's ABLE Tool, developed during the CHESS study, as a method to identify the need for formal assessment of learning and behavioural difficulties in children with epilepsy.

Systematically recording the views of children and families will provide a richer understanding as to why so many experience academic difficulties. All participating children will receive a report outlining their needs & supports, & parents/teachers will get a psychological report to aid educational planning.

Through this study, a clear understanding of the needs of children with epilepsy and good teaching practice, derived from our entire education research evidence suite, will be developed into national guidelines for both mainstream and special schools, with digital resources for teachers and parents in 2020.

References

1. Fenton V & Menlove L (2013) **What Helps? What Hinders - Inclusion in Education for Children with Epilepsy**. *Young Epilepsy.* Publication Number 257.
2. Reilly C, Mensah A, Neville B (2014) **The identification of educational problems in childhood epilepsy: The Children with Epilepsy in Sussex Schools (CHESS) Study**. *Young Epilepsy*. Publication Number 298.
3. Reilly C, Atkinson P, Das KB, Chin R, Aylett SE, Burch V, Gillberg C, Scott RC, Neville B (2014) **Neurobehavioral Comorbidities in Children With Active Epilepsy: A Population-Based Study**. *Pediatrics*. 133(6):e1586-e1593.
4. Reilly C, Jones C, Muggeridge A (2017) **The psychosocial impact of epilepsy on young children and their families: The Sussex Early Epilepsy and Neurobehaviour (SEEN) Study.** *Young Epilepsy*. Publication Number 399.
5. Reilly C, Atkinson P, Memon A, Jones C, Dabydeen L, Gillberg C, Neville B, Mahoney M, Scott RC (2018) **Global development and adaptive behaviour in children with early-onset epilepsy: a population-based case–control study**. *Developmental Medicine & Child Neurology*. PMID: 29862505.
6. Reilly C, Atkinson P, Memon A, Jones C, Dabydeen L, Das KB, Gillberg C, Neville B, Scott RC (2018) **Symptoms of depression, anxiety, and stress in parents of young children with epilepsy: a case controlled population-based study**. *Epilepsy & Behavior*. 80:177-183.
7. Reilly C, Atkinson P, Memon A, Jones C, Dabydeen L, Cross JH, Das KB, Gillberg C, Neville B, Scott RC (2018) **Child and parental sleep in young children with epilepsy: a population-based case-control study**. *Epilepsia Open*. 3(3):383-391.
8. Jones C, Atkinson P, Cross JH, Reilly R (2018) **Knowledge of and attitudes towards epilepsy among teachers: A systematic review**. *Epilepsy & Behavior*. 87:59-68.

New Reasearch Projects

The neuropathology of focal epilepsy in children

Project Aim: To understand the biology underlying the diseases that cause focal epilepsy.

Investigators: Tom Jacques, Helen Cross, Martin Tisdall, Darren Hargrave

Summary: We are focussing on brain tumours and on malformations of cortical development. This is leading to changes in our diagnostic practice for children undergoing epilepsy surgery and is improving our understanding of how these diseases develop.

What this means: This is a group of new projects which aim to define the causes of focal epilepsy. This work is vital to obtaining faster, more accurate diagnoses and also to improving and developing successively better treatment options. Currently, most epilepsy treatments are symptomatic and focus on seizures. We need to understand more about what causes epilepsy to be able to develop and offer curative rather than symptomatic treatment.

Multiscale modelling of epileptic networks from SEEG recordings

Project Aim: This work, in the first instance, aims to provide a quantitative understanding of network dynamics in the epileptic brain at different scales. In the future, we are hoping to develop these approaches to help predict network changes after epilepsy surgery and thus guide decision making and improving outcomes for patients undergoing presurgical evaluation.

Investigators: Richard Rosch, Stasa Tumpa, Rachel Thornton, Martin Tisdall, Karl Friston

Summary: Resective surgery is an effective treatment for many focal epilepsies. Yet epilepsy is increasingly understood to be a disorder of brain networks, with abnormal brain activity emerging not from the isolated activity of individual regions, but from concerted activity of many coupled sources. Understanding this integrated epileptic network is far from intuitive – even apparently simple networks can show complex dynamics that are difficult to predict.

Computational models may offer a strategy to improve our understanding of epileptic networks. In this project, we are fitting computational network models of neuronal coupling to stereotactically recorded intracranial EEG (SEEG). Through the use of computational models, we are able to test what the network organisation that underlies epileptic dynamics on the SEEG is. This can be done at the level of microcircuits around focal brain abnormalities (e.g. looking at local coupling between tuber cores and peritubular cortex in tuberous sclerosis patients), and at the level of whole brain circuits (e.g. identifying whole-network changes after interventions in patients undergoing therapeutic radiofrequency thermocoagulation).

What this means: We know that epilepsy is often a disorder of networks across the brain rather than the result of a single disruptive section. This means that entire networks must be considered when evaluating someone's suitability to undergo epilepsy surgery. This project sets out to really understand the workings of these networks so that the pre-surgical team can have a better grasp of the effect that any surgery, however relatively 'simple' may have on a person's functioning.

Memory profile and reorganisation after epilepsy surgery in children with intractable Temporal Lobe Epilepsy (TLE)

Project Aim: The project aims to 1) characterise the memory profile of children and young people with TLE as well as their post-surgical memory outcome and 2) depict functional and structural reorganisation of memory networks in temporal lobe epilepsy before and after surgery, using functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI) magnetic resonance. We hope this may help to refine the prognostic accuracy of the preoperative workup, guide neurosurgical resection, and reduce the risk of memory impairment after surgery.

Investigators: Filipa Bastos, Faraneh Vargha-Khadem, Helen Cross, Jonathan Clayden, Sarah Buck

Update: Medically intractable temporal lobe epilepsy (TLE) is the main indication for epilepsy surgery in both adults and children and yields good outcome regarding seizure freedom. However, due to the medial temporal lobe's central role in memory, long-term memory and learning, difficulties are reported in patients with TLE. Routine pre-operative memory assessment in children with TLE consists of behavioural testing with protocols with suboptimal sensitivity to detect deficits in the paediatric population. Furthermore, memory lateralisation predictions are extrapolated from language lateralisation even though the interdependence of these two functions in children is not well documented, particularly in children with temporal lobe pathology.

This project involves memory testing using an application on a tablet developed by one of the investigators (Sarah Buck) as well as undertaking an MRI. Patients are seen before surgery and again 4 and 12 months after surgery. Patient recruitment will be ongoing until the Summer of 2019 but data collection and analysis will carry on further as patients have to be seen 1 year after surgery.

What this means: We want to ensure that children with TLE undergoing surgery will have the best possible outcomes with regard to their memory function. To do this we have developed an app-based test to be used by the child, alongside MRI imaging which will help us to better understand how memory works and is organised in the brains of children rather than relying on evidence from adult research. This will enable much more accurate understanding of how the surgery could affect an individual and therefore, thus continually improving the process of surgical evaluation.

Multicentre Epilepsy Lesion Detection (MELD) Project

Project Aim: To create open-access, robust and generalisable tools for Focal Cortical Dysplasia (FCD) detection that can be used in the pre-surgical evaluation of patients with drug-resistant epilepsy.

Investigators: Sophie Adler-Wagstyl, Konrad Adler-Wagstyl, Kirstie Whitaker, Helen Cross, David Carmichael, Martin Tisdall, Torsten Baldeweg

Summary: The MELD project is a multi-centre collaboration for lesion detection involving the incorporation of data and sequences from multiple sites. This will involve training classifiers on data from multiple centres and tailoring classifiers according to the needs of the individual epilepsy centres. Each site will be given detailed protocols to follow in order to pre-process the data from their site. The anonymised data matrices along with some clinical information (such as age, age of onset of epilepsy, surgery, histopathology and Engel outcome) will be shared. This will allow classifiers to be trained on the data from all participating centres. Any developed classification tools and/or code will be shared. We hope that this will create open-access, robust and generalisable tools for FCD detection that can be used in the pre-surgical evaluation of patients with drug-resistant epilepsy.

What this means: We hope to create new and more robust tools to detect FCD in children and adults with drug resistant epilepsy. These tools will be co-created across many hospitals and will become openly accessible for any hospital to use when evaluating someone for FCD. The tools would then be continually improved to ensure that more and more people would have access to accurate diagnosis and possible surgery.

The "Pair Test": an App to diagnose learning and memory impairments in children with Temporal Lobe Epilepsy (TLE)

Project Aim: The aims are to 1) provide better informed diagnosis of memory impairments in children with epilepsy and 2) predict outcome after surgery in the temporal lobe, using the Pair Test.

Investigators: Sarah Buck, Torsten Baldeweg, Faraneh Vargha-Khadem

Summary: The "Pair Test" uses a tablet-based paired-associate learning paradigm to disentangle impairments in different memory processes, and different components of the neural network within the medial temporal lobes. The test provides behavioural evidence regarding the functional integrity of the hippocampi and their interaction with the neocortical learning system. The Pair Games can be used to (a) diagnose the status of memory and learning, (b) monitor progression of disease, (c) assess the efficacy of pharmacological and/or surgical interventions by providing pre- and post-treatment measures of function. Overall, the test provides better informed diagnoses than standardised tools, with more precise indication of the types of memory deficits and the underlying processing impairment.

What this means: This project has created and is trialling an app-based test which will better help clinicians understand the type and complexity of learning and memory problems in children with TLE. For instance, we may know that someone has trouble with their memory but we don't know if this is one memory problem or several. This test helps clinicians to see the full picture. They hope that this will not only lead to better support and treatment but also to make a more accurate predictions of how epilepsy surgery may affect someone's learning and memory.

Improving the standard of speech and language assessment for children with Dravet syndrome

Project Aim: To improve speech and language assessment in Dravet Syndrome by clarifying profiles and community therapist experience and understanding.

Investigators: Rosie Shuttleworth, Christina Hawkins, Maria Clark

Summary: Twelve children with Dravet Syndrome had a retrospective case note review, supplemented by questionnaires from community Speech and Language Therapists. This identified that children with Dravet syndrome tended to have uneven profiles, with weaker communication skills and high levels of autism. Community teams had limited experience and requested training and support to meet the children's needs.

What this means: We know that people with Dravet syndrome have significant developmental needs. Greater understanding of their profile and support for local teams will facilitate identification and support of these needs so that children can reach their potential.

What we do

Prospective multicenter study on localization accuracy and clinical utility of automated electric source imaging in presurgical evaluation (PROMAESIS)

Project Aim: To elucidate the accuracy and the clinical utility of automated electric source imaging (ESI) in presurgical evaluation.

Investigators: Friederike Moeller, Rachel Thornton, Sándor Beniczky

Summary: Electrical source imaging combines high density EEG and MRI in to identify the sources of inter-ictal activity and seizures in focal epilepsy. Published data has shown that it identifies region co-localised with the seizure onset zone, but the clinical utility of the technique is yet to be established.

The PROMAESIS study is a multi-centre evaluation of electrical source imaging including the use of automated analysis techniques. In particular, it aims to assess the utility of the technique in the pre-surgical evaluation of individuals (including children) with focal epilepsy. Children will be recruited from a number of sites including Great Ormond Street Hospital and from across the European Reference Network, EpiCARE.

Primary outcome: Accuracy measures (sensitivity, specificity, positive and negative predictive values, overall accuracy).

Secondary outcomes: Clinical utility (change in patient management decisions); inter-ESI-methods agreement (at sub-lobar level).

What this means: We know that electrical source imaging can locate parts of the brain causing seizure activity, but not yet how to use the technique most effectively in care. This project aims to understand the accuracy of the technique and identify how to best incorporate it into clinical processes across the UK and Europe.

Optimisation and bioperformance of a novel formulation of pyridoxal 5'-phosphate for treatment of pyridox(am)ine 5'-phosphate oxidase deficiency induced epilepsy in children

Project Aim: To test the efficacy of a new treatment for children with pyridox(am)ine 5'-phosphate oxidase deficiency induced epilepsy.

Investigators: Catherine Tuleu, Peter Clayton, Philippa Mills, Emma Footitt, Ahad Rahim and Simon Heales

Summary: Some children have a specific type of epilepsy (called *pyridox(am)ine 5'-phosphate oxidase deficiency induced epilepsy*) that can be treated with a form of vitamin B6 called pyridoxal-5-phosphate (PLP). However, the current medication is not ideal. PLP is only available as a nutritional supplement in tablet or capsule forms. Unlike pharmacy-only medicines, this product is not regulated and can be problematic for clinical use. It is difficult to prepare and administer, unpalatable and unstable. Additionally, our preliminary data has shown that there is a high risk of inaccurate dosing and when mixed in water, these products are not stable, forming compounds that may be dangerously toxic to the liver. We are therefore investigating a new, more stable, formulation. We are evaluating purity and taste of this new drug, making sure that it can be absorbed in the gut and ensuring that it meets safety requirements (i.e. not liver toxic) for administration, even to babies.

What this means: We hope to produce a tolerable and regulated formulation of PLP which will improve both safety and quality of life for children who are taking PLP.

Research Project Update

The fast without the spurious: developing a system for robust and rapid simultaneous EEG-fMRI measurements

GOAL 01

Project Aim: To develop more advanced EEG-fMRI scans that may better detect brain areas active at the start of seizures. To do this we are trying new motion-correction technology that tells the scanner where the head, is using a camera and a marker attached to a dental retainer, and updates the scanner accordingly.

Investigators: Amy McDowell, Danilo Maziero, David Carmichael, Helen Cross, Kelly St Pier, Nikolaus Weiskopf

Update: This project is now coming to a close and we are writing up both another advancement to improve EEG quality during subject movement and our assessment of more rapid fMRI sequences. In addition, we are about to publish a paper regarding the optimal scanning rate for these and other fMRI studies. We have collected a small case series to test our new EEG-fMRI acquisition and are writing this up for publication. Mirja Steinbrenner, a neurologist from Berlin has joined the team on a research placement to do this.

What this means: This project has developed a system to improve the accuracy of brain imaging to better understand which parts of the brain are active just before and during a seizure. It has also been developed to improve accuracy when the patient is moving. Any movement, no matter how small, will affect most imaging techniques but it is not always possible to get a patient to stay perfectly still for a length of time, particularly if the patient is a child or a child with complex needs. This work will greatly improve the accuracy of imaging for these patients.

Effect of paroxysmal events in early onset neurological disease on cerebral tissue oxygenation & metabolism: a NIRS pilot study

GOAL 01

Project Aim: To better understand energy consumption during epileptic seizures.

Investigators: Helen Cross, Aikaterini Vezyroglou, Ilias Tachtsidis, Rachel Thornton, David Carmichael.

Update: We are using broadband Near Infrared Spectroscopy (bNIRS) to investigate the changes of oxygenated and deoxygenated haemoglobin, as well as of cytochrome c oxidase during epileptic seizures alongside EEG. We designed headgear to record bNIRS simultaneously with routine EEG and recruited 15 patients to this pilot study.

This project is now coming to a close. We were lucky to capture seizures in 9 patients and are now analysing our results.

What this means: We are investigating whether the bNIRS, and especially the cytochrome c oxidase measurement, is affected during an epileptic seizure. As cytochrome c oxidase is part of the mitochondrial respiratory chain, any changes in cytochrome c oxidase during epileptic events might be a biomarker of energy consumption during seizures. Better understanding of energy consumption during seizures might help us investigate how seizures affect the brain in the long term.

Using new quantitative MRI tissue parameter maps to detect and delineate Focal Cortical Dysplasia (FCD)

Project Aim: To develop better imaging methodology by investigating whether using quantitative MRI parameter mapping, together with quantitative analysis, can provide improved detection, delineation and classification of FCD lesions. This is the first application of these scanning and analysis methods to epilepsy and may lead to a change in local, national and international practice in imaging childhood epilepsy.

Investigators: Sara Lorio, David Carmichael, Helen Cross, Nikolaus Weiskopf, Karin Shmueli, Thomas Jacques, Chris Clark, Kling Chong, Torsten Baldeweg

Update: Sara Lorio has been working on improving the proton density maps that we obtain and has developed new methodology that can be used in clinical situations such as where there are large lesions or previous surgery. This is currently in-revision with a leading neuroimaging journal. We have processed new advanced diffusion maps that show contrast changes radiologically and quantitatively, and seem to differentiate between FCDIIa and IIb. These diffusion results are being written up for publication. We have also made quantitative susceptibility maps that show strong contrast in a handful of cases – this may relate to calcium levels which we are investigating and writing up for publication.

What this means: This project is developing new imaging techniques to increase the accuracy of detecting and analysing the lesions in the brain which cause epileptic activity in children with FCD. If successful, this work will change the way that imaging is conducted and will lead to improvements in surgical success and allow more people to be offered surgery as a treatment option.

Restoring healthy brain connectivity dynamics under image guidance: A pilot of transcranial electrical current stimulation in Juvenile Myoclonic Epilepsy (EPICONN TM)

Project Aim: A pilot study to measure a reduction in epileptiform activity associated with transcranial alternating current stimulation (tACS) and attention. We look to measure changes in brain connectivity and understand their relationship to epileptiform activity reduction. We hypothesise that in epilepsy brain networks can be targeted by weak electric fields applied to the scalp (tACS) to modulate the brain's connectivity to minimise epileptic activity and maximise cognitive performance.

Investigators: David Carmichael, Frederike Moeller, Elhum Shamshiri, Mirja Steinbrenner, Helen Cross

Update: This project has won funding from Epilepsy Research UK to undertake the pilot phase: *'Restoring healthy brain connectivity dynamics under image guidance: A pilot of transcranial electrical current stimulation in Juvenile Myoclonic Epilepsy'*. Mirja Steinbrenner aslo won Rogue Resolutions' BrainBox Initiative Research Challenge 2018 to explore the *'Reduction of cerebral excitation through combination of GSR biofeedback and tDCS'*. This funding will allow us to understand how to manipulate brain activity at a large scale to reduce epileptic activity and allow for the non-invasive optimisation of electrical stimulation therapy.

What this means: We want to know more about how non-invasive electrical stimulation of the brain affects the brain and how this may be used to control seizures. Current electrical stimulation treatment for epilepsy is limited by our understanding of how it affects brain activity. We are looking into ways of better understanding, and improving, the mechanism of this treatment.

We know surgery is not always successful and not everyone responds to antiepileptic drugs (AEDs). This project looks at a pioneering, and cost effective, new treatment as an addition or alternative to surgery/AEDs.

Prognosis in Landau-Kleffner Syndrome and continuous spikes in slow-wave sleep syndromes – epileptic Encephalopathy Longitudinal Multicentre Omics study (ELMO)

Project Aim: This is an international, longitudinal, prospective multicentre cohort study which seeks to primarily determine if laboratory markers improve upon clinical prediction of disease course and response to treatment in children with difficult to treat epilepsy. Secondarily the project will evaluate longitudinal changes in gene expression and gene methylation status that occur during the course of epilepsy from the time of diagnosis.

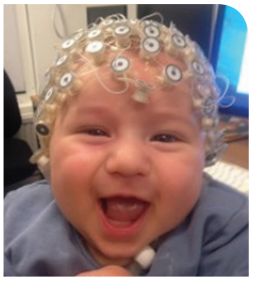
Chief Investigator: Deb Pal

Local Principal Investigator: Helen Cross

Update: Participants were recruited to the study from sites in the UK (London, Leeds, Leicester and Liverpool), Belgium (Brussels) and Italy (Rome). The recruitment window has now closed, however follow-up appointments are ongoing into 2019. Initial lab work is underway and the research team looks forward to analysing the data over the coming year.

What this means: Epilepsies that seriously affect someone's normal development of cognition and behaviour are termed "epileptic encephalopathies" (EEs). However, the cause of 85% of cases remains unsolved. We want to better understand the effects these conditions have on the brain and to see if we can find a biomarker in the blood to better determine the cause of the problem in order to improve treatment and understanding of what to expect as the condition develops. We know this has been done for people with autism and Alzheimer's so we are hoping to use a similar approach with EE.

The infant baby enrichment research programme – ENRICH



Project Aim: To explore the possibility of measuring the cortical response from the scalp of infants using standard non-invasive EEG techniques, due to the activation of CT afferents and how the cortical response changes in regard to age.

Investigators: Ronit Pressler, Geraldine Boylan

Update: This is a single-centre, proof of concept, translational study to determine how and when Somato-sensory evoked potentials develop over the first 4 months of life. We have completed the recruitment phase of this study and are in the process of assessing participants. The total amount of mothers/parents approached was >100 with a total of 43 recruited. We have lost 20 of these recruits to follow up, with all but one being lost prior to any testing being conducted.

What this means: This study seeks to understand how responses in the brain to certain sensory stimuli are developed over the first four months of life. We want to understand whether if a pleasant touch is administered to a baby's forearm in the supine and prone positions, will we observe a cortical response, and if so, can it be recorded and how does it develop over time. This will require additional EEGs being taken at the age of four weeks and also at four months.

What we do

A multicenter, open-label, single-arm study to evaluate the pharmacokinetics, efficacy, and safety of Brivaracetam in neonates with repeated electroencephalographic seizures (PETITE)

Project Aim: The purpose of the study is to evaluate the pharmacokinetics of Brivaracetam in neonates who have seizures that are not adequately controlled with phenobarbital treatment and to identify the optimal Brivaracetam dose (Exploratory Cohort) for the treatment of subjects enrolled into the Confirmatory Cohorts of this study.

Investigators: Ronit Pressler, Marios Kaliakatsos

Update: Petite is a European, UCB Biopharma-led neonatal study exploring the efficacy of Brivaracetam. The study has now been set up and at present 6 sites are active across Europe (two UK sites - GOSH and Cambridge) but no baby has been recruited so far.

The 'Exploratory Cohort' will receive a low dose of Brivaracetam intravenous (iv) solution for injection following one or multiple therapeutic doses of midazolam. 3 additional iv Brivaracetam doses, up to a total of 4 can be administered during the 48-hour Evaluation Period.

The dose and dosing frequency of Brivaracetam will be adjusted for the 'Confirmatory Cohorts' based on the analysis of the data collected for the Exploratory Cohort.

What this means: We are working with UCB Biopharma to understand the best way to use Brivaracetam in newborn babies with seizures who do not respond to Phenobarbital.

Is pyridox(am)ine 5'-phosphate oxidase deficiency, an eminently treatable cause of epilepsy, under-recognised in children?

Project Aim: Improve diagnosis and treatment of children with pyridox(am)ine 5'-phosphate oxidase (PNPO) deficiency by using a novel rapid screening dry blood spot assay.

Investigators: Peter Clayton, Philippa Mills, Helen Cross, Ronit Pressler

Update: This project has been granted ethical approval and is currently awaiting funding before work can begin.

What this means: The research team has developed a new, quick test to check if someone has an epilepsy disorder called pyridox(am)ine 5'-phosphate oxidase (PNPO) deficiency which responds to treatment with vitamin B6. We want to see how employing this test in clinical practice improves the diagnosis and treatment of children with PNPO as it is often overlooked. Early detection and treatment with vitamin B6 will help to prevent disability. We also hope this study may uncover other causes of epilepsy which may benefit from vitamin B6 treatment.

Epilepsy in Infancy: relating phenotype to genotype (EPIPEG)

Project Aim: To identify and follow-up a cohort of children with new onset of epilepsy under 12 months of age to enable definition of neuro-behavioural phenotypes; identify risk factors for neurodevelopmental problems and later intellectual disability; determine novel genetic mutations as a cause for early onset epilepsy, and relate to clinical presentation.

Investigators: Helen Cross, Manju Kurian, Rod Scott, Christin Eltze, Finbar O'Callaghan, Michelle De Haan, Elaine Hughes, Jane Kung, Manuela Pisch, Katy Barwick

Update: Recruitment has now closed and we are collating all of the data for analysis. We received 195 referrals, of these 181 were eligible and a further 119 recruited to the assessment arm of the study. The final samples for Whole Exome Sequencing are being prepared for analysis and we are preparing to visit a subset of the 53 sites to investigate how many, if any, eligible cases were missed.

There have been a number of troubleshooting requirements and the current database is used for the safe storage of data but the take-up by recruitment sites has not been as hoped. This is due to the simple time capacity of sites and the less intuitive design of the database.

An early review of the data shows that our patients are almost twice as likely to be male than female; are born full-term; have a normal birth weight range of 2.32-3.9kg (~5-8lbs); are mostly Caucasian in ethnicity, describing themselves as 'white other' or 'white British' and have a family history of epilepsy in almost half of cases.

Analysis of the first 50 patients indicates that Interictal EEG findings and seizure type are strongly correlated with language and motor skills at presentation, and interestingly, response to medication did not result in better developmental scores - weakening the correlation between seizure burden and developmental outcome at 12months. Sleep variables differ from typically developing infants shortly after diagnosis and are associated with age at seizure onset, response to medication, and seizure type.

What this means: We want to understand the specific areas of need in the early onset epilepsies and how to spot the earliest possible signs of epilepsy so that we can better help families know what to expect, and help doctors to understand what to look for and treat.

Many people with epilepsy never learn what causes their epilepsy, which is why we are looking at the child as a whole and including a wide range of genetic testing to find an answer. Research like this aims to understand the unknown causes of epilepsy in the hope of paving the way to new and better treatments. We hope that this project will provide the basis for a longer study, which will follow these babies as they grow up.

The genetics of early onset epileptic encephalopathy

Project Aim: The project aims to identify novel early onset epileptic encephalopathy genes which will contribute to the understanding of the disease mechanisms involved in such epilepsies.

Investigators: Amy McTague, Helen Cross, Dimitri Kullmann, Rod Scott, Manju Kurian

Update: Following investigation in the early onset epileptic encephalopathy cohort, 12 patients have been identified to have mutations in KCNT1. This series has now been published in Neurology in early 2018. Further gene discovery work is ongoing and investigation of the cohort has also lead to expansion of the phenotypes of known genes such as KCNQ2, RARS2, PLCB1, GABRB3, TBC1D24, FOXG1 and GNA01.

What this means: We want to know what has caused the epilepsy so we can better understand the processes in the brain that have gone wrong. We hope to use some new treatments for these processes that might not only apply to this rare epilepsy but also to some more common epilepsies. So far, we have found a previously unidentified gene which causes a severe early onset epilepsy.

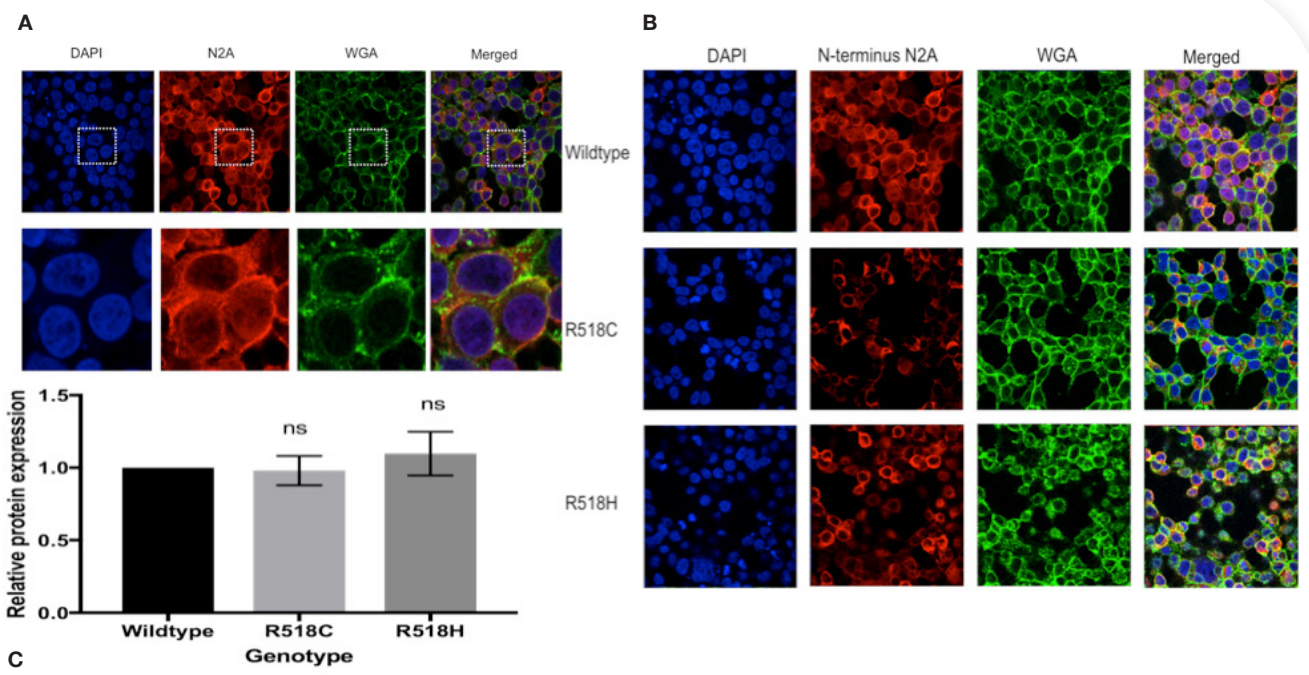
The genetics of Landau Kleffner Syndrome

Project Aim: The project aims to identify novel genes which will contribute to the understanding of the disease mechanisms causing language impairment and seizures in this epileptic disorder.

Investigators: Adeline Ngoh, Maria Clark, Brian Neville, Helen Cross, Rebecca Greenaway, Rob Harvey, Dimitri Kullmann, Manju Kurian

Update: The team has identified GRIN2A mutations in seven patients (12%). Functional investigations on the identified missense mutations have shown that these result in reduced surface protein expression and markedly reduced agonist potency. Analysis of whole exome sequencing continues and evaluation of interesting potential candidate genes is underway.

What this means: We aim to identify the genes responsible for Landau Kleffner Syndrome in the hope this will help us to understand why it causes seizures and language difficulties. Understanding this will lead to more targeted and earlier treatment.



A: Representative confocal microscopy image of HEK-293 cells co-transfected with wildtype N1 and wildtype N2A (x63), enlarged to show co-localization of surface N2A with membrane marker Wheat Germ Agglutinin (WGA).

B: Comparison of confocal microscopy images of HEK-293 cells transfected with wildtype N1 and wildtype-N2A, R518C-N2A, or R518H-N2A (x63).

C: Plot of relative fluorescence intensity of surface N2A-R518C and N2A-R518H compared to N2A-Wildtype (average measurements from 3 independent transfections). **p= <0.005, ****p= <0.0001; ns = not significant

Corticosteroids or clobazam for ESES Syndrome: A European, multicentre, randomised, controlled clinical trial (RESCUE ESES)

Project Aim: An international, multicentre randomised controlled clinical trial with blinded outcome assessment to determine the best treatment for children with Electrical Status Epilepticus in Sleep (ESES) Syndrome.

Chief Investigator: Floor Jansen, Utrecht

Local Principal Investigator: Helen Cross

Update: This condition is extremely rare and so recruitment is very slow but steady. We have opened at three UK sites (London, Edinburgh, Glasgow), and other European Union countries including Italy (Pavia), France (Paris, Lyon, Strasbourg), Belgium (Brussels, Leuven), Germany (Kehl, Freiburg, Kiel, Vogtareuth), Denmark (Dianalund), Finland (Helsinki), Romania (Bucharest), Bulgaria (Sofia) and Spain (Madrid).

Analysis of the Netherlands cohort found that in children with ESES, cognitive improvement after treatment was strongly associated with EEG spike wave index (SWI) decrease, while it was not reflected by a significant IQ increase. Steroid treatment was found to be most successful in improving cognitive performance in this cohort.

What this means: Electrical Status Epilepticus in Sleep (ESES) Syndrome is a rare epilepsy syndrome of childhood that is characterised by epileptic activity during sleep and problems with cognition or behaviour. ESES resolves spontaneously in puberty, but cognitive problems often remain. Adequate treatment is mandatory to prevent or reverse these cognitive deficits. However, it is unknown which treatment is the best. Treatment with "standard" antiepileptic drugs is not very effective. Some studies suggest that clobazam and steroid treatment may be the best option. The only way to prove which treatment is best is to let a lottery decide which treatment a child gets (randomisation) and then compare the effects of both treatments.

Ketogenic diet in Infants With Epilepsy (KIWE)

Project Aim: This is a randomised controlled trial to determine the effectiveness on seizure control of the ketogenic diet compared to alternative further antiepileptic drug treatment. Patients are children with epilepsy aged 3 months to 2 years who have failed to respond to two or more pharmacological treatments.

Investigators: Christin Eltze, Ruth Williams, Nicholas Freemantle, Simon Heales, Rachel Kneen, Louise Marston, Tim Martland, Irwin Nazareth, Helen McCullagh, Alasdair Parker, Shakti Agrawal, Archana Desurkar, Anita Devlin, Jeen Tan, Anita Devlin, Helen Basu, Penny Fallon, Andrew Mallick, Andrew Lux, Rajib Samanta, Laura Lyons, Maryam Balogun, Helen Cross, Natasha Schoeler

Update: The project is currently recruiting at 12 centres across the UK. There have been numerous barriers to recruitment, but we have achieved 75 recruited patients to date. We have applied to the NIHR for a 12 month extension which would allow us to continue recruitment until November 2019. With the extension, we hope to recruit at least 94 patients in total.

What this means: We want to know if the ketogenic diet is an effective treatment for epilepsy in infants who have not responded to two or more antiepileptic drugs. We want to know if it is an effective alternative to trying additional antiepileptic drugs. We know the ketogenic diet works well for some older children but no-one has determined systematically if it works for infants. If it does, then it provides further options for early treatment.

What we do

Cardiac Arrhythmias in Dravet Syndrome (CADS)

Project Aim: An international study to assess the prevalence of cardiac arrhythmias in patients with Dravet Syndrome (DS) and to compare the prevalence of cardiac arrhythmias between these patients and those with other types of epilepsy.

Investigators: Roland Thijs, Sharon Shmuely, Sanjay Sisodiya, Helen Cross

Update: We included 59 DS cases between June 2015 and January 2018. In 14 cases no seizures were recorded due to a seizure free period (n=8) or premature termination of the study (n=6), thus leaving 45 cases with ictal ECG recordings. Two historical epilepsy controls were selected for each case. Median age in DS was 16years (range 6 to 66years) and 19years in controls (range 6 to 63years); 51% were female in both groups.

We analysed 547 seizures in the cases (300 convulsive seizures (CS)) and 169 in the controls (119 CS). No asystole occurred. Bradycardia was more common in controls (n=11, 6.5%) compared to DS subjects (n=2, 0.36%; p=0.003). Assessments of peri-ictal heart rate variability and QTc intervals, and possible conduction abnormalities will be incorporated into the final analysis.

What this means: This is an international study, led by the Stichting Epilepsie Instellingen Nederland (SEIN) and conducted in the Netherlands, Germany and the UK. We know that people with Dravet Syndrome have a higher risk of Sudden Unexpected Death in Epilepsy (SUDEP) and we want to understand if this is connected to heart problems. We hope to evidence the need for treatment pathways to include both cardiac and neurological monitoring as standard care in Dravet Syndrome. The team have finished collecting data and are beginning to look at the emerging trends.

Betashot - A feasibility study of the use of Betashot, a medium chain triglyceride-based (MCT) formula for special medical purposes in children and adults with epilepsy

Project Aim: This feasibility study is to evaluate the use of Betashot, a MCT based food for special medical purposes. This study aims to determine whether a product, primarily consisting of Decanoic Acid (C10) is well tolerated in a population of individuals with epilepsy.

Investigators: Matthew Walker, Helen Cross, Sanjay Sisodiya, Simon Heales, Natasha Schoeler

Update: Study recruitment was completed in March 2018. A total of 38 adults and 38 children with complex epilepsy were recruited. Analyses are underway to determine the tolerability of Betashot and any effects that the product had.

What this means: This is a tolerability study related to the ketogenic diet. We want to know if patients are happy to take it and whether they have any positive or negative side effects. We do not fully understand how the ketogenic diet works but research suggests that medium chain fatty acids (MCTs) may be key in the efficacy of the diet. We hope this product, if tolerable by patients, will ease the demanding ketogenic diet administration.

What I Need in School (WINS) – Developing guidelines for best practice for young people with epilepsy in schools in the UK

Project Aim: To garner the views and experiences of school age children (6-15 years) with epilepsy, their parents and teachers regarding the impact of epilepsy on school functioning and their current and desired educational supports for young people with epilepsy.

Investigators: Colin Reilly, Patricia Atkinson, Emma Johnson, Chloe Jones, Helen Cross

Update: To date we have received referred 45 patients across 2 sites. We have completed the focus group phase and are now delivering structured interviews which focus on the needs of children with epilepsy in educational settings as well as the needs of parents and teachers.

We have amended the project to include the validation of the Assessment of Learning and Behaviour in Epilepsy Tool (Young Epilepsy CHESS Study outcome 2014) for which we will now undertake a full psychological assessment for each child with epilepsy.

Chloe Jones recently published a literature report on teacher attitudes to epilepsy, following which, we have developed a teacher survey to capture the general awareness of and attitudes towards epilepsy among teachers within our catchment area.

What this means: We know epilepsy can have a profound effect on a young person's learning and we want to ask them, their parents and their teachers to tell us what they feel they need support with and what type of support they would like. We hope this project will enable us to write guidelines for schools to support young people with epilepsy achieve their academic potential. We will also test a screening instrument to help teachers and parents identify whether a child may have additional learning or behavioural needs. Knowing this will lead to getting the right support at school.

Improving Care in Epilepsy (ICE) for children, young people and families

Project Aim: To implement an innovative model of care that improves outcomes by better reflecting the broad impact epilepsy has on the individual person, by virtue of being young person and family-centred, integrated across different sectors providing care, and measured on meaningful outcomes.

Investigators: Amit Bali, Carol Long, Monica Lakhanpaul, Kerry Robinson, Helen Cross, Dougal Hargreaves, Christina Petropoulos

Update: This is a collaborative project between Young Epilepsy, UCL Great Ormond Street Institute of Child Health, UCLPartners and Whittington Health.

Current work streams include the development of a learning healthcare system for paediatric epilepsy, linked to individualised care plan; the co-creation of young people's networks; and the commissioning of an economic evaluation of the true economic impact of epilepsy at individual, family, service and national levels.

We have been struggling to fund these projects. Each bid is met with great interest and support but not with a dedication of funds. Encouragingly, we have seen recent change in digital innovation funding which may provide the necessary opportunity. We hope to begin these projects in 2019.

What this means: We want to ensure services for epilepsy are joined up, and are provided in partnership with young people and families. We want to ensure they receive personalised, holistic care. Our work to date has told us this is imperative. This requires improved communication, understanding what outcomes really matter, tailoring care and thinking with a whole systems strategy across all sectors.

Mental Health in Children with Epilepsy (MICE)

Project Aim: Establish the feasibility of routine screening and brief telephone intervention for mental health disorders in paediatric neurology clinics so children and young people with difficulties are able to access the support they need.

Investigators: Roz Shafran, Helen Cross, Sophie Bennett, Sarah Byford, Bruce Chorpita, Anna Coughtrey, Emma Dalrymple, Caroline Dore, Peter Fonagy, Tamsin Ford, Isobel Heyman, Rona Moss-Morris, Colin Reilly, Jonathan A Smith, Terence Stephenson, Sophia Varadkar

Update: Our NIHR funded Programme Grant began in October 2017. The first year of the Programme aimed to develop an epilepsy-specific version of the Modular Approach to Therapy for Children with Anxiety, Depression, Trauma or Conduct Problems. We met with our Patient and Participant Involvement Research Advisory Group and Health Professionals Advisory group every month to discuss the study protocol and the intervention. We used their input along with feedback from families to help us to create epilepsy-specific materials, such as a roadmap of resources for parents, an additional session on the relationship between epilepsy and mental health and Frequently Asked questions about mental health, epilepsy and the treatment. We also added epilepsy-specific examples throughout the treatment manual. In early October, the MATCH-ADTC team flew from the US to train clinicians from several sites across London and the UK to deliver this intervention over the telephone. The therapists include epilepsy nurses so that the treatment is fully integrated with patients' physical healthcare. We are now supporting the therapists to deliver this intervention within their service, before commencing the full trial in April 2019.

What this means: Children and young people with epilepsy are more likely to have emotional or behavioural difficulties than children and young people who do not have a chronic illness. There are lots of studies showing that there are effective treatments for emotional and behavioural difficulties in children, but we don't know whether they also work in children who have epilepsy. We want to know if an online assessment and a talking treatment delivered over the telephone can help us to pick up and treat emotional and behavioural difficulties in children and young people with epilepsy.

European Reference Network on rare and complex epilepsies (EpiCARE)

EpiCARE is a European Reference Network (ERN) coordinated by Professor Helen Cross for GOSH, which was launched in June 2017.

One of 24 approved ERNs on rare disorders, EpiCARE has 28 members, spanning 13 countries. EpiCARE aims to improve access for patients to diagnostic and therapeutic expertise, by engaging multidisciplinary experts through the network.

EpiCARE Update

- ✓ 22 cases have been discussed across EpiCARE to advise surgical evaluation. Following this success, EpiCARE was selected to participate in an EU film highlighting the importance of cross border working.
- ✓ Over 70 training courses, educational workshops and scientific meetings are organized by the EpiCARE centres.
- ✓ The cloud based Standardized Computer-based Organized Reporting of EEG (SCORE) software was made available to all EpiCARE members in March 2018. This has directly fed into the PROMAESIS project.
- ✓ Prof Ingmar Blumcke, the Neuropathology Lead, has initiated the development of a cross-ERN digital pathology database. EpiCARE, along with ERKNet (ERN for Rare Kidney Diseases), has invited all histopathology experts to join forces to develop a common, web-based digital pathology network.
- ✓ A formal partnership has been agreed between EpiCARE and the Human Brain Project (HBP). HBP develops research and platforms at the intersection of neuroscience, computer science, and information technology. This partnership will contribute to the development of the Medical Informatics Platform (MIP), an innovative open-source IT infrastructure that offers a unique inter-operability solution to connect hospitals across Europe. The MIP will allow the simultaneous query of multiple databases across multiple hospitals. This presents an opportunity to test and implement novel diagnostic and disease-management tools based on deep learning and artificial intelligence by enabling GDPR-compliant processing of individual patients' data. The MIP, which is currently installed at seven sites, shall be deployed in 30 plus major EU hospitals by April 2020.
- ✓ Development of Babylink, a bespoke IT platform for collaboration, education and training on neonatal seizures within the EpiCARE ERN. Babylink was developed by the INFANT research centre to provide support to non-expert EEG centres on the recognition of neonatal seizures.
- ✓ The Guidelines Development Group is developing evidence-based clinical practice guidelines on the selected three topics: Lennox-Gastaut syndrome, infantile spasms, and Dravet syndrome.

Impact of Britain leaving the European Union

The EU have been conscious of ensuring the continued functioning of the ERNs, however should no deal be agreed, or a 'Hard Brexit' initiated, the UK centres will no longer be able to participate in the ERNs.

Six ERNs are coordinated by UK centres, including EpiCARE. Each of the six have been asked to make provision for an alternative centre to coordinate the network from 30th March 2019. After due consideration, Hospices Civils de Lyon, France, will coordinate EpiCARE and Professor Alexis Arzimanoglou will take key responsibility with continued involvement of staff including Professor Cross at GOSH.

Completed Projects

Improving epilepsy surgery in childhood using fMRI and EEG

Investigators: *David Carmichael, Tim Tierney, Elhum Shamshiri, Maria Centeno, Daniel Kohn, Chris Clark, Jonathan Clayden, Ronit Pressler, Helen Cross*

Surgical treatment in epilepsy is effective if the epileptogenic zone (EZ) can be correctly localised and characterised. Here we used simultaneous electroencephalography–functional magnetic resonance imaging (EEG-fMRI) data to derive EEG-fMRI and electrical source imaging (ESI) maps. We evaluated their yield, individual and combined ability to localise the EZ and predict seizure outcome.

Fifty-three children with drug-resistant epilepsy underwent EEG-fMRI. Interictal discharges were mapped using both EEG-fMRI hemodynamic responses and ESI. EEG-fMRI combined with ESI was found to provide a simple unbiased localisation that may predict surgery better than each individual test, including in MRI-negative patients. Our computerised classifier was able to correctly detect the epileptic abnormalities in 73% of the patients. It even worked in the very young patients.

This shows great technological progress and now we are planning to go one step further by testing the programme on new patients with abnormalities that the Neuroradiologist cannot currently identify. The hope is that more children with drug-resistant epilepsy will be able to be considered for epilepsy surgery, and the surgery itself will have greater accuracy and therefore higher chances of freedom from seizures. We hope these results will motivate the development of clinical services for GOSH and Children's Epilepsy Surgery Service (CESS).

The 'Koala Project'

Investigators: *Caroline Skirrow, Rosie Coleman, Louise Weiss-Croft, Torsten Baldeweg, Helen Cross and many more*

Named after the surgical ward at GOSH, this project evaluated the long-term cognitive outcomes after epilepsy surgery in a new cohort of children with temporal and extra-temporal epilepsy.

The study is a major long-term outcome study in children who underwent epilepsy surgery, showing general cognitive improvements extending over a longer (>3-5 years) follow-up duration. It is also the first study to have used identical pre- and post-operative neuroimaging, together with detailed neuropsychological assessments.

A total of 83 participants were recruited into the study, including 18 sibling controls. The cognitive improvements seen in the surgery group were associated with cortical growth, both globally and in discrete frontal regions, known to be supporting intellectual functioning. This study also confirmed that surgical removal of the some critical language regions can be associated with some decline in verbal abilities, calling for future exploration of more tailored surgical techniques and further developments in non-invasive neuroimaging.

The project funding (funded by ERUK and GOSHCC), has enabled us to conduct a major benchmark study with importance for the field of paediatric epilepsy surgery worldwide and to undertake a detailed evaluation of non-invasive neuroimaging methods. This study has also highlighted important areas of further development in neuroimaging and surgical methods, which will further improve long-term outcomes of children with medication-resistant epilepsy.

An LC-MS/MS-Based Method for the Quantification of Pyridox(am)ine 5'-Phosphate Oxidase (PNPO) Activity in Dried Blood Spots from Patients with Epilepsy

Investigators: *Matthew Wilson, Emma Footitt, Ronit Pressler, Peter Clayton, Philippa Mills*

The first patients described with PNPO-deficiency had neonatal onset seizures refractive to conventional anticonvulsants and pyridoxine but responsive to high doses of pyridoxal phosphate (PLP). Recently, however, we have shown that approximately 40% of PNPO-deficient patients respond to treatment with pyridoxine and for some PLP aggravated seizures.

Prognosis of these patients relies upon rapid diagnosis as PNPO-deficiency can lead to potentially fatal early infantile epileptic encephalopathy, severe developmental delay, and other features of neurological dysfunction. A normal developmental outcome can result if appropriate treatment is given promptly. Diagnosis can be challenging however as patients often have multisystem pathology, their response to treatment may not be immediate or total, and no clinical assay for this disorder has been available.

This study developed a rapid mass spectrometry-based clinical PNPO enzyme assay. Dried blood spots from 18 genetically-defined PNPO deficient patients, 13 children with other seizure disorders receiving B6 supplementation, 37 child hospital controls and seven healthy adults were analysed. PNPO-deficient patients had PNPO activity levels lower than all other groups; no false positives or negatives were identified.

Using this assay we have shown R116Q, previously a variant of uncertain significance, is pathogenic dramatically affecting erythrocyte PNPO activity. This variant was initially thought to be a polymorphism in PNPO due to its prevalence in the general population and co-segregation, in some instances, with known pathogenic PNPO homozygous variants. Five children have been reported that are homozygous for this variant which appears to result in a milder phenotype; 3/5 have a good developmental outcome, 4/5 presented with seizures after 5months of age, one presented at 3years. The story is likely to be complicated however as not all individuals homozygous for R116Q-PNPO present with seizures.

This assay will enable us to better define the clinical spectrum of PNPO-deficiency and will ensure that these patients are diagnosed more rapidly.

Effect of Cannabidiol on drop seizures in Lennox Gastaut Syndrome

Investigators: *Helen Cross, Sameer Zuberi and many more*

This study was a multicentre, international, random controlled trial looking at the effect of Cannabidiol (CBD) as an add-on therapy in the treatment of seizures associated with Lennox Gastaut Syndrome.

Across 30 centres, individuals were randomised to three experimental conditions; a placebo or one of two doses of CBD (Epidiolex®, GW Pharmaceuticals). The primary outcome achieved, was to observe a significant reduction in drop seizures in the CBDI groups. However, previously described adverse events were observed, chiefly somnolence and diarrhoea.

The results were published this year in the New England Journal of Medicine. Study data were submitted along with the data on Dravet Syndrome, another form of complex epilepsy, to the European Medicines Agency for licensing consideration. Data will also contribute to policy reviews with regard to whether medication will be available on NHS if licenced.

Cannabidiol as add-on treatment in complex epilepsies of childhood

Investigators: *Aikatarini Vezyroglou, Christin Eltze, Sophia Varadkar, Lucinda Carr, Catherine O' Sullivan, Emma Ninnis, Helen Cross*

This study was an open label, compassionate use programme looking at the effect of Cannabidiol (CBD) as an add-on therapy in the treatment of children with drug resistant epilepsy who were not eligible for the Dravet Syndrome or Lennox Gastaut Syndrome trials.

Oral CBD (Epidiolex®, GW Pharmaceuticals) was initiated in 24 children, aged 2 to 19 (mean age 10) years, with epilepsy of underlying structural (7), genetic (5), metabolic (1), inflammatory (3), and unknown (8) cause. Patients had previously failed 3-11 antiepileptic drugs.

Three continue in up titration with < 3months of treatment. One received only 5 days of CBD treatment as part of acute treatment for ultimately fatal status epilepticus (presumed FIRES) and was excluded. In the remaining 20, doses reached 6-45 (mean 19.95) mg/kg/d. Eight (40%) reported >50% seizure reduction, while 12(60%) showed little change.

Adverse events were diarrhoea (n=4, 20%), somnolence (n=2, 10%), loss of appetite (n=2, 10%), weight loss (n=1, 5%) and respiratory depression due to increased clobazam levels (n=1, 5%). One patient passed away due to pneumonia during the trial, a routine trial investigation confirmed that this was unrelated to CBD.

After 1-19 months 7 discontinued treatment, 4 due to lack of efficacy, and to 3 lack of efficacy and side effects. All patients reporting benefit (n=8) remain on the drug.

With publication of the randomised controlled trials in Dravet Syndrome and Lennox Gastaut Syndrome, a submission of data has been made to the European Medicines Agency for licencing.

There are now several cohort studies of differing epilepsies within the literature, and our series will be written up for full publication. Our experience has contributed to the national debate on the use of cannabinoid products in the epilepsies.

The International Collaborative Infantile Spasms Study (ICISS)

Investigators: *Finbar O'Callaghan, Stuart Edwards, Fabienne Dietrich Alber, Elaenor Hancock, Anthony Johnson, Colin Kennedy, Andrew Lux, Marcus Likeman, Mark Mackay, Andrew Mallick, Richard Newton, Melinda Nolan, Ronit Pressler, Dietz Rating, Bernhard Schmitt, Christopher Verity, John Osborne and many more*

This was an international, multicentre, randomised controlled trial to investigate whether the two classical therapies (hormonal therapy and vigabatrin) were best used separately or in combination to treat infantile spasms. Investigators assessing electro-clinical outcome were blind to therapy but parents and clinicians were not.

Previous research indicates that combining hormone therapy with vigabatrin is associated with more infants achieving spasm cessation. We wanted to test this and whether combination therapy would also be associated with better developmental outcomes at 18 months.

Eligible infants had a clinical diagnosis of infantile spasms (West Syndrome), a hypsarrhythmic EEG or similar, and no more than 7 days from clinical diagnosis. Between 7 March 2007 and 2 July 2014, 103 participating hospitals across Australia (3), Germany (11), New Zealand (2), Switzerland (3) and the UK (84) screened 766 eligible infants and randomised 377 to either the hormonal treatment alone (191) or combinations therapy of hormonal treatment with vigabatrin (186).

The primary outcome was no observed spasms between days 14 and 42 of treatment. 71.5% on combination therapy had no witnessed spasms between day 14 and 42 of treatment compared with 56.5% on hormonal therapy alone (p=0.002). Combination therapy is significantly more effective at stopping spasms and the observed absence of spasms from treatment day 14 to 42 suggests that the effect may be sustained.

The secondary outcome measure was greater developmental outcome at 18 months of age. Developmental and epilepsy data at 1months of age were available for 362 patients. The observed cessation of spasms between treatment day 14 and 42 was associated with a better developmental outcome (median Vineland Adaptive Behaviour Scales 78 versus 61, p<0.001), and better epilepsy outcome (83% with an early clinical response had no epilepsy at 18 months versus 48%, p<0.001).

Treatment type, however was not associated with better epilepsy or developmental outcome (p=0.5 in both). Early cessation of spasms was key to both better epilepsy and developmental outcome, but combination therapy was associated with significantly more infant achieving spasm cessation.

Awarded PhD's - Congratulations!

Sophie Adler-Wagstyl

2017
Cortical morphology and MRI signal intensity analysis in paediatric epilepsy

Sophie is a MBPhD student who completed her PhD at the ICH on the quantitative analysis of structural MRI scans in paediatric epilepsy, including developing a framework for the automated detection of focal cortical dysplasias. She is now co-lead of the Multi-centre Epilepsy Lesion Detection (MELD) project alongside completing medical school.

Amy McTague

2018
The molecular genetic investigation of epilepsy of infancy with migrating focal seizures

In the next stage of her research, Amy aims to create a stem cell model of early onset epilepsy, to model disease and also as a platform to both discover and test novel therapies. She has recently been awarded the NIHR GOSH BRC Catalyst Fellowship and a Rosetrees Seedcorn award to launch this project, with a plan to apply for further funding in 2019.

Sophie Bennett

2017
Mental health of children and young people with neurological conditions

Sophie's group have now been awarded an NIHR Programme Grant for Applied Research, which builds on the screening and intervention studies reported in her PhD. The 'Mental Health In Epilepsy (MICE)' study started in October 2018 and will train epilepsy nurses in the UK to deliver mental health interventions in children with epilepsy.

Tom Stone

2017
Genomic classification and analysis of epilepsy-associated glioneuronal tumours

Tom now holds a post-doctoral position in Tom Jacques' research group. He is using the methods learned during his PhD to try to analyse and characterise a wide range of paediatric low-grade brain tumours, with a particular focus on rare diagnoses.

Sarah Buck

2018
Memory in paediatric Temporal Lobe Epilepsy

Sarah is now working as a post-doctoral fellow at the Institute of Neurology at Queen Square with Meneka Sidhu and John Duncan on memory fMRI in adults with Temporal Lobe Epilepsy.

Tim Tierney

2017
Development and application of functional Magnetic Resonance Imaging in paediatric focal epilepsy

Tim is now working on a collaborative project to further develop the wearable MEG system and test its clinical effectiveness in a custom designed shielded room at Young Epilepsy.

What we do

Mind The Gap VI

In May 2018 we held the sixth Mind The Gap symposium, the series was brain child of the late Professor Brian Neville and is hosted by Professor Cross and Professor Christopher Gillberg. The initiative is to bring comprehensive care to children and young people with epilepsy by integrating seizure management with cognitive/ educational and behavioural/psychiatric assessment and management.

This year, Mind The Gap was dedicated to sharing the latest views on the problems associated with childhood epilepsy beyond seizures to a multidisciplinary audience.

The challenges of epilepsy beyond seizures are well documented and we know that cognitive impairment is the greatest associated problem with childhood epilepsy. In many children, their cognitive impairment will have a greater long-term impact than seizures. We also know that the additional challenges of childhood epilepsy affects family functioning and mental health. This knowledge indicates the need for structural changes in training, research and clinical practice.

Mind the Gap is an open symposium but this year, we altered the format to include a second day of workshops on the key themes of the talks given the previous day. These workshops were designed to really delve into the challenges of putting research into practice, specifically for the child in school, and to create a strong, multidisciplinary dialogue regarding potential solutions and suggestions to research.

The symposium and workshop were highly successful, bringing together individuals across different disciplines and national systems. Discussion at the workshops focused on the challenge of closing the 'gaps' in improving recognition, management and support for the high rate (95%) of unrecognised difficulties of children with epilepsy in schools published by the CHESS study (Reilly *et al*, 2014).

Closing these gaps may often be multifaceted, depending on the cognitive problem, comorbidity or age of the child. We know that early diagnosis in all of these areas is the key to better outcomes; however, there is a need to evidence the need for, and subsequently the efficacy of, evidence-based interventions.

It was agreed that a review of best practice was the best first step, at both local and national levels. The review will address best practice across:

- pupil age
- stage of education (e.g. preschool, school, transition and beyond)
- support giver (schools or parents).

As a group, the next steps agreed were to develop a dedicated working group to evaluate the screening possibilities, and begin to collect best practice data.

We will reconvene in 2020 for Mind The Gap VII – watch this space!

Paediatric Epilepsy Research Retreat 2018

19 projects discussed

86 guests from over 30 organisations and 7 countries

Our Research Retreat, hosted by Professor Cross, The Prince of Wales's Chair of Childhood Epilepsy, is an annual gathering of researchers and collaborators across our research unit. This meeting gives researchers, at all stages of their careers, the opportunity to discuss ongoing projects, completed projects and future directions of research with a unique range of epilepsy specialists.

This year we presented 19 current projects and welcomed 86 guests from over 30 organisations and 7 countries. Almost every attendee has a direct clinical role in supporting children and young people with epilepsy. We welcomed back previous speakers and were able to see the outcomes of discussions started at previous Retreats reflected in the year's work through sub-projects, collaborations and shared data.

2018 marked our 8th Retreat and we were honoured to welcome Professor Kees Braun as Research Moderator. Professor Braun is Professor of Paediatric Neurology at the Rudolf Magnus Brain Centre at Utrecht University, Netherlands. He is President of the Dutch Society of Paediatric Neurology, a member of the European Task Force for Epilepsy Surgery in Children (U-Task), the European Network for Epilepsy Research (ENER), and work-package leader under EpiCARE. Professor Braun coordinates epilepsy research across the Rudolf Magnus Brain Centre and his areas of expertise are: refractory paediatric epilepsy, epilepsy surgery, imaging in epilepsy, and childhood arteriopathic stroke, in particular moyamoya treatment.

Discussions at the end of each presentation give investigators the opportunity to receive comments and feedback from fellow researchers and principal investigators representing a vast array of different fields. We altered the format to ensure every speaker had 30 minutes which allowed ample time for discussion.

What we do

The Retreat is also a highly social occasion, giving international and domestic researchers what is often their single annual opportunity to meet colleagues and peers face to face. This vital networking truly highlights the breadth of epilepsy research being undertaken across the unit. The meeting critically serves as a way of motivating early-career researchers to recognise this diversity and to form the collaborations which underpin excellent science and practical outcomes.

Last year, the Research Retreat was extended into a series of monthly satellite meetings held at ICH which resulted in a multidisciplinary Rasmussen Syndrome Working Group, the aims of which are to assess and improve the clinical pathway of children with this syndrome. At the 2019 Retreat we look forward to this group presenting their data.

The Research Retreat and additional meetings are a critical contributor to creating a collegiate environment across the unit and nurturing new talent in paediatric epilepsy research.

Speakers use half their time to present their project because leaving opportunity for discussion with the multidisciplinary audience is just as important

"An excellent group of researchers…a lovely example of the global development of the field."

Paediatric Neurologist

The Research Retreat is refreshingly non-competitive.

Research can be a very competitive world and we create a nurturing environment in which to support future stars

Research Publications

Primary Research

1. Abdulkadir M, Londono D, Gordon D, Fernandez TV, Brown LW, Cheon KA, Coffey BJ, Elzerman L, Fremer C, Fründt O, Garcia-Delgar B, Gilbert DL, Grice DE, Hedderly T, **Heyman I**, Hong HJ, Huyser C, Ibanez-Gomez L, Jakubovski E, Kim YK, Kim YS, Koh YJ, Kook S, Kuperman S, Leventhal B, Ludolph AG, Madruga-Garrido M, Maras A, Mir P, Morer A, Müller-Vahl K, Münchau A, Murphy TL, Plessen KJ, Roessner V, Shin EY, Song DH, Song J, Tübing J, van den Ban E, Visscher F, Wanderer S, Woods M, Zinner SH, King RA, Tischfield JA, Heiman GA, Hoekstra PJ, Dietrich A (2018) **Investigation of previously implicated genetic variants in chronic tic disorders: a transmission disequilibrium test approach**. *Eur Arch Psychiatry Clin Neurosci*. 268(3):301-316.

2. Adler S, Hong SJ, Liu M, **Baldeweg T, Cross JH**, Bernasconi A, Bernhardt BC, Bernasconi N (2018) **Topographic principles of cortical fluid-attenuated inversion recovery signal in temporal lobe epilepsy**. *Epilepsia*. 59(3):627-635.

3. Amin S, Lux A, Calder N, Laugharne M, Osborne J, **O'callaghan F** (2017) **Causes of mortality in individuals with tuberous sclerosis complex**. *Dev Med Child Neurol*. 59(6):612-617.

4. Amin S, Lux A, Khan A, **O'Callaghan F** (2017) **Sirolimus Ointment for Facial Angiofibromas in Individuals with Tuberous Sclerosis Complex**. *Int Sch Res Notices*.8404378.

5. Aoki S, Hashimoto K, Mezawa H, Hatakenaka Y, Yasumitsu-Lovell K, Suganuma N, **Gillberg C** et al (2018) **Development of a new screening tool for neuromotor development in children aged two - the neuromotor 5min exam 2-year-old version (N5E2)**. *Brain Dev*. 40(6):445-451.

6. Apps JR, Carreno G, Gonzalez-Meljem JM, Jani N, Haston S, Hölsken A, Pettorini B, Beynon RJ, Simpson DM, Fraser HC, Hong Y, Hallang S, Stone TJ, Virasami A, Donson AM, Jones D, Aquilina K, Spoudeas H, Joshi AR, Grundy R, Storer LCD, Korbonits M, Hilton DA, Tossell K, Thavaraj S, Ungless MA, Gil J, Buslei R, Hankinson T, Hargrave D, Goding C, Andoniadou CL, Brogan P, **Jacques TS**, Williams HJ, Martinez-Barbera JP (2018) **Tumour compartment transcriptomics demonstrate the activation of inflammatory and odontogenic programmes in human adamantinomatous craniopharyngioma and identify the MAPK/ERK pathway as a novel therapeutic target**. *Acta Neuropathologica*. 135(5):757-777.

7. Arichi T, Whitehead K, Barone G, **Pressler R**, Padormo F, Edwards AD, Fabrizi L (2017) **Localization of spontaneous bursting neuronal activity in the preterm human brain with simultaneous EEG-fMRI**. *Elife*. 12:6.

8. Bale G, Mitra S, de Roever I, Sokolska M, Price D, Bainbridge A, **Gunny R**, Uria-Avellanal C, Kendall GS, Meek J, Robertson NJ, Tachtsidis I (2018) **Oxygen dependency of mitochondrial metabolism indicates outcome of newborn brain injury**. *J Cereb Blood Flow Metab*. 18:271678X18777928.

9. Baud M, Perneger T, Racz A, Pensel M, Elger CE, Rydenhag B, Malmgren K, **Cross JH**, McKenna G, **Tisdall M**, Lamberink H, Rheims S, Ryvlin P, Isnard J, Mauguiere F, Arzimanoglou A, Akkol S, Deniz K, Ozkara C, Losius M, Rektor I, Kälviäinen R, Vanhatalo LM, Dimova P, Minkin K, Maren A, Steinhoff B, Kalina A, Kresk P, Marusic P, Jordan Z, Fabo D, Carrette E, Boon P, Rocka S, Mameniškien R, Vulliemoz S, Pittau F, Braun K, Seeck M (2018) **European Trends in Epilepsy Surgery**. *Neurology*. 91(2):e96-e106.

10. Bell GS, de Tisi J, Gonzalez-Fraile JC, Peacock JL, McEvoy AW, **Harkness WFJ**, Foong J, Pope RA, Diehl B, Sander JW, Duncan JS (2017) **Factors affecting seizure outcome after epilepsy surgery: an observational series**. *J Neurol Neurosurg Psychiatry*. 88(11):933-940.

11. Beniczky S, Aurlien H, Brøgger JC, Hirsch LJ, Schomer DL, Trinka E, **Pressler RM** *et al* (2017) **Standardized computer-based organized reporting of EEG: SCORE - Second version**. *Clin Neurophysiol*. 128(11):2334-2346.

12. Bennett SD, Coughtrey AE, **Heyman I**, Greally S, Clarkson H, Bhattacharyya T, Lewis C, Varadkar S, Shafran R (2018) **Guided self-help for mental health disorders in children and young people with chronic neurological conditions: A qualitative evaluation**. *Eur J Paediatr Neurol*. 22(4):620-631.

13. Blumcke I, Spreafico R, Haaker G, Coras R, Kobow K, Bien CG, Pfäfflin M, Elger C, Widman G, Schramm J, Becker A, Braun KP, Leijten F,Baayen JC, Aronica E, Chassoux F, Hamer H, Stefan H, Rössler K, Thom M, Walker MC, Sisodiya SM, Duncan JS, McEvoy AW, Pieper T, Holthausen H, Kudernatsch M, Meencke J, Kahane P, Schulze-Bonhage A, Zentner J, Heiland DH, Urbach H,Steinhoff BJ, Bast T, Tassi L, Lo Russo G, Özkara C, Oz B, Krsek P, Vogelgesang S, Runge U, Lerche H, Weber Y, Honavar M, Pimentel J, Arzimanoglou A, Ulate-Campos A, Noachtar S, Hartl E, Schijns O, Guerrini R, Barba C, **Jacques TS, Cross JH**, Feucht M, Mühlebner A, Grunwald T, Trinka E, Winkler PA, Gil-Nagel A, Toledano Delgado R, Mayer T, Lutz M, Zountsas B, Garganis K, Rosenow F, Hermsen A, von Oertzen TJ, Diepgen TL, Avanzini G for the EEBB Consortium (2017) **Histopathological Findings in Brain Tissue Obtained during Epilepsy Surgery**. *NEJM*. 377(17):1648-1656.

14. Brotschi B, **Gunny R**, Rethmann C, Held U, Latal B, Hagmann C (2017) **Relationship between temperature variability and brain injury on magnetic resonance imaging in cooled newborn infants after perinatal asphyxia**. *J Perinatol*. 37(9):1032-1037.

15. Castellheim A, Lundstrom S, Molin M, Kuja-Halkola R, **Gillberg C** (2018) **The role of general anesthesia on traits of neurodevelopmental disorders in a Swedish cohort of twins**. *J Child Psychol Psychiatry*. 59(9):966-972.

16. Curatolo P, Nabbout R, Lagae L, Aronica E, Ferreira JC, Feucht M, Hertzberg C, Jansen AC, Jansen F, Kotulska K, Moavero R, **O'Callaghan F**, Papavasiliou A, Tzadok M, Jóźwiak S (2018) **Management of epilepsy associated with tuberous sclerosis complex: Updated clinical recommendations**. *Eur J Paediatr Neurol*. S1090-3798(17):32057-3.

17. De Blasi B, Barnes A, Boscolo Galazzo I, Hua CH, Shulkin B, Koepp M, **Tisdall M** (2018) **Age-specific 18F-FDG image processing pipelines and analysis are essential for individual mapping of seizure foci in paediatric patients with intractable epilepsy**. *J Nucl Med*. 59(10):1590-1596.

18. de Vries PJ, Belousova E, Benedik MP, Carter T, Cottin V, Curatolo P, Dahlin M, D'Amato L, d'Augères GB, Ferreira JC, Feucht M, Fladrowski C, Hertzberg C, Jozwiak S, Kingswood JC, Lawson JA, Macaya A, Marques R, Nabbout R, **O'Callaghan F**, Qin J, Sander V, Sauter M, Shah S, Takahashi Y, Touraine R, Youroukos S, Zonnenberg B, Jansen AC; TOSCA Consortium and TOSCA Investigators (2018) **TSC-associated neuropsychiatric disorders (TAND): findings from the TOSCA natural history study**. *Orphanet J Rare Dis*. 13(1):157.

19. Devinsky O, Patel AD, **Cross JH**, Villanueva V, Wirrell EC, Privitera M, Greenwood S, Roberts C, Checketts D, VanLandingham K, Zuberi SM (2018) **Effect of Cannabidiol on Drop Seizures in Lennox-Gastaut Syndrome**. *NEJM*. 378:1888-1897.

20. Dragoumi P, Emery J, Chivers F, Brady M, Desurkar A, **Cross JH, Das KB** (2018) **Crossing the lines between epilepsy syndromes: a myoclonic epilepsy variant with prominent eyelid myoclonia and atonic components**. *Epileptic Disord*. 20(1):35-41.

21. Faramand AM, Barnes N, Harrison S, **Gunny R, Jacques T**, Tahir MZ, **Varadkar SM, Cross HJ, Harkness W, Tisdall MM** (2018) **Seizure and cognitive outcomes after resection of glioneuronal tumors in children**. *Epilepsia*. 59(1):170-178.

22. Fernell E, Landgren M, Johnson M, **Gillberg C** (2017) **Place pediatrics and child psychiatry at "the same table"**. *Lakartidningen*. 114.

23. Fisher RS, **Cross JH**, D'Souza C, French JA, Haut SR, Higurashi N, Hirsch E, Jansen FE, Lagae L, Moshé SL, Peltola J, Roulet Perez E, Scheffer IE, Schulze-Bonhage A, Somerville E, Sperling M, Yacubian EM, Zuberi SM (2017) **Instruction manual for the ILAE 2017 operational classification of seizure types**. *Epilepsia*. 58(4):531-542.

24. Forzano F, Foley PA, Keane MR, Brain CE, Smith GD, Yates RW, Ellershaw D, Calder AD, **Scott RH** (2018) **Contiguous gene deletion of TBX5 and TBX3: report of another case**. *Clin Dysmorphol*. 27(1):6-8.

25. Gardner JF, Cushion TD, Niotakis G, Olson HE, Grant PE, **Scott RH**, Stoodley N, Cohen JS, Naidu S, Attie-Bitach T, Bonnières M, Boutaud L, Encha-Razavi F, Palmer-Smith SM, Mugalaasi H, Mullins JGL, Pilz DT, Fry AE (2018) **Clinical and Functional Characterization of the Recurrent TUBA1A p.(Arg2His) Mutation**. *Brain Sci*. 8(8):e145.

26. Graham D, Gill D, Dale RC, **Tisdall MM** (2018) **Corpus Callosotomy Outcomes Study Group. Seizure outcome after corpus callosotomy in a large paediatric series**. *Dev Med Child Neurol*. 60:199-206.

27. Hamandi K, Beniczky S, Diehl B, Kandler RH, **Pressler RM**, Sen A, Solomon J, Walker MC, Bagary M; with ILAE British Chapter Workshop Attendees (2017) **Current practice and recommendations in UK epilepsy monitoring units. Report of a national survey and workshop**. *Seizure*. 50:92-98.

28. **Heyman I**, McGeough E (2018) **Cross-disciplinary partnerships between police and health services for mental health care**. *J Psychiatr Ment Health Nurs*. 25(5-6):283-284.

29. Hikmat O, Tzoulis C, Chong WK, Chentouf L, Klingenberg C, Fratter C, Carr LJ, Prabhakar P, Kumaraguru N, Gissen P, **Cross JH, Jacques TS**, Taanman JW, Bindoff LA, **Rahman S** (2017) **The clinical spectrum and natural history of early-onset diseases due to DNA polymerase gamma mutations**. *Genetics in Medicine*. 19(11):1217-1225.

30. Jansen AC, Belousova E, Benedik MP, Carter T, Cottin V, Curatolo P, Amato LD, Augeres GBD, De Vries PJ, Ferreira JC, Feucht M, Fladrowski C, Hertzberg C, Jozwiak S, Lawson JA, Macaya A, Marques R, Nabbout R, **O'Callaghan F**, Qin J, Sander V, Shah S, Takahashi Y, Touraine R, Youroukos S, Zonnenberg B, Kingswood JC (2017) **Quality of life and burden of disease in Tuberous Sclerosis Complex (TSC): findings from TOSCA research project**. *Journal of Intellectual Disability Research*. 61(9):829-829.

31. Kane N, Acharya J, Benickzy S, Caboclo L, Finnigan S, Kaplan PW, Shibasaki H, **Pressler R**, van Putten M (2017) **A revised glossary of terms most commonly used by clinical electroencephalographers and updated proposal for the report format of the EEG findings**. *Clin Neurophysiol Practice*. 2:170-185.

32. Karaa A, **Rahman S**, Lombès A, Yu-Wai-Man P, Sheikh MK, Alai-Hansen S, Cohen BH, Dimmock D, Emrick L, Falk MJ, McCormack S, Mirsky D, Moore T, Parikh S, Shoffner J, Taivassalo T, Tarnopolsky M, Tein I, Odenkirchen JC, Goldstein A, Mito Working Group Member Participants (2017) **Common data elements for clinical research in mitochondrial disease: a National Institute for Neurological Disorders and Stroke project**. *J Inherit Metab Dis*. 40(3):403-414.

33. Kingswood JC, Belousova E, Benedik MP, Carter T, Cottin V, Curatolo P, Dahlin M, D' Amato L, d'Augères GB, de Vries PJ, Ferreira JC, Feucht M, Fladrowski C, Hertzberg C, Jozwiak S, Lawson JA, Macaya A, Marques R, Nabbout R, **O'Callaghan F**, Qin J, Sander V, Sauter M, Shah S, Takahashi Y, Touraine R, Youroukos S, Zonnenberg B, Jansen AC, TOSCA Consortium and TOSCA Investigators (2018) **Renal angiomyolipoma in patients with tuberous sclerosis complex: findings from the TuberOus SClerosis registry to increase disease Awareness**. *Nephrol Dial Transplant*. PMID: 29697822.

34. Krebs G, de la Cruz LF, Monzani B, Bowyer L, Anson M, Cadman J, **Heyman I**, Turner C, Veale D, Mataix-Cols D (2017) **Long-Term Outcomes of Cognitive-Behavioral Therapy for Adolescent Body Dysmorphic Disorder**. *Behav Ther*. 48(4):462-473.

35. Lamberink HJ, Boshuisen K, Otte WM, Geleijns K, Braun KPJ, **TimeToStop Study Group** (2018) **Individualized prediction of seizure relapse and outcomes following antiepileptic drug withdrawal after pediatric epilepsy surgery**. *Epilepsia*. 59(3):e28-e33.

36. Liu J, Reeves C, **Jacques TS**, McEvoy A, Miserocchi A, Thompson P, Sisodiya S, Thom M (2017) **Nestin-expressing cell types in the temporal lobe and hippocampus: morphology, differentiation and proliferative capacity**. *Glia*. 66(1):62-77.

37. Marcus HJ, Vakharia VN, Ourselin S, Duncan J, **Tisdall M**, Aquilina K (2018) **Robot-assisted stereotactic brain biopsy: systematic review and bibliometric analysis**. *Childs Nerv Syst.* 34(7):1299-1309.

38. Martinos MM, Pujar S, **Gillberg C**, Cortina-Borja M, **Neville BGR, De Haan M, Scott RC**, Chin RFM (2017) **Long-term behavioural outcomes after paediatric convulsive status epilepticus: a population-based cohort study**. *Dev Med Child Neurol.* 60(4):409-416.

39. McTague A, Nair U, Malhotra S, Meyer E, Trump N, Gazina E, Papandreou A, Ngoh A, Ackermann S, Ambegaonkar G, Appleton R, Desurkar A, Eltze C, Kneen R, Kumar AV, Lascelles K, Montgomery T, Venkateswaran R, Samanta R, **Scott RH**, Tan J, Whitehouse W, Poduri A, Scheffer IE, Chong WK, **Cross JH**, Topf M, Petrou S, **Kurian MA** (2018) **Clinical and molecular characterisation of KCNT1-related severe early onset epilepsy**. *Neurology*. 90(1):e55-e66.

40. McWilliams A, **Reilly C, Heyman I** (2017) **Non-epileptic seizures in children: Views and approaches at a UK child and adolescent psychiatry conference**. *Seizure-European Journal of Epilepsy*. 2017. 53:23-25.

41. Mohamed-Ahmeda AHA, Wilson MP, Albueraa M, Chena T, **Mills PB**, Footitt EJ, Clayton PT, Tuleu C (2017) **Quality and stability of extemporaneous pyridoxal phosphate preparations used in the treatment of paediatric epilepsy**. *J Pharm Pharmacol*. 69(4):480-488.

42. Myers K, Lightfoot P, Patel S, **Cross JH**, Scheffer IE (2018) **Stiripentol efficacy and safety in Dravet syndrome: a 12-year observational study**. *Dev Med Child Neurol.* 60(6):574-578.

43. Narizzano M, Arnulfo G, Ricci S, Toselli B, **Tisdall M**, Canessa A, Fato MM, Cardinale F (2017) **SEEG assistant: a 3DSlicer extension to support epilepsy surgery**. *BMC Bioinformatics*. 18:124.

44. Northam GB, Adler S, Eschmann KCJ, Chong WK, Cowan FM, **Baldeweg T** (2018) **Developmental conduction aphasia after neonatal stroke**. *Ann Neurol*. 83(4):664-675.

45. **O'Callaghan FJ**, Edwards SW, Alber FD, Borja MC, Hancock E, Johnson AL, Kennedy CR, Likeman M, Lux AL, Mackay MT, Mallick MA, Newton RW, Nolan M, **Pressler R**, Rating D, Schmitt B, Verity CM, Osborne JP (2018) **Vigabatrin with hormonal treatment versus hormonal treatment alone (ICISS) for infantile spasms: 18-month outcomes of an open-label, randomised controlled trial**. *The Lancet Child & Adolescent Health*. 2(10):715-725.

46. O'Reilly MA, Bathelt J, Sakkalou E, Sakki H, Salt A, Dale NJ, **de Haan M** (2017) **Frontal EEG asymmetry and later behavior vulnerability in infants with congenital visual impairment**. *Clin Neurophysiol*. 128(11):2191-2199.

47. Perani S, Tierney TM, Centeno M, Shamshiri EA, Yaakub SN, O'Muircheartaigh J, **Carmichael DW**, Richardson MP (2018) **Thalamic volume reduction in drug-naive patients with new-onset genetic generalized epilepsy**. *Epilepsia*. 59(1):226-234.

48. **Pressler RM**, Seri S, Kane N, Martland T, Goyal S, Iyer A, Warren E, Notghi L, Bill P, **Thornton R**, Appleton R, Doyle S, Rushton S, Worley A, **Boyd SG**, CESS Clinical Neurophysiology working group (2017) **Consensus-based guidelines for Video EEG monitoring in the pre-surgical evaluation of children with epilepsy in the UK**. *Seizure*. 50:6-11.

49. Pronicka E, Ropacka-Lesiak M, Trubicka J, Pajdowska M, Linke M, Ostergaard E, Saunders C, Horsch S, van Karnebeek C, Yaplito-Lee J, Distelmaier F, Õunap K, **Rahman S**, Castelle M, Kelleher J, Baris S, Iwanicka-Pronicka K, Steward CG, Ciara E, Wortmann SB (2017) **A scoring system predicting the clinical course of CLPB defect based on the foetal and neonatal presentation of 31 patients**. *J Inherit Metab Dis*. 40(6):853-860.

50. Pujar SS, Martinos MM, Cortina-Borja M, Chong WKK, De **Haan M, Gillberg C, Neville BG, Scott RC**, Chin RF, North London Epilepsy Research Network (2017) **Long-term prognosis after childhood convulsive status epilepticus: a prospective cohort study**. *Lancet Child Adolesc Health.* 2:103-111.

51. Pujar SS, Seunarine KK, Martinos MM, **Neville BGR, Scott RC**, Chin RFM, **Clark CA** (2017) **Long-term white matter tract reorganization following prolonged febrile seizures**. *Epilepsia.* 58(5):772-780.

52. **Reilly C, Atkinson P**, Memon A, Jones C, Dabydeen L, **Cross JH, Das KB, Gillberg C, Neville BGR, Scott RC** (2018) **Child and parental sleep in young children with epilepsy: A population-based case-control study**. *Epilepsia Open*. 3(3):383-391.

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

54. **Reilly C, Atkinson P**, Memon A, Jones C, Dabydeen L, **Das KB, Gillberg C, Neville BGR**, Mahoney JM, **Scott RC** (2018) **Global development and adaptive behaviour in children with early-onset epilepsy: a population-based case-control study**. *Dev Med Child Neurol*. PMID: 29862505.

55. **Reilly C**, Taft C, Edelvik A, Olsson I, Malmgren K (2017) **Health-related quality of life and emotional wellbeing improve in parents after their children have undergone epilepsy surgery - A prospective population-based study**. *Epilepsy & Behavior*. 75:196-202.

56. Rosch R, **Baldeweg T**, Moeller F, Baier G (2018) **Network dynamics in the healthy and epileptic developing brain**. *Netw Neurosci*. 2(1):41-59.

57. Rudebeck SR, Shavel-Jessop S, **Varadkar S**, Owen T, **Cross JH, Vargha-Khadem F, Baldeweg T** (2018) **Pre- and postsurgical cognitive trajectories and quantitative MRI changes in Rasmussen syndrome**. *Epilepsia*. 59(6):1210-1219.

58. Sa M, Hacohen Y, Alderson L, Chong WKK, Anderson G, **Jacques TS**, Neubauer D, Szczepanik E, Lim M, Kaliakatsos M (2018) **Immunotherapy-responsive childhood neurodegeneration with systemic and central nervous system inflammation**. *Eur J Paediatr Neurol*. 22(5):882-888.

59. Schwalbe E, Lindsey J, Nakjang S, Crosier S, Smith A, Hicks D, Rafiee G, Hill RM, Iliasova A, Stone T, Pizer B, Michalski A, Joshi A, Wharton SB, **Jacques TS**, Bailey S, Williamson D, Clifford SC (2017). **Novel molecular subgroups for clinical classification and outcome prediction in childhood medulloblastoma: a cohort study**. *The Lancet Oncology*. 18(7):958-971.

60. Shelmerdine SC, Hutchinson JC, Sebire NJ, **Jacques TS**, Arthurs OJ (2017). **Post-mortem magnetic resonance (PMMR) imaging of the brain in fetuses and children with histopathological correlation**. *Clinical Radiology*. 72(12):1025-1037.

61. Stone TJ, Keeley A, Virasami A, **Harkness W, Tisdall M**, Izquierdo Delgado E, Gutteridge A, Brooks T, Kristiansen M, Chalker J, Wilkhu L, Mifsud W, Apps J, Thom M, Hubank M, Forshew T, **Cross JH**, Hargrave D, Ham J, **Jacques TS** (2018) **Comprehensive molecular characterisation of epilepsy-associated glioneuronal tumours**. *Acta Neuropathol*. 135(1):115-129.

62. Stotesbury H, Kirkham FJ, Kölbel M, Balfour P, Clayden JD, Sahota S, Sakaria S, Saunders DE, Howard J, Kesse-Adu R, Inusa B, Pelidis M, Chakravorty S, Rees DC, Awogbade M, Wilkey O, Layton M, **Clark CA**, Kawadler JM (2018) **White matter integrity and processing speed in sickle cell anemia**. *Neurology*. 90(23):e2042-e2050.

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

64. Szychot E, Seunarine K, Mankad K, Thust S, **Clark C**, Gaze MN, Michalski A (2017) **Impact of induction chemotherapy, hyperfractionated accelerated radiotherapy and high-dose thiotepa on brain volume loss and functional status of children with primitive neuroectodermal tumour**. *Pediatric Blood & Cancer*. 64(11):e26619.

65. Tansley SL, Betteridge ZE, Simou S, **Jacques TS**, Pilkington C, Wood M, Warrier K, Wedderburn LR, McHugh NJ for the Juvenile Dermatomyositis Research Group (2017) **Anti-HMGCR Autoantibodies in Juvenile Idiopathic Inflammatory Myopathies Identify a Rare but Clinically Important Subset of Patients**. *The Journal of Rheumatology*. 44(4):488-492.

66. Thom M, Liu J, Bongaarts A, Reinten RJ, Paradiso B, Jager HR, Reeves C, Somani A, An S, Marsdon D, McEvoy A, Miserocchi A, Thorne L, Newman F, Bucur S, Honavar M, **Jacques TS**, Aronica E (2017) **Multinodular and vacuolating neuronal tumours in epilepsy: dysplasia or neoplasia?** *Brain Pathology.* 28(2):155-171.

67. Tierney TM, Holmes N, Meyer SS, Boto E, Roberts G, Leggett J, Buck S, Duque-Muñoz L, Litvak V, Bestmann S, **Baldeweg T**, Bowtell R, Brookes MJ, Barnes GR (2018) **Cognitive neuroscience using wearable magnetometer arrays: Non-invasive assessment of language function**. *Neuroimage*. 181:513-520.

68. Titre-Johnson S, Schoeler N, Eltze C, Williams R, Vezyroglou K, McCullagh H, Freemantle N, Heales S, Kneen R, Marston L, Martland T, Nazareth I, Neal E, Lux A, Parker A, Agrawal S, Fallon P, **Cross JH** (2017) **Ketogenic diet in the treatment of epilepsy in children under the age of 2 years: study protocol for a randomised controlled trial**. *Trials.*18(1):195.

69. Toescu SM, Hettige S, Phipps K, Smith RP, Haffenden V, **Clark C**, Hayward R, Mankad K, Aquilina K (2018) **Post-operative paediatric cerebellar mutism syndrome: time to move beyond structural MRI.** *Child's Nervous System*. 34:2249-2257.

70. Turnbull C, **Scott RH**, Thomas E, Jones L, Murugaesu N, Pretty FB, Halai D, Baple E, Craig C, Hamblin A, Henderson S, Patch C, O'Neill A, Devereaux A, Smith K, Martin AR, Sosinsky A, McDonagh EM, Sultana R, Mueller M, Smedley D, Toms A, Dinh L, Fowler T, Bale M, Hubbard T, Rendon A, Hill S, Caulfield MJ, 100 000 Genomes Project (2018) **The 100 000 Genomes Project: bringing whole genome sequencing to the NHS**. *BMJ*. 361:k1687 Erratum in: 361:k1952.

71. Tye C, Thomas LE, Sampson JR, Lewis J, **O'Callaghan F**, Yates JRW, Bolton PF (2018) **Secular changes in severity of intellectual disability in tuberous sclerosis complex: A reflection of improved identification and treatment of epileptic spasms?** *Epilepsia Open*. 3(2):276-280.

72. Vakharia VN, Sparks R, Rodionov R, Vos SB, Dorfer C, Miller J, Nilsson D, **Tisdall M**, Wolfsberger S, McEvoy AW, Miserocchi A, Winston GP, O'Keeffe AG, Ourselin S, Duncan JS (2018) **Computer-assisted planning for the insertion of stereoelectroencephalography electrodes for the investigation of drug-resistant focal epilepsy: an external validation study**. *J Neurosurg*. 13:1-10.

73. **Varadkar S** (2018) **Cannabidiol for drop seizures in Lennox-Gastaut syndrome**. *Lancet*. 391(10125):1006-1007.

74. **Varadkar S** (2018) **Continuous spike-wave during sleep: treating an epilepsy without seizures**. *Dev Med Child Neurol*. 60(3):220.

75. Vezyroglou K, **Eltze C, Varadkar S**, Carr L, Sullivan CO, Ninnis E, **Cross JH** (2017) **Efficacy and safety of cannabidiol as add-on therapy in drug-resistant epilepsy, a single centre experience**. *European Journal of Paediatric Neurology.* 21(1):e87.

76. Villaluz MM, Boissé Lomax L, Jadhav T, **Cross JH**, Scheffer IE (2018) **The ketogenic diet is effective for refractory epilepsy due to acquired structural epileptic encephalopathy**. *Dev Med Child Neur.* 60(7):718-723.

77. Warne RR, Carney OM, Wang G, Bhattacharya D, Chong WK, **Aylett SE**, Mankad K (2018) **The Bone Does Not Predict the Brain in Sturge-Weber Syndrome**. *AJNR Am J Neuroradiol*. 39(8):1543-1549.

78. Wilmshurst JM, Ibekwe RC, **O'Callaghan FJK** (2017) **Epileptic spasms - 175 years on: Trying to teach an old dog new tricks**. *Seizure*. 44:81-86.

79. Wilson MP, Footitt EJ, Papandreou A, Uudelepp ML, **Pressler R**, Stevenson DC, Gabriel C, McSweeney M, Baggot M, Burke D, Stödberg T, Riney K, Schiff M, Heales SJR, Mills KA, Gissen P, Clayton PT, **Mills PB** (2017) **An LC-MS/MS-Based Method for the Quantification of Pyridox(am)ine 5'-Phosphate Oxidase Activity in Dried Blood Spots from Patients with Epilepsy**. *Anal Chem*. 89(17):8892-8900.

80. Yozawitz E, Stacey A, **Pressler RM** (2017) **Pharmacotherapy for Seizures in Neonates with Hypoxic Ischemic Encephalopathy**. *Paediatr Drugs*.19(6):553-567.

Reviews, editorials and letters

1. Augustin K, Khabbush A, Williams S, Eaton SJ, Orford M, **Cross JH**, Heales SJ, Walker M, Williams R (2018) **Medium chain triglyceride ketogenic diet in neurological and metabolic disorders**. *Lancet Neurol*. 17:84-93.

2. **Cross JH**, Spoudeas H (2017) **Medical Management of Hypothalamic Hamartoma**. *Epilepsia*. 58:16-21.

3. Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, **Cross JH**, Elger CE, Engel J Jr, Forsgren L, French JA, Hesdorffer DC, Lee BI, Mathern GW, Moshe SL, Perucca E, Scheffer IE, Tomson T, Watanabe M, Wiebe S (2017) **How long for epilepsy remission in the ILAE definition?** *Epilepsia*. 58(8):1486-1487.

4. Harden C, Tomson T, Gloss D, Buchhalter J, **Cross JH**, Donner E, French JA, Gil-Nagel A, Hesdorffer DC, Smithson WH, Spitz MC, Walczak TS, Sander JW, Ryvlin P (2017) **Practice Guideline Summary: Sudden Unexpected Death in Epilepsy Incidence Rates and Risk Factors: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Epilepsy Society**. *Epilepsy Curr*. 17(3):180-187.

5. **Harkness WFJ** (2017) **Presidential address 2017 William Harkness FRCS October 10th 2017 Denver, Co USA: 2017-annus mirabilis, a global view of neurosurgery for children**. *Childs Nerv Syst*. 34(10):1817-1836.

6. **Jacques TS** (2018) **Editorial**. *Neuropathology and Applied Neurobiology*. 44(2):135-136.

7. Kalser J, **Cross JH** (2018) **The epileptic encephalopathy jungle - from Dr West to the concepts of aetiology-related and developmental encephalopathies**. *Current Opinions in Neurology*. 31(2):216-222.

8. Keshavan N, **Rahman S** (2018) **Natural history of mitochondrial disorders: a systematic review**. *Essays in Biochemistry.* 62(3):423-442.

9. **O'Callaghan FJ** (2018) **The essential symbiosis of academic and clinical neurology**. *Dev Med Child Neurol*. 60(1):5.

10. Prager C, **Cross JH** (2018) **Diagnosis and management of the epilepsies in children**. *Prescriber*. 29.04.

11. Rahman J, **Rahman S** (2018) **Mitochondrial Medicine in the Omics Era**. *The Lancet*. 391(10139):2560-2574.

12. **Rahman S** (2018) **Mitochondrial diseases and status epilepticus**. *Epilepsia*. 59(2):70-77.

13. **Reilly C**, Grant M, Bennett S, Murphy T, **Heyman I** (2018) **Physical exercise in Tourette syndrome - a systematic review**. *Child and Adolescent Mental Health*. DOI: 10.1111/camh.12263.

14. Stone TJ, Rowell R, Jayasekera BAP, Cunningham MO, **Jacques TS** (2018) **Molecular characteristics of long-term epilepsy-associated tumours (LEATs) and mechanisms for tumour-related epilepsy (TRE)**. *Neuropathology and Applied Neurobiology*. 44(1):56-69.

Edited books

1. **Gillberg C** (2018) **ESSENCE on ADHD, autism and other developmental deviations [ESSENCE om ADHD, autism och andra utvecklingsavvikelser]**. *Natur & Kultur, Stockholm.*

Edited chapters in books

1. **Baldeweg T,** Liegeois F (2018) **Functional MRI in Pediatric Epilepsy Surgery** *In: Pediatric Epilepsy Surgery: Preoperative Assessment and Surgical Treatment, 2nd Edition*. Editors: Cataltepe O, Jallo G. *Thieme, New York*.

2. **Rahman S** (2018) **Chapter 2: Clinical approach to mitochondrial diseases in children** *In: Clinical Mitochondrial Medicine*. Editors: Chinnery PF, Keogh M. *Cambridge University Press*.

3. **Rahman S** (2018) **Mitochondrial epilepsies** *In: The Causes of Epilepsy, 2nd Edition*. Editors: Shorvon S, Guerrini R, Trinka E, Schachter S. *Cambridge University Press*.

4. Smith C, **Jacques TS**, Reichard R (2018) **Pediatric Head Injury** *In: Developmental Neuropathology*. Editor: Harding B. *International Society of Neuropathology*.

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International League Against Epilepsy (ILAE)

Helen Cross
Chair of the Research Committee (2015-2019)
British Paediatric Neurology Association (BPNA)

Helen Cross
Chair of the Clinical Research Network (Children)
National Institute for Health Research (NIHR) Neurosciences Clinical Studies Group

Helen Cross
Chair of Medical Board
Hope for Hypothalamic Hamartoma

Helen Cross
Chair of Medical Board
Matthew's Friends

Helen Cross
Chair of the Neurosciences Clinical Studies Group (CSG)
Medicines for Children Research Network (MCRN)

Thomas Jacques
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Colin Reilly
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ILAE

Finbar O'Callaghan
Secretary and Board Member
European Paediatric Neurology Society (EPNS)

Helen Cross
Elected to Board
International Child Neurology Association

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Shamima Rahman
Editor
Journal of Inherited Metabolic Disease

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Associate Editor
BMC Neurology

Michelle De Haan
Affiliated Scientist
British Autism Study of Infant Siblings Network

Ronit Pressler
Affiliated Member
Paediatric Neurosciences Clinical Reference Group (CRG), NHS England

Helen Cross *et al*
Founding Members of the Rasmussen Syndrome Working Group
Young Epilepsy, GOSH and UCL GOS - ICH

Christopher Gillberg
Founder/Director of the Autism and Rett Syndrome Work Group
Swedish Medical Research Council

David Carmichael
Member of the MRI expert task force
E-PILEPSY E-PROCESSING

Helen Cross
Member
MHRA Paediatric Medicines Expert Advisory Group

Helen Cross
Member of the Medical Board
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Michelle De Haan
Membership of Steering Committees
Centre for Developmental Cognitive Neuroscience UCL

Christopher Gillberg
Member
Norwegian Academy of Sciences

Thomas Jacques
Member of the Histopathology of Epilepsy Associated Tumours Group
ILAE

Manju Kurian
Member of the Scientific Board
Epilepsy UK

Ronit Pressler
Council Member
British Society for Clinical Neurophysiology

Ronit Pressler
Member of the Medical Therapy in Children Task Force
ILAE

Ronit Pressler
Member of the Editorial Board
European Journal of Paediatric Neurology

Shamima Rahman
Member of the Medical Advisory Board
Lily Foundation

Shamima Rahman
Member of the Medical Advisory Board
Freya Foundation

Shamima Rahman
Member of the Scientific Council of the AFM-Telethon
French Muscular Dystrophy Association

Shamima Rahman
Member of the Steering Committee
Collaborative International Leigh Syndrome Task Force

Shamima Rahman
Member
Australian Mitochondrial Disease Foundation's Clinical and Scientific Review Panel

Shamima Rahman
Member
Scientific Council of the AFM-Telethon Molecular and Physiopathological Basis of Other NeuroMuscular Diseases Commission

Rod Scott
Member of the Editorial Board
Epilepsia, Journal of the ILAE

Rod Scott
Member of the Workshop on Neurobiology of Epilepsy (WONOEP) Scientific Committee
ILAE Neurobiology Commission Conference

Faraneh Vargha-Khadem
Member of the Scientific Advisory Board
Max Planck Society

What we do

Unit Roles in Education

Torsten Baldeweg
Chairman of Exam Board, MSc Paediatric Neuropsychology
University College London

Torsten Baldeweg
Module organiser and lecturer, MSc Paediatric Neuropsychology
University College London

Helen Cross
Member of the PhD Review Panel
UCL GOS - ICH

Helen Cross & Christopher Gillberg
Mind the Gap VI
Young Epilepsy

Michelle De Haan
Course Speaker, MSc in Cognitive Neuroscience, Translational Research Module
University College London

Michelle De Haan
Deputy Director, MSc in Clinical & Applied Paediatric Neuropsychology
UCL GOS - ICH

Michelle De Haan
Director, MSc in Infancy and Early Childhood Development
UCL GOS - ICH

Ronit Pressler
Course Director, EEG in the first two years of life
ILAE

Shamima Rahman
Contributor, MSc courses
UCL GOS - ICH and UCL Institute of Neurology and Genomics England

Shamima Rahman
Training Advisor for Inherited Metabolic Medicine
Royal College of Paediatrics and Child Health

Shamima Rahman
Senior Adviser, Education and Training Advisory Committee
Society for the Study of Inborn Errors of Metabolism

Colin Reilly
Course Contributor, Educational Psychology
University College London

Colin Reilly
Annual workshops for trainee educational psychologists
University College London

Martin Tisdall
Honorary Senior Lecturer
UCL GOS - ICH and UCL Institute of Neurology

Professional Recognition and Awards

Helen Cross

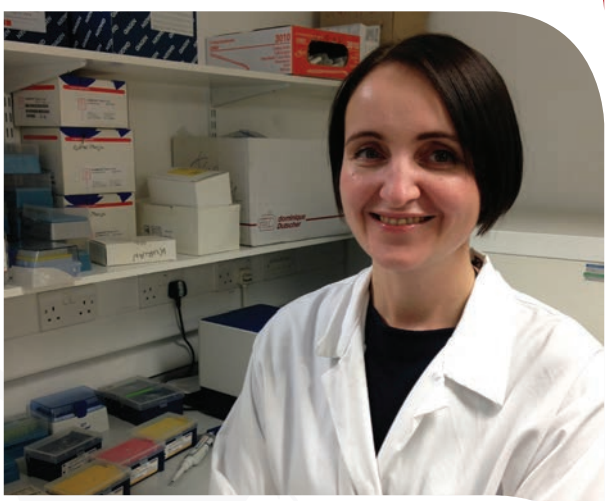
Clinical Science Research Award
2018
American Epilepsy Society

Frank Ford Award
2018
International Child Neurology Association

Manju Kurian

The Sir Jules Thorn Award for Biomedical Research
2017
Sir Jules Thorn Charitable Trust

Professor of Neurogenetics
2017
UCL GOS - Institute of Child Health



Amy McTague

Jon Driver Neuroscience Prize
2017
University College London

NIHR GOSH BRC Catalyst Fellowship
2018
NIHR and GOSH

Sophie Adler-Wagstyl

Cordwainer's Prize for Best MB PhD Thesis
2017
University College London

Michelle De Haan

Professor of Infant and Child Development
2017
UCL GOS - Institute of Child Health

Birgit Pimpel

Academic Representative of the Year
2018
UCL GOS - Institute of Child Health

Mirja Steinbrenner

BrainBox Initiative Research Challenge
2018
Rogue Resolutions

Faraneh Vargha-Khadem

Rapporteur
2018
Max Planck Society

At Young Epilepsy we want to create better futures for young lives.

As a national charity and a centre of expertise for all young people with epilepsy, we have over 125 years experience to share.
Let's work together.

For more information on our research or if you want to get involved please contact:

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Research Manager
Tel: 01342 831274
Email: research@youngepilepsy.org.uk

Download our free epilepsy management app:
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