Research Projects

Young Epilepsy

This document outlines the new, ongoing, and competed projects during July 2020 to June 2021.

The projects are presented under the workstream they most contribute to. They have coloured, numbered icons in the top right corner which illustrate all of the goals to which they contribute. Each project also features a purple 'what this means?' box which gives a summary of the work and intended impact.

youngepilepsy.org.uk

Completed Projects

Workstream 1- Understanding Childhood Epilepsies

Functional effects of SCN1A mutations – New insights from biophysics and computational modelling

Project Aim: Linking functional properties of SCN1A miss-sense mutations with their resultant phenotypes

Investigators: Richard Rosch, Elaine Hughes, Kathleen Gorman, Colin Peters, Peter Ruben

Summary: Changes to the gene SCN1A is one of the most thoroughly investigated genetic causes of epilepsy. This gene controls sodium channel functionality – a critical component of cell structure. Yet even within the well-known SCN1A-related epilepsies, new phenotypes are still emerging, and the complexities of genotype-phenotype relationships remain only partially understood.

We combine biophysical measurements of the functional properties of the sodium channel variants found in patients with epilepsy, with computational modelling of neuronal function to understand better how different miss-sense mutation in the same gene – SCN1A – result in a wide range of phenotypes.

Goal 1

What this means: Even when patients have apparently the same genetic mutation, there are still differences within the individual. This is because whilst we may have identified the cause of a particular epilepsy – such as a genetic mutation – we still might not understand exactly how it works or how each part of the mechanism of that gene/mutation results in the particular epilepsy syndrome of each patient.

By investigating in detail, the effects of specific mutations in a single gene, we hope to improve our understanding of the effects of genetic mutations in individual patients, and ultimately improve our treatments for each patient individually.

Neuro-LinK: Determining long-term outcomes in children with chronic neurological conditions (ICH Data science initiative)

Project Aim: Determine the long-term health outcomes of children treated at GOSH in three well-defined cohorts via data linkage with The Hospital Episode Statistics (HES) database

Investigators: Jessica Pickles, Deborah Ridout, Torsten Baldeweg, Darren Hargrave, Thomas Jacques, Katie Harron, Vandana Ayyar Gupta, Francesco Muntoni

Summary: We are interested in obtaining long-term outcome data, including hospital admissions and education outcome, for children with neurological conditions such as brain tumours, Duchenne Muscular Dystrophy and epilepsy surgery candidates. In particular, we are interested in those patients with neurological chronic disease who manage their condition over extensive periods, often require multiple interventions and may receive several forms of treatment. We will engage with PPI groups to discuss our project aims. Their feedback and advice will be instrumental in developing our application to seek approval.

Goal 1 Goal 2 Goal 3

There is a clear absence of long-term clinical outcomes associated with large paediatric cohorts, hindering the translation of research findings to our patients' life course and their expected clinical progression of disease. The project is aiming to access health outcomes for specific patient groups to appreciate the extent of the burden of disease for patients both during and after receiving their primary care at GOSH.

What this means: There is not enough information of the long-term outcome trajectory of children with chronic neurological conditions. We want to truly understand the burden of such conditions on patients so that we can better understand how to manage and treat them within the NHS.

Gene-STEPS: Shortening Time of Evaluation in Paediatric epilepsy Services: a multi-centre prospective evaluation of the impact of early genetic diagnosis on patient outcomes

Project Aim:

1. Implement rapid trio WGS for all children presenting to our health systems with epilepsy onset under 12 months of age
2. Utilize electronic healthcare records and research databases to unite phenotypic and genomic data and to create a "virtual" registry across all institutions that will promote ongoing discovery.
3. Assess the impact of early genetic diagnosis on epilepsy, developmental, and health economic outcomes through formal longitudinal assessments of all children enrolled.

Investigators: Amy McTague, Helen Cross, Lyn Chitty, Neil Sebire. With Annapurna Poduri (Boston Childrens), Katherine Howell, Ingrid Scheffer (Royal Childrens Hospital Melbourne), Gregory Costain, Vann Chau (The Hospital for Sick Children Toronto)

Summary: In the past decade, the genomic revolution has led to the identification of underlying genetic aetiologies for childhood epilepsy, in the form of monogenic disorders affecting ion channels, neurotransmitter receptors, synaptic proteins, and other families of proteins. In a growing number of cases, the specific genetic diagnosis informs prognosis and genetic counselling, leads to the opportunity to participate in natural history studies, and even to changes in treatment that, to date anecdotally, may change outcomes in seizures and in neurodevelopment. However, a major challenge in clinical practice is that early intervention requires early diagnosis.

Currently the diagnostic odyssey in early-onset epilepsy is long and arduous for patients and their families. The timing and nature of genetic testing for such patients varies widely within and across countries and institutions. Our collective expertise includes epilepsy genetics research, genomic research, clinical epilepsy, clinical trials, and team science across four leading paediatric institutions in the IPCHiP Consortium: Boston Children's Hospital (US), Great Ormond Street Hospital and UCL Great Ormond Street Institute of Child Health (UK), Royal Children's Hospital Melbourne and Murdoch Children's Research Institute (Australia), and The Hospital for Sick Children ("Sick Kids", Canada). Each of our institutions has a proven track record of discovery and translation to patients, and our combined efforts in epilepsy will set a new standard for multi-institutional research, data sharing, and improvement

To investigate our hypothesis that rapid genetic diagnosis and tailored management could improve outcomes, we propose a novel approach to streamline and accelerate diagnostics in these severely affected children.

Funders: Young Epilepsy, GOSH charity, GOSH NIHR BRC, UCL International Office

Multicentre Epilepsy Lesion Detection (MELD) Project

Project Aim: Create open-access, robust and generalisable tools for understanding and detecting focal cortical dysplasias (FCDs) that can assist the pre-surgical evaluation of patients with drug-resistant epilepsy.

Investigators: Sophie Adler-Wagstyl, Kirstie Whitaker, Armin Raznahan, MELD consortium, Helen Cross, Torsten Baldeweg, Konrad Adler-Wagstyl

Summary: The MELD project has created the largest neuroimaging cohort of FCDs to date, including data from over 580 patients and 380 controls. Using this unique dataset alongside statistical and machine-learning techniques, we are currently working on 3 projects. 1) Mapping the distribution of FCDs across the brain and creating predictive models of lesion location and seizure freedom. 2) Linking the distribution of FCDs across the cortex to the underlying brain structure. 3) Creating machine-learning algorithms to automatically detect FCDs on MRI scans.

What this means: Through the MELD project we hope to better understand this important cause of medication-resistant epilepsy and create tools that can be used to inform clinical decision making. These include predictive maps of lesion locations, deep-learning tools for the detection of FCDs and models for the prediction of post-surgical seizure freedom. These tools will be validated on data from 20 hospitals and will be made openly accessible for any hospital to use when evaluating a patient with a suspected FCD.

Shining a light on the genetic basis of Sunflower syndrome

Project Aim: Investigate the genetic basis of this rare photosensitive epilepsy

Investigators: Amy McTague, Manju Kurian

Summary: Sunflower syndrome is a rare, photosensitive epilepsy, named for sun-seeking behaviour or stereotyped reflex seizures in bright light. Affected patients have many hand-waving episodes per day (the patient waves their hand in front of their own eyes and this stimulates a seizure). Hand-waving episodes are resistant to treatment and significantly impair quality of life.

Children with Sunflower Syndrome also experience other seizure types including absences, eyelid and other myoclonias and generalised tonic clonic seizures. Sunflower syndrome is often associated with significant neurodisability; many patients have co-morbid learning difficulties, autistic spectrum disorder, attention deficit hyperactivity disorder, anxiety and depression.

There remain a number of unanswered questions including whether the hand-waving episodes represent a reflex seizure or compulsive self-induction of seizures.

Goal 1

We have established an international cohort of patients including families with significant family history and will undertake trio whole genome sequencing which will be analysed using Ingenuity and Alamut software, initially for known disease-causing genes followed by analysis for copy number variants and novel genes using differing inheritance models. Putative variants will be validated by Sanger sequencing and functional validation of likely disease-causing variants will be undertaken.

What this means: Sunflower Syndrome is a rare photosensitive epilepsy characterised by self-induction of seizures in children. We don't yet know what causes Sunflower Syndrome but we believe it has a genetic basis and we will be looking at an international cohort of patients and sequencing their entire genome alongside their biological parents. We will cross reference this with known epilepsy causing genes, against variations of these and will look for previously unknown epilepsy causing genes.

Short-term findings of this study will immediately improve the current genetic screening for epilepsy. We hope the long-term findings will reveal causal genes - giving a strong basis on which to develop targeted treatment for this condition.

Modelling childhood genetic epilepsies in zebrafish larvae

Project Aim: Identifying whole-brain network dysfunction at single neuron resolution in larval zebrafish models of genetic epilepsies

Investigators: Richard Rosch, Dominic Burrows, Jade Lau, Martin Meyer

Summary: There are many limitations to what we can understand about epilepsy from measuring its effects in humans, or the commonly used rodent models with the available recording methods. Zebrafish larvae offer a unique perspective in that they are transparent and small enough in size so that they allow whole-brain calcium imaging at single cell resolution during epileptic seizures.

Zebrafish are a novel experimental model for the investigation of some of the most severe epilepsy syndromes of childhood, with the future potential to guide and trial novel therapeutic approaches for translation into human patients.

Goal 1 Goal 2

In this research project we identify and characterise whole-brain abnormalities in genetic models of childhood epilepsies at single cell resolutions, in order to identify novel treatment strategies for some of the most complex epilepsy syndromes.

What this means: We are using Zebrafish larvae instead of mouse models to better understand some of the most severe genetic epilepsies of childhood. Zebrafish larvae are transparent, and this means we can see how each brain cell is functioning. This level of resolution will allow a much greater understanding of the brain networks involved in these complex epilepsies and lead to new, targeted, treatments.

Autism spectrum diagnosis (ASD) and epilepsy

Project Aim: The assessment of autism for children with complex epilepsy poses many challenges; from fluctuating profiles to diagnostic overshadowing and atypical presentations. This project reviews the issues involved by drawing on more than 20 years' experience of neurodevelopmental assessment of children with complex epilepsy at GOSH.

Investigators: Harriet Holmes, Francesca Sawer, Maria Clark

Summary: Lots of the behavioural and communication weaknesses of autism are also commonly present in children with epilepsy. However, the trajectory of these difficulties over time and fluctuating nature of the developmental profile, is often very different to "typical" ASD and in our experiences, can often mirror the fluctuations of epilepsy, leading us to question its formal classification.

Goal 1

The uniqueness and rarity of the presentations we see, means that making a child's difficulties understandable and accessible/treatable often means using mainstream diagnoses such as autism which may not be the best fit. We aim to explore issues around assessment, confounding comorbidities and high-risk groups as well as exploring challenges faced by families. We aim to publish the findings as a practice paper.

What this means: We will review the challenges in diagnosis autism in children with epilepsy experienced over 20 years at GOSH to try to learn whether there is a more effective model to support children with epilepsy who present also with symptoms of autism.

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

Update: 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.

Goal 1

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.

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: Investigation of this cohort is ongoing and our results have led to several publications including a Gene Reviews summary of SLC12A5 and a review of the genetic landscape of epilepsy-dyskinesia.
In addition, we have taken part in an international cohort study on the genetics of Epilepsy of Migrating Focal Seizures of Infancy and have identified a novel gene for epilepsy-dyskinesia, CACNA1B.

Goal 1 Goal 2

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. Recently, we have identified a new gene which causes both a severe early onset epilepsy and a movement disorder.

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.

Goal 1 Goal 2

This project involves memory testing using an application on a tablet developed by Sarah Buck as well as undertaking an MRI. Patients are seen before surgery and again 4 and 12 months after surgery.

Patient recruitment, which was due to continue until Spring 2020, was cut short in February 2020 due to the COVID-19 pandemic. Patient follow up is currently on hold for the same reason. We hope to be able to resume patient follow up in the Spring of 2021, and hopefully present results during the second trimester of 2022.

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.

Development in Hypothalamic Hamartoma

Project Aim: To review the developmental profiles of children with hypothalamic hamartoma in relation to their medical presentation and treatment.

Investigators: Hanna Richardson, Leah Bull, Varsha Siyani

Summary: Hypothalamic hamartoma is a rare epilepsy caused by a benign tumour-like formation on the hypothalamus. The growth causes very difficult to control seizures, early puberty and developmental and cognitive problems. Children with hypothalamic hamartoma have high levels of comorbidity and their profiles can change over time. The behavioural impact can be very severe and there are plans to look at this further with neuropsychiatry at GOSH.

Goal 2

We conducted a case note review of children with hypothalamic hamartoma to better understand how their development links to their medical presentation and treatment.

What this means: The more we understand about how hypothalamic hamartoma affects development, the better we will be able to treat all aspects of the condition. This is particularly important in cases where we are unable to remove the hamartoma by surgery.

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 Sarah Buck as well as undertaking an MRI. Patients are seen before surgery and again 4 and 12 months after surgery.

Patient recruitment, which was due to continue until Spring 2020, was cut short in February 2020 due to the COVID-19 pandemic. Patient follow up is currently on hold for the same reason. We hope to be able to resume patient follow up in the Spring of 2021, and hopefully present results during the second trimester of 2022.

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.

A natural history of Pyruvate Dehydrogenase Complex deficiency

Project Aim: To describe the natural history of Pyruvate Dehydrogenase Complex (PDC) deficiency from childhood to adulthood, including the spectrum of molecular diagnoses in affected patients in order to identify genotype/phenotype correlations and predictors of poor prognosis.

Investigators: Nandaki Keshavan, Shamima Rahman

Summary: PDC deficiency is one of the most common mitochondrial disorders. Patients with this condition develop a combination of problems including seizures, neurodisability and have a reduced life expectancy. It is essential to understand the mechanisms underlying the disease in order to identify new treatments, and to understand the natural history of disease in order to prepare for clinical trials. To date, a natural history study of PDC deficiency has not been undertaken in the UK. In collaboration with the Freya Foundation and tertiary paediatric metabolic and neurology centres nationally, we will undertake a multicentre retrospective study to describe the spectrum of symptoms, disease severity, molecular diagnosis, management and outcomes in both children and adult patients with PDC deficiency. We will then collate the data and analyse it to determine whether there are any correlations between clinical/laboratory findings and outcomes. We will also biobank patient blood samples for future multi-omic studies in order to elucidate pathophysiological mechanisms.

What this means: We want to understand what are the predictors of poor outcomes in patients with PDC deficiency by undertaking the first natural history study of PDC deficiency in the UK. It is important that we understand how patients are currently being treated at different tertiary centres to inform best practice. At present we know little about the mechanisms that cause disease symptoms and in future aim to investigate this further in hope that we may be able to identify new effective treatments.

Novel network analysis of intracranial stereoelectroencephalography (SEEG)

Project Aim: To characterize interictal abnormalities in single unit neural dynamics and to establish whether the regions that display abnormal dynamics are consistent with the epileptogenic zone.

Investigators: Rod Scott, Martin Tisdall, Aswin Chari, Rachel Thornton

Summary: Epilepsy surgery is a neurosurgical operation to remove parts of the brain that generate seizures. A proportion of children being evaluated for surgery have electrodes inserted into their brains as part of their clinical assessment, termed stereoelectroencephalography (SEEG), to help localise these regions. Subsequent surgery is not always successful - up to 40% of children will have ongoing seizures 5 years after surgery.

The purpose of this study is to assess the utility of specially designed SEEG electrodes which can measure signals from single brain cells. These electrodes record the same clinical information as normal SEEG electrodes and are implanted in the same way, but can give the research team extra information at the same time. The investigators aim to assess whether studying the changes in the firing of individual cells, both during and between seizures, improves our ability to localise seizures and therefore improve outcomes following surgery. This study will be carried out in children undergoing invasive recordings as part of evaluation for epilepsy surgery.

The project has gained ethical approval and, over the course of late 2019 and 2020, has recruited 4 patients. The project's progress has been slow due to a number of technical challenges involved in recording these signals and the temporary pause on intracranial recordings necessitated by the COVID-19 pandemic but we look forward to making progress in the near future with some new equipment and new strategies!

What this means: We want to know if data gathered during and between seizures can improve the use of SEEG electrodes to find the epileptogenic region.

Non-invasive modulation of brain network dynamics to suppress epileptic activity and improve cognition (EPICONN TM)

Project Aim: A pilot study to measure a reduction in epileptiform activity associated with transcranial electrical stimulation (TES). We look to modulate brain connectivity and understand its relationship to epileptiform activity reduction. We hypothesise that in epilepsy brain networks can be targeted by weak electric fields applied to the scalp (TES) to modulate the brain's connectivity to reduce epileptic activity.

Investigators: David Carmichael, Frederike Moeller, David Sharp, Helen Cross, Mirja Steinbrenner, Martin Tisdall, Mark Richardson, Ines Violante, Rory Piper

Update: This project is funded by an ERUK pilot grant to commence study in patients with Juvenile Myoclonic Epilepsy. We have obtained first data in a few patients just before COVID struck and are analysing the results as the basis for larger research grants.

Rory piper a surgeon training in Oxford performed a research placement investigating thalamic connectivity in epilepsy with us and has recently been awarded a PhD to continue to work with us.

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. 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.

Multiscale modelling of epileptic networks from SEEG recordings

Project Aim: Epilepsy surgery aims to change epileptic brain networks in a way that will reduce the likelihood of future seizures. In this project we aim to use state of the art network modelling approaches to characterise these epileptic brain networks from intracranial EEG recordings, and in future help in predicting the effects of surgical intervention on those networks.

Investigators: Richard Rosch, Rachel Thornton, Martin Tisdall, Karl Friston, Ulrich Stoof

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, see Tumpa et al (2019) bioRxiv doi. org/10.1101/691170), and at the level of whole brain circuits (e.g. identifying whole-network changes after interventions in patients undergoing therapeutic radiofrequency thermocoagulation).

A new PhD student has been appointed with funding awarded by the Oakgrove Foundation to develop the computational tools necessary for this analysis.

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.

Landau-Kleffner syndrome: Patterns in the recovery phase

Project Aim: A retrospective case note review examining cognitive and language trajectories across different phases of Landau-Kleffner syndrome (LKS).

Investigators: Maria Clark, Christina Hawkins, Gemma Wilson, Harriet Holmes

Summary: LKS is a rare epilepsy which has an active phase, characterised by the loss of language skills and a distinct sleep EEG abnormality, referred to as Continuous Spike and Wave in Sleep (CSWS) or Electrical Status Epilepticus during Sleep (ESES). The active phase is followed by the recovery phase which continues for many years but in that time a child may regain skills. We have been asked to write a practice paper about LKS for the Paediatrics and Child Health Journal.

What this means: We are investigating past data to better inform future management and treatment of LKS.

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 neurobehavioural 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, Aikaterini Vezyroglou

Summary: We received 200 referrals, of these 186 were eligible and a further 119 were recruited to the assessment arm of the study. We are currently investigating the genetic aetiologies in patients from the study suspected to have an underlying disorder of genetic origin. A cohort of patients were recruited for whole exome triome analysis. To date, several genetic diagnoses (e.g. SCN-related genes, PRRT2) have been established in approximately 15% of the cohort. Variants of unknown significance in known epilepsy gene, requiring further evidence for proof of pathogenicity have been reported in 42%, and analysis for novel mutant genes is ongoing in 43%.

We plan to collect developmental follow up data from the 119 recruited participants and begin to establish a long term data set or these individuals.

What this means: We have been looking at children following first presentation with seizures from the EPIPEG cohort. In some patients, we suspect that their epilepsy may be 'genetic', that is related to a fault or spelling mistake in their genetic makeup. We've investigated a number of children now and so far, found a genetic problem in 1/6 of the cases. 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, 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. This project will provide the basis for a longer study, which will follow these children as they grow up.

Realising the potential of 7T MRI for paediatric imaging

Project Aim: To enable the first 7 Tesla (7T) magnetic resonance imaging (MRI) of paediatric patients with epilepsy being evaluated for surgery at GOSH and Kings College London Hospital (KCLH)

Investigators: David Carmichael, Helen Cross, Martina Callaghan, Shaihan Malik, Thomas Booth, Sila Dokumaci, Fred Dick, Dr Simon Richardson, Serena Counsell, Alex Hammers, Jonathan O'Muircheartagh

Summary: The current standard resolution for clinical Magnetic Resonance Imaging (MRI) in neurology is 1.5 - 3 Tesla (a measure of the power of the magnet used). This study will look into the practical application and benefit of the 7 Tesla (7T) MRI machines at GOSH and KCLH.

3T MRI machines can show details of the brain as small as 1mm, a 7T machine can show details 50% smaller than this; small enough to detail network connectivity in real time. We believe that the potential of this technology will enable a significant increase in our ability to detect and stratify structural abnormalities causing epilepsy, particularly those due to cortical abnormalities, and through greater accuracy, allow more children to be considered for epilepsy surgery.

We have been developing scan protocols for Paediatric Epilepsy patients, n parallel, we have been developing patient friendly head cushions to improve scan performance and tolerance.

What this means: We are working to understand the potential of this enhanced imaging technology and how best to use it for children.

Workstream 2 – Outstanding Treatments

The CADET Trial: The Children's Adaptive Deep brain stimulation for Epilepsy Trial

Project Aim: To determine the efficacy of DBS in reducing seizure frequency in children with Lennox Gastaut Syndrome. We also wish to determine the effect on seizure severity and quality of life, the safety of the procedure (complications and adverse events) and the best stimulation patterns to provide seizure control.

Investigators: Martin Tisdall, J Helen Cross, Hakim-Moulay Debhi, Tim Denison, Harutomo Hasegawa, Elaine Hughes, Marios Kaliakatsos, Kei Landin, Rory Piper, Ali Resaei Haddad, Richard Sleway, Ioannis Stavropoulos, Antonio Valentin

Summary: Lennox-Gastaut syndrome (LGS) is a rare yet severe form of childhood epilepsy - a disorder that causes seizures. LGS is typically resistant to medications and children continue to experience seizures that impair their quality of life and development. Early trials in adults with LGS have shown that deep brain stimulation (DBS) of a specific region of the thalamus of the brain (the centromedian nucleus (CMN)) is effective in reducing the number of seizures. No such trials, however, have been performed to demonstrate this benefit in children. Providing this therapy earlier in the course of the disease may improve long-term seizure control, brain development, and quality of life.

Goal 1 Goal 2

We will engage with advancements in neuro-engineering in order to translate DBS technologies into an effective and tailored treatment for children with LGS. Our aims are to reduce the frequency of seizures and improve the quality of life of children with complex epilepsy.

The CADET Trial will be a Phase II clinical trial of DBS for children with LGS. 22 children (5-15 years) will undergo DBS using a new device that allows continuous stimulation and has features attuned to the particular needs of children. Patients will either be randomised to active ('on') versus inactive ('off') stimulation for three-months. All children will thereafter complete six-months of active stimulation and the change in seizure frequency in the last month will be the primary outcome that will determine effectiveness.

Funders: LifeARC/GOSH-CC

Development of a lifespan compliant magnetoencephalography system

Project Aim: Build an OP-MEG system for children aged 0-15years, that will offer direct clinical applicability, increased practicality, better data, and lower cost compared to current systems.

Investigators: Matthew Brookes, Richard Bowtell Gareth Barnes, Helen Cross, Rosemarie Pardington

Summary: Conventional MEG systems use sensors that are cryogenically cooled and fixed in a one-size-fits-all helmet. Performance is limited by a gap between the head and sensors, which is larger for infants, greatly reducing sensitivity. Further, movement relative to the sensors causes dramatic reductions in data quality (even 5mm movements render data unusable). For these reasons, conventional MEG is inadequate for infants.

Goal 3

The new OP-MEG sensors do not rely on cryogenics. They are small, lightweight, and can be mounted on the patient's head within a helmet. Because the sensors are closer to the head, OPMs afford vastly better performance, and removing cryogenics results in a much cheaper system. Based on this, we now have a unique opportunity to develop a MEG scanner for infants.

In this project we will look to solve the issues of different sensor arrangements according to head size and develop appropriate, tolerable helmets for the new wearable OP-MEG system.

What this means: The different head sizes of children and infants present a challenge to MEG scanning and we hope to develop a series of appropriate, comfortable and tolerable helmets for children aged 0-15 years.

Wearable magnetoencephalography (MEG) at Young Epilepsy

MEG Project 1: The Young Epilepsy Diagnostic Suite

Investigators: Tim Tierney, Stephanie Mellor, Geroge O'Neill, Gareth Barnes, Helen Cross, Rosemarie Pardington, Amy Muggeridge, Megan Brady, Kelly St Pier, Mark Devlin, Niall Holmes, Elena Boto, Ryan Hill, Gill Roberts, James Leggett, Richard Bowtell, Matt Brookes, Nick Murby, Eliot Dawson, Nick van de Wydeven, Courtney Veenswyk-Colvin, Peter Fierlinger, David Woolger, Cassandra Hugill, Sophie Perry, Vishal Shah, Torsten Baldeweg, Sarah Buck, Umesh Vivekananda, Matthew Walker, Vladimir Litvak, Eleanor Maguire, Daniel Barry, Andrew Levy, Sven Bestmann, Leo Dunque-Munoz, Jose Lopez

Summary: The new Diagnostic Suite offers upgraded electroencephalogram (EEG), sleep telemetry and home telemetry services alongside the world's first wearable Optically Pumped (OP) magnetoencephalography (MEG) unit within a lightweight magnetically shielded room (Mu-Room). The overarching goal of the Young Epilepsy Diagnostic Suite is to offer world leading clinical neuroimaging technology in a comfortable and seamless environment for patients and their families.

Goal 3 Goal 5

Currently MEG is a neuroimaging tool which is of very limited availability to children and young people with epilepsy, due to the equipment expense, weight, maintenance cost, fixed sensor location, intimidating aesthetic and the need to be perfectly still during the investigation. The OP-MEG and lightweight Mu-Room system overcomes each of these barriers to clinical use – chiefly the need to stay still. For the first time, MEG is a clinically feasibly tool in the diagnosis and surgical evaluation of children and young people with epilepsy – particularly those with complex needs who cannot tolerate other forms of neuroimaging such as EEG or magnetic resonance imaging (MRI).

What this means: The primary outcome of this project is to provide clinicians with a novel technology which informs earlier and more accurate interventions for children with epilepsy. Epilepsy has enormous impact on a person's life and is usually present with additional developmental needs. The longer a child has uncontrolled seizures, the more likely there will be an impact in the longer term. Early, accurate intervention is critical to improving patient outcomes and quality of life in childhood epilepsy.

MELD (Multi-centre Epilepsy Lesion Detection) as an Adjunct for SEEG Trajectories (MAST) trial

Project Aim: Assess the utility of a novel machine learning algorithm in helping to plan electrode trajectories in children undergoing stereoelectroencephalography (SEEG)

Investigators: Sophie Adler, Konrad Wagstyl, Aswin Chari, Zubair Tahir, Martin Tisdall

Summary: This clinical trial is a pilot study aimed at assessing the utility of a locally developed machine-learning lesion detection algorithm in planning SEEG electrode trajectories. It is a rare prospective study of novel artificial intelligence technology and aims to recruit 20 patients over the next 2 years.

Goal 3

Prior to setting up the trial, we assessed whether the algorithm may have been useful in previous SEEG cases and found that many of the lesions identified corresponded to where the seizures arose from. Interestingly, in 3/34 cases, a seizure onset zone was not found on SEEG and the algorithm identified lesions that were not being targeted.

What this means: We hope to show how useful a novel artificial intelligence software (that we developed here at ICH) is at improving the detection of abnormalities associated with epilepsy. We are starting with a first stage 'pilot' study to get a better idea of how we can use it and ensure it is safe before deciding on whether or not we should conduct a larger study. At the time of writing, we have already recruited 4 patients to the study!

Modelling neuronal dysfunction in early onset epilepsies; a patient-centric approach

We have three overarching aims:

To create and characterise a patient-derived induced pluripotent stem cell (iPSC) organoid model of Epilepsy of Infancy with Migrating Focal Seizures (EIMFS).
The creation of patient-derived cerebral organoids will enable study of the effects of the mutations in their native neuronal and genetic milieu. Fibroblasts from patients with SLC12A5, KCNT1 or SCN2A mutations have been transformed into induced pluripotent stem cells (iPSCs) and are being differentiated into cerebral organoids. Currently we are validating organoids for layer specific and regional markers of neuronal identify and maturity. In the next year patient lines will also be differentiated into medial ganglionic eminence-like organoids containing interneurons, which will be fused with the cerebral organoids.

To investigate the neuronal phenotype of EIMFS at a cellular and network level.
A number of assays will be undertaken to investigate disease mechanisms including Western blotting and immunofluorescence to assess cell surface expression, patch clamping and multi-electrode array analysis to assess impact on channel and transporter function, multi-electrode array analysis to measure network formation and single-cell RNA sequencing to evaluate gene expression differences.

To investigate the impact of novel therapies.
We will use a gene therapy approach or antisense oligonucleotides to rescue the phenotype as an initial proof of concept. If successful, these approaches will be developed in future funding applications.

Investigators:
Amy McTague, Dimitri Kullmann, Gabriele Lignani, Jenny Lange, Manju Kurian

Summary: In Epilepsy of Infancy with Migrating Focal Seizures (EIMFS), affected babies have very frequent seizures, often up to sixty per day, which usually do not respond to currently available medications. Abnormalities in three genes, known as KCNT1, SLC12A5 and SCN2A can cause EIMFS. These genes make important proteins in the brain that, when abnormal, cause seizures in young babies. However, it is not clear how they lead to epilepsy. Using a new state-of-the art brain cell model made from skin cells taken from patients in the study, we will investigate how abnormalities in these genes lead to epilepsy and developmental problems in patients. Skin cells from each patient will be converted into stem cells. Stem cells have the potential to convert into any of the cell types in the body. The stem cells will be converted into three dimensional structures, or organoids, which after maturation for several months will be made up of layers of neurons. If we can work out precisely how the abnormal genes cause seizures, this may help us identify better drugs for both this form of epilepsy and other epilepsies.

What this means: We want to improve our understanding of how these abnormal genes lead to epilepsy and development problems which will help in the development of new treatments, with the ultimate aim of improving quality of life for patients and their families.

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 1 month to 2 years who have failed to respond to two or more pharmacological treatments.

Investigators: Helen Cross, Laura Lyons, Sally Halsall, Natasha Schoeler, Maryam Balogun, Christin Eltze, Simon Heales, Helen McCullagh, Rachel Kneen, Tim Martland, Jeen Tan, Andrew Mallick, Andrew Lux, Alasdair Parker, Helen McCullagh, Archana Desurkar, Penny Fallon, Helen Basu, Anita Devlin, Rajib Samanta, Shakti Agrawal, Manish Prasad, Rohini Rattihalli, Elma Stephen, Andreas Brunklaus, Martin Kirkpatrick, Ailsa McLellan, Nick Freemantle, Louise Marston, Irwin Nazareth

Update: Recruitment continued until June 30 2021, by which time we had recruited 136 children which should enable 80% power for the study. We are in the process of data cleaning, and aim to report on results by April 2022

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 C Tactile (CT) afferents and how the cortical response changes in regard to age.

Investigators: Ronit Pressler, Geraldine Boylan

Update: A total of 24 infants were recruited into the study, of which 20 attended both somatosensory nervous system pathway (SSEP) assessments at 4 weeks and 4 months of age and developmental assessments at 4 months. Group analysis of potentials during gentle stroking did not reveal a clear reproducible response. We are currently improving the test protocol and aim to test a further 20 infants. This second phase will be conducted in Cork, Ireland.

Goal 1 Goal 3

ENRICH was run by UCC (Cork) and GOSH was involved in a small part which was called Gentle Touch – evaluating the cortical response to gentle touch (like stroking or massage) using evoked potentials. We finished the clinical part but unfortunately were not able to see a clear response. This was probably due to technical problems, so UCC had planned to take this further by using our data to make changes to the recording set up but this was impossible due to COVID-19 pandemic.

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.

A multicentre, 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) and we have recruited our first participant.

Goal 1 Goal 3

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.

The study has now successfully included 5 babies (within Europe) and concluded the exploratory phase. The study has been reviewed by the Data Management Committee and they approved the start of the confirmatory phase which will start in 2021. GOSH will not be recruiting but UCLH will.

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.

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

We have two aims:

- Provide better informed diagnosis of memory impairments in children with epilepsy.
- Predict outcome after surgery in the temporal lobe, using the Pair Test.

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

Update: 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.

Goal 2 Goal 3 Goal 4

What this means: The Pair Test is an app-based tool which will better help clinicians understand the type and complexity of learning and memory problems in children with Temporal Lobe Epilepsy (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.

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, Simon Heales

Update: Some children have a specific type of epilepsy, called pyridox(am)ine 5'-phosphate oxidase deficiency induced epilepsy, which 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 have developed a more stable, formulation and have evaluated the purity and taste of this new drug. We are currently evaluating whether this product meets the safety requirements (i.e. not liver toxic) for administration to humans.

Goal 3 Goal 5

This work has been delayed by the COVID-19 pandemic, and we are still evaluating the new formulation having done some toxicity studies in mice models.

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.

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. The COVID-19 pandemic has delayed progress.

Goal 1 Goal 3

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.

Antisense oligonucleotides for the treatment of ALDH7A1-deficiency

Project aim: A proof of principal project to show that antisense oligonucleotide therapy can prevent the accumulation of the toxic metabolites that occur in patients with a-aminoadipic semialdehyde dehydrogenase (ALDH7A1) deficiency, a vitamin B6-dependent epilepsy disorder.

Investigators: Philippa Mills, Haiyan Zhou, Paul Gissen

Summary: Humans rely on vitamin B6 for the proper functioning of their nervous, endocrine and immune systems. They are not able to make this micronutrient themselves and must therefore get it from their diet. There are many different dietary forms of vitamin B6 which our bodies convert to the active form of this vitamin. This is known as pyridoxal phosphate (PLP). PLP is essential for enzymes involved in metabolism of proteins, fats and carbohydrates to work properly.

Whilst a dietary deficiency of vitamin B6 is rare, there are several genetic disorders which result in insufficient PLP within the cells of the body. PLP plays an important role in the brain therefore children with these disorders present with epilepsy.

The most common of these epilepsy disorders occurs when there are mutations in a gene that is responsible for making an enzyme called a-aminoadipic semialdehyde dehydrogenase. This enzyme is involved in the pathway which converts lysine, an amino acid which is present in the food we eat, into energy. Mutations in this gene result in an accumulation of metabolites which interact with PLP thereby reducing the amount of PLP available for the brain. The resulting epilepsy can be treated by giving supraphysiological doses of vitamin B6.

Goal 2 Goal 3

Unfortunately, the compounds that accumulate, besides interacting with PLP, are also toxic to the brain. This toxicity results in intellectual disability and developmental problems. Treatment with B6 does not correct this. One way of preventing the accumulation of these compounds is to restrict the amount of lysine in the child's diet. Children do not like this diet and the improvements seen have only been partial. Better treatments are therefore needed. We will investigate the use of antisense oligonucleotides as a way of preventing an accumulation of these toxic compounds in this disorder.

We are currently looking to see if we can patent the work we have been doing but the COVID-19 pandemic has caused delays.
amount of lysine in the child's diet. Children do not like this diet and the improvements seen have only been partial. Better treatments are therefore needed. We will investigate the use of antisense oligonucleotides as a way of preventing an accumulation of these toxic compounds in this disorder.

This work has been delayed by the COVID-19 pandemic, and we are still evaluating the new formulation having done some toxicity studies in mice models.

What this means: We are looking to develop a more tolerable treatment for ALDH7A1-deficiency.

Workstream 3 – Outstanding Support

Epilepsy Carers Uniting with Researchers (E-Cure) PPI network

Project aim: Strengthen the voice of children and young people with epilepsy in our research by establishing the UKs first network of parents, carers and young people who volunteer to shape childhood epilepsy research

Investigators: Amy Muggeridge, Samantha Chan, Amy McTague, Helen Cross

Summary: The sole purpose of the network is to consult on the development of research ideas, methodologies, and delivery to ensure research reflects the true needs of patients and families. Members choose their level of participation and interests. Roles for members can be as simple as participating in surveys, up to becoming formal members of project management groups as patient representatives. The network currently has almost 140 members.

Goal 5

What this means: Working with patients and their families is critical to the success of research. This network is a key component of research design across the unit.

Epilepsy Pathway Innovation in Africa (EPInA)

Goal 2 Goal 3 Goal 5 Goal 6

We have four aims:

- **Diagnose:** improve the rate of accurate diagnosis of epilepsy by refining app-based technologies.
- **Treatment:** increase the adherence to medication using text messaging.
- **Societal change:** ensure an enduring, positive change by improving public awareness and reducing the stigma experienced by people with epilepsy in sub-Saharan Africa.
- **Prevent:** reduce the incidence of infection and peri-natal injury in an endemic region in Tanzania and the subsequent risk of epilepsy.

Investigators: Charles Newton, Helen Cross, Arjune Sen, David McDaid, Albert Akpalu, Damazo Kadengye, Gershim Asiki, Patrick Adjei, Sloan Mahone, Symon Kariuki, Tarun Dua, Thomas Kwasa, Mohammed Mnacho, John Geddes, Josemir Sander, Richard Walker, William Matuja

Summary: Epilepsy is one of the most common serious neurological conditions and is particularly widespread in sub-Saharan Africa (SSA). This high incidence is, in at least a quarter of cases, because of preventable factors, yet many people who may have had seizures are not diagnosed and even fewer receive appropriate treatments. These factors are compounded by enduring social stigma that can make it hard for Africans with epilepsy to obtain employment, form relationships or feel valued.

We have chosen to work in three countries – Ghana, Kenya and Tanzania. We will bring together work across all three countries to better understand the history of epilepsy, investigate why people with epilepsy are so disadvantaged and then set out to improve things. We will develop an app to help healthcare workers to better diagnose epilepsy, and pilot a text messaging scheme to help people to remember to take their medication. We will train local people in epilepsy care and develop epilepsy healthcare specialists to lead future projects.
In Tanzania, which has a higher incidence of epilepsy, possibly due to onchocerciasis infection, we are also going to see if reducing the rate of onchocerciasis infection can lower the number of people with epilepsy.

Funding: NIHR

What this means: By implementing measures to improve the prevention, diagnosis, treatment and cultural understanding of epilepsy, we think this project can dramatically change the lives of people with epilepsy in sub-Saharan Africa. If successful we will use all that we learn to ensure similar work is carried out across other low-income countries.

Epilepsy Pathway Innovation in Africa (EPInA)

We have four aims:

- **Diagnose:** improve the rate of accurate diagnosis of epilepsy by refining app-based technologies.
- **Treatment:** increase the adherence to medication using text messaging.
- **Societal change:** ensure an enduring, positive change by improving public awareness and reducing the stigma experienced by people with epilepsy in sub-Saharan Africa.
- **Prevent:** reduce the incidence of infection and peri-natal injury in an endemic region in Tanzania and the subsequent risk of epilepsy.

Investigators: Charles Newton, Helen Cross, Arjune Sen, David McDaid, Albert Akpalu, Damazo Kadengye, Gershim Asiki, Patrick Adjei, Sloan Mahone, Symon Kariuki, Tarun Dua, Thomas Kwasa, Mohammed Mnacho, John Geddes, Josemir Sander, Richard Walker, William Matuja

Summary: Epilepsy is one of the most common serious neurological conditions and is particularly widespread in sub-Saharan Africa (SSA). This high incidence is, in at least a quarter of cases, because of preventable factors, yet many people who may have had seizures are not diagnosed and even fewer receive appropriate treatments. These factors are compounded by enduring social stigma that can make it hard for Africans with epilepsy to obtain employment, form relationships or feel valued.

We have chosen to work in three countries – Ghana, Kenya and Tanzania. We will bring together work across all three countries to better understand the history of epilepsy, investigate why people with epilepsy are so disadvantaged and then set out to improve things. We will develop an app to help healthcare workers to better diagnose epilepsy, and pilot a text messaging scheme to help people to remember to take their medication. We will train local people in epilepsy care and develop epilepsy healthcare specialists to lead future projects.
In Tanzania, which has a higher incidence of epilepsy, possibly due to onchocerciasis infection, we are also going to see if reducing the rate of onchocerciasis infection can lower the number of people with epilepsy.

Funding: NIHR

What this means: By implementing measures to improve the prevention, diagnosis, treatment and cultural understanding of epilepsy, we think this project can dramatically change the lives of people with epilepsy in sub-Saharan Africa. If successful we will use all that we learn to ensure similar work is carried out across other low-income countries.

PsyKD - Understanding of the impact of the ketogenic diet on child and parental quality of life

Project aim: Gain an understanding of the needs and experiences of families considering a Ketogenic Diet Therapy (KDT) and the subsequent impact of the diet on children and their parents.

Investigators: Colin Reilly, Natasha Schoeler, Helen Cross, Victoria Whiteley, Anita Devlin, Christin Eltze, Emma Williams

Summary: Adherence to a KDT may not always be easy and depends on physician, parental and healthcare system-related factors. Despite the range of prescriptible and non-prescriptible ketogenic products available, KDTs still require stringent dietary restriction, which places significant burden on families and requires major effort on the part of the child and family. Little is known about the impact of KDTs on child behavioural and emotional functioning and child quality of life.

In order to have a better understanding of the impact of KDTs on children with epilepsy and on parental functioning, we propose to conduct a pilot study assessing functioning and views before commencement of dietary treatment and at three months and one year follow up. The study would be the first of its kind and would make a significant contribution to the research evidence base for treatment of epilepsy with KDTs on psychosocial outcomes.

The project has been delayed by the COVID-19 pandemic and is currently seeking funding. It is a collaboration between Young Epilepsy, Matthews Friends, GOSH, Addenbrookes Hospital, Royal Manchester Children's Hospital and Newcastle upon Tyne Hospitals.

What this means: Adherence to a KDT is a lifestyle change and we want to better understand how to best support families to make the most of this treatment.

Physical Activity in Childhood Epilepsy (PACE)

Project aim: The primary aim is to compare levels of physical activity in secondary school-aged children with 'active' epilepsy, and matched healthy controls, using both survey methods and activity trackers.

A secondary aim is to understand factors (e.g. age, gender, seizure related factors, sleep, behaviour-emotional functioning, school learning and parent wellbeing) which may be associated with physical activity, including structured exercise/sports participation, in children with epilepsy.
A third aim is to gather pilot data on physical activity levels in children with epilepsy and explore the feasibility of implementing an intervention to improve levels of physical activity in children with epilepsy.

Investigators: Colin Reilly, Emma Johnson, Helen Cross, Lauren Sherar, Monica Lakhanpaul, Kerry Robinson, Amit Bali, Patricia Atkinson, Natalie Pearson, Kathryn Simpson

Summary: Anecdotal evidence suggests that children with epilepsy engage in less physical activity than their peers. This does not mean engagement in team sports, rather, just being active. There is, however, limited research on this and no previous studies in the UK.

We will compare levels of physical activity in 150 secondary school-aged (11-15years) children. Half of them will have epilepsy and the other half not have epilepsy. Of the 150 children, 50 of them will attend special schools and 100 attend mainstream schools.

Activity will be measured by using activity trackers. We also want to know whether factors other than just their epilepsy may affect how active they are – things like their age, gender, how they feel, and sleep quality etc.

Depending on what we find, we may use this evidence to explore strategies which may improve access to being active, for children with epilepsy. This project is fully funded and ethical approval has been granted. The study was suspended due to the COVID-19 pandemic and is due to reopen as an entirely remote study in January 2021.

What this means: We want to understand the attitudes, barriers and enablers to children with epilepsy participating in physical activity in order to provide the best support.

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, Helen Cross, Monica Lakhanpaul, Kerry Robinson, Dougal Hargreaves, Christina Petropoulos

Summary: This is a collaborative programme of projects between Young Epilepsy, UCL Great Ormond Street Institute of Child Health, UCL Partners and Whittington Health, led by Amit Bali.
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 the economic study. Bids are met with great interest and support but not with a dedication of funds. We are currently revising the approach to fund this study. The development of a learning healthcare system has been incorporated into Young Epilepsy's Digital Strategy 2019-24 and will constitute one of two arms of the project. This project will partner with the Epilepsy12 National Audit to record patient reported measures and we hope to integrate this as a patient held record and epilepsy registry within the NHS by 2024.

What this means: We want to ensure services for epilepsy are joined up, and are provided in partnership with young people and families and empowers them. 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.

Prevention of Epilepsy by reducing Neonatal Encephalopathy (PREVENT) study

Project aim: Our aim is to examine if a care bundle approach to improve the maternal care around delivery will reduce the number of babies sustaining serious birth related brain injury and epilepsy.

Investigators: Sudhin Thayyil, Helen Cross, Ronit Pressler, and many more

Summary: Led by Imperial College London, the PREVENT study is the world's largest study on babies with brain injuries. Brain injury during labour or childbirth is one of the leading causes of epilepsy in babies. The proportion of babies sustaining serious brain injury around the time of birth (40 per 1000 livebirths) in public sector hospitals in India is 10 times higher than that of the UK. Approximately 12 million people with epilepsy live in India.

Although epilepsy is not curable in most cases, by reducing birth related brain injury a substantial number of these cases can be prevented. In many cases, this can be prevented by simple, evidenced based and low-cost interventions tailored to the local needs. Our aim is to examine if a care bundle approach; a series of simple and interventions administered consistently, which includes intelligent foetal heart rate monitoring, an e-partogram, brain oriented neonatal resuscitation, and birth companions, will improve the maternal care around delivery will reduce the number of babies sustaining serious birth related brain injury and epilepsy. We have assembled a team of experts in neonatal brain injury and neuroimaging, obstetrics, midwifery, qualitative research, epilepsy, global health, electrophysiology, care bundle development, health economics, public health, statistics, implementation research from leading academic centres in the UK and India, along with parent representatives to undertake this work.

The study will be conducted over 4 years in two adjacent public sector hospitals in Tamil Nadu, India, where the total number of babies sustaining birth related brain injury is the same as the total UK annual burden of birth related brain injury. During the first year of the study, we will collect accurate base-line data on brain injury, and develop and pilot the care bundle. The care bundle will be then implemented during the second year, and the outcome evaluated during the 3rd and 4th years.

The main outcome is to assess whether the proportion of babies (per 1000 live births) developing birth related brain injury is different before and after the introduction of this care bundle. We will also examine and compare the number of infants that develop epilepsy by their first birthday before and after the introduction of the care bundle. We will compare our findings with data from 44 nonparticipating public sector hospitals to identify any natural reduction in the incidence of brain injuries. Finally, we will examine the views of the stakeholders and cost-effectiveness of this care bundle for adoption into the national health policy in India.

What this means: There is a high incidence of epilepsy in India due to complications during birth. We want to address the issues surrounding safe childbirth and through this aim to reduce the incidence of epilepsy due to birth complications.

Assessment of profound intellectual disability in complex epilepsy

Project aim: To develop a robust assessment tool for children with complex epilepsy

Investigators: Maria Clark, Gemma Wilson, Lucy Pepper

Summary: Current assessments do not capture the skills of children with complex epilepsy and are not sensitive enough to record change over time or after intervention. We are trying to develop new ways to assess this group that is meaningful for their families and allows them to be included in research or outcome data. We have been awarded a small grant through the Patient Public Involvement scheme at GOSH to allow us to run some focus groups with families to advance the project.

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

Summary: Our NIHR funded Programme Grant began in October 2017. At therapists' requests we hosted a booster training session in March 2019 which gave therapists the opportunity to feedback on their experience on delivering the intervention during the training phase and discuss key learning points in preparation for the trial. During this session, we conducted qualitative interviews which provided further insight into their experience and the practicalities of physical healthcare staff delivering a telephone-based psychological intervention within epilepsy services. We also obtained participants' perspectives of receiving the intervention and the impact it has had on both their child's mental wellbeing and quality of family life. We received very positive, promising feedback from both therapists and families, and incorporated any feedback and suggestions into our planning for the main trial where necessary.

In April 2019 we were awarded the second half of our funding based on successful outcomes from the 6-month training phase. The trial commenced in May 2019 when the first participant was recruited, and screening is now underway across all 7 sites. Due to demand, we have trained additional therapists and staff to help with screening at other sites. We continue to meet with our Patient and Participant Involvement Research Advisory Group and Health Professionals Advisory group every 2-3 months. They advise on trial related procedures, for example the recruitment process in clinics and have contributed to plain English summary for families. We are currently opening St Piers School at Young Epilepsy as a study site.

We started recruiting patients into the main trial in 2019 and have now recruited over 130 participants of our planned 334. We were very pleased to be able to continue our research and support families during the COVID-19 pandemic as all of the assessment and treatment is completed over the telephone or via video conferencing. We've had some really good feedback from participants so far.

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.

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

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, Mirja Steinbrenner

Update: This project is now being finalised. We have published our assessment of more rapid fMRI sequences 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. The COVID-19 pandemic has caused delays to this project but we have moved to the analysis stage.

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.

European Reference Network on rare and complex epilepsies (EpiCARE)

Summary: EpiCARE is a European Reference Network (ERN) for rare and complex epilepsies, coordinated by Professor Alexis Arzimanoglou, Director of the Epilepsy, Sleep and Paediatric Neurophysiology Department at the University Hospitals of Lyon, France. Advances in brain scanning as well as genetic and metabolic investigations have determined an increasing number of causes behind epileptic seizures, resulting in the description of more than 130 rare diseases.

The European Reference Networks (ERNs) were launched in 2017. They involve more than 900 highly specialised health care teams, located in more than 300 hospitals in 26 European countries. The main mission of the ERNs is to help patients with rare or low-prevalence complex diseases.

The ERN EpiCARE brings together highly specialized health centres (28 full members and 15 affiliated partners) in 24 European countries with expertise in rare and complex epilepsies. The centers closely collaborate with the scientific societies (ILAE, EAN, EPNS, Epilepsy Alliance Europe) and a number of other epilepsy teams in the EU with expertise in specific domains. EpiCARE offers a coordinated approach for epilepsy diagnostics and treatment by using e-tools and cross-country e-consultancy.

One of 24 approved ERNs on rare disorders, EpiCARE now has 52 members, spanning 13 countries. EpiCARE aims to improve access for patients to diagnostic and therapeutic expertise, by engaging multidisciplinary experts through the network.

EpiCARE aims to:

- To improve accessibility of detailed diagnostics to individuals of all ages with rare and complex epilepsies across Europe, including clinical evaluation and investigation.
- To develop treatment protocols and monitor standardised outcomes of rare and complex epilepsies.
- To improve awareness and accessibility to protocols for physicians and individuals with rare and complex epilepsies across Europe for treatment.
- To enhance educational activities and training opportunities across Europe by interchange across the network.

To enhance opportunities for registries, and collaborative research for the benefit of individuals with rare and complex epilepsies across Europe.

Completed Projects

Workstream 1- Understanding Childhood Epilepsies

Epilepsy Dossier: *Autism and epilepsy: laying out the evidence*

Project Aim: Undertake a systematic review of factors associated with the occurrence of epilepsy in individuals with autism

Investigators: Colin Reilly, Sophie Bennett, Roz Shafran, Amy McTague, Emma Dalrymple, David Skuse, Neha Batru, Eleni Zarakoviti

Summary: Epilepsy is a common co-occurring condition in people with autism. We systematically reviewed quantitative and qualitative studies which have focused on the health economic aspects of living with both autism and epilepsy. We focused on the lived experience of individuals which allows us to consider the social, educational, human and economic costs of having both conditions.

Data from the systematic reviews were combined with data from PPI groups to create a dossier. Three key themes emerged:

1. Risk factors of co-occurring epilepsy and autism
2. Living with co-occurring autism and epilepsy
3. A need for economic analysis of costs of co-occurring autism and epilepsy

Goal 2

What this means:
Future research recommendations

1. Qualitative research with autistic people who have epilepsy and their families
2. Key relevant economic interventions for this population remain unclear and need to be identified
3. Further research is needed on long term non healthcare costs and outcomes
4. Research on the impact on being autistic with epilepsy has on job/employment prospects

Read now: http://pageflip.en-route.co.uk/books/lofr/mobile/index.html

---

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

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

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

Summary: We used 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. 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. We designed headgear to record bNIRS simultaneously with routine EEG and recruited 15 patients to this pilot study. We were lucky to capture seizures in 9 patients. Analysis of our bNIRS and EEG data during repeated seizures in one of our patients showed a significant increase in blood oxygenation adjacent to the epileptic focus and a significant decrease in cytochrome c oxidase in the region of the epileptic focus. This might indicate a relative brain tissue hypoxia and energetic deficiency in the region of the epileptic focus during seizures.

Goal 1

What this means:
We are investigating how the bNIRS, and especially the cytochrome c oxidase measurement, is affected during an epileptic seizure. Better understanding of energy consumption during seizures will help us understand how seizures affect the brain in the long term.

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

Project Aim: To develop better imaging methodology for classification of FCD lesions

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

Summary: We aimed 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 in childhood epilepsy. We have published our study looking at diffusion changes in the cortex that demonstrated greater sensitivity of advanced diffusion maps to FCD lesions. We have also analysed quantitative susceptibility maps (QSM), a new MRI measure that has not been tested in many epilepsy patients before. QSM maps showed strong visual contrast in a handful of cases – and changes in cortical structure in FCD patients when evaluated quantitatively. Reduced susceptibility values were found across the cortex and an absence of a peak in susceptibility found in healthy cortex. Working with Po-Wah So at KCL we have compared our results to alterations in metal content using the diamond light source (https://www.diamond.ac.uk) to show changes in iron, calcium and zinc.

This work is now available in preprint form from https://www.medrxiv.org/content/10.1101/2020.09.15.20157123v1 and has been submitted for publication.

Workstream 2 – Outstanding Treatments

Children's Epilepsy Surgery Service (CESS) network stereoelectroencephalography (SEEG) outcomes

Project Aim: Assess the outcomes of children undergoing SEEG across the UK

Investigators: Aswin Chari, Rachel Thornton, Martin Tisdall & the entire CESS SEEG team

Summary: Multicenter retrospective cohort study of all children undergoing SEEG at six of seven UK Children's Epilepsy Surgery Service centers from 2014 to 2019. Demographics, noninvasive evaluation, SEEG, and operative factors were analyzed to identify variables associated with the identification of a seizure onset zone (SOZ) and subsequent seizure freedom following SEEG-guided epilepsy surgery. Findings: One hundred thirty-five patients underwent 139 SEEG explorations using a total of 1767 electrodes. A putative SOZ was identified in 117 patients (85.7%); odds of successfully finding an SOZ were 6.4 times greater for non-motor seizures compared to motor seizures (p = 0.02) and 3.6 times more if four or more seizures were recorded during SEEG (p = 0.03). Of 100 patients undergoing surgical treatment, 47 (47.0%) were seizure free at a median follow-up of 1.3 years.

Goal 3

What this means: This large nationally representative cohort illustrates that SEEG-guided surgery can still achieve high rates of seizure freedom. Seizure presentation and the number of seizures recorded during SEEG are important factors in the identification of a SOZ, and the indication for SEEG is an important factor in postoperative outcomes.

Early surgery for radiologically evident focal cortical dysplasia

Project Aim: Assess the proportion of children with a radiologically evident focal cortical dysplasia that become medication resistant and subsequently undergo surgery

Investigators: Ido Ben Zvi, Noelle Enright, Aswin Chari, Christin Eltze, Martin Tisdall

Summary: This study incorporated a survey within a regional paediatric epilepsy network and a retrospective database review of a paediatric epilepsy centre serving the network to identify children with epilepsy and a presumed FCD on MRI. The survey revealed that 86% of the patients with epilepsy and presumed FCD on MRI within the network were referred to our centre. Of 139 paediatric patients included in the study, 131 (94.2%) had drug-resistant epilepsy. One hundred and ten (83.9%) patients were referred to epilepsy surgery, of whom 97 underwent surgery. Of 92 with one-year postoperative follow-up, 59.8% had an Engel Class 1 (seizure-free) outcome. Concordance of location between MRI and ictal EEG was strongly associated with Engel Class 1 outcome ($p<0.001$), as was older age at seizure onset ($p=0.03$). Time from diagnosis to surgery, number of medications, type of surgery and histology were not associated with improved outcome.

Goal 3

What this means: Data suggest that most children presenting with seizures and a radiological diagnosis of FCD will develop drug-resistant epilepsy and are candidates for epilepsy surgery.

Workstream 3 – Outstanding Support

What I Need in School (WINS)

Project Aim: Developing guidelines for best practice for young people with epilepsy in schools in the UK

Investigators: Colin Reilly, Patricia Atkinson, Emma Johnson, Helen Cross, Amy Muggeridge

Summary: There is a lack of knowledge about epilepsy in schools and we aimed to gain an understanding of the views of parents of children with epilepsy regarding the process of securing educational and therapeutic supports and the changes they would like to make to this provision.

Parents (n=68) of children (born between 2003 and 2014) with 'active' epilepsy (at least one seizure in last year) resident in the RH10-RH13 postcode areas of West Sussex, were interviewed using a semi-structured interview schedule The interviews were conducted between October 2018 and March 2020 and coded using Thematic Analysis by two independent raters.

Parents reported difficulties accessing both educational and therapeutic supports. They often felt that they had to drive the process to gain supports themselves. They reported little professional support, and inadequate communication regarding their child's needs with school staff and between school staff and/or medical/therapeutic professionals. Parents of children with severe intellectual disability (ID) and/or who attended a special school generally reported finding the process easier. Parents of children with mild to moderate ID who attended mainstream schools reported the most difficulties. Regarding changes parents would like to make to their child's current educational and/or therapeutic supports, they highlighted the need for school staff to recognise the impact of epilepsy on learning and behaviour and to support their child more holistically. Many wanted greater access to assessment and therapeutic provision in relation to their child's learning and behaviour. They also highlighted the need for the child's schoolwork to be appropriate to their cognitive ability and profile.

Goal 4

Parents of school-aged children with epilepsy report difficulties accessing appropriate educational and therapeutic supports for their child and would like more support in the process. Parents also highlight the need for increased knowledge of the impact of epilepsy on learning and behaviour and want more resources for assessment in these areas.

What this means: This work will feed into the resources to education professional provided by Young Epilepsy and we further hope to write guidelines for schools to support young people with epilepsy achieve their academic potential. We plan to 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.

Research Funding

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

Our collaborative funding strategy has enabled us to build the world's largest paediatric epilepsy research unit and network of multidisciplinary practitioners.

Between July 2019 and June 2020, research across the unit has secured over £25million in new research grants.

Alongside academic grants raised by the researchers and their academic institutions, we rely on the additional multidisciplinary fundraising by Young Epilepsy, which allow us to redirect funds where the need is greatest within a project. This flexibility is vital and provides stability during challenges such as delays.

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
Autistica
Brain Tumour Charity
Cancer Research UK
Child Health Research Trust
Children with Cancer UK
Epilepsy Research UK
Ethypharm
European Association of Neurosurgical Societies
European Commission
Freya Foundation
Google Cloud Platform Research Credit Award
GOSH NIHR BRC
Great Ormond Street Children's Charity
GW Pharmaceuticals
Innovate UK
James Lewis Foundation
LifeARC - GOSHCC
Medical Research Council Clinician Scientist Fellowship
National Institute of Health Research (NIHR)
NIHR GOSH Biomedical Research Centre
NIHR GOSH BRC PPIE Small Grants
Novartis
Novel Network Analysis of Intracranial EEG: 2019-2022
Nutricia
Oakgrove Foundation
Role of the Piriform Cortex in the Epileptic Connectome: 2021-2024 (awarded 2020)
Rosetree's Trust
Sir Henry Wellcome Fellowship
Sobell foundation
The Brain Tumour Charity
UCB BioPharma
UCL Child Health Research CIO Strategic Initiatives Pump-Priming Fund
Veriton Pharma
Vitaflo
Waterloo Foundation
Wellcome Research Enrichment - Public Engagement
Wyfold Charity Trust
Young Epilepsy