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GREAT ORMOND STREET INSTITUTE OF CHILD HEALTH

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NHS Foundation Trust

THE NATIONAL CENTRE FOR YOUNG PEOPLE WITH EPILEPSY CHARITABLE TRUST

Paediatric Epilepsy Research and Impact Report

2022

Young Epilepsy

Contents

Introduction

I am delighted to present our annual research report for the period July 2021 to June 2022 for the paediatric epilepsy research unit across Young Epilepsy, UCL GOS - Institute of Child Health and Great Ormond Street Hospital for Children.

During the past year, our research programme has continued to conduct over 40 active projects. Despite the ongoing impact of COVID-19 on all our lives, we initiated seven new research projects. These projects focused on a vast array of topics, including the development of web-based interventions for staff currently supporting children with epilepsy, the advancement of cutting-edge neuroimaging techniques, and a six-year follow-up study investigating the neurodevelopmental status of children who presented with epilepsy in the first year of life. Whilst these new projects are just a snapshot of the entire research programme; their diversity demonstrates our commitment to encouraging work in all areas of epilepsy research. Whilst we continue to conduct research into understanding and treating epilepsy, we recognise the importance of providing outstanding support through educational, psychosocial, and service-based research.

In the past year alone, the research unit has been responsible for the publication of 89 peer-reviewed items of primary research, as well as 26 chapters in books, reviews and commentaries of expert opinion.

In January 2022, we hosted our 12th international Paediatric Epilepsy Research Retreat, moderated by Professor Elaine Wirrell. The Retreat is a one-of-a-kind event where early career and seasoned researchers meet to constructively share their research and forge new collaborations. Unfortunately, due to the ongoing impact of COVID19, the event had to be hosted online for the second consecutive year. Nonetheless, we attracted our biggest-ever audience, with 157 attendees. Despite the virtual format, there were an excellent array of high-quality presentations, and the feedback received from participants was that they found this unique environment and network just as informative and motivating as ever.

This year's report closely mirrors last year's, highlighting the impact of our research over the past decade and casting a spotlight on our key projects and trends whilst briefly summarising all our ongoing projects. For those of you who are interested, there is a link on page seven where you can find out more detail on any of the research projects summarised in this report.

Young Epilepsy's vision is to create a society where children and young people with epilepsy are enabled to thrive and fulfil their potential. A society in which their voices are respected and their ambitions realised. Our research programme supports this vision and exists to establish successively better outcomes by driving early diagnosis and intervention in every aspect of childhood epilepsy, and I do hope you will enjoy reading this report.

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

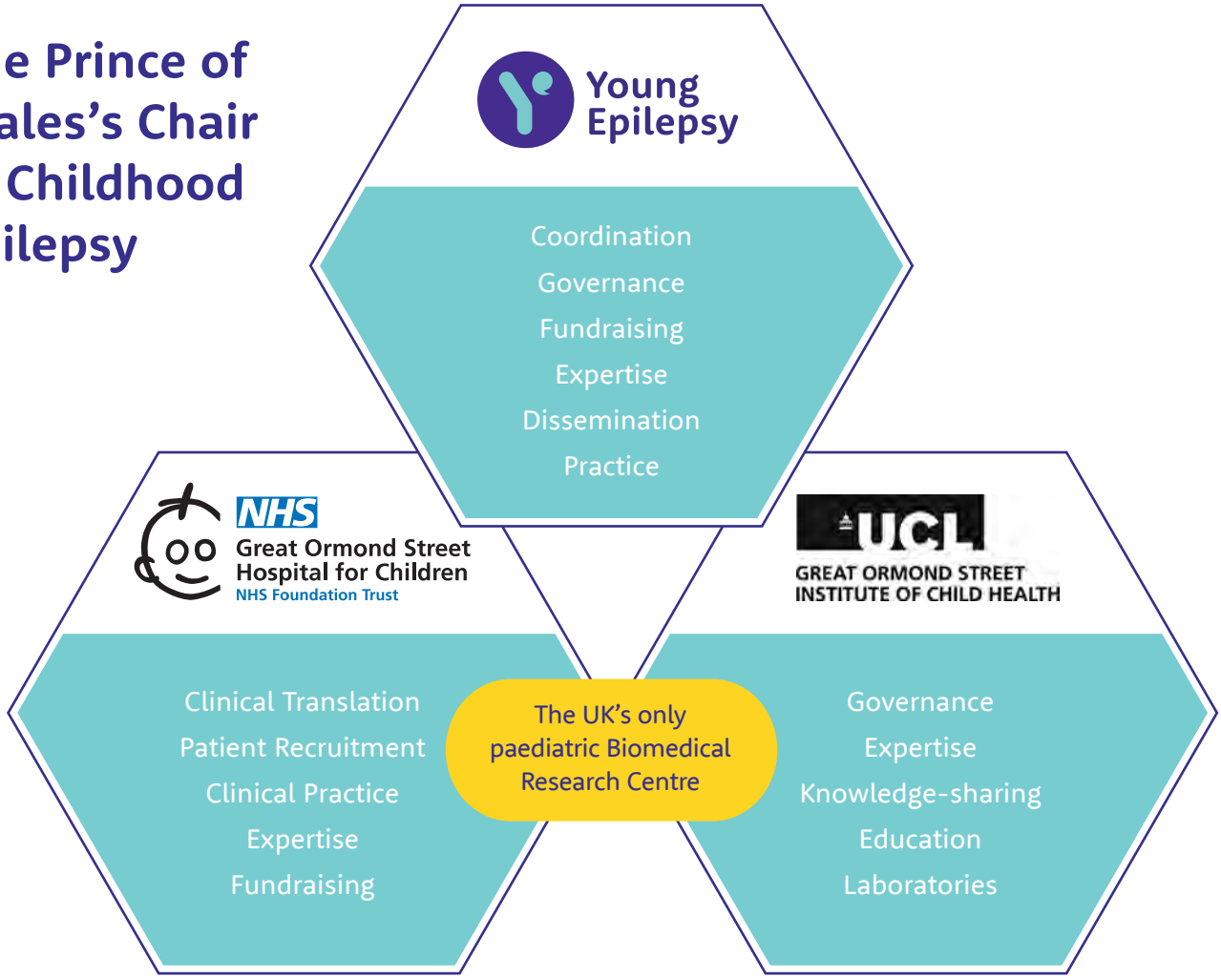
Who we are

Led by the Prince of Wales's Chair of Childhood Epilepsy, Professor Helen Cross, our research programme is a collaborative scheme between Young Epilepsy, Great Ormond Street Hospital and UCL GOS - Institute of Child Health.

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

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

The Prince of Wales's Chair of Childhood Epilepsy



Young Epilepsy exists to create a society where children and young people with epilepsy are enabled to thrive and fulfil their potential. A society in which their voices are respected and their ambitions realised.

Under our three key offers; health and research, voice and support and St Piers special education, we aim to:

- Coordinate research that improves diagnosis and treatments, and deliver cutting-edge health services.
- Campaign for children's rights, supporting them in school and college, and providing innovative tools, information, and practical help for living day-to-day life.
- Provide an innovative and creative environment for children and young people with epilepsy, autism, and severe learning difficulties.

Great Ormond Street Hospital for Children (GOSH) is an international centre of excellence in child healthcare, at the forefront of paediatric training in the UK. Together with UCL GOS - Institute of Child Health, GOSH forms the UK's only Biomedical Research Centre specialising in paediatrics. Most of the children we care for are referred from other hospitals throughout the UK and overseas. There are 63 different clinical specialties at GOSH; the UK's widest range of specialist health services for children on one site. 60% of the UK's epilepsy surgeries are carried out at GOSH.

University College London Great Ormond Street-Institute of Child Health (ICH) together with its clinical partner Great Ormond Street Hospital for Children (GOSH), forms the largest concentration of children's health research in Europe.

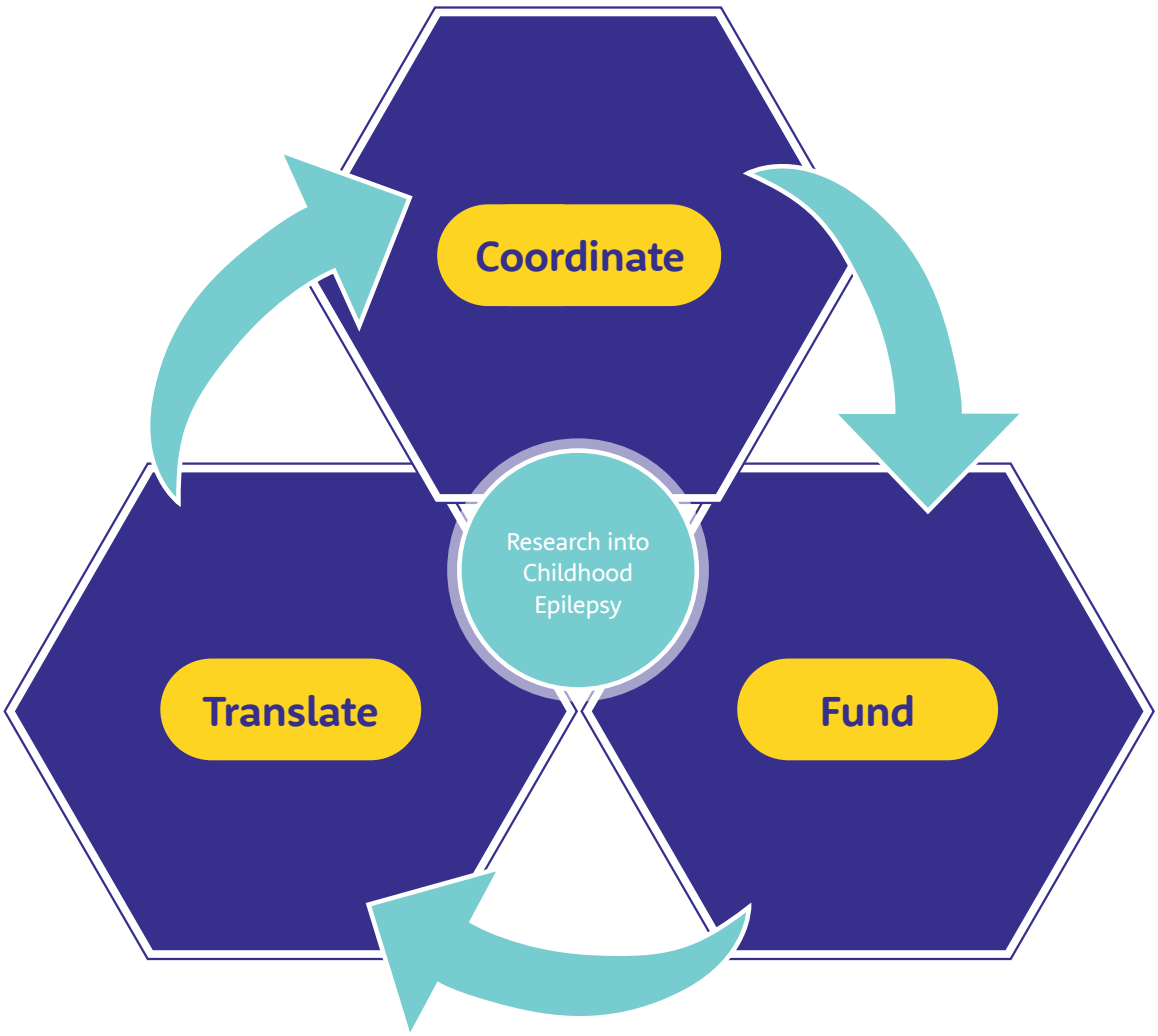
The inspirational mission of the UCL Great Ormond Street Institute of Child Health is to "improve the health and well-being of children, and the adults they will become, through world-class research, education and public engagement".

The academic strategy of GOS ICH is focused on five scientific research and teaching departments:

- Developmental Biology and Cancer
- Developmental Neurosciences
- Genetics and Genomic Medicine
- Infection, Inflammation and Immunology
- Population Policy and Practice

What we do

Our research programme exists to ensure the best outcome for every child by optimising diagnosis, treatment, and support for all aspects of childhood epilepsy.



* The welfare of animals used in research is very important to Young Epilepsy, GOSH and ICH. Researchers would prefer not to use animals at all so we follow the guidance of the Association of Medical Research Charities. These principles are called the 3Rs:

- **Replace** the use of animals with alternative techniques or avoid the use of animals altogether.
- **Refine** the way experiments are carried out, to make sure animals suffer as little as possible. This includes better housing and improvements to procedures which minimise pain and suffering and/or improve animal welfare.
- **Reduce** the number of animals used to a minimum by seeking ways to find out information from fewer animals or more information from the same number of animals.

Workstream 1: Understanding Childhood Epilepsies

Around half of people diagnosed with epilepsy never learn the cause of it. This is concerning from both the personal and clinician perspective. The more we know about what causes epilepsy and how else the underlying cause is affecting the individual patient, the better clinicians can manage and treat, and the better the patient can understand themselves.

GOAL 01

Gain a better understanding of the medical causes of epilepsy

The majority of epilepsy treatment is symptomatic. The more we know about the underlying causes of the epilepsies, the more chance there is of developing curative, targeted treatments. Under this goal we run:

- Cohort studies to evaluate prevalence, natural history and outcome of comorbidities
- Studies to determine the molecular or genetic basis to the epilepsies
- Collaborative outcome studies
- Correlative neurophysiology and neuropsychology studies
- Enhanced structural studies using neuroimaging to increase detection of structural correlates
- Pathological examination of tissue from surgical specimens to enhance our understanding of structural correlates and related epileptogenesis

25% projects currently contribute to this goal

GOAL 02

Gain a better understanding of how epilepsy affects development and behaviour

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

- Cohort epidemiological studies to determine incidence, prevalence and outcome
- Population and family studies to gain further insights into new treatments
- Correlative studies in neurophysiology to enhance detection of origin
- Experimental animal model studies* to examine the effects of epileptiform discharges on development
- Correlative neurophysiology and neuropsychology studies

21% projects currently contribute to this goal

Workstream 2: Outstanding Treatment

Epilepsy treatments have not changed very much over time and the process of finding the right combination of treatments for each patient takes a long time. This is very hard on patients – especially if they are young. Continued advancement of imaging, surgery, dietetics, genomics and targeted treatment, and new medicines is crucial in the quest to effectively treat, and one day perhaps cure, every epilepsy.

GOAL 03

Improving diagnosis and treatment to determine the benefits of early interventions in improving long-term outcomes

The longer one has epilepsy, the longer its underlying cause is able to threaten or cause damage. Effective diagnostic processes, optimal treatments and early intervention are vital in slowing or halting any damage.

- Short and long-term evaluation of outcome following early epilepsy surgery
- Evaluation of new medical treatments
- Evaluation of educational intervention
- Novel diagnostic and imaging methods

28% projects currently contribute to this goal

Workstream 3: Outstanding Support

This workstream is set to tackle the wider challenges associated with growing up with epilepsy and in treating childhood epilepsies. It is important to know what epilepsy is and how to treat it but if the systems and supports are not in place to act on this knowledge then patients cannot benefit.

GOAL 04

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

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

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

6% projects currently contribute to this goal

GOAL 05

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

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

- Patient and public inclusion and representation in research design and management
- Interventional behaviour programmes
- Rehabilitation and follow-up studies
- Assessment of service provision
- Evaluation of the impact of epilepsy on family life
- Evaluation of the economic costs involved in epilepsy care

16% projects currently contribute to this goal

GOAL 06

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

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

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

4% projects currently contribute to this goal

Summary of Research Projects

This section provides a brief overview of two key projects from this year's work. This is followed by a summary list of the current and competed projects during July 2021 to June 2022.

The projects are presented under the workstream that they contribute to most.

To find out more details about each of these projects please visit:

www.youngepilepsy.org.uk/for-professionals/research

Young Epilepsy

Key Projects

The Young Epilepsy Diagnostic Suite

It has been a busy year for the Diagnostic Suite following the launch of the ground-breaking wearable Optically Pumped (OPM) magnetoencephalography (MEG) system in September 2021. Clinical evaluation is ongoing and trials have been carried out on healthy adult and paediatric volunteers. In January 2023 we will begin the next phase of the clinical evaluation involving trials in children with epilepsy.

Running in parallel to the clinical trials, we are collecting OPM-MEG data with concurrent 64-channel EEG. Recording OPM-MEG and EEG simultaneously is a crucial step towards a quantitative comparison between EEG and OPM-MEG, helping to inform clinical interpretation of the OPM-MEG signal. The overarching goal of the Young Epilepsy Diagnostic Suite is to offer world leading clinical neuroimaging technology alongside our existing diagnostic clinical encephalography (EEG) service which is all co-located in a comfortable, child-friendly environment for patients and their families.

We attended and contributed to the BIOMAG 2022 conference in Birmingham in August. This international conference has a focus on the measurement of magnetic signals from the human brain, as well as the development of new magnetic sensors including our novel OPM sensors. This biomagnetism community is highly productive and generates thousands of high-profile publications a year on cognitive neuroscience, clinical neuroscience and YE was cited in a number of abstracts and presentations throughout this 4-day conference. We will also be presenting our work in healthy adults at the BPNA 2023 conference in Edinburgh in January.

From a pure research perspective, this OPM-MEG technology will offer ground-breaking opportunities for research to continue pushing boundaries in medical sciences to further epilepsy investigations and other applications such as ADHD, autism and concussion. We are collaborating with a number of UK and international research teams exploring the numerous applications of this new technology. The Diagnostic Centre continues to also be available to hire during allocated times, for PHD students and other researchers to conduct their investigations.

Developing the wearable Optically Pumped (OPM) Magnetoencephalography (MEG) unit within a lightweight magnetically shielded room (Mu-Room)

It is widely recognised that wearable OPM-MEG will overtake conventional MEG, which has been inaccessible to many children to date. The YE OPM-MEG system is a more child friendly technology which will be crucial in evaluating the suitability of young patients for brain surgery. This system will allow children to be assessed for epilepsy surgery at an earlier age and will provide much more accurate data for brain surgery, resulting in better outcomes for patients and their families.

Following completion of clinical evaluation and regulatory approval of this inovative neuroimaging solution, OPM-MEG will become part of the current clinical offer at the Young Epilepsy Diagnostic Centre alongside our existing diagnostic EEG service.

The Mental Health Intervention for Children with Epilepsy (MICE) Project

Chief Investigators:
Professor Roz Shafran and Professor Helen Cross

Co-Investigators:
Dr. Sophie Bennett, Dr. Anna Coughtrey, Professor Sarah Byford, Professor Bruce Chorpita, Professor Caroline Dore (replaced by Dr. Hakim-Moulay Dehbi), Emma Dalrymple, Professor Peter Fonagy, Professor Tamsin Ford, Professor Isobel Heyman, Professor Rona Moss-Morris, Dr. Colin Reilly, Professor Jonathan Smith, Professor Terence Stephenson, Dr. Sophia Varadkar

Comprehensive Clinical Trials Unit (CCTU) MICE Team:
James Blackstone, Kashfia Chowdhury

MICE is an NIHR funded research study that is testing the efficacy of an evidence-based psychological treatment for young people with epilepsy and mental health problems. It began in October 2017. The aim of the project is to improve the treatment of mental health problems in young people with epilepsy.

Background
At least half of young people with epilepsy also have mental health problems such as depression, anxiety and behaviour difficulties. Many young people have more than one of these problems. These difficulties have a very significant negative impact on the quality of life of the young people with epilepsy and their families and often have a greater impact than the epileptic seizures.

Existing epilepsy services are separate from mental health services and mental health problems in young people with epilepsy may not be identified or if identified not treated as well as they could be.

Study Methodology
The MICE team worked with health professionals, parents, children and young people to modify the Modular Approach to Therapy for Children ('MATCH-ADTC') so the treatment meets the special mental health needs of young people with epilepsy.

This was done by developing an extra module specifically to help children and young people with anxiety, depression or behaviour problems in the context of epilepsy. The researchers recruited young people, aged 3-18, with epilepsy across sites in England, to complete the Strengths and Difficulties Questionnaire (SDQ) within the young person's epilepsy service.

Those who scored above the clinical threshold using an algorithm developed in our Programme Development Grant (PDG) were invited to complete the Development and Wellbeing Assessment ('DAWBA') online to establish if they met DSM-V diagnostic criteria for a common mental health disorder. Those that met diagnostic threshold were invited to participate in the Randomised Controlled Trial (RCT), until a sample of 334 had been recruited.

Half of the 334 children were randomly assigned to receive the modified version of MATCH-ADTC in addition to their usual care. The other half were randomly assigned to receive an enhanced version of their usual care. Therapists and their clinical supervisors were trained across sites to deliver MATCH.

The purpose of the RCT was to evaluate the clinical and cost-effectiveness of adding MATCH (with the additional epilepsy-specific module) to standard care for mental health disorders. The primary outcome measure was the SDQ, independently assessed six months post-randomisation. All analyses were conducted on an intention-to treat basis and blind to treatment assignment. Measures were repeated one year post-randomisation.

While receiving the MATCH intervention, 24 participants have been invited to take part in two in-depth interviews, one before their therapy starts and one six months later. The experiences of young participants and/or their carers, with regards to how their epilepsy and psychological and emotional wellbeing evolve over time is being explored.

The aim is to complement the quantitative measures to evaluate the intervention's effectiveness in terms of outcomes and processes. The interviews are being analysed longitudinally using Interpretative Phenomenological Analysis (IPA), a method widely used to understand individual experience in health psychology.

The public and patient involvement (PPI) research advisory group and epilepsy charities have ensured that the research has focussed on issues that matter most to them. Epilepsy Research UK (ERUK) have published a blog based on our PPI members' experiences of being involved in research and most importantly what they wish they would have known about caring for a child with epilepsy from the start.

Analysis

The two groups are being compared 6 and 12 months after the start of treatment to see if there are differences in terms of the mental and physical health of children and young people. We are also seeing if the new treatment provides good value for money and talking to the young people and families to understand their experience of the treatment and how it might be improved in the future.

Progress

Recruitment for the MICE study was concluded in February 2022. Overall, 334 participants were included in the trial. As of September 2022, data collection for the 6-month follow-up is complete and 317 people have completed 6-month assessments. A total of 94.91% of participants who were randomised have, therefore, provided information at this time point. 12-month follow-up data collection remains on track, with 278 people having completed the 12-month assessments so far.

MICE at Young Epilepsy

In addition to the main MICE trial a substudy at Young Epilepsy involves gathering pilot data regarding the possible utility of MICE in children and young people with epilepsy attending a specialist school for children with epilepsy. St. Piers School is a school for children with epilepsy and other neurodevelopmental difficulties. The substudy began in autumn 2022.

Current projects

Workstream 1: Understanding Childhood Epilepsies

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

Project Aim: Linking functional properties of SCN1A mis-sense mutations with their resultant phenotypes.
Investigators: Richard Rosch, Elaine Hughes, Kathleen Gorman, Colin Peters, Peter Ruben

02 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

03 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: To implement rapid trio WGS for all children, utilise electronic healthcare records and research databases to unite phenotypic and genomic data and 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)

04 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

05 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, Mathilde Ripart, Hannah Spitzer, MELD consortium, Helen Cross, Torsten Baldeweg, Konrad Adler-Wagstyl

06 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

07 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

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

Project Aim: To characterise the memory profile of children and young people and 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.
Investigators: Filipa Bastos, Faraneh Vargha-Khadem, Helen Cross, Jonathan Clayden, Sarah Buck

09 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

10 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.
Investigators: Nandaki Keshavan, Shamima Rahman

11 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

12 Novel network analysis of intracranial stereoelectroencephalography (SEEG)

Project Aim: To characterise 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

13 Multiscale modelling of epileptic networks from SEEG recordings

Project aim: Develop analysis techniques that allow us to understand how changes in brain networks in patients with drug-resistant epilepsy undergoing epilepsy surgery result in the patients' epilepsy.
Investigators: Richard Rosch, Ulrich Stoof, James Wilsenach, Aswin Chari, Martin Tisdall, Gerald Cooray, Karl Friston

14 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, Gemma Wilson

15 EAGLET: EEG vs aEEG to improve the diagnosis of neonataL seizures and Epilepsy - a Randomised Trial

Project Aim: EAGLET is a prospective multicentre randomised controlled trial to evaluate whether the combination of cEEG with aEEG is superior to aEEG in the real time evaluation and diagnosis of neonatal seizures and in reducing time to treatment.
CIs: Ronit Pressler and David Rowitch, Co-investigators: Topun Austin, Paul Clarke, Claudia Chetcuti-Ganado

16 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).
Investigators: David Carmichael, Frederike Moeller, David Sharp, Helen Cross, Mirja Steinbrenner, Martin Tisdall, Mark Richardson, Ines Violante, Rory Piper, Zachary Cohen

17 The Meerkat Project

Project Aim: The Meerkat project aims to develop non-contact monitoring for neonates in intensive care. A collaboration between the Departments of Engineering and Paediatrics at the University of Cambridge, as well as universities in the UK and Europe, the project will leverage expertise in image processing and machine learning to improve neonatal care.
CI: Kathy Beardsall, co-investigators: Alex Grafton, Peter Marschik, Ronit Pressler, Oliver Bonner

18 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 neurobehavioral phenotypes; identify risk factors for neurodevelopment and later intellectual disability.
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

19 Turning6 - A Clinical and Neurodevelopmental follow up of EpiPEG participants at 72 months

Project Aims:

- ✓ Characterise the neurodevelopmental (cognition, behaviour, sleep) status of children who had epilepsy in the first year of life
- ✓ Examine the association between initial neurodevelopmental and clinical assessment results and performance at follow-up
- ✓ Examine factors including epilepsy factors and neurodevelopmental status associated with current performance and changes in performance between initial assessment and follow-up

Investigators: Colin Reilly, Finbar O'Callaghan, Manuela Pisch, Colette Meades, Bhavna Sidphara, Amy Muggeridge, Lara Carr and Helen Cross.

20 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

21 The 7T Temporal Lobe Epilepsy Study

Project aim: The 7-TLE study is a prospective neuroimaging study that is using super-high-field (7-Tesla) MRI to investigate the network abnormalities in children and adults with temporal lobe epilepsy.
Investigators: Rory Piper, Shan-Shan Tang, Alexander Hammers, Atta Siddiqui, John Duncan, Martin Tisdall and David Carmichael, Torsten Baldeweg

22 Dynamic variability in the epileptic brain

Short Project aim: Investigate how epileptic brain activity changes over time at multiple scales (seconds, minutes, days), in order to understand how our diagnosis and interventions can be targeted appropriately.
Investigators: Richard Rosch, Jamie Norris, Stuart Smith, Martin Tisdall, Gerald Cooray, Karl Friston

Current projects

Workstream 2: Outstanding Treatment

23 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.
Investigators: Martin Tisdall, J Helen Cross, Rory Piper, Marios Kaliakatsos, Hakim-Moulay Debhi, Harutomo Hasegawa, Elaine Hughes, John Fleming, Richard Selway, Ioannis Stavropoulos, Antonio Valentin, Tim Denison

24 Wearable magnetoencephalography (MEG) at Young Epilepsy

Project Aim: To develop a new Epilepsy Diagnostic Suite at Young Epilepsy centered around the installation and evaluation of the OPM-MEG technology.
Investigators: Gareth Barnes, Richard Bowtell, Matthew Brookes, Helen Cross, Tim Tierney, Torsten Baldeweg, Rosemarie Pardington, Kelly St Pier, Zelekha Seedat, Konrad Wagstyl, Umesh Vivekananda, David Woolger.

25 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, Zelekha Seedat, Rosemarie Pardington

26 Clinical deployment of wearable functional neuroimaging

Project Aim: This project aims to fast-track regulatory approval of a new OPM-MEG system, making it the first, and only OPM-MEG system in the world to be approved for human use.
Investigators: Elena Boto, Prof. Matthew Brookes, Eliot Dawson, Freya Jackson, Rosemarie Pardington, Kelly St. Pier, Zelekha Seedat, David Woolger

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

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

Project Aims:

- ✓ To create and characterise a patient-derived induced pluripotent stem cell (iPSC) organoid model Epilepsy of Infancy with Migrating Focal Seizures (EIMFS).
- ✓ To investigate the neuronal phenotype of EIMFS at a cellular and network level.
- ✓ To investigate the impact of novel therapies.

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

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

Project Aim: To 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

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

Project Aim: To provide better informed diagnosis of memory impairments in children with epilepsy and predict outcome after surgery in the temporal lobe, using the Pair Test.
Investigators: Sarah Buck, Torsten Baldeweg, Filipa Bastos, Faraneh Vargha-Khadem

31 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 performance in the lab and in vivo of an improved pyridoxal 5'-phosphate (PLP) option 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

32 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

Current projects

Workstream 3: Outstanding Support

33 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, Lara Carr, Samantha Chan, Amy McTague, Helen Cross

34 Epilepsy Pathway Innovation in Africa (EPInA)

Project Aims:

- Societal change: ensure an enduring, positive change by improving public awareness and reducing the stigma experienced by people with epilepsy in sub-Saharan Africa.
- Diagnose: To improve the rate of accurate diagnosis of epilepsy by primary health care workers with app-based technologies.
- Treatment: increase the adherence to medication using text messaging.
- 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, Arjune Sen, Helen Cross, Josemir Sander, Albert Akpalu, Patrick Adjei, Symon Kariuki, Damazo Kadengye, Gershim Asiki, Thomas Kwasa, Bruno Mmbando, Dan Bhwana, Tarun Dua, William Matuja, Sloan Mahone, David McDaid, Richard Walker

35 European Reference Network on rare and complex epilepsies (EpiCARE)

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.
Project Aims:

- 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.

36 Prevention of Epilepsy by reducing Neonatal Encephalopathy (PREVENT) study

Project Aim: To examine a care bundle approach to improve the maternal care around delivery to reduce number of babies sustaining serious birth related brain injury and epilepsy.
Investigators: Sudhin Thayyil, Helen Cross, Ronit Pressler et al.

37 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, Steve Rose, Karen Ray

38 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 can 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 MossMorris, Colin Reilly, Jonathan A Smith, Terence Stephenson, Sophia Varadka

39 Physical Activity in Childhood Epilepsy (PACE)

Project Aims:
- ✓ 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.
- ✓ To better understand factors which may be associated with physical activity, including structured exercise/sports participation, in children with epilepsy.
- ✓ Identify the barriers to engagement in physical activity for young people with epilepsy.
- ✓ Explore the feasibility of implementing an intervention to improve levels of physical activity in children with epilepsy

Investigators: Colin Reilly, Joan Idowu, Natalie Pearson, Colette Meades, Lauren Sherar, Monica Lakhanpaul, Kerry Robinson, Amy Muggeridge, and Helen Cross.

40 Epilepsy in Schools: Developing web-based training for educational staff who support children with epilepsy in mainstream schools

Project Aims: The overall aim of this project is to develop, pilot and assess the feasibility of web-based interventions for staff currently supporting children with epilepsy. The specific aims of this project are to:
- ✓ Co-develop web-based training for teachers and other educational staff who support children with epilepsy in mainstream schools.
- ✓ Conduct a pilot study of the developed web-training focusing on the knowledge and attitudes of e ducational staff in mainstream schools before and after the training.

Investigators: Colin Reilly, Joan Idowu, Sophie Bennett and Helen Cross

Completed projects

Workstream 2 – Outstanding Treatments

41 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

42 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

Workstream 3 – Outstanding Support

43 Autism spectrum diagnosis (ASD) and epilepsy

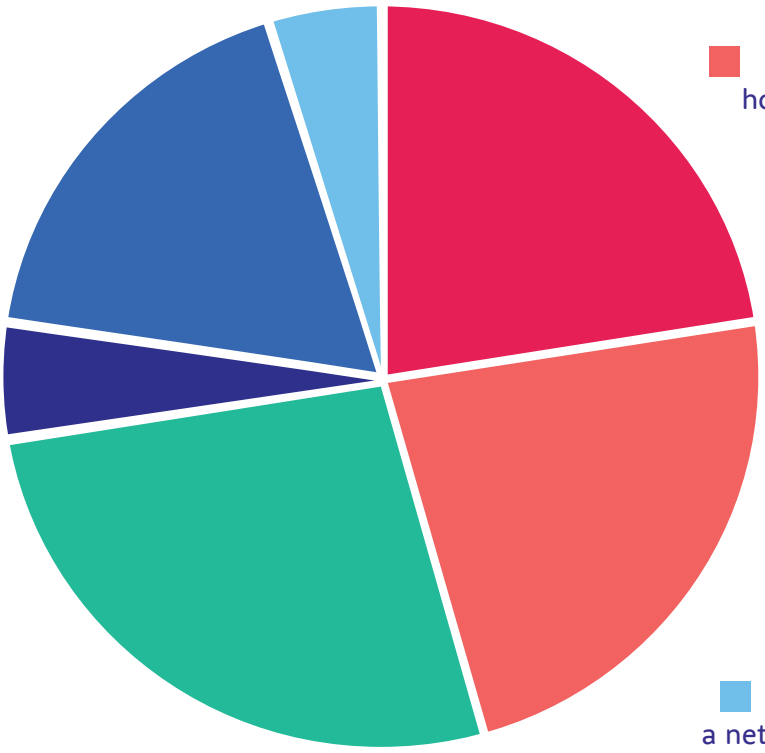
Project Aim: The assessment of autism for children with complex epilepsy poses many challenges; from fluctuating profiles to diagnostic overshadowing and atypical presentations. This project reviews the issues involved by drawing on more than 20 years' experience of neurodevelopmental assessment of children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

Impact of our research

Young Epilepsy

Current & Past Impact

Between **July 2021** and **June 2022** the programme portfolio consisted of **25%, 21%, 28%, 6%, 16%** and **4%** contribute to each goal respectively



25% of projects contributed to understanding the medical causes of epilepsy

21% of projects contributed to understanding how epilepsy affects development and behaviour

28% of projects contributed to improving diagnosis and treatment to determine the benefits of early intervention in improving long-term outcomes

6% of projects contributed to understanding the barriers to learning and determining the benefits of educational interventions

16% of projects contributed to making life better for children and families and making support systems more effective

4% of projects contributed to developing a network of multidisciplinary professionals to strengthen our research and shape the education of future practitioners

Year on year most of our projects address

Workstream 1
Understanding Childhood Epilepsies

Workstream 2
Outstanding Treatments

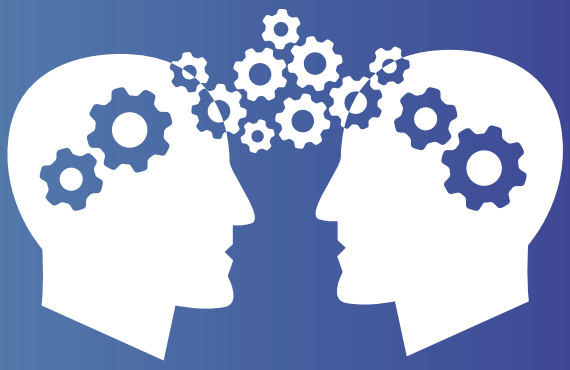
But we are growing our work in

Workstream 3
Outstanding Services

89 published
peer-reviewed items of primary research

25 reviews and a further chapter in
1 book

Specialist PPI network for childhood epilepsy with **140 members**

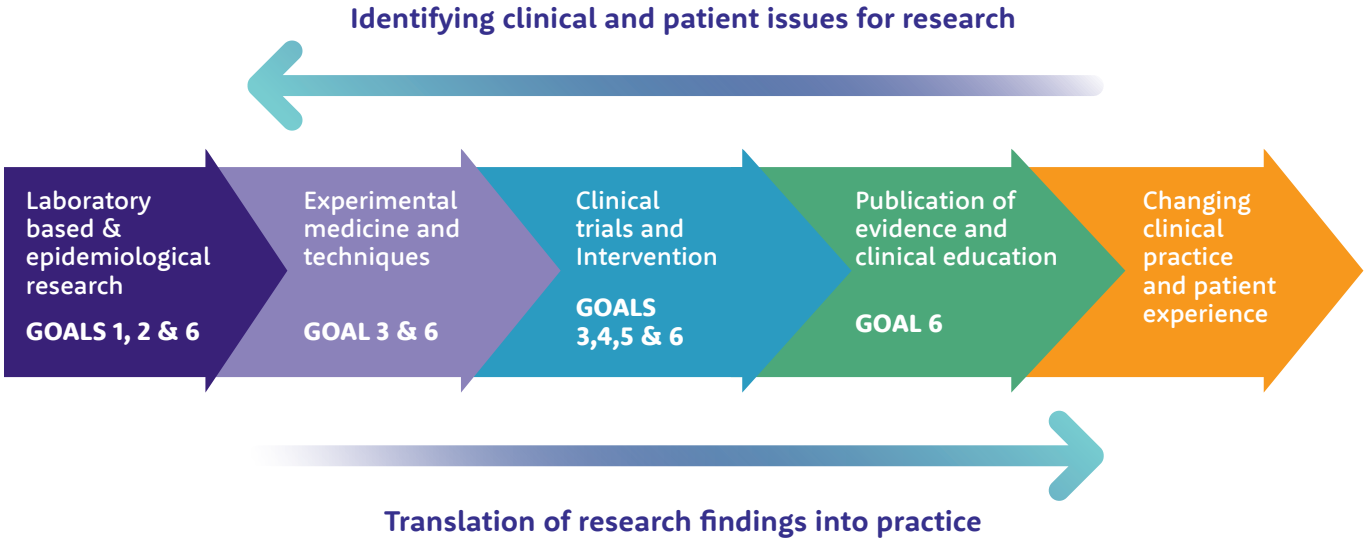


Largest Research Retreat to date – with **157 researchers** coming together to share knowledge and discuss projects

Meeting our research goals

Our research originates from the identification of clinical problems and feedback from patients. Ideas are then developed into project plans for which funding is sought and an expert team assembled.

The end result is to publish results as original research which has stood up to the review and critique of independent experts – a process known as peer review. This ensures robust evidence on which we can implement changes and/or conduct further research.



The number of research projects within the partnership was slightly lower than last year (Figure 1) which is likely to reflect the lasting impact of covid. We track the contribution of active projects to the three workstreams and six goals (Figure 2). We are historically strongest in addressing Workstream 1 and 2 – Understanding Childhood Epilepsies and Outstanding Treatments (Figure 3). Given our clinical origins this is unsurprising, but we continue to encourage research under Workstream 3, Outstanding Support, through educational, psychosocial, and service-based research.

Figure 1: Number of active research projects per year

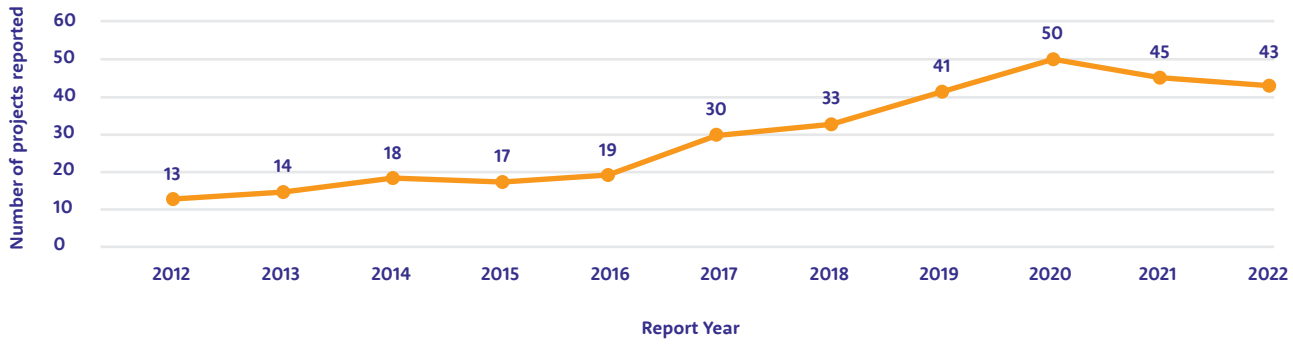


Figure 2: Number of active projects contributing to each goal

Many projects contribute to more than one workstream and/or goal

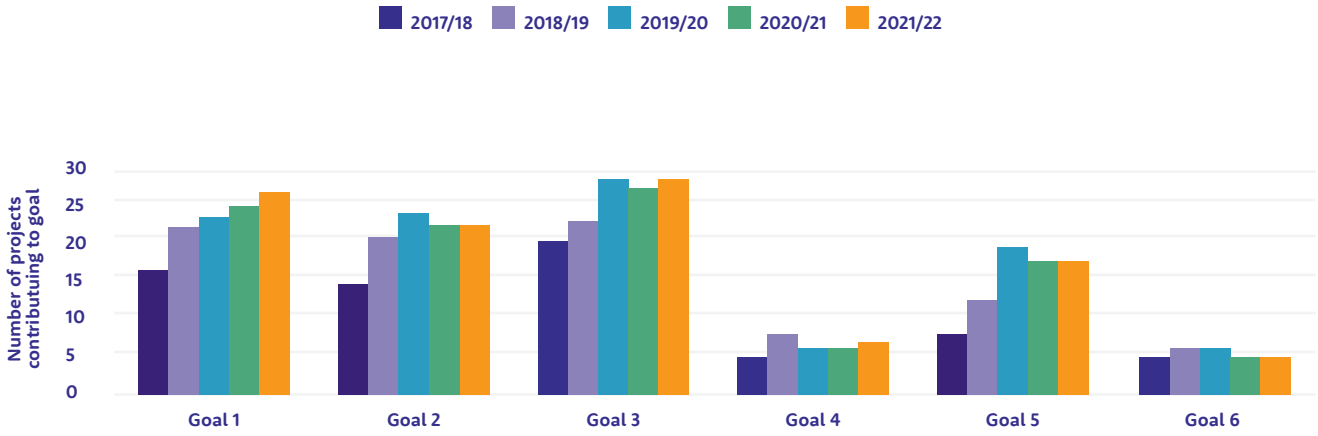
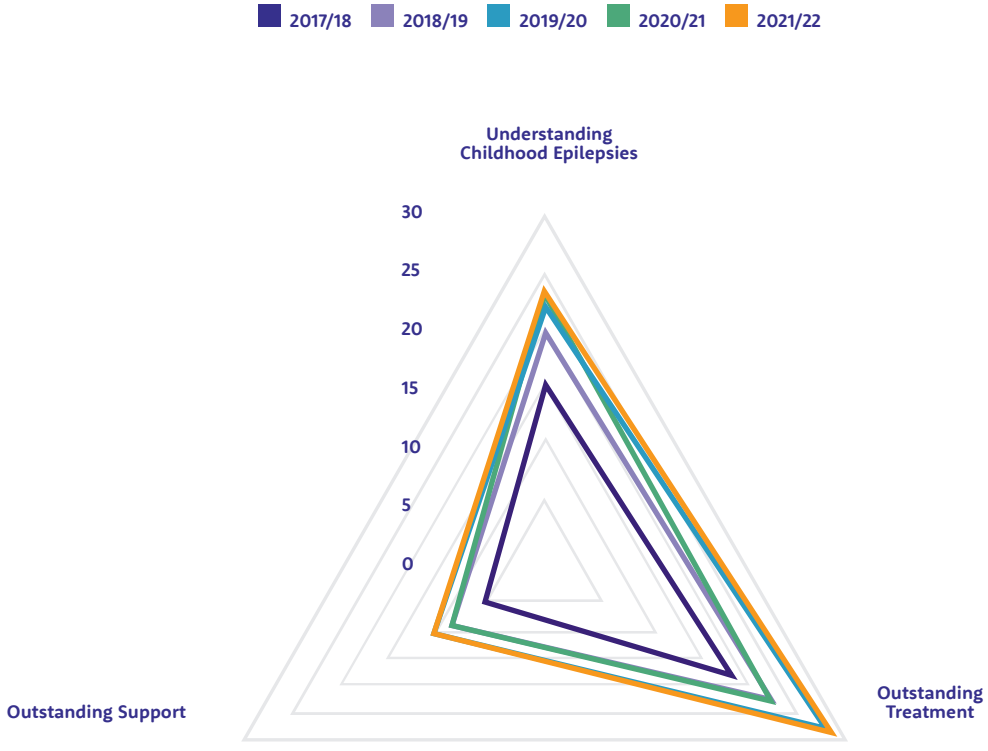


Figure 3: The relative work under each workstream year by year

(Number of projects contributing to each workstream annually, weighted by number of goals per workstream)



The strength of the evidence we publish

Over the past 12 years, our research programme has grown from having just 4 Principal Investigators (the leaders of research units and laboratories, often Professors), to having 33 Principal Investigators supervising 18 PhD students and working alongside an additional 37 international collaborating researchers (Figure 4).

This growth is reflected in the number of research projects and publications produced across the unit each year (Figure 5). 2022 has seen a rise in the number of publications of both original research and reviews or communications of expert opinion (Figure 5).

Figure 4: Annual growth of the Research Unit Network

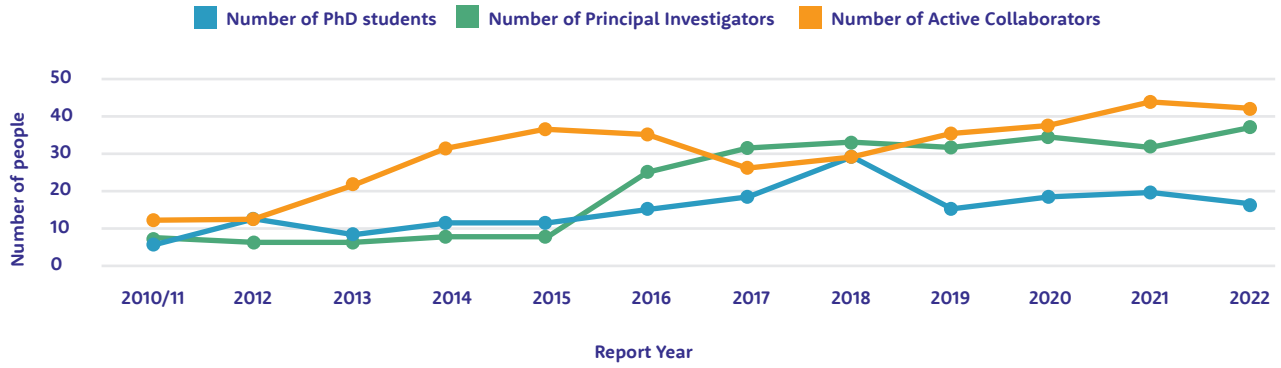
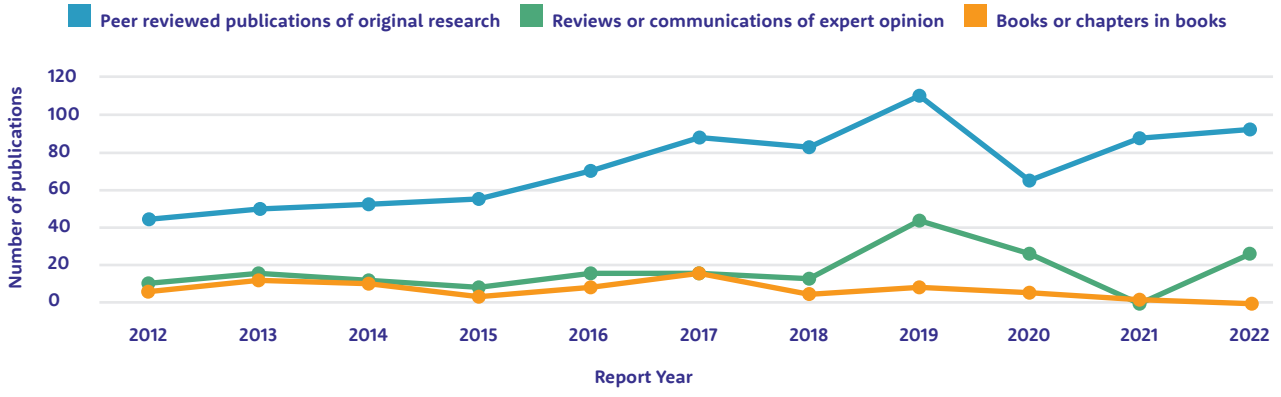
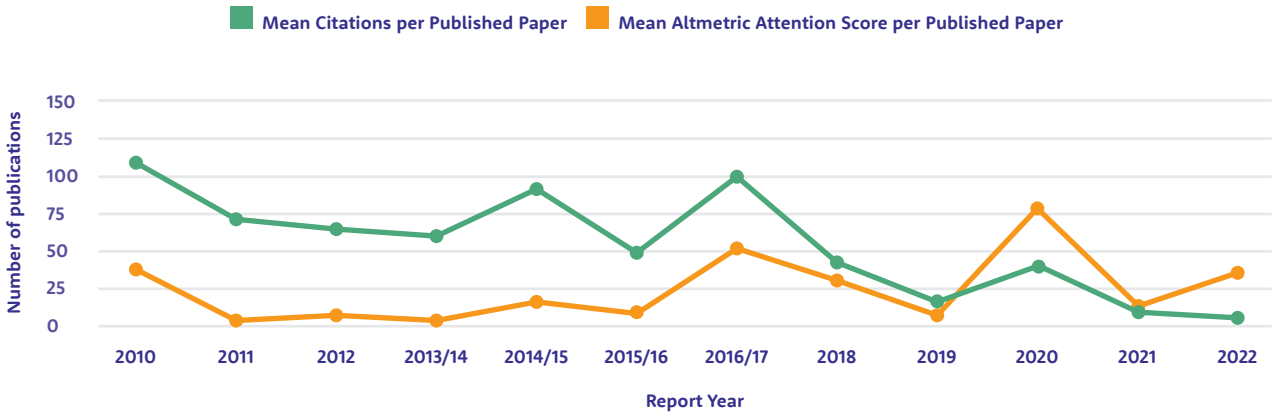


Figure 5: Number of research publications produced per year



We track the progress and influence of these research publications over time using two metrics – citations and an altmetric attention score (Figure 6). A citation is counted when an individual research paper is referred to in a later research publication as a source of evidence. The altmetric attention score that we use is produced by an independent bibliographic data organisation, Dimensions.ai, and is calculated based on the public attention that an individual publication has received across news articles, social platforms, and policy documents.

Figure 6: Impact of research publications



These data reveal to us that as well as producing more publications this year (115), compared to last year (90), our publications have also made more immediate impact. Whilst this years' publications have been cited less times, this can be expected as the longer a publication is available, the more citations you can expect it to accrue. There is, however, a clear increase in the mean altmetric attention score, which is 12.24 for last year, and 32.75 for this year (Figure 6). To put this in context, last year, no papers had an altmetric attention score of > 100. This year there are 5 papers with an altmetric score > 100, meaning that they were in the top 5% of all the research papers tracked by Dimensions.ai, with one publication receiving an altmetric score > 1,000. This difference is likely due to the increasing access to research and increasing ability to track this access, but in these extreme cases, it is perhaps due to links with current global interests, such as Genomics.

Topics of the 2021/22 high impact papers cover:

- The application of whole genome sequencing to better understand and treat rare diseases in the NHS
- The feasibility of a new anti-seizure medication for drug resistance epilepsy
- The efficacy of hypothermia for treating neonatal encephalopathy in low-income and middle-income countries
- The safety, feasibility, and outcomes of epilepsy surgery in infants up to 3 months of age
- Guidance on Dravet syndrome from infant to adult care
- The safety and efficacy of a new treatment for patients with CDKL5 deficiency disorder

Importance of PPI

How do we ensure research is developed to reflect the real needs of clinicians and patients?

Our Research collaboration with GOSH and ICH ensures that the focus of our research is developed from clinical needs. As part of this, we consider the views of all individuals who are affected by research. This not only includes the researchers and consultants, but also nurses, support workers, caregivers, parents and crucially the young people themselves. The practice of involving patients in research is called Patient and Public Involvement (PPI) and it is critical in the development of practical, relevant research. The E-CURe (Epilepsy Carers Uniting with Researchers) network exists to strengthen the voice of children and young people with epilepsy in our research. We currently have 140 members but would welcome more. Please see page 44 for details on how to get involved.

“

Research is such an integral part of our nursing practice; it allows us to ensure we continually provide “best practice” to any child or young person under our care. Research empowers nurses to apply their initiatives to clinical and academic excellence, whilst utilising high-quality evidence in order to obtain improved health outcomes for our patients.

Epilepsy Nurse Consultant

“

Taking part in research projects is a valuable way of ‘giving something back’; sharing our experience to provide hard evidence to inform and improve policy and practice.

Parent of a child with epilepsy

“

Research helps us understand the support that children with epilepsy need to thrive. We can then use that evidence to influence decision making and improve children’s lives.

Senior Policy and Advocacy manager

Top 10 Epilepsy Research Priorities

In partnership with Epilepsy Research UK, Young Epilepsy were proud to be part of the UK Epilepsy Priority Setting Partnership (PSP).

The UK PSP were tasked with investigating the health priorities of people with Epilepsy. A survey, completed by 2,014 individuals, identified approximately 5,418 research priorities. From these 110 research questions were drafted, of which 57 were moved forward for prioritisation. 25 of these were shortlisted for discussion at the UK Epilepsy PSP workshop, with the aim of selecting the top 10 priorities for Epilepsy research.

The selected Top 10 Epilepsy Research Priorities were:

01	What are the causes and contributing factors of epilepsy-related deaths, including Sudden Unexpected Death in Epilepsy (SUDEP), and how can these deaths be prevented?
02	What underlying mechanisms cause epilepsy in children and adults?
03	What impact do epilepsy, seizures and anti-seizure medication (ASMs) have on brain health – including, cognition, memory, learning, behaviour, and mental health?
04	How does epilepsy and epilepsy treatment impact neurodevelopment, and can this be managed or prevented?
05	How can targeted, personalised medicine, such as gene therapy, be used to treat and/or prevent epilepsy?
06	How can tools, devices and biological markers be used to accurately predict and prevent seizures and the onset of epilepsy?
07	How do hormonal changes in women throughout the lifespan (e.g., puberty, pregnancy, menopause) impact epilepsy, and how can this impact be addressed?
08	How can quality of life be improved for people with epilepsy, their family and carers, including those bereaved by epilepsy?
09	What causes drug-resistant (refractory) epilepsy, and how can it be best treated?
10	How can big data analysis, through artificial intelligence (AI) and machine learning, aid the diagnosis and management of epilepsy?

Creating clearly defined research priorities with input from the entire epilepsy community, allows future research to concentrate on the research areas that matter most. Young Epilepsy will, therefore, be carefully considering these in the ongoing development of our research programme.

Retreat 2022

Young Epilepsy Paediatric Epilepsy Research Retreat 2022

The Young Epilepsy Research Retreat, hosted by The Prince of Wales's Chair of Childhood Epilepsy, is an annual gathering of researchers and collaborators across our research unit. This meeting gives researchers the opportunity to share ongoing and/or completed projects, as well as discuss and explore future directions of research. The uniqueness of the event enables researchers, to engage with a rich and diverse network of colleagues from a wide range of backgrounds and thereby benefit from each other's experience and expertise.

Last year, for the second consecutive year, we had to change plans at the last minute and move to holding the event virtually instead of in person. Nonetheless, the event was a huge success and resulted in the largest attendance yet with over 157 participants registering.

Our Moderator

Professor Elaine Wirrell

2022 marked our 12th Retreat and Professor Cross opened and presided over the event for the two days. Alongside Professor Cross we were delighted to welcome as our Moderator, Professor Elaine Wirral. Professor Wirrell is the Director of Paediatric Epilepsy, Professor of Neurology and Program Director of Child and Adolescent Neurology at the Mayo Clinic in Rochester, Minnesota. The two days were packed with back-to-back presentations from across the wide portfolio of our research projects. There was an excellent array of presentations and the discussions at the end of each presentation gave investigators the opportunity to receive comments and feedback from fellow researchers and principal investigators representing many different fields.

So, whilst our 2022 retreat was not in the format we originally envisaged, the feedback received from participants was that they found this unique environment and network just as informative and motivating as ever.

Research Funding

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

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

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 due to unforeseen circumstances.

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 out work.

Action Medical Research
Anna Mueller Grocholski Foundation
Autistica
Brain Tumour Charity
BRC Cambridge
Cancer Research UK
Child Health Research Trust
Children with Cancer UK
D'Oyly Carte Charitable Trust
Epilepsy Research UK
Ethypharm
European Association of Neurosurgical Societies
European Commission
Evelyn Trust
Freya Foundation
The George E Neville Foundation
Google Cloud Platform Research Credit Award
GOSH NIHR BRC
GOSH-CC
Great Ormond Street Children's Charity
GW Pharmaceuticals
The Hospital Saturday Fund
Human Brain Project
Innovate UK
James Lewis Foundation
Medical Research Council Clinician Scientist Fellowship
Michael Cornish Charitable Trust
National Institute of Health Research (NIHR)
Nevilles PLC
NIHR GOSH Biomedical Research Centre
NIHR GOSH BRC PPIE Small Grants
Novartis
Nutricia
The Oakdale Trust
Oakgrove Foundation
Rosetree's Trust
Sir Henry Wellcome Fellowship
UCB BioPharma
UCL Child Health Research CIO Strategic Initiatives Pump-Priming Fund
Veriton Pharma
Vitaflo
Waterloo Foundation
Wellcome Research Enrichment - Public Engagement
Wolfson Foundation
Wyfold Charity Trust
Young Epilepsy

Researchers

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

Principal Investigators

Professor Helen Cross OBE The Prince of Wales's Chair of Childhood Epilepsy and Director UCL GOS - ICH

Young Epilepsy; UCL GOS - Institute of Child Health and Great Ormond Street Hospital for Children

Additional Roles:

Elected President (2021-2025) International League Against Epilepsy (ILAE)

Chair Research Council - European Reference Network for Rare and Complex Epilepsies (EpiCARE)

President - Epilepsy Research UK

Clinical Advisor - Children's Epilepsy Surgery Service (CESS)

Clinical Advisor - Epilepsy Action

Chair of Medical Board - Hope for Hypothalamic Hamartoma

Chair of Medical Board - Matthew's Friends

Chair of the Medical Board - Dravet UK

Professor Torsten Baldeweg Professor of Developmental Cognitive Neuroscience, Head of UCL GOS - ICH Developmental Neurosciences Programme

UCL GOS - Institute of Child Health

Additional Roles:

External Expert to the French Higher Research Council - University of Amien

Chairman of Exam Board, MSc Paediatric Neuropsychology - University College London

Module organiser and lecturer, MSc Paediatric Neuropsychology - University College London

Editor (Until December 2019) - Journal of Developmental Cognitive Neuroscience

Professor Gareth Barnes Head of Magnetoencephalography

Wellcome Centre for Neuroimaging

Professor Chris Clark Professor of Imaging and Biophysics, Head of UCL GOS – ICH Developmental Imaging and Biophysics Section

UCL GOS - Institute of Child Health

Professor Michelle De Haan Professor in Infant and Child Development

UUCL GOS - Institute of Child Health and Great Ormond Street Hospital for Children

Additional Roles:

Affiliated Scientist - British Autism Study of Infant Siblings Network

Course Speaker, MSc in Cognitive Neuroscience, Translational Research Module - University College London

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

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

Membership of Steering Committees - Centre for Developmental Cognitive Neuroscience UCL

Professor Isobel Heyman CConsultant Child and Adolescent Psychiatrist

UCL GOS - Institute of Child Health and Great Ormond Street Hospital for Children

Professor Tom Jacques Professor of Paediatric Neuropathology

UCL GOS - Institute of Child Health and Great Ormond Street Hospital for Children

Additional Roles:

Editor in Chief - Journal of Neuropathology and Applied Neurobiology

Lead - Paediatric Tumour Genomics England Clinical Interpretation Partnership (GeCIP)

Pathology representative on the Central Nervous System subgroup - National Cancer Research Institute (NCRI) Children's Cancer and Leukaemia Clinical Studies Group

Professor Manju Kurian NIHR Research Professor and Professor of Neurogenetics

UCL GOS - Institute of Child Health

Additional Roles:

Chair - BPNA Research Committee

Member of the Scientific Advisory Committee - Epilepsy Research UK

Professor Finbar O'Callaghan Professor of Paediatric Neuroscience, Head of UCL GOS - ICH Clinical Neurosciences Section

UCL GOS - Institute of Child Health and Great Ormond Street Hospital for Children

Additional Roles:

President - British Paediatric Neurology Association (BPNA)

Secretary and Board Member- European Paediatric Neurology Society (EPNS)

Professor Shamima Rahman Professor of Paediatric Metabolic Medicine

UCL GOS - Institute of Child Health and Great Ormond Street Hospital for Children

Additional Roles:

Adviser to Statutory Approvals Committee - Human Fertilisation and Embryology Authority

Contributor, MSc courses - UCL GOS ICH, UCL Division of Biosciences, UCL Institute of Cardiovascular Science, UCL QS Institute of Neurology and Genomics England

Editor-in-Chief - Journal of Inherited Metabolic Disease

Council Member, Society for the Study of Inborn Errors of Metabolism (SSIEM)

Member, Medical Research Council Clinical Training Panel

Assessment Advisor for Inherited Metabolic Medicine - Royal College of Paediatrics and Child Health

Coordinator of Mitochondrial Subnetwork - Metabolic European Reference Network (MetabERN)

Lead of Mitochondrial Subdomain - Genomics England Clinical Interpretation Partnership (GeCIP)

Member of the Medical Advisory Board - Freya Foundation

Member of the Medical Advisory Board - Lily Foundation
Member of the Scientific Advisory Board – Khondrion
Member of the Steering Committee - Collaborative International Leigh Syndrome Task Force
Member of the Steering Group - Rare Mitochondrial Disorders Priority Setting Partnership, James Lind Alliance and Genetic Alliance UK
Senior Editor - Annals of Human Genetics

Professor Rosamund Shafran Chair in Translational Psychology

UCL GOS - Institute of Child Health and Great Ormond Street Hospital for Children

Professor Rod Scott Professor of Paediatric Neuroscience

UCL GOS - Institute of Child Health; Great Ormond Street Hospital for Children and University of Vermont, USA

Additional Roles:
Associate Editor - BMC Neurology
Member of the Basic Science Committee - American Epilepsy Society
Member of the Editorial Board - Epilepsia, Journal of the ILAE
Member of the Workshop on Neurobiology of Epilepsy (WONOEP) - ILAE Neurobiology Commission Conference
Reviewer - National Institute of Health Research (NIHR)

Professor Faraneh Vargha-Khadem Professor of Developmental Cognitive Neuroscience, Head of UCL GOS - ICH Cognitive neurosciences Section

UCL GOS - Institute of Child Health and Great Ormond Street Hospital for Children

Additional Roles:
Member of the Scientific Advisory Board - Max Planck Society

Dr Patricia Atkinson Consultant Community Paediatrician

Sussex Community NHS Foundation Trust

Dr Sarah Aylett Consultant Paediatric Neurologist

Great Ormond Street Hospital for Children

Additional Roles:
Caldicott Guardian Postgraduate Teaching - ICH-UCL

Dr Stewart Boyd Consultant Clinical Neurophysiologist

UCL GOS - Institute of Child Health and Great Ormond Street Hospital for Children

Dr David Carmichael Honorary Reader in Neuroimaging and Biophysics, Reader in Magnetic Resonance Physics

UCL GOS - Institute of Child Health and Wellcome / EPSRC Centre for Medical Engineering, Kings College London

Additional Roles:
Member of the MRI expert task force - E-PILEPSY E-PROCESSING

Dr Maria Clark Consultant Paediatric Neurologist

UCL GOS - Institute of Child Health and Great Ormond Street Hospital for Children

Dr Felice D'Arco Consultant Paediatric Neuroradiologist

Great Ormond Street Hospital for Children

Additional Roles:
Chair - GOSH MRI Safety Group
Honorary Senior Lecturer - UCL GOS - ICH and UCL Institute of Neurology
Lecturer - European Course of Paediatric Neuroradiology
Member - European Network for Brain Malformations
Member of the Editorial Board - Journal of the European Society of Neuroradiology

Dr Krishna Das Consultant Paediatric Neurologist

Young Epilepsy and Great Ormond Street Hospital for Children

Dr Christin Eltze Consultant Paediatric Neurologist

UCL GOS - Institute of Child Health and Great Ormond Street Hospital for Children

Dr Marios Kaliakatsos Paediatric Neurologist

Great Ormond Street Hospital for Children

Dr Amy McTague MRC Clinician Scientist Fellow and Honorary Consultant Paediatric Neurologist

UCL GOS - Institute of Child Health

Additional Roles:
Member of work package 2, Laboratory Diagnostics - EpiCARE
Scientific Adviser - Apollo London translational medicine network
Scientific Adviser - KCNT1 Epilepsy Foundation

Professor Philippa Mills Associate Professor of Inherited Paediatric Metabolic Disease

UCL GOS - Institute of Child Health

Additional Roles:
Course Contributor - UCL GOS - ICH
Treasurer - Society of the Study of Inborn Errors of Metabolism

Dr Friederike Moeller Consultant Clinical Neurophysiologist

UCL GOS - Institute of Child Health and Great Ormond Street Hospital for Children

Dr Ronit Pressler Consultant in Clinical Neurophysiology and Clinical Lead of GOSH Telemetry Unit, Honorary Associate Professor in Clinical Neuroscience

UCL GOS - Institute of Child Health and Great Ormond Street Hospital for Children

Additional Roles:
Council Member and Honorary secretary of the BSCN (British Society for Clinical Neurophysiology)
Council member of the ILAE UK Branch
Course Director, EEG in the First Year of Life teaching course – ILAE
Member of the Editorial Board of European Journal of Paediatric Neurology and Neurophysiology Clinique Associated Editor for Epilepsia Open
Web based teaching: e-brain and VIREPA (paediatric EEG)
Member of the Medical Therapy in Children Task Force – ILAE

Dr Colin Reilly Educational Psychologist

Young Epilepsy and UCL GOS - Institute of Child Health

Additional Roles:
Chair Paediatric Psychiatric Issues Committee – ILAE
Member ILAE research Advocacy Task Force
Member EpiCARE working group - Neuropsychology in CSWS
Member of the Editorial Board - Epilpesy & Behavior

Dr Robert Robinson Consultant Paediatric Neurologist

UCL GOS - Institute of Child Health and Great Ormond Street Hospital for Children

Dr Richard Rosch Sir Henry Wellcome Postdoctoral Fellow

King's College London, University of Pennsylvania

Additional Roles:
Clinical Fellow - Great Ormond Street Hospital for Children

Dr Richard Scott Consultant in Clinical Genetics

UCL GOS - Institute of Child Health and Great Ormond Street Hospital for Children

Dr Rachel Thornton Consultant in Neurophysiology

Addenbrookes Hospital, Cambridge

Mr Martin Tisdall Consultant Paediatric Neurosurgeon and Honorary Associate Professor

UCL GOS - Institute of Child Health; Great Ormond Street Hospital for Children and National Hospital for Neurology and Neurosurgery

Additional Roles:
Honorary Senior Lecturer - UCL GOS - ICH and UCL Institute of Neurology

Dr Sophia Varadkar Consultant Paediatric Neurologist

UCL GOS - Institute of Child Health and Great Ormond Street Hospital for Children

Additional Roles:
Chair - North Thames Neurosciences Network for the Neurosurgical Child
Chair of the Steering Committee - BPNA Paediatric Epilepsy Training Programme
Co-Chair - UK Paediatric Vagus Nerve Stimulation (VNS) expert group
Council Member - ILAE British Chapter
Medical Advisor - Children's Trust, Tadworth
Medical Advisor and Trustee - Ring 20 Research and Support UK
Member - RCPCH Epilepsy Programme Board

Research Staff

Sophie Adler-Wagstyl Research Associate

Konrad Adler-Wagstyl Research Associate

Katy Barwick Genetics Associate - EpiPEG

Anne Brown Research Administrator

Lara Carr Research Coordinator, Young Epilepsy (From *October 2022)*

Emma Dalrymple PPI Lead – MICE

Emma Johnson Assistant Research Psychologist - WINS

Louise Jones
Research Administrator

Laura Lyons Trial Manager - KIWE

Elaina Maldonado Research Associate

Amy Muggeridge Research Manager, Young Epilepsy *(Until November 2022)*

Liz Neal Honorary Research Dietitian

Nicola Openshaw-Lawrence EpiCARE ERN Operational Helpdesk Coordinator and Data Manager

Rosemarie Pardington
Director of Health, Research & Compliance, Young Epilepsy

Manuela Pisch Research Associate

Natasha Schoeler Senior Research Dietitian

Tom Stone Research Associate

PhD Students

Fatimah Almousawi *Pathways and mechanisms affected in individuals with vitamin B6-responsive epilepsy*

Filipa Bastos *Memory outcome after temporal lobectomy*

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

Dominic Burrows *Brain-wide abnormal dynamics during epileptic seizures at single cell resolution*

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

Rosie Coleman *Functional and structural plasticity after epilepsy surgery*

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

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

Nandaki Keshavan *Gene Therapy for Deoxyguanosine Kinase Deficiency*

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

Mei-Ju Lai *Investigating cellular identity in childhood epilepsy*

Adeline Nogh *Molecular Genetic Investigation of Landau-Kleffner Syndrome*

Jamie Norris *Variability in epilpetiform activity and the brain's response to stimulation*

Jack O'Brien *Cairney Novel models of autoimmune epilepsies*

Rory Piper *Network-guided epilepsy surgery for children*

Izabella Smolicz *The biology of paediatric central nervous system tumours at post-mortem*

Ulrich Stoof *Multiscale modelling of epileptic networks from SEEG recordings*

Aitkaterini Vezyroglou *Deep phenotyping of alternating hemiplegia in childhood*

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Young Epilepsy

Research Publications

Primary Research

1. Amin, S., Monaghan, M., Aledo-Serrano, A., Bahi-Buisson, N., Chin, R. F., Clarke, A. J., ... & Benke, T. A. (2022). **International consensus recommendations for the assessment and management of individuals with CDKL5 deficiency disorder**. *Frontiers in Neurology*, 826. DOI: 10.3389/fneur.2022.874695.

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Young Epilepsy

Epilepsy in childhood:
Carers
Uniting with
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...join the conversation"

We Need You

to help us strengthen the voice of children and young people with epilepsy and their families in research.

Following the launch of the first network of young people with epilepsy and their parents, whose sole purpose is to consult on the development of research projects across our partnership, we are keen to continue to grow. If you would like your experiences to ensure epilepsy research is answering the right questions in the right way, please get in contact and sign up to the E-CURe network by scanning the QR code below.

Glossary

Animal models
A non-human species used in medical research because it can mimic aspects of a disease found in humans

Assays
An investigative procedure in laboratory medicine for measuring the presence, amount, or functional activity of a target entity

Biophysical
Methods used in physics to study biological phenomena

Calcium imaging
A technique to optically measure the calcium levels in a cell or tissue

Chronic
Long term

Co-morbidities
Medical conditions that are simultaneously present in a patient

Computational modelling
A mathematical model to study the behaviour of a complex system by computer simulation

Copy number variants
When the number of copies of a particular gene varies between individuals

Cortical
Relating to the outer layer of the uppermost part of the brain

Cox regression
A statistical test

Cryogenic
The production of, and behaviour of, materials at very low temperature

Dietetics
Branch of knowledge concerned with the diet and its effects on health

Electroencephalography (EEG)
A test that detects electrical activity in your brain using small electrodes attached to your scalp. Your brain cells communicate via electrical impulses and activity shows up as wavy lines on an EEG recording

Epidemiological
The branch of medicine which deals with the incidence, distribution, and control of diseases

Epilepsy-dyskinesia
Disorders characterised by recurrent episodes of abnormal movements, co-occurring with epilepsy or other episodic neurological symptoms

Epileptiform discharges
Seen on an EEG, meaning spikes, polyspikes, sharp waves, or spike and slow-wave complexes without observed clinical seizures

Epileptogenesis
The gradual process by which a normal brain develops epilepsy or, the area of epileptogenesis is the area of the brain which causes a patient's epilepsy

Functional validation (of disease-causing genes)
The process of determining whether a particular genetic mutation is causing a disease

Genomics
The study of whole genomes of organisms, and incorporates elements from genetics

Genotype
An organism's set of heritable genes that can be passed down from parents to offspring

Health economics
The study and understanding of how society allocates resources to healthcare and the resource needs of specific healthcare issues

Hemiparesis
Weakness of one entire side of the body

Immunofluorescence
A method in biology that relies on the use of antibodies chemically labelled with fluorescent dyes to visualise molecules under a light microscope

Intractable
Untreatable, hard to manage

Language lateralisation
The phenomenon in which one hemisphere (typically the left) shows greater involvement in language functions than the other

Lesion
A region in an organ or tissue that is abnormal from injury or disease

Magnetoencephalography (MEG)
Functional neuroimaging technique for mapping brain activity by recording magnetic fields produced by electrical currents occurring naturally in the brain

Memory lateralisation
The phenomenon in which one hemisphere (typically the left) shows greater involvement in memory functions than the other

Miss-sense mutation
A point mutation in a gene in which a single nucleotide change results in a codon that codes for a different amino acid

Multi-omic
Or *integrative omics*, is a biological analysis approach in which the data sets are multiple "omes", such as the genome, proteome, transcriptome, epigenome, metabolome, and microbiome

Myoclonia
A form of epileptic seizure manifesting with jerks of the muscles

Natural history
The progression of a disease process in an individual over time, in the absence of treatment

Optically pumped magnetometers (OPM)-MEG
A new type of MEG instrumentation, promising several advantages compared with conventional scanners: higher signal sensitivity, better spatial resolution, more uniform coverage, lifespan compliance, free movement of participants during scanning, and lower system complexity.

Pancytopenia
A condition that occurs when a person has low counts for all three types of blood cells: red blood cells, white blood cells, and platelets

Pathophysiological mechanisms
The cause of a disease associated injury

Phenotype
An individual's observable traits, such as height, eye colour, and blood type. The genetic contribution to the phenotype is called the genotype

PPI
Patient and public involvement

Practice paper
Evaluative summaries of scientific and evidence-based information that address practice topics. Practice papers are often done in emerging areas that might not have sound scientific data yet

Putative variants
A segment of DNA that is believed to be a gene. Putative genes can share sequence similarities to already characterised genes and thus can be inferred to share a similar function, yet the exact function of putative genes remains unknown

Sanger sequencing
A method for determining the nucleotide sequence of DNA

Status epilepticus
A single seizure lasting more than five minutes or two or more seizures within a five-minute period without the person returning to normal between them

Structural correlates
Structural anomalies which correlate to symptoms

Targeted treatment
Treatments which target specific symptoms and potential causes of disease. These treatments are disease modifying

Therapeutic radiofrequency thermocoagulation
A technique of controlled thermal ablation of tissues

Trio whole genome sequencing (WGS)
Whole exome sequencing is a comprehensive method for analysing entire genomes. Trio whole exome sequencing refers to the sequencing of the entire genome of a patient and their biological parents

Western blotting
A widely used analytical technique in molecular biology and immunogenetics to detect specific proteins in a sample of tissue extract

Young Epilepsy, the children and young people's epilepsy charity

We exist to create a society where children and young people with epilepsy are enabled to thrive and fulfil their potential. A society in which their voices are respected and their ambitions realised.

together we create possible.

For more information on our research, or to get involved please contact:

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