

# Paediatric Epilepsy Research Report 2015/16



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# Introduction

I am delighted to present our annual Research Report for the period March 2015 to April 2016. This document summarises the work of the research unit across Young Epilepsy, UCL GOS Institute of Child Health and Great Ormond Street Hospital for Children.

We are committed to optimising long-term outcomes and reducing the overall burden of epilepsy on young lives and families. Our research continues to focus on all aspects of childhood epilepsy, championing a holistic and multidisciplinary approach to aetiology, diagnosis and treatment. As a unit, we are especially fortunate to have the facilities and expertise to document the entire journey of translational research and use this evidence to vanguard practical outcomes for young people, reflected in public policy.

New projects initiated over the past year have included:

- A pilot study which aims to determine whether a dietary product is well tolerated in a population of individuals with epilepsy.
- A randomised controlled trial which will assess whether early postoperative antiepileptic drug (AED) withdrawal improves cognitive function compared with late withdrawal.
- A Phase 3 observational study of Cannabidiol as a new treatment for drug resistant epilepsies.
- Further development of our work to integrate services and improve outcomes for young people with epilepsy. This work looks to develop a strategy for a new integrated model of care.

In addition we have, as a unit, been responsible for 70 peer-reviewed publications of primary research, as well as a further 24 publications of chapters, reviews and commentaries of expert opinion.

In January 2016, we hosted our sixth annual Paediatric Epilepsy Research Retreat for researchers and collaborators, moderated by Professor Leiven Lagae of KUL University Hospitals, University of Leuven, Belgium. This inspirational event really strengthens the research community and provides a rare opportunity to exhibit current work to a multidisciplinary audience of experienced professionals and peers. The Retreat is an open forum to explore and debate the future directions of epilepsy research.

Under renewed strategic objectives, Young Epilepsy moves to deliver a dedicated education and social care research arm, strengthening our evidence base for service models internationally. As a unit, our research continues to work towards improving the recognition of epilepsy as a healthcare priority in every part of the world.

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



# Research Partners



## Young Epilepsy

Young Epilepsy is the national charity working exclusively on behalf of children and young people with epilepsy and associated conditions. With over 100 years expertise it provides world-class diagnosis, assessment and rehabilitation for children and young people with epilepsy. The charity also operates an internationally renowned research programme.

Young Epilepsy has a specialist school and college, providing day, residential and short break services, for young people up to the age of 25 years, offering education and healthcare for children and young people with epilepsy, autism and other neurological conditions. We have just opened our £10m new School and Education Resource

Centre. This state-of-the-art facility will provide the cornerstone for our education research programme.

Young Epilepsy aims to achieve better futures for young lives with epilepsy; campaigning to raise awareness and understanding of epilepsy and issues associated with the condition. The charity provides support and information for parents, children and young people as well as training for professionals. It campaigns for better access to, and quality of, health and education services, and offers tailor-made training across the country for parents, children, young people, health, social care and education professionals.

## UCL GOS Institute of Child Health

The University College London Great Ormond Street Institute of Child Health (ICH) is one of the world's pioneering paediatric research centres. ICH represents the largest concentration of people dedicated to advancing paediatrics outside of the United States.

ICH pursues an integrated, multidisciplinary approach to enhance understanding, diagnosis, therapy and prevention of childhood disease. A broad range of paediatric issues is covered, from molecular genetics to population health sciences. All specialties as they relate to children's health are included so that ICH fulfils the role of a world-leading academic establishment in paediatrics. In keeping with a commitment to disease prevention, ICH is active in teaching and research aimed at developing interventions to promote health both during childhood and in the later years of life.



The Research Excellence Framework (REF) is the system for assessing the quality of research in UK higher education institutions. In REF2014 ICH was part of a UCL return to the Clinical Medicine sub-panel of Main Panel A. In this sub-panel, 80% of UCL research was graded as either world-leading (43%) or internationally excellent (37%). UCL's research power performance was top in the UK. The strength and range of child health research at UCL was specifically commended. As part of this exercise, case impact studies were submitted to the REF2014 database to illustrate the impact of research on the wider society.

Two aspects of this research unit's work were submitted to REF2014 and are available for review – work on early treatment with ketogenic diet and surgery, and the work on status epilepticus.

## Great Ormond Street Hospital for Children

Great Ormond Street Hospital (GOSH) is an international centre of excellence in child healthcare. The hospital is dedicated to children's healthcare and to finding new and better ways to treat childhood illnesses.

GOSH is at the forefront of paediatric training in the UK; playing a leading role in training paediatric doctors and training more children's nurses than any other hospital.

The hospital is committed to carrying out pioneering research to find treatments and cures for some of the most complex illnesses.

Over the last three years, the hospital, together with the UCL GOS Institute of Child Health, has been in the top five centres in the world for research published.

## Research Funding

We remain ever grateful for the generosity and dedication of the organisations and individuals who support this great body of work. Central to the research programme is the ability to apply for and manage research grants and donations. Our research activities are funded through a combination of research grants associated with specific projects as well as donations from individuals and charitable organisations. We simply could not achieve the outcomes we strive for without such generosity.

### **We extend a special thanks to the Funders of our 2015 research programme:**

- Action Medical Research
- Charles Wolfson Foundation
- Epilepsy Research UK
- European Commission
- FP7-HEALTH-2013-INNOVATION-1
- George E Neville Foundation
- Great Ormond Street Hospital Children's Charity
- Maurice Wohl Foundation
- McGrath Foundation
- NIHR EME Programme
- Rita Lila Howard Foundation
- SPARKS
- True Colours Trust
- Vitaflo Limited
- Willie and Mabel Morris Charitable Trust
- Wolfson Foundation

# Research Strategy

Young Epilepsy, UCL GOS Institute of Child Health and Great Ormond Street Hospital

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

Collaboration and integrated working across the unit puts us in a unique position to:

- Incorporate reviews of children across the entire range of complexity and at all stages of diagnosis and care.
- Extend the continuation of our work into adulthood, through UCL, allowing study across the whole age range.
- Improve vital interventional understanding beyond medical treatment, through the diagnostic, educational and behavioural expertise within Young Epilepsy.

## GOAL 1

To gain a better understanding of underlying mechanisms and aetiologies responsible for seizures.

### This will be achieved by:

- ★ Cohort epidemiological studies to determine incidence, prevalence and outcome.
- ★ Collaborative and in-house studies to determine the molecular basis to the epilepsies, using population and family studies with the aim of further insights into new treatments.
- ★ Enhanced structural studies using neuroimaging to increase detection of structural correlates of the epilepsies.
- ★ Correlative studies in neurophysiology to enhance detection of origin.
- ★ Pathological examination of tissue from surgical specimens to enhance our understanding of structural correlates and related epileptogenesis.

## GOAL 2

To widen our understanding of the underlying mechanisms of neurodevelopmental and behavioural compromise in childhood epilepsy by including:

- ★ The development of experimental animal studies to examine the effects of epileptiform discharges on development.
- ★ Cohort studies to evaluate prevalence, natural history and outcome of comorbidities in childhood epilepsy.
- ★ Correlative neurophysiology/ neuropsychology studies.
- ★ Collaborative outcome studies across the age range.

**GOAL**  
**3**

To determine the benefits of early interventions in improving long-term outcome in childhood epilepsy.

**This will be achieved by:**

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

**GOAL**  
**5**

To reduce the overall burden of epilepsy in childhood to the individual, family and agencies involved through:

- ★ Interventional behaviour programmes.
- ★ Rehabilitation.

**GOAL**  
**4**

To gain a better understanding of barriers to learning in children with epilepsy across all educational settings. To determine the benefits of newer educational interventions in improving academic achievement in epilepsy across all settings.

**This will be achieved by:**

- ★ Evaluation of measures of progress in children with severe impairments.
- ★ Evaluation of targeted educational interventions across all settings.
- ★ Enhance the understanding of possible impairments and interventions of those working with children with epilepsy in educational environments.

**GOAL**  
**6**

To develop a milieu of senior researchers working both together and independently towards overriding goals of the unit, so enhancing training for academia, promoting a collegiate environment for junior staff and moving forward academic careers.

**This will be achieved by:**

- ★ Development of training fellowships.
- ★ Projects involve working towards higher degrees with encouragement for independent working thereafter.
- ★ Joint working between UCL GOS - ICH, GOSH and Young Epilepsy.
- ★ Enhancing research across all areas of expertise.

# Research Update



Below is a brief update on the research projects currently being undertaken across the unit:

## Epilepsy in Infancy: relating phenotype to genotype (EPIPEG)

**Project Aim:** To improve diagnosis and treatment outcome for young people with epilepsy by studying newly presenting patients, under 12 months of age, and their response to treatment. A clinical database will be established to be used as a resource for health practitioners when determining the best course of treatment for a particular diagnosis.

**Investigators:** Helen Cross, Manju Kurian, Rod Scott, Christin Eltze, Finbar O'Callaghan, Elaine Hughes, Jane Kung, Manuela Pisch, Michelle Downes

**Update:** Having registered in excess of 60 centres across the South East, with access to a bespoke database, we initiated the pilot phase of recruitment in February 2015. We have now moved to the substantive phase; recruitment will be complete by the end of June 2017. We also have funding and ethics approval for an extension to evaluate sleep patterns in the infants.

## 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:** Mutations in SLC12A5 have been identified as a novel cause of epilepsy of infancy with migrating focal seizures, with functional work in cell and zebrafish models published in Nature Communications in 2015. Further gene discovery work in our large cohort of children with early onset epilepsy is ongoing. Investigation of the cohort has also led to expansion of the phenotypes of known genes such as RARS2, PLCB1 and GABRB3.

## The genetics of Landau Kleffner Syndrome

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

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

**Update:** The team has screened 50 patients for mutations in the gene, GRIN2A, previously reported to be a cause of Landau Kleffner syndrome and related epilepsy syndromes in 8-20% of patients. Mutations were identified in six patients (12%). GRIN2A negative patients have had coding regions of their DNA screened for other disease-causing genes and analysis of this data is currently underway.



## Sleep and memory in children with focal epilepsy

**Project Aim:** To evaluate the role of sleep in learning (specifically memory consolidation) in children with different types of focal epilepsy, and determine whether this is disrupted compared to healthy children. This should lead to a better understanding of the causes of cognitive impairment in epilepsy.

**Investigators:** Samantha Chan, Torsten Baldeweg, Stewart Boyd, Rod Scott, Krishna Das, Ronit Pressler, Helen Cross

**Update:** Recruitment is now complete and data analysis ongoing. We are currently writing up the primary findings for publication. Additionally, we are performing further analyses on the EEG data in collaboration with colleagues from Zurich. The project has been presented widely across the unit and UCL GOS ICH particularly.



## Evaluating dietary intervention before surgical treatment for epilepsy (EDIBLE)

**Project Aim:** This is a work package of the European Union FP7 funded project DESIRE (Development and Epilepsy – Strategies for Innovative Research to improve diagnosis, prevention and treatment in children with difficult to treat epilepsy). The work package is a randomised controlled trial to determine whether seizure freedom is more likely when resective surgery is performed after a ketogenic diet, in the treatment of epilepsy associated with focal cortical dysplasia type II.

**Investigators:** Helen Cross is the leader of this work package and chief investigator of the randomised controlled trial. The trial will be conducted across 15 sites in Europe, including six in the UK. It is coordinated through the Clinical Trials Unit at Liverpool University by the Research Coordinator Christiana Papamichael

**Update:** Ethics has been approved in the UK and three sites initiated. The first patient will soon be recruited! Steady progress is being made towards opening sites in the remaining countries.

### **Ketogenic diet in infants with epilepsy (KIWE)**

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

**Investigators:** Christin Eltze, Nicholas Freemantle, Simon Heales, Rachel Kneen, Louise Marston, Tim Martland, Irwin Nazareth, Elizabeth Neal, Finbar O'Callaghan, Helen McCullagh, Alasdair Parker, Dr Shakti Agrawal, Ruth Williams, Penny Fallon, Andrew Lux, Siobhan Titre-Johnson, Helen Cross

**Update:** The project has received full ethics and MHRA approvals and is currently open to recruitment at Great Ormond Street Hospital, Evelina Children's Hospital, Addenbrookes Hospital, Leeds and Birmingham Hospitals. Recruitment of participants is underway and the trial is approaching the end of its feasibility phase with the aim to expand recruitment to further centres in the UK by July 2016.

### **Improving epilepsy surgery in childhood using fMRI and EEG**

**Project Aim:** To have a better understanding of the feasibility and the utility of EEG-fMRI in the presurgical evaluation of children with drug resistant focal epilepsy.

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

**Update:** Led by the clinical research fellow, Dr Maria Centeno, we have scanned 53 patients undergoing presurgical evaluation at Great Ormond Street Hospital and 21 control subjects. We have published two papers, the first validating our child-friendly approach and a second with colleagues in Geneva looking at the connectivity of the epileptic network. A third is submitted looking at the effects of interictal events on 'cognitive' brain networks. We are writing up our results that show EEG-fMRI, in particular when used with electrical source imaging is effective at localising the epileptogenic area even when there is no MRI lesion and predicting surgical outcome. We are also planning to translate this research into a pioneering clinical service at GOSH on the basis of these findings.

### **EEG investigation of brain networks in Childhood Absence Epilepsy (CAE) and Juvenile Myoclonic Epilepsy (JME) using EEG-fMRI**

**Project Aim:** The project aims to look at brain networks involved in CAE and JME, to determine how the networks thought to be responsible for the clinical expression of epilepsy are altered before treatment.

**Investigators:** Suejen Perani, Maria Centeno, Helen Cross, Mark Richardson, David Carmichael

**Update:** This is a collaborative study with Professor Mark Richardson at Kings College. Data from CAE and JME drug-naïve patients have been acquired and recruitment is complete. Analyses are underway and preliminary results show structural and functional changes in brain regions, including the thalamus, in drug-naïve patients.

### Cerebral blood flow changes preceding epileptic events in children

**Project Aim:** To use the techniques of simultaneous scalp EEG-NIRS (Near Infrared Spectroscopy) and EEG-fMRI during seizures and interictal events to have a better understanding of cerebral blood flow and the haemodynamic responses that may precede epileptic events with implications for utilising these methods in seizure prediction.

**Investigators:** Elhum Shamshiri, David Carmichael, Helen Cross

**Update:** 10 patients have been recruited for scalp EEG-NIRS and analysis of the EEG-fMRI data is advancing showing some interesting preliminary results indicating haemodynamic responses preceding.

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

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

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

**Update:** Sara Lorio has joined to lead this project. The team obtained seven patient datasets and have been working on motion correction software and hardware. The retrospective arm of the project is underway. The team is identifying participants based on their clinical and genetic groupings to look for phenotypic morphometric changes. In addition they are looking at new MRI image contrasts to help delineate epileptic lesions.

### The disability complex of early onset epilepsies: Sussex Early Epilepsy and Neurobehaviour (SEEN, previously reported as the Under Fives project)

**Project Aim:** To investigate neurobehaviour and parental wellbeing in young children with epilepsy and a comparison group with non-epilepsy related neurodisability.

**Investigators:** Brian Neville, Colin Reilly, Patricia Atkinson, Chloe Jones, Ayesha Memon, KB Das, Christopher Gillberg, Rod Scott

**Update:** Data collection commenced in September 2014 and will continue until June 2016. Results will be available in 2016 and 2017. Initial findings with respect to parental wellbeing were presented at BPNA conference in January 2016. These preliminary findings show that, overall, mothers of children with epilepsy reported significantly higher levels of anxiety, depression and fatigue compared to fathers. Additionally, mothers of children with epilepsy reported significantly higher levels of anxiety and depression when compared with mothers of children with non-epilepsy related neurodisability. Further findings echo reports of parent frustration with lack of support, access to specialists and long waiting lists for diagnostics such as EEG.

### **Pilot study of cardiac rhythm in Dravet Syndrome: a cause of SUDEP?**

**Project Aim:** To determine whether heart rhythm abnormalities are aggravated at times of illness in children with Dravet Syndrome and establish whether this in turn has implications for management and monitoring at times of illness. We hope this might lead to studies of acute preventative therapies at such times.

**Investigators:** Helen Cross, Juan Pablo Kaski, Sarah Aylett, Elaine Hughes, Sanjay Sisodiya

**Update:** This study involves parents retaining an ECG machine at home, and recording the heart rhythm during illness. Five families have been recruited and have participated to date. Data collection is ongoing.

### **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

**Update:** We have recently recruited Amy McDowell who will work part-time on this project. We are optimising faster fMRI scans and have developed an in-scanner EEG motion artefact correction method that is just published in NeuroImage. This was led by Danilo Maziero a PhD student from Sao Paolo who visited us for a year. He demonstrated, for the first time, that we could prospectively correct fMRI using our camera tracking technology and retrospectively correct the simultaneous EEG at the same time.

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

**Project Aim:** This feasibility study is to evaluate the use of Betashot, a medium chain triglyceride (MCT) based food for special medical purposes (FSMP) in 80 participants:

- 40 children diagnosed with epilepsy - 20 with Dravet syndrome, 20 with another early onset epilepsy, the result of a genetic mutation
- 40 adults diagnosed with epilepsy.

Participants will take Betashot daily for twelve weeks whilst continuing with their normal diets but excluding foods high in complex sugars. Assessments of product tolerance, acceptability and compliance will be made.

**Investigators:** Matthew Walker, Helen Cross, Sanjay Sisodiya, Simon Heales, Rumana Jalil

**Update:** Ethics approval has been obtained. Patient recruitment starts June 2016.



### **Cannabidiol - Safety, tolerability and efficiency of Cannabidiol as add-on therapy in severe childhood epilepsies**

**Project Aim:** This is a Phase 3 observational study of Cannabidiol as a new treatment for drug resistant epilepsies.

**Investigators:** Helen Cross, Katharina Vezyroglou

**Update:** We have participated in the open label named patient programme of Cannabidiol in severe epilepsies and were able to utilise the medication in 25 patients. Results are being analysed and will be submitted for presentation in early 2016. We have also recruited to the international randomised control trials of Cannabidiol in Dravet and Lennox Gastaut Syndrome.

### **A European pilot network of reference centres in refractory epilepsy and epilepsy surgery (E-PILEPSY)**

**Project Aim:** To trigger accelerated development of epilepsy surgery by promoting cooperation between highly specialised neurology, clinical neurophysiology and neurosurgery centres in all EU regions. The primary expected outcome is to increase the number and proportion of patients cured from their refractory epilepsy by improving delivery of optimal epilepsy surgery throughout Europe.

**Lead Investigators:** Philippe Ryvlin, Helen Cross

**Update:** We are now in the third and final year of this endeavour. A website has been established, virtual multidisciplinary discussion of patients, and systematic reviews on presurgical evaluation and outcomes in progress. An application to the European call for Reference Networks, for an extension to develop a network for Rare and Complex Epilepsies, was recently submitted incorporating E-epilepsy as the surgical therapeutic arm. Great Ormond Street Hospital (Professor Cross) led on this application as the coordinator.

### **Improving Care in Epilepsy (ICE) for children, young people and families (formerly the Darzi Fellowship Project)**

**Project Aim:** To implement an innovative model of care that reflects the broad impact epilepsy has on the individual person by virtue of being person and family-centred, integrated across different sectors, and based on meaningful outcomes. This is a collaborative project between Young Epilepsy, UCL-ICH, UCL Partners and Whittington Health.

**Project Team:** Amit Bali, Carol Long, Monica Lakhanpaul, Kerry Robinson, Helen Cross

**Update:** Current workstreams include the development of a pilot epilepsy registry linked to individualised care plans, the co-creation of young people's networks, and the commissioning of an economic analysis that quantifies the benefits of a multi-sector, integrated approach.

### **'What I need in school' - Developing guidelines for best practice for young people with epilepsy in schools in the UK**

**Project Aim:** To garner the views and experiences of school age children (6-15 years) with epilepsy, their parents and teachers regarding:

- Impact of epilepsy on school functioning
- Current and desired educational supports for young people with epilepsy.

**Investigators:** Patricia Atkinson, Colin Reilly, Helen Cross

**Update:** Project is due to commence in early 2017.



### **Validation of the Assessment of Behaviour and Learning in Epilepsy (ABLE) a screening instrument for the neurobehavioral comorbidities of childhood epilepsy**

**Project Aim:** To provide validation data on the Assessment of Behaviour Learning Epilepsy (ABLE) (parent and teacher versions) screening instrument.

**Investigators:** Colin Reilly, Isobel Heyman, Tara Murphy, Helen Cross

**Update:** Methodology has been developed to validate the tool; the project is due to commence in late 2016.

# Research Team

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

## Principal Investigators

**Professor Helen Cross OBE** The Prince of Wales's Chair of Childhood Epilepsy and Head of University College London Great Ormond Street - Institute of Child Health Neurosciences Unit

**Professor Torsten Baldeweg** Professor of Developmental Cognitive Neuroscience

**Professor Chris Clark** Professor of Imaging and Biophysics

**Professor Christopher Gillberg** Visiting Professor in Child and Adolescent Psychiatry

**Professor Isobel Heyman** Consultant Child and Adolescent Psychiatrist and Honorary Professor

**Professor Brian Neville** Emeritus Professor of Childhood Epilepsy

**Professor Shamima Rahman** Professor of Paediatric Metabolic Medicine

**Professor Rod Scott** Professor in Paediatric Neurology

**Professor Faraneh Vargha-Khadem** Professor of Developmental Cognitive Neuroscience

**Dr Sarah Aylett** Consultant Paediatric Neurologist

**Dr Stewart Boyd** Consultant Clinical Neurophysiologist

**Dr David Carmichael** Lecturer in Neuroimaging and Biophysics

**Dr Michelle De Haan** Reader in Developmental Cognitive Neuroscience

**Dr Roxanna Gunny** Consultant Neuroradiologist

**Dr Tom Jacques** Reader in Paediatric Neuropathology

**Dr Marios Kaliakatsos** Honorary Senior Lecturer, Neurology

**Dr Manju Kurian** Consultant Paediatric Neurologist and Clinician Scientist

**Dr Philippa Mills** Lecturer in Genetics and Genomic Medicine Programme

**Dr Finbar O'Callaghan** Head of Clinical Neurosciences Section and Reader in Paediatric Neurology

**Dr Ronit Pressler** Consultant in Clinical Neurophysiology and Clinical Lead of Telemetry Unit

**Dr Colin Reilly** Educational Psychologist

**Dr Richard Scott** Consultant in Clinical Genetics

**Dr Rachel Thornton** Consultant in Neurophysiology

**Mr Martin Tisdall** Consultant Paediatric Neurosurgeon

**Dr Sophia Varadkar** Consultant Paediatric Neurologist



## PhD Students

**Sophie Adler** *1. Cortical infolding in epilepsy 2. Morphology in Paediatric Epilepsy*

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

**Sarah Buck** *Organisation of the memory circuit in paediatric Temporal Lobe Epilepsy*

**Samantha Chan** *Sleep and cognition in epilepsy: Sleep and memory in children with focal epilepsy*

**Rosie Coleman** *Functional and structural plasticity after epilepsy surgery*

**Bianca De Blasi** *Quantitative PET analysis in paediatric epilepsy*

**Jane Kung** *EPIPEG: Epilepsy in infancy; relating genotype to phenotype*

**Amy McTague** *The genetics of early onset epileptic encephalopathy*

**Adeline Ngoh** *The genetics of Landau Kleffner Syndrome*

**Suejen Perani** *Investigation of brain networks in Childhood Absence Epilepsy and Juvenile Myoclonic Epilepsy using EEG-fMRI*

**Birgit Pimpel** *High-resolution cortical mapping for epilepsy surgery in children*

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

**Elhum Shamshiri** *Understanding cerebral blood flow changes preceding epileptic events in children*

**Tim Tierney** *Retrospective motion correction in fMRI data*

**Siobhan Titre-Johnson** *Ketogenic diet in infancy*

## Research Staff

**Amit Bali** Clinical Leadership Fellow

**Michelle Downes** Research Associate

**Rumana Jalil** Trial Coordinator

**Chloe Jones** Assistant Research Psychologist

**Esther Meyer** Research Fellow

**Amy Muggeridge** Research Manager

**Liz Neal** Honorary Research Dietician

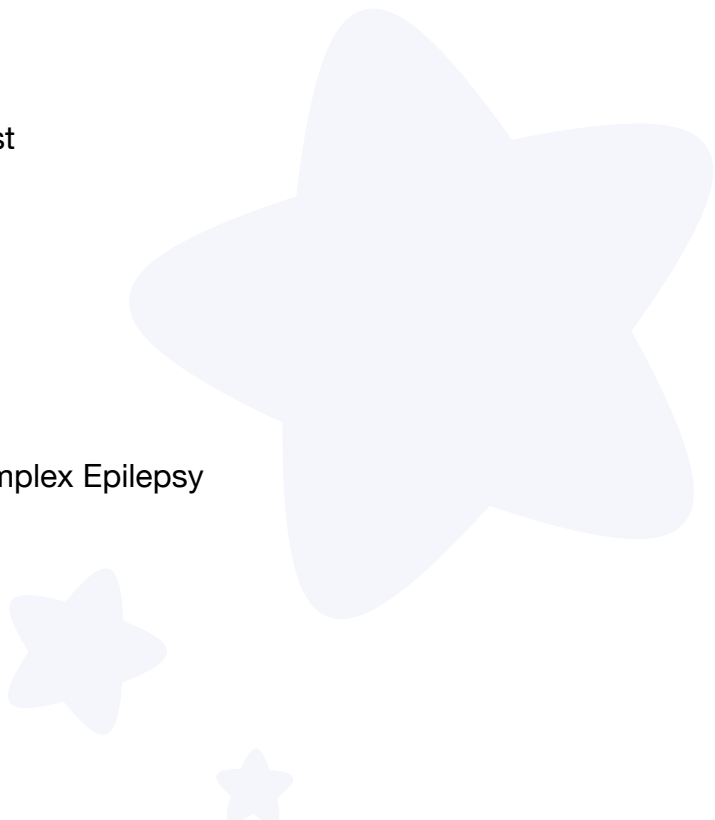
**Manuela Pisch** Research Associate

**Natasha Schoeler** Dietetic Assistant

**Siobhan Titre-Johnson** Trial Manager

**Anna Tyler** Postdoctoral Research Fellow

**Katharina Vezyroglou** Clinical Fellow for Complex Epilepsy





## Clinicians in neuroscience active in epilepsy research

**Dr Patricia Atkinson** Consultant Community Paediatrician  
**Dr Sarah Aylett** Consultant Paediatric Neurologist  
**Dr Stewart Boyd** Consultant Neurophysiologist  
**Dr Maria Clark** Consultant Paediatric Neurologist  
**Dr Krishna Das** Consultant Paediatric Neurologist  
**Dr Christin Eltze** Consultant Paediatric Neurologist  
**Mr William Harkness** Consultant Paediatric Neurosurgeon  
**Dr Cheryl Hemingway** Consultant Paediatric Neurologist  
**Dr Friederike Moeller** Consultant Clinical Neurophysiologist  
**Dr Marios Kaliakatsos** Paediatric Neurologist  
**Dr Robert Robinson** Consultant Paediatric Neurologist  
**Dr Rachel Thornton** Consultant in Clinical Neurophysiology  
**Mr Martin Tisdall** Consultant Paediatric Neurosurgeon  
**Dr Sophia Varadkar** Consultant Paediatric Neurologist

## Active Collaborators

**Professor Nick Freemantle** Professor of Clinical Epidemiology and Biostatistics  
*PRIMENT Clinical Trials Unit, UCL Great Ormond Street - Institute of Child Health*

**Professor Simon Heales** Professor of Clinical Chemistry *UCL Great Ormond Street - Institute of Child Health and Great Ormond Street Hospital*

**Professor Gregory Holmes** Professor of Neurology and Paediatrics *University of Vermont, USA*

**Professor Matthias Koepp** Professor of Neurology *UCL - Institute of Neurology*

**Professor Irwin Nazareth** Professor of Primary Care *PRIMENT Clinical Trials Unit, UCL Great Ormond Street - Institute of Child Health*

**Professor Sanjay Sisodiya** Professor of Neurology *UCL - Institute of Neurology*

**Professor Matthew Walker** Professor of Neurology *UCL - Institute of Neurology*

**Professor Robin Williams** Professor of Molecular Cell Biology *Royal Holloway Hospital*

**Dr Shakti Agrawal** Consultant Paediatric Neurologist *Birmingham Children's Hospital*

**Dr Richard Chin** Clinical Senior Lecturer *University of Edinburgh*

**Dr Elaine Hughes** Consultant Paediatric Neurologist *Evelina Children's Hospital*

**Dr Thomas Jacques** Clinical Senior Lecturer *UCL Great Ormond Street - Institute of Child Health*

**Dr Rachel Kneen** Consultant Paediatric Neurologist *Royal Liverpool University Hospital*

**Dr Andrew Lux** Consultant Paediatric Neurologist *Bristol Children's Hospital*

**Dr Louise Marston** Trial Statistician *PRIMENT Clinical Trials Unit, UCL Great Ormond Street - Institute of Child Health*

**Dr Tim Martland** Consultant Paediatric Neurologist *Royal Manchester Children's Hospital*

**Dr Helen McCullagh** Consultant Paediatric Neurologist *Leeds Teaching Hospital*

**Dr Ailsa McLellan** Consultant Paediatric Neurologist *Royal Hospital for Sick Children, Edinburgh*

**Dr Alasdair Parker** Consultant Paediatric Neurologist *Cambridge University Hospital*

**Dr Ruth Williams** Consultant Paediatric Neurologist *Evelina Children's Hospital*



## Paediatric Epilepsy Research Retreat 2016

**'Wonderfully open meeting providing a constructive way to shape my work.'**

**Clinical Research Fellow**

**'Provides a vital input through refreshingly non-competitive discussion'**

**Paediatric Research Fellow**

The Epilepsy Research Retreat serves as an annual gathering of researchers and collaborators across the unit. This meeting gives researchers the opportunity to discuss ongoing projects, completed projects and future directions of research with a unique range of specialists in epilepsy.

The 2016 research retreat took place on 21-22 January at the Felbridge Hotel in East Grinstead. Our Research Moderator this year was the pre-eminent Professor Lieven Lagae of KUL University Hospitals, University of Leuven, Belgium.

The meeting brought together 104 researchers from Young Epilepsy, UCL GOS - Institute of Child Health, UCL - Institute of Neurology and Great Ormond Street Hospital as well as collaborators from Evelina Children's Hospital, Royal Holloway, Crawley Hospital, King's College Hospital and elsewhere in the UK as well as collaborators from the University of Vermont, USA, and University of Calgary Cumming School of Medicine, Canada.







Research fellows presented updates on 26 current projects under the following themes:

- Aetiology
- Networks and Connectivity
- Interventions
- Outcomes

Discussions at the end of each presentation gave investigators the opportunity to receive comments and feedback from fellow researchers and principal investigators representing a vast array of different fields.

The Retreat is also a highly social occasion, giving researchers what is often their single annual opportunity to meet colleagues and peers face to face. This vital networking truly highlights the breadth of epilepsy research being undertaken across the unit. The meeting critically serves as a way of motivating young researchers to understand this diversity whilst forming the collaborations which underpin excellent science.

**'A wonderful meeting'**

**Professor of Paediatric Neurology**

**'A hugely enjoyable forum with a uniquely broad range of experts to meet and constructively share research'**

**Research Coordinator**

# Research Publications

## Primary Research 2015/16

1. Avberšek A, Miserocchi A, McEvoy AW, Patel AV, Aronica E, Blümcke I, **Jacques TS**, Acheson J, Thom M, Sisodiya SM (2015) **Multiphasic presentation of Rasmussen's encephalitis** *Epileptic Disorders* 17(3):315-20
2. Baker K, Astle DE, Scerif G, Barnes J, Smith J, Moffat G, Gillard J, **Baldeweg T**, Raymond FL (2015) **Epilepsy, cognitive deficits and neuroanatomy in males with ZDHHC9 mutations** *Ann. Clin. Transl. Neurol.* 2(5):559-69
3. Balestrini S, Milh M, Castiglioni C, Lüthy K, Finelli MJ, Verstreken P, Cardon A, Gnidovec Stražičar B, Lloyd Holder J, Lesca G, Mancardi MM, Poulat AL, Repetto GM, Banka S, Bilo L, Birkeland LE, Bosch F, Brockmann K, **Cross JH**, Doummar D, Félix TM, Giuliano F, Hori M, Hüning I, Kayserili H, Kini U, Lees MM, Meenakshi G, Mewasingh L, Pagnamenta AT, Peluso S, Mey A, Rice GM, Rosenfeld JA, Taylor JC, Troester MM, Stanley CM, Ville D, Walkiewicz M, Falace A, Fassio A, Lemke JR, Biskup S, Tardif J, Ajeawung NF, Tolun A, Corbett M, Gecz J, Afawi Z, Howell KB, Oliver KL, Berkovic SF, Scheffer IE, de Falco FA, Oliver PL, Striano P, Zara F, Campeau PM, Sisodiya SM (2016) **TBC1D24 genotype-phenotype correlation: epilepsies and other neurological features** *Neurology* (in press)
4. Bassetti C, Berkovic SF, Bisulli F, Cirignotta F, **Cross JH**, Derry CP, Gambardella A, Guerrini R, Halasz P, Hesdorffer DC, Kahane P, Licchetta L, Mahowald MW, Manni R, Marini C, Mostacci B, Naldi I, Nobili L, Ottman R, Parrino L, Picard F, Provini F, Pugliatti M, Ryvlin P, Scheffer IE, Tassi L, Tinuper P, Vigeveno F, Vignatelli L, Zucconi M (2016) **Definition and Diagnostic Criteria of Sleep-related Hypermotor Epilepsy (SHE)** *Neurology* 10;86(19):1834-42
5. Bennett S, Shafran R, Coughtrey A, Walker S, **Heyman I** (2015) **Psychological interventions for mental health disorders in children with chronic physical illness: a systematic review** *Arch. Dis. Child.* 100(4):308-316
6. Boshuisen K, van Schooneveld M, Uiterwaal C, **Cross JH**, Harrison S, Polster T, Daehn M, Djimjadi S, Yalnızoğlu D, Turanlı G, Sassen R, Hoppe C, Kuczaty S, Barba C, Kahane P, Schubert S, Reuner G, Bast T, Strobl K, Mayer H, de Saint Martin A, Seegmuller A, Laurent Agathe, Arzimanoglou A, Braun K (2015) **IQ improves after AED withdrawal following paediatric epilepsy surgery** *Ann Neurol.* 78(1):104-14
7. Boshuisen K, Lamberink HJ, Schooneveld MMJ, **Cross JH**, Arzimanoglou A, Geleijns K, Uiterwaal CSPM, Braun KPJ (2015) **TimeToStop (TTS) Trial, A pragmatic randomized clinical trial on cognitive consequences of early versus late antiepileptic drug withdrawal after paediatric epilepsy surgery** *Trials* 16:482
8. Centeno M, Tierney T, Perani S, Shamshiri E, StPier K, Wilkinson C, Konn D, Banks T, Vulliemoz S, Lemieux L, **Pressler R, Clark CA, Cross JH, Carmichael DW** (2016) **Optimising EEG-fMRI for Localisation of Focal Epilepsy in Children** *PLoS One* DOI:10.1371/journal.pone.0149048
9. Chaudhary UJ, Centeno M, **Thornton RC**, Rodionov R, Vulliemoz S, McEvoy AW, Diehl B, Walker MC, Duncan JS, **Carmichael DW**, Lemieux L (2016) **Mapping preictal and ictal haemodynamic networks using simultaneous intracranial EEG-fMRI** *Neuroimage Clinical* 11:486-93
10. Coan AC, Chaudhary UJ, Campos BM, Perani S, Ciantis A, Vulliemoz S, Diehl B, Beltramini GC, **Carmichael DW, Thornton RC**, Covolan RJ, Cendes F, Lemieux L (2016) **EEG-fMRI in the presurgical evaluation of temporal lobe epilepsy** *J. Neurol. Neurosurg. Psychiatry.* 87(6):642-9
11. Cukiert A, Rydenhag B, Harkness W, **Cross JH**, Gaillard WD, on behalf of the Task Force for Paediatric Epilepsy Surgery for the ILAE Commissions of Paediatrics and Surgical therapies (2016) **Technical aspects of paediatric epilepsy surgery: Report of a multicentre, multinational web-based survey by the ILAE Task Force on Paediatric Epilepsy Surgery** *Epilepsia* 57(2):194-200
12. Das D, **Varadkar S**, Das KB (2016) **Oral clomethiazole treatment for paediatric non-convulsive status epilepticus** *Epileptic. Disord.* 1;18(1):87-91
13. Downes M, Greenaway R, Clark M, **Cross JH**, Jolleff N, Harkness W, **Kaliakatsos M, Boyd S, White S, Neville BG** (2015) **Outcome following multiple subpial transection in Landau-Kleffner syndrome and related regression** *Epilepsia* 56(11):1760-6



14. Falk MJ, Shen L, Gonzalez M, Leipzig J, Lott MT, Stassen AP, Diroma MA, Navarro-Gomez D, Yeske P, Bai R, Boles RG, Brilhante V, Ralph D, DaRe JT, Shelton R, Terry SF, Zhang Z, Copeland WC, van Oven M, Prokisch H, Wallace DC, Attimonelli M, Krotoski D, Zuchner S, Gai X; MSeqDR Consortium participants: Bale S, Bedoyan J, Behar D, Bonnen P, Brooks L, Calabrese C, Calvo S, Chinnery P, Christodoulou J, Church D, Clima R, Cohen BH, Cotton RG, de Coo IFM, Derbenevoa O, den Dunnen JT, Dimmock D, Enns G, Gasparre G, Goldstein A, Gonzalez I, Gwinn K, Hahn S, Haas RH, Hakonarson H, Hirano M, Kerr D, Li D, Lvova M, Macrae F, Maglott D, McCormick E, Mitchell G, Mootha VK, Okazaki Y, Pujol A, Parisi M, Perin JC, Pierce EA, Procaccio V, **Rahman S**, Reddi H, Rehm H, Riggs E, Rodenburg R, Rubinstein Y, Saneto R, Santorsola M, Scharfe C, Sheldon C, Shoubridge EA, Simone D, Smeets B, Smeitink JA, Stanley C, Suomalainen A, Tarnopolsky M, Thiffault I, Thorburn DR, Van Hove J, Wolfe L, Wong LJ (2015) **Mitochondrial Disease Sequence Data Resource (MSeqDR): A global grass-roots consortium to facilitate deposition, curation, annotation, and integrated analysis of genomic data for the mitochondrial disease clinical and research communities** *Mol. Genet. Metab.* 114(3):388-396
15. Fosi T, Chu C, Chong WK, **Clark C, Scott RC, Boyd S, De Haan M, Neville B** (2015) **Quantitative magnetic resonance imaging evidence for altered structural remodelling of the temporal lobe in West syndrome** *Epilepsia* 56(4):608-16
16. Gardiner AR, Jaffer F, Dale RC, Labrum R, Erro R, Meyer E, Xiromerisiou G, Stamelou M, Walker M, Kullmann D, Warner T, Jarman P, Hanna M, **Kurian MA**, Bhatia KP, Houlden H (2015) **The clinical and genetic heterogeneity of paroxysmal dyskinesias** *Brain* 138(12):3567-80
17. Graham D, **Tisdall M**, Gill D (2016) **Corpus callosotomy outcomes in paediatric patients: a systematic review** *Epilepsia* doi: 10.1111/epi.13408
18. Hatch J, Coman D, Clayton P, **Mills P**, Calvert S, Webster RI, Riney K (2015) **Normal Neurodevelopmental Outcomes in PNPO Deficiency: A Case Series and Literature Review** *JIMD Rep.* 26:91-7
19. Hoffman CE, Ochi A, Snead III OC, Widjaja E, Hawkins C, **Tisdal M**, Rutka JT (2016) **Rasmussen's encephalitis: advances in management and patient outcomes** *Child's Nervous System* 32(4):629-640
20. Horvath GA, Demos M, Shyr C, Matthews A, Zhang L, Race S, Stockler-Ipsiroglu S, Van Allen M, Mancarci O, Toker L, Pavlidis P, Ross CJ, Wasserman WW, Trump N, Heales S, Pope S, **Cross JH**, van Karnebeek CDM (2016) **Secondary neurotransmitter deficiencies in epilepsy caused by voltage-gated sodium channel mutations: A potential treatment target?** *Molecular Genetics and Metabolism* 117(1):42-48
21. Hunter RM, **Reilly C**, Atkinson P, Das KB, **Gillberg C**, Chin RF, **Scott RC, Neville BG**, Morris S (2015) **The health, education, and social care costs of school-aged children with active epilepsy: A population-based study** *Epilepsia* 1;56(7):1056-64
22. Jaffer F, Avbersek A, Vavassori R, Fons C, Campistol J, Stagnaro M, De Grandis E, Veneselli E, Rosewich H, Gianotta M, Zucca C, Ragona F, Granata T, Nardocci N, Mikati M, Helseth AR, Boelman C, Minassian BA, Johns S, Garry SI, Scheffer IE, Gourfinkel-An I, Carrilho I, **Aylett SE**, Parton M, Hanna MG, Houlden H, **Neville B, Kurian MA**, Novy J, Sander JWA, Lambiase PD, Behr ER, Schyns T, Arzimanoglou A, **Cross JH**, Kaski JP, Sisodiya SM (2015) **Faulty cardiac repolarisation reserve in alternating hemiplegia of childhood broadens the phenotype** *Brain* 138(10):2859-74
23. Japaridze N, Muthuraman M, Reinicke C, Moeller F, Anwar AR, Mideksa KG, **Pressler R**, Deuschl G, Stephani U, Siniatchkin M (2015) **Neuronal Networks during Burst Suppression as Revealed by Source Analysis** *PLoS One.* 30;10(4):e0123807
24. Jullien V, **Pressler R**, Boylan G, Blennow M, Marlow N, Chiron C, Pons G, NEMO Consortium (2016) **Neonatal Seizure Treatment with Medication Off-Patent. Pilot evaluation of the population pharmacokinetics of bumetanide in term newborn infants with seizures** *J. Clin. Pharmacol.* 56(3):284-90
25. Kobulashvili T, Höfler J, Dobesberger J, Ernst F, Ryvlin P, **Cross JH**, Braun K, Dimova P, Francione S, Hecimovic H, Helmstaedter C, Kimiskidis VK, Lossius MI, Malmgren K, Marusic P, Steinhoff BJ, Boon P, Craiu D, Delanty N, Fabo D, Gil-Nagel A, Guekht A, Hirsch E, Kalviainen R, Mameniskienė R, Özkara Ç, Seeck M, Rubboli G, Krsek P, Rheims S, Trinka E (2016) **Current practices in long-term video-EEG monitoring services: a survey among partners of the E-PILEPSY pilot network of reference for refractory epilepsy and epilepsy surgery** *Seizure, European Journal of Epilepsy* 38:38-45
26. Leu C, Balestrini S, Maher B, Hernández-Hernández L, Heggeli K, Schoeler N, Novy J, Willis J, Plagnol V, Ellis R, Reavey E, O'Regan M, O. Pickrell W, Thomas RH, Chung SK, Delanty N, Nashef L, Zuberi S, Rees MI, Cavalleri GL, Sander L, Hughes E, **Cross JH**, Scheffer IE, Palotie A and Sisodiya SM (2015) **Genome-wide polygenic burden of rare deleterious variants in sudden unexpected death in epilepsy** *Ebiomedicine* 2(9):1063-1070

27. Levtova A, Camuzeaux S, Laberge AM, Allard P, Brunel-Guitton C, Diadori P, Rossignol E, Hyland K, Clayton PT, **Mills PB**, Mitchell GA (2015) **Normal Cerebrospinal Fluid Pyridoxal 5'-Phosphate Level in a PNPO-Deficient Patient with Neonatal-Onset Epileptic Encephalopathy** *JIMD. Rep.* 22:67-75
28. Lotte J, Bast T, Borusiak P, Coppola A, **Cross JH**, Dimova P, Fogarasi A, Graneß I, Guerrini R, Hjalgrim H, Keimer R, Korff CM, Kurlemann G, Leiz S, Linder-Lucht M, Loddenkemper T, Makowski C, Mühe C, Nicolai J, Nikanorova M, Pellacani S, Philip S, Ruft S, Sánchez Fernández I, Schlachter K, Striano P, Sukhudyen B, Valcheva D (2016) **Effectiveness of antiepileptic therapy in patients with PCDH19 mutations** *Seizure* 35:106-110
29. Magner M, Dvorakova V, Tesarova M, Mazurova S, Hansikova H, Zahorec M, Brennerova K, Bzduch V, Spiegel R, Horovitz Y, Mandel H, Eminoglu FT, Mayr JA, Koch J, Martinelli D, Bertini E, Konstantopoulou V, Smet J, **Rahman S**, Broomfield A, Stojanović V, Dionisi-Vici C, van Coster R, Morava-Kozicz E, Sperl W, Zeman J, Honzik T (2014) **TMEM70 deficiency: long-term outcome of 48 patients** *J. Inherit. Metab. Dis.* 38(3):417-26
30. Mathieson S, Rennie J, Livingstone V, Temko A, Low E, **Pressler RM**, Boylan GB (2016) **In-depth performance analysis of an EEG based neonatal seizure detection algorithm** *Clinical Neurophysiology* 127(7):2643-2660
31. McGinnity CJ, Koepp MJ, Hammers A, Riaño Barros DA, **Pressler RM**, Luthra S, Jones PA, Trigg W, Micallef C, Symms MR, Brooks DJ, Duncan JS (2015) **NMDA receptor binding in focal epilepsies** *J. Neurol. Neurosurg. Psychiatry.* 86(10):1150-7
32. McMahan KQ, Papandreou A, Ma M, Barry BJ, Mirzaa GM, Dobyns WB, **Scott RH**, Trump N, **Kurian MA**, Paciorkowski AR (2015) **Familial recurrences of FOXG1-related disorder: Evidence for mosaicism** *Am. J. Med. Genet. A.* 167(12):3096-102
33. McWilliams A, **Reilly C**, McFarlane FA, Booker E, **Heyman I** (2016) **Nonepileptic seizures in the pediatric population: A qualitative study of patient and family experiences** *Epilepsy & Behavior.* 30(59):128-36
34. Mefford HC, Zemel M, Geraghty E, Cook J, Clayton PT, Paul K, Plecko B, **Mills PB**, Nordli DR, Gospe SM (2015) **Intragenic deletions of ALDH7A1 in pyridoxine-dependent epilepsy caused by Alu-Alu recombination** *Neurology* 85(9):756-762
35. Moutaen BE, Rados M, Huiskamp GJ, Van Eijsden P, Leijten FS, Braun KPJ, on behalf of the **E-PILEPSY consortium (2016) Current use of imaging and electromagnetic source localization procedures in epilepsy surgery centers across Europe** *Epilepsia* 57(5):770-6
36. Ngoh A, Bras J, Gurreiro R, Meyer E, McTague A, Dawson E, Mankad K, **Gunny R**, Clayton P, **Mills P**, Thornton R, Lai M, Forsyth R, **Kurian M** (2016) RARS2 mutations in a sibship with infantile spasms *Epilepsia* 57(5):97-102
37. Nowell M, Sparks R, Zombori G, Miserocchi A, Rodionov R, Diehl B, Wehner T, Baio G, Trevisi G, **Tisdall M**, Ourselin S, McEvoy AW, Duncan J (2015) **Comparison of computer-assisted planning and manual planning for depth electrode implantations in epilepsy** *J. Neurosurg.* 4:1-9
38. **O'Callaghan FJ** (2015) **Epilepsy in childhood and quality of life** *Eur. J. Paed. Neurol.* 19(3):276-7
39. Panagiotakaki E, De Grandis E, Stagnaro M, Heinzen EL, Fons C, Sisodiya S, de Vries B, Goubau C, Weckhuysen S, Kemlink D, Scheffer I, Lesca G, Rabilloud M, Klich A, Ramirez-Camacho A, Ulate-Campos A, Campistol J, Giannotta M, Moutard M, Doummar D, Hubsch-Bonneaud C, JafferF, **Cross JH**, Gurrieri F, Tiziano D, Nevsimalova S, Nicole S, **Neville B**, van den Maagdenberg AMJM, Mikati M, Goldstein DB, Vavassori R, Arzimanoglou A, The Italian IBAHC Consortium, The French AHC Consortium, The International AHC Consortium (2015) **Clinical profile of patients with ATP1A3 mutations in Alternating Hemiplegia of Childhood—a study of 155 patients** *Orphanet Journal of Rare Diseases* 10:123
40. Papandreou A, McTague A, Trump N, Ambegaonkar G, Ngoh A, Meyer E, **Scott RH**, **Kurian MA** (2016) **GABRB3 mutations: a new and emerging cause of early infantile epileptic encephalopathy** *Dev. Med. Child. Neurol.* 58(4):416-420
41. Papandreou A, Schneider RB, Augustine EF, Ng J, Mankad K, Meyer E, McTague A, Ngoh A, Hemingway C, Robinson R, **Varadkar SM**, Kinali M, Salpietro V, O'Driscoll MC, Basheer SN, Webster RI, Mohammad SS, Pula S, McGowan M, Trump N, Jenkins L, Elmslie F, **Scott RH**, Hurst JA, Perez-Duenas B, Paciorkowski AR, **Kurian MA** (2016) **Delineation of the movement disorders associated with FOXG1 mutations** *Neurology* 86(19):1794-1800
42. Patel A, **Thornton R**, Mitchell TN, Michell AW (2016) **Advances in EEG: home video telemetry, high frequency oscillations and electrical source imaging** *Journal of Neurology, 2016 in press*
43. **Pressler RM**, Boylan GB, Marlow N, Blennow M, Chiron C, **Cross JH**, de Vries LS, Hallberg B, Hellström-Westas L, Jullien V, Livingstone V, Mangum B, Murphy B, Murray D, Pons G, Rennie J, Swarte R, Toet MC, Vanhatalo S, Zohar S, Neonatal seizure treatment with Medication Off-patent (NEMO) consortium (2015) **Bumetanide for the treatment of seizures in newborn babies with hypoxic ischaemic encephalopathy (NEMO): an open-label, dose finding, and feasibility phase 1/2 trial** *Lancet Neurol.* 14(5):469-77

44. Raimondi F, **Mills P**, Clayton PT, Giudice ED (2015) **A preterm neonate with seizures unresponsive to conventional treatment** *BMJ Case Reports* doi:10.1136/bcr-2015-209743
45. Rajakulendran S, Pitceathly RDS, Taanman J-W, Costello H, Sweeney MG, Woodward CE, Jaunmuktane Z, Holton JL, **Jacques TS**, Harding BN, Fratter F, Hanna MG and **Rahman S** (2016) **Clinical, neuropathological and genetic study of homozygous A467T POLG-related mitochondrial disease** *PLoS One* 11(1):e0145500. doi: 10.1371/journal.pone.0145500. PMID: 26735972
46. Reid ES, Williams H, Stabej PL, James C, Ocaka L, Bacchelli C, Footitt EJ, **Boyd S**, Cleary MA, **Mills PB**, Clayton PT (2015) **Seizures Due to a KCNQ2 Mutation: Treatment with Vitamin B(6)** *JIMD Rep.* 27:79-84
47. **Reilly C**, Atkinson P, Chin RF, Das KB, **Gillberg C**, **Aylett SE**, Burch V, **Scott RC**, **Neville BG** (2015) **Symptoms of anxiety and depression in school-aged children with active epilepsy: a population-based study** *Epilepsy & Behavior* 30(52):174-9
48. **Reilly C**, Atkinson P, Das KB, Chin RF, **Aylett SE**, Burch V, **Gillberg C**, **Scott RC**, **Neville BG** (2015) **Features of autism spectrum disorder (ASD) in childhood epilepsy: a population-based study** *Epilepsy Behav.* 42:86-92
49. **Reilly C**, Atkinson P, Das KB, Chin RF, **Aylett SE**, Burch V, **Gillberg C**, **Scott RC**, **Neville BG** (2015) **Cognition in school-aged children with "active" epilepsy: A population-based study** *J. Clin. Exp. Neuropsychol.* 37(4):429-38
50. **Reilly C**, Atkinson P, Das KB, Chin RF, **Aylett SE**, Burch V, **Gillberg C**, **Scott RC**, **Neville BG** (2015) **Features of developmental coordination disorder in active childhood epilepsy: a population-based study** *Dev. Med. Child. Neurol.* 57(9):829-34
51. **Reilly C**, Atkinson P, Das KB, Chin RF, **Aylett SE**, Burch V, **Gillberg C**, **Scott RC**, **Neville BG** (2015) **Factors associated with quality of life in active childhood epilepsy: a population-based study** *Eur. J. Paediatr. Neurol.* 19(3):308-13
52. **Reilly C**, McWilliams A, Heyman, I (2015) **What's in a name? 'Psychogenic' non-epileptic events in children and adolescents** *Developmental Medicine and Child Neurology* 57(1):100-101
53. **Reilly C**, Taft C, Nelander M, Malmgren K, Olsson I (2015) **Health-related quality of life and emotional well-being in parents of children with epilepsy referred for presurgical evaluation in Sweden** *Epilepsy & Behavior* 31(53):10-4
54. Ruggieri L, Giannuzzi V, Baiardi P, Bonifazi F, Davies EH, Giaquinto C, Bonifazi D, Felisi M, Chiron C, **Pressler R**, Rabe H, Whitaker MJ, Neubert A, Jacqz-Aigrain E, Eichler I, Turner MA, Ceci A; on behalf of the GRiP Consortium (2015) **Successful private-public funding of paediatric medicines research: lessons from the EU programme to fund research into off-patent medicines** *Eur. J. Pediatr.* 174(4):481-91
55. Sauro KM, Holroyd-Leduc J, Wiebe S, Quan H, Cooke L, Cross JH, Mathern GW, Armson H, Stromer J, Jetté N (2014) **Knowledge translation of an online tool for referral for epilepsy surgery evaluation** *Neurol. Clin. Pract. (in press)*
56. Schoeler NE, **Cross JH**, Drury S, Lench N, McMahon JM, Mackay MT, Scheffer IE, Sander JW, and Sisodiya SM (2015) **A favourable response to ketogenic dietary therapies is rarely due to undiagnosed glucose 1 transporter deficiency syndrome** *Dev. Med. Child. Neurol.* 57(10):896-897
57. Schoeler NE, Leu C, White J, Plagnol V, Ellard S, Matarin M, Yellen G, Thiele EA, Mckay M, McMahon JM, Scheffer IE, Sander JW, **Cross JH**, Sisodiya SM (2015) **Variants in KCNJ11 and BAD do not predict response to ketogenic dietary therapies for epilepsy** *Epilepsy Research* 118:22-28
58. Shahni R, Cale CM, Anderson G, Osellame LD, Hambleton S, **Jacques TS**, Wedatilake Y, Taanman JW, Chan E, Qasim W, Plagnol V, Chalasani A, MR, Gilmour KC and **Rahman S** (2015) **Signal transducer and activator of transcription 2 (STAT2) is a novel regulator of mitochondrial fission** *Brain* 138(Pt 10):2834-46
59. Shamshiri EA, Centeno M, Tierney TM, St Pier K, **Pressler R**, Perani S, **Cross JH**, **Carmichael DW** (2016) **Assessing the impact of interictal discharges on resting state network connectivity in focal epilepsy using EEG fMRI and a natural stimulus task** *Epilepsia* 56:26-27
60. Skirrow C, **Cross JH**, Harrison S, Cormack F, Harkness W, Coleman R, Meierotto E, Gaiottino J, **Vargha-Khadem F**, **Baldeweg T** (2015) **Temporal lobe surgery in childhood and neuroanatomical predictors of long-term declarative memory outcome** *Brain* 138(1):80-93
61. Spagnoli C, Kugathasan U, Brittain H, **Boyd SG** (2015) **Epileptic spasms and early-onset photosensitive epilepsy in Patau syndrome: An EEG study** *Brain. Dev.* 37(7):704-13

62. Stöberg T, McTague A, Ruiz AJ, Hirata H, Zhen J, Long P, Farabella I, Meyer E, Kawahara A, Vassallo G, Stivaros SM, Bjursell MK, Stranneheim H, Tigerschiöld S, Persson B, Bangash I, Das K, Hughes D, Lesko N, Lundeberg J, **Scott RC**, Poduri A, Scheffer IE, Smith H, Gissen P, Schorge S, Reith ME, Topf M, Kullmann DM, Harvey RJ, Wedell A, **Kurian MA** (2015) **Mutations in SLC12A5 in epilepsy of infancy with migrating focal seizures** *Nature Communications* 6:8038
63. Tierney TM, Weiss-Croft LJ, Centeno M, Shamshiri EA, Perani S, **Baldeweg T, Clark CA, Carmichael DW** (2015) **FIACH: a biophysical model for retrospective noise control in fMRI** *Neuroimage* 124:1009-1020
64. Trump N, McTague A, Brittain H, Papandreou A, Meyer E, Ngoh A, Palmer R, Morrogh D, Boustred C, Hurst JA, Jenkins L, **Kurian MA, Scott RH** (2016) **Improving diagnosis and broadening the phenotypes in early-onset seizure and severe developmental delay disorders through gene panel analysis** *Journal of Medical Genetics* 53(5):310-317
65. **Varadkar S, Tisdall M** (2016) **Language after Hemispherotomy in Rasmussen Syndrome** *Pediatric Neurology Briefs* 30(2):13
66. Waelchli R, **Aylett SE**, Atherton D, Thompson DJ, Chong WK, Kinsler VA (2015) **Classification of neurological abnormalities in children with congenital melanocytic naevus syndrome identifies magnetic resonance imaging as the best predictor of clinical outcome** *Br. J. Dermatol.* 173(3):739-50
67. Wedatilake Y, Plagnol V, Anderson G, Paine S, Clayton P, Jacques T, **Rahman S** (2015) **Tubular aggregates caused by serine active site containing 1 (SERAC1) mutations in a patient with a mitochondrial encephalopathy** *Neuropathol. Appl. Neurobiol.* 41(3):399-402
68. Weeke LC, Toet MC, van Rooij LG, Groenendaal F, Boylan GB, **Pressler RM**, Hellström-Westas L, van den Broek MP, de Vries LS (2016) **Lidocaine response rate in aEEG-confirmed neonatal seizures: Retrospective study of 413 full-term and preterm infants** *Epilepsia* 57(2):233-42
69. Werner K, Fosi T, Boyd SG, **Baldeweg T, Scott RC, Neville BG** (2015) **Temporal lobe impairment in West syndrome: event-related potential evidence** *Ann. Neurol.* 77(1):47-57
70. Wilmshurst JM, Burman R, Glauser T, Gaillard W, **Cross JH** (2015) **Treatment of Infants with epilepsy: Common practice across the world** *Epilepsia* 56(7):1033-46

## Reviews, editorials and letters

1. Bhalla D, Aziz H, Bergen D, Birbeck GL, Carpio A, Cavalheiro E, Chivorakoun P, **Cross JH**, Houinato D, Newton CR et al (2015) **Undue regulatory control on phenobarbital-an important yet overlooked reason for the epilepsy treatment gap** *Gray Matters Epilepsia* 56(4):659-662
2. **Cross H** (2015) **Epilepsy: behavioural, psychological, and ketogenic diet treatments** *BMJ Clinical Evidence: Systematic review* 1214
3. **Cross JH** (2015) **Epilepsy: Generalised seizures** *BMJ Clinical Evidence: Systematic review* 1201
4. Guerrini R, Duchowny M, Jayakar P, Krsek P, Kahane P, Tassi L, Melani F, Polster T, Andre VM, Cepeda C, Krueger DA, **Cross JH**, Spreafico R, Cosottini M, Gotman J, Chassoux F, Ryvlin P, Bartolomei F, Bernasconi A, Stefan H, Miller I, Devaux B, Najm I, Giordano F, Vonck K, Barba C, Blumcke I (2015) **Diagnostic methods and treatment options for focal cortical dysplasia** *Epilepsia* 56(11):1669-1686
5. Jones C, **Reilly C** (2016) **Parental anxiety in childhood epilepsy: A systematic review** *Epilepsia* 57(4):529-37
6. Koepp MJ, Caciagli L, **Pressler RM**, Lehnertz K, Beniczky S (2016) **Reflex seizures, traits, and epilepsies: from physiology to pathology** *Lancet. Neurol.* 15(1):92-105
7. Lake NJ, Compton AG, **Rahman S**, Thorburn DR (2015) **Leigh Syndrome: One disorder, more than 75 monogenic causes** *Ann. Neurol.* 79(2):190-203
8. McTague A, Howells KB, **Cross JH, Kurian MA**, Scheffer IE (2016) **The genetic landscape of the epileptic encephalopathies of infancy and childhood** *Lancet. Neurol.* 15:304-316
9. Ormazabal A, Casado M, Molero M, Montoya J, **Rahman S**, Aylett S, Hargreaves I, Heales S, Artuch R (2015) **Can folic acid play a role in mitochondrial disorders?** *Drug Discovery Today* 20(11):1349-54



10. **Pressler RM**, Boylan GB, Marlow N, de Vries LS, Blennow M, Chiron C, **Cross JH**, Hallberg B, Hellström-Westas L, Jullien V, Mangum B, Murphy B, Murray D, Pons G, Rennie J, Toet MC, Zohar S; NEMO consortium (NEonatal seizure treatment with Medication Off-patent) (2015) **Bumetanide for neonatal seizures-back from the cotside** *Nat. Rev. Neurol.* 11(12):724
11. **Rahman S** (2015) **Emerging aspects of treatment in mitochondrial disorders** *J. Inherit. Metab. Dis.* 38(4):641-53
12. **Rahman S** (2015) **Pathophysiology of mitochondrial disease causing epilepsy and status epilepticus** *Epilepsy. Behav.* 49:71-5
13. **Reilly C** (2015) **GRAY MATTERS. Indications and expectations for neuropsychological assessment in routine epilepsy care: Report of the ILAE Neuropsychology Task Force, Diagnostic Methods Commission, 2013–2017** *Epilepsia* 56(8):1315-24
14. **Varadkar S, Cross JH** (2015) **Rasmussen Syndrome and other inflammatory epilepsies** *Semin. Neurol.* 35(3):259-68
15. Verity C, Philip S, Martland T, Carter M, **Varadkar S**, Harkness W, **Cross JH**, Walsh R (2015) **Misleading data in Shastin et al's paper** *Child's Nervous System* 31(7):1017-8
16. Wilmshurst JM, Gaillard WD, Puthenveetil V, Tsuchida T, Plouin P, Van Bogaert P, Carrizosa J, Elia M, Craiu D, Jovic N, Nordli D, Hirtz D, Wong V, Glauser T, Mizrahi E, Kim HD, **Cross JH** (2015) **Summary of Recommendations for the Management of Infantile Seizures: Task Force Report for the ILAE Commission of Pediatrics** *Epilepsia* 56(8):1185-97

## Edited books

1. Malmgren K, **Cross JH**, Baxendale S Ed. **Long term outcome of epilepsy surgery** (2015) *Springer, New York*
2. Moshe S, **Cross JH**, de Bellescize J, Nordli D, Vigeveno F, de Vries L Ed. **Seizures and syndromes of onset** *In: The First Two Years of Life* Editor: John Libbey (2015) *Eurotext, Paris*

## Edited chapters in books

1. **Baldeweg T**, Skirrow C **Long-term cognitive outcomes after epilepsy surgery in children** *In: Long-term Outcomes of Epilepsy Surgery in Adults and Children* Editors: Malmgren K, Baxendale S, **Cross JH** (2015) *Springer Verlag*
2. **Cross JH** **Childhood epilepsy** *In: Cambridge Encyclopedia of Child Development* Editors: Brian Hopkins, Elena Geangu, Sally Linkenauger (2015) *Cambridge University Press*
3. **Heyman I**, Skuse D, Goodman, R **Brain Disorders and Psychopathology, Chap 31 pg 998-1019** *In: Child and Adolescent Psychiatry* Editors: Rutter, Taylor (2015) *Wiley*
4. Mizrahi EM, **Pressler RM** **Foundations of neonatal epileptology: classification of seizures and epilepsies in the neonate and their aetiology, electroencephalography, prognosis and pathophysiology** *In: Seizures of Onset in the First Two Years of Life* Editors: N Moshé et al (2015) *McGraw Hill*
5. Skirrow C, **Baldeweg T** **Educational and employment outcomes following epilepsy surgery in childhood** *In: Long-term Outcomes of Epilepsy Surgery in Adults and Children* Editors: Malmgren K, Baxendale S, **Cross JH** (2015) *Springer Verlag*
6. Smith ML, **Baldeweg T** **Cognition, Language, and Memory Outcomes** *In: Pediatric Epilepsy Surgery (Section V: Following Surgery)* Editors: Arzimanoglou A, **Cross JH**, Gaillard WD, Holthausen H, Jayakar P, Kahane P, Mathern G (2016)

## **Unit Involvement in Educational Programmes**

Epilepsy in Infants and Young Children: A Guide for Parents (2016)  
Brochure and interactive online PDF  
*Young Epilepsy*

Workshop for teenagers with epilepsy and parents (2016)  
*Great Ormond Street Hospital NHS Trust*

London Brain Project: Beyond Seizures (Nov 2013 - present)  
*University College London*

Paediatric Epilepsy Masterclasses (2012, 2014, 2016)  
*Young Epilepsy*

Neuropsychiatry residential course (2014, 2015)  
*Oxford*

Course Director for the UK ILAE EEG course  
*International League against Epilepsy (ILAE)*

Faculty Member and Advisory Group Member of the Paediatric Epilepsy Training Programme (PET) course  
*British Paediatric Neurology Association*

## **Unit Roles**

Editor, Developmental Cognitive Neuroscience (Elsevier) since (Dec 2014-present)  
*University College London*

Reviewing and expert opinion roles including reviewing for NIHR central commissioning facility (Research for Patient Benefit Program) (2011-present)  
*National Institute for Health Research (NIHR)*

Vignettes for NIHR Psychological and Community Therapies Panel of the NETSCC (HTA program) (2011-present)  
*National Institute for Health Research (NIHR)*

# Professional Recognition and Awards



**Helen Cross**

Officer of the Most Excellent Order of the British Empire  
(June 2015)

*The Sovereign of the United Kingdom*



**Michelle Downes**

2015-16 Provost's Awards  
for Public Engagement -  
Student Engager of the Year  
Award (June 2015)

*University College London*



**Isobel Heyman**

Psychiatrist of the Year 2015  
(first paediatric recipient!)

*Royal College of  
Psychiatrists*



**Faraneh Vargha-Khadem**

Distinguished Career Award  
(May 2016)

*International  
Neuropsychological Society*



**Ronit Pressler**

Readership in Clinical  
Neuroscience (June 2015)  
*University College London*



**Sophie Bennett**

Young Epilepsy Champions  
Awards 2016 - Discovery  
Award (May 2016)

*Young Epilepsy*



**Helen Cross**

NIHR Senior Investigator  
(2016-2020)

*The NHS National Institute  
for Health Research (NIHR)*

**Sophie Adler**

Merit Abstract Award (June  
2016)

*Organisation of Human Brain  
Mapping*

**Sarah Rudebeck**

Marit Korkman Award for the best submission on a  
paediatric neuropsychology topic by a graduate student,  
intern or post-doctoral fellow (July 2016)

*International Neuropsychological Society*

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

As a national charity and a centre of expertise for all young people with epilepsy, we have over 100 years' experience to share;  
**let's work together.**

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

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Research Manager  
Tel: 01342 831274  
Email: [research@youngepilepsy.org.uk](mailto:research@youngepilepsy.org.uk)



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