



Paediatric Epilepsy Research Annual Report 2011



Great Ormond Street
Hospital for Children



NHS Trust

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About Young Epilepsy

Young Epilepsy is the national charity working exclusively on behalf of children and young people with epilepsy aged 25 years and under. With over 100 years expertise it provides world class diagnosis, assessment and rehabilitation for children and young people with epilepsy. The charity also operates internationally renowned research programme co-ordinated by Professor Helen Cross, the Prince of Wales's Chair of Childhood Epilepsy. Young Epilepsy has a specialist school and college, providing day, residential and short break services for children and young people with epilepsy, autism and other neurological conditions.

Young Epilepsy aims to achieve better futures for young lives with epilepsy and to raise awareness and understanding of epilepsy and issues associated with the condition. The charity provides support and information for parents, children and young people and training for professionals. It campaigns for better access to, and quality of, health and education services. We offer tailor-made training across the country for parents, teenagers and health, social care and education professionals and also work in schools.

Introduction



It is with great pleasure that I introduce our research report for 2011 for the epilepsy unit across UCL-Institute of Child Health, Great Ormond Street Hospital & Young Epilepsy.

Our research continues to focus on all aspects of childhood epilepsy looking toward optimising outcomes in children with epilepsy. New projects initiated over the past year have included a genetic study examining a possible genetic basis to treatment outcome with the ketogenic diet, a study assessing the feasibility and utility of EEG-fMRI in the presurgical evaluation of children with drug resistant focal epilepsy, and a newly-funded study to evaluate the role of sleep in learning and memory consolidation in children with focal epilepsy.

We have secured new grant monies totalling £510,868 over this period. Further, we have as a unit been responsible for 44 peer reviewed publications of primary research, and 10 publications including reviews and commentaries of expert opinion.

We hosted our second annual research retreat for researchers and collaborators in January, moderated by Professor Solomon Moshé from New York. Here, many of our projects were presented and discussed enabling further ideas to be explored.

Over the last 12 months we unfortunately said goodbye to Professor Charles Newton who moved to Oxford and Dr Richard Chin who moved to Edinburgh. They however continue to collaborate on many projects. We also welcomed Dr Manju Kurian, Clinician Scientist, who will further our research into the genetics of early onset epileptic encephalopathies.

Our aim over the next year is to widen our focus of research into education; to look at interventions that may improve outcomes following on from research into underlying mechanisms of cognitive dysfunction.

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

Research Strategy for Childhood Epilepsy

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

The overriding goal of epilepsy research within this joint unit is to enable a better long outcome and to reduce the overall burden for children with epilepsy. The unit - encompassing the UCL-Institute of Child Health, Great Ormond Street Hospital for Children and Young Epilepsy - is in a unique position of incorporating review of children with a range of severity from newly diagnosed to complex. Further collaboration across UCL allows continuation of work into adulthood, allowing study across the whole age range. The educational and behavioural expertise within Young Epilepsy allows interventional study beyond medical treatment.

Research Partners

UCL Institute of Child Health

UCL Institute of Child Health (ICH) is one of the world's pioneering paediatric research centres and 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.

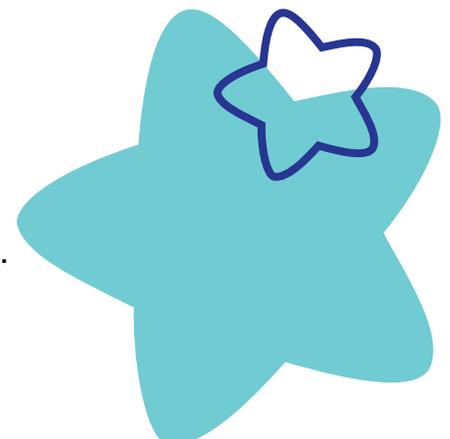
In keeping with a commitment to disease prevention, ICH is active in teaching and research aimed at developing interventions to promote health both during childhood and in the later years of life.

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. There are more than 50 different clinical specialties at GOSH.

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

The hospital is committed to carrying out pioneering research to find treatments and cures for some of the most complex illnesses, for the benefit of children here in the UK and worldwide.



Research Update

Below is a brief update on the research projects being carried out within the unit:

The impact of reducing anti-epileptic drug load on quality of life in children with refractory epilepsy

Project Aim: To prospectively determine the effect of reducing Anti-Epileptic Drug (AED) load on the quality of life and seizure control in children with refractory epilepsy who are on AED polytherapy

Investigators: Rod Scott, Krishna Das, Suresh Pujar, Archana Desurkar, Kirsten McHale, Brian Neville

Update: Recruitment of research participants from St Piers School and College at Young Epilepsy is underway.

Educational problems of children with epilepsy: their identification and management

Project Aim: To determine the prevalence of learning and behaviour difficulties in school-age children with epilepsy

Investigators: Brian Neville, Colin Reilly, Patricia Atkinson, Rod Scott, Victoria Burch, Paul McCrone, Richard Chin, Sarah Aylett, Krishna Das, Dame Philippa Russell, Christopher Gillberg

Update: The Educational Psychologist is in post and the initial screening and detailed assessments is in progress.

Prevalence and clinical outcome of Rasmussen Encephalitis in children

Project Aim: To collate information on the prevalence, symptomology, management and outcome of children with Rasmussen syndrome in the UK

Investigators: Kate Lamb, Robert Robinson, Helen Cross

Update: Information is being collated from clinicians across the UK who report through the British Paediatric Neurology Surveillance Unit (BPNSU) who have managed or are currently managing a child with Rasmussen Encephalitis.



Research Update

Beyond IQ: Cognitive-behavioural profiles of children with complex epilepsy and intellectual disability

Project Aim: To establish whether age- and IQ-matched groups of young people with mild-to-moderate intellectual disability (ID) and complex focal (FE) or generalised epilepsy (GE) would perform differently on cognitive tasks of executive function, everyday memory, and social communication.

Investigators: Sara Shavel-Jessop, Chris Barker, Peter Rankin, Sarah Aylett

Update: The project has been completed and is being written up for publication. It is suggested, on the basis of the findings of this study, that having focal or generalised epilepsy does not appear to differentially affect performance on a range of specific and general ability tasks in young people with mild-to-moderate intellectual disability. The study also demonstrates the utility of standardised age-appropriate assessment in this population, and supports its wider use in research and clinical practice.

Epilepsy genomics in childhood: finding the causes, directing treatment

Project Aim: To investigate whether some children have a genetic predisposition to epilepsy, and if this is common in certain types of epilepsy

Investigators: Anna Tostevin, Helen Cross, Sanjay M. Sisodiya

Update: Data collection is underway. Over 150 participants have so far been recruited. So far there has been a 10% rate of abnormality detected.

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

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

Update: The initial year funding has been secured for the research fellow who will be in post from March 2012.

The encephalopathy of infantile spasms

Project Aim: To describe the encephalopathy of infantile spasms using ERPs and MRIs with controls

Investigators: Brian Neville, Rod Scott, Stewart Boyd, Tang Fosi

Update: This is now being written up with important findings.



Research Update

A genetic basis for response to the Ketogenic Diet

Project Aim: To determine whether there is a genetic basis to treatment outcome with the Ketogenic Diet in drug-resistant epilepsy

Investigators: Natasha Payne, Helen Cross, Sanjay M. Sisodiya

Update: Recruitment of research participants is underway from Great Ormond Street Hospital, Evelina Children's Hospital, Young Epilepsy (in conjunction with Matthew's Friends), The National Hospital for Neurology and Neurosurgery and Birmingham Children's Hospital. R&D approval has also been obtained for St George's, Addenbrooke's and Bristol, where recruitment is to begin shortly.

Elucidation of the Biochemical Mechanisms Responsible for the Efficacy of the Ketogenic Diet

Project Aim: To determine changes seen in medium chain fatty acids in children treated with the ketogenic diet, and determine their possible role in the underlying mechanism of effect

Investigators: Sean Hughes, Helen Cross, Simon Heales

Update: Research participants will be recruited from Great Ormond Street Hospital from March 2012.

The effect of a child's epilepsy on sibling quality of life

Project Aim: To assess how having a brother or sister with epilepsy affects a child's quality of life compared to siblings of children who have a neurological disorder other than epilepsy

Investigators: Sanam Memon, Krishna Das, Victoria Burch, Richard Chin

Update: The project has been completed and is being written up for publication. Sanam Memon was awarded The Association of Physicians Elective Prize in July 2011 from the University of Aberdeen for this project. This is awarded to a student who submits a project that has achieved a high standard of excellence. Results from this preliminary study did not show any significant difference between cases and controls. Learning disability and behavioural difficulties were reported as the main cause of worry for siblings rather than seizures.

Research Update

The spectrum of epileptic spasms in children

Project Aim: Retrospective study to evaluate the range of phenotype of epileptic spasms in children captured on video-EEG

Investigators: Daniel Carranza, Helen Cross, Ingrid Scheffer

Update: This is a collaborative study with investigators from Melbourne, Australia. Over 600 cases have been exclusively confirmed on video-EEG from a wide retrospective cohort of children with epileptic spasms from the UK and Australia. The reviewed data shows a wide age distribution with a significant proportion (15%) of non-infantile onset spasms (>1 year old at onset). Newly described etiologies, particularly subtle structural lesions and genetic causes, are represented in a small proportion of cases.

Long term outcomes of childhood status epilepticus

Project Aim: To characterise the prevalence, nature and structural substrates of epilepsy 5-10 years after an episode of convulsive epilepticus in childhood and to identify early predictors of who will develop epilepsy

Investigators: Suresh Pujar, Rod Scott, Chris Clark, Michelle de Haan, Kling Chong, Brian Neville, Richard Chin

Update: Preliminary results is showing that the mortality within 10 years following convulsive status epilepticus (CSE) is substantial, presence of prior neurological impairment being the main determinant, but the outcome is good in children with no neurological impairments before the episode of CSE.

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, Chris Clark, Jonathan Clayden, Ronit Pressler, Helen Cross

Update: This project is in collaboration with the Department of Biochemistry, UCL-ICH. Research participants will be recruited from Great Ormond Street Hospital from March 2012.



The Research Team

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

Principal investigators

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

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

Dr Manju Kurian *Consultant and Clinician Scientist*

Professor Brian Neville *Emeritus Professor of Childhood Epilepsy*

Dr Ronit Pressler *Consultant and Honorary Senior Lecturer in Clinical Neurophysiology*

Dr Rod Scott *Reader in Paediatric Neuroscience*

PhD students

Alex Bender (jointly with Dartmouth College) – *Neurophysiological mechanisms of cognitive impairments in Dravet Syndrome*

Samantha Chan – *Sleep and memory in children with focal epilepsy*

Ben Duffy – *Experimental Imaging Studies Post-Status Epilepticus*

Tang Fosi – *The neurological basis for cognitive and autistic regression in infants with West syndrome (infantile spasms)*

Amanda Hernan (jointly with Dartmouth College) – *The effects of early life seizures on short term plasticity in the prefrontal cortex*

Sean Hughes (jointly with Biochemistry, ICH) – *Elucidation of the Biochemical Mechanisms Responsible for the Efficacy of the Ketogenic Diet*

Jonathan Kleen (jointly with Dartmouth College) – *Characteristics and mechanisms of cognitive impairment in epilepsy. (MD/PhD). Awarded 2011. Currently completing medical training*

Marcella Lucas (jointly with Dartmouth College) – *Mechanisms of cognitive impairment in rats with malformations of cortical development*

Natasha Payne (jointly with ION) – *A Genetic Basis for Response to the Ketogenic Diet in Epilepsy*

Suresh Pujar – *The outcomes 5-10 years after childhood convulsive status epilepticus: a population based study*

Ali Titiz (jointly with Dartmouth College) – *The impact of epileptic discharges on memory consolidation during sleep*

Michael Yoong – *The consequences and outcomes of convulsive status epilepticus in childhood*

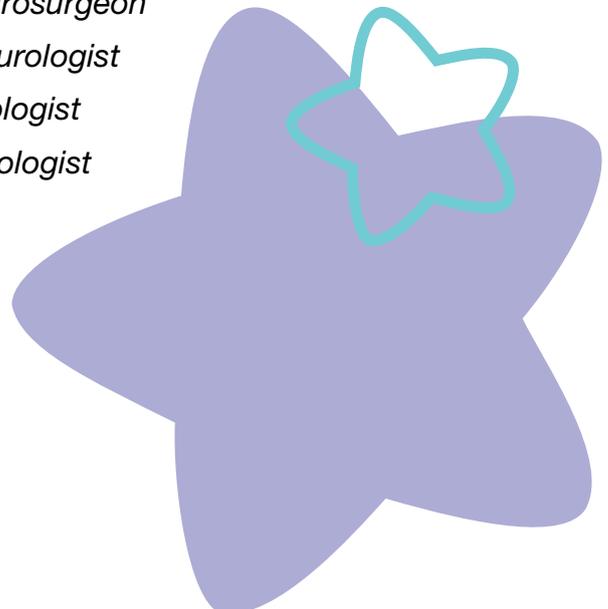
The Research Team

Research staff

Daniel Carranza *Clinical/Research Fellow*
Antionietta Coppola *Research Fellow*
Havinder Hara *NEMO Coordinator*
Marina Martinos *Postdoctoral Neuropsychologist*
Kirsten McHale *Research Nurse*
Amy Mctague *Clinical/Research Fellow*
Angela Mensah *Research Coordinator*
Esther Meyer *Research Fellow*
Colin Reilly *Research Psychologist*
Anna Tostevin *Research Assistant*

Clinicians in neuroscience active in epilepsy research

Dr Patricia Atkinson *Consultant Community Paediatrician*
Dr Sarah Aylett *Consultant Paediatric Neurologist*
Dr Stewart Boyd *Consultant Neurophysiologist*
Mr Aabir Chakraborty *Consultant Paediatric Neurosurgeon*
Dr Maria Clark *Consultant Paediatric Neurologist*
Dr Krishna Das *Consultant Paediatric Neurologist*
Dr Archana Desurkar *Consultant Paediatric Neurologist*
Dr Christin Eltze *Consultant Paediatric Neurologist*
Mr William Harkness *Consultant Paediatric Neurosurgeon*
Dr Cheryl Hemingway *Consultant Paediatric Neurologist*
Dr Robert Robinson *Consultant Paediatric Neurologist*
Dr Sophia Varadkar *Consultant Paediatric Neurologist*



Epilepsy Research Retreat

The Epilepsy Research Retreat serves as an annual get together of researchers and collaborators across the unit. This has followed models from other centres around the world and gives researchers the opportunity to discuss ongoing projects, completed projects and possible future directions of research.

The 2012 research retreat took place on 26-27 January at Alexander House Hotel in East Grinstead with Professor Solomon Moshé as the moderator. Professor Moshé is Professor of Neurology, Neuroscience & Paediatrics at Einstein College of Medicine, New York as well as the current President of the International League Against Epilepsy (ILAE). The meeting brought together 70 researchers from Young Epilepsy, UCL-Institute of Child Health, UCL-Institute of Neurology, Great Ormond Street Hospital and Dartmouth College, USA.



Epilepsy Research Retreat

There were presentations on 23 of the projects taking place across the unit ranging from neuropathology to neuroimaging, genetics to academic achievement as well as results of animal work from our collaborators in Dartmouth. Discussions at the end of each presentation gave investigators the opportunity to receive comments and feedback from fellow researchers and principal investigators.

The retreat also proved to be a highly social occasion. This aside, it successfully highlighted the breadth of epilepsy research being undertaken across the unit and also served as a way of motivating young researchers who may not have previously had the opportunity to meet other members of the unit.



Publications - 2011

Peer Reviewed Publications

1. Cormack F, Vargha-Khadem F, Wood SJ, **Cross JH**, Baldeweg T. Memory in paediatric temporal lobe epilepsy: Effects of lesion type and side. *Epilepsy Res.* 2011 Oct 29. [Epub ahead of print].
2. D'Argenzio L, Colonnelli MC, Harrison S, Jacques TS, Harkness W, Vargha-Khadem F, **Scott RC**, **Cross JH**. Cognitive outcome after extratemporal epilepsy surgery in childhood. *Epilepsia.* 2011 Nov; 52(11):1966-72.
3. Gaillard WD, **Cross JH**, Duncan JS, Stefan H, Theodore WH; Task Force on Practice Parameter Imaging Guidelines for International League Against Epilepsy, Commission for Diagnostics. Epilepsy imaging study guideline criteria: commentary on diagnostic testing study guidelines and practice parameters. *Epilepsia.* 2011 Sep;52(9):1750-6.
4. Catarino CB, Liu JY, Liagkouras I, Gibbons VS, Labrum RW, Ellis R, Woodward C, Davis MB, Smith SJ, **Cross JH**, Appleton RE, Yendle SC, McMahon JM, Bellows ST, Jacques TS, Zuberi SM, Koepp MJ, Martinian L, Scheffer IE, Thom M, Sisodiya SM. Dravet syndrome as epileptic encephalopathy: evidence from long-term course and neuropathology. *Brain.* 2011 Oct;134(Pt 10):2982-3010.
5. Illingworth MA, Hanrahan D, Anderson CE, O'Kane K, Anderson J, Casey M, de Sousa C, **Cross JH**, Wright S, Dale RC, Vincent A, **Kurian MA**. Elevated VGKC-complex antibodies in a boy with fever-induced refractory epileptic encephalopathy in school-age children (FIRES). *Dev Med Child Neurol.* 2011 Nov;53(11):1053-7.
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8. **Cross JH**. Epilepsy in the WHO European region: fostering epilepsy care in Europe. *Epilepsia.* 2011 Jan;52(1):187-8.
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12. Kariuki SM, Abubakar A, Holding PA, Mung'ala-Odera V, Chengo E, Kihara M, **Neville BG**, Newton CR. Behavioral problems in children with epilepsy in rural Kenya. *Epilepsy Behav.* Epub 2011 Nov 26.
13. Burton K, Rogathe J, Hunter E, Burton M, Swai M, Todd J, **Neville B**, Walker R, Newton C. Behavioural comorbidity in Tanzanian children with epilepsy: a community-based case-control study. *Dev Med Child Neurol.* 2011 Dec;53(12):1135-42.
14. Fons C, Campistol J, Panagiotakaki E, Giannotta M, Arzimanoglou A, Gobbi G, **Neville B**, Ebinger F, Nevšimalová S, Laan L, Casaer P, Spiel G, Ninan M, Sange G, Artuch R, Schyns T, Vavassori R, Poncelin D; ENRAH Consortium. Alternating hemiplegia of childhood: metabolic studies in the largest European series of patients. *Eur J Paediatr Neurol.* Epub 2011 Sep 25.

Publications - 2011

15. Pujar SS, **Neville BG**, **Scott RC**, Chin RF; North London Epilepsy Research Network. Death within 8 years after childhood convulsive status epilepticus: a population-based study. *Brain*. 2011 Oct;134 (Pt 10):2819-27.
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18. Kleen JK, Wu EX, Holmes GL, **Scott RC**, Lenck-Santini PP. Enhanced oscillatory activity in the hippocampal-prefrontal network is related to short-term memory function after early-life seizures. *J Neurosci*. 2011 Oct 26;31(43):15397-406.
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Publications - 2011

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Publications - 2011

Guidelines/Reviews/Editorials/Letters

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6. Reilly C, Agnew R, **Neville BG**. Depression and anxiety in childhood epilepsy: a review. *Seizure*. 2011 Oct;20(8):589-97.
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8. Pritchett R, Kemp J, Wilson P, Minnis H, Bryce G, **Gillberg C**. Quick, simple measures of family relationships for use in clinical practice and research. A systematic review. *Fam Pract*. 2011 Apr;28(2): 172-87.
9. **Cross JH**, Kossoff EH. Dietary treatments: The road from Phoenix to Edinburgh. *Epilepsy Res*. 2011 Sep 26. [Epub ahead of print].
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Chapters in Books

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Better futures for young lives with epilepsy

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