

**EPILEPSY RESEARCH  
CENTRE**

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**Professor Samuel Berkovic**  
Neurologist



**Professor Ingrid Scheffer**  
Paediatric Neurologist

**RECENT NEWS**

Last year we published exciting discoveries into the causes of severe epilepsies beginning in the first year of life, including epilepsies associated with vaccination. Our publication in *Lancet Neurology* describing *SCN1A* mutations in "vaccine encephalopathies" was considered to be the most important epilepsy publication for 2006. See page 2 for more details.



THE UNIVERSITY OF  
MELBOURNE



**EPILEPSY GENETICS**

*Newsletter*

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2007

Another successful year has passed at the Epilepsy Research Centre filled with important scientific discoveries and significant publications. Our research continues to grow as we recruit more individuals, twins and families, who are essential in our endeavour to discover genes important in epilepsy. We are in our 18th year conducting epilepsy genetics research and the number of participants has now reached close to 6500. We wish to extend our heartfelt thanks to all participants and their families who have taken part in this research, as well as the clinicians who have referred them, for without them, our research would not be possible. With your support we hope to continue investigating the mechanisms that cause epilepsy, which will hopefully one day lead to improvements in the treatment and the lives of people with seizures.

2006 saw us bid a fond farewell to neurology fellow Dr Christopher Derry who, after four and a half years with us, has submitted his PhD and returned to the United Kingdom to take up a clinical neurology position. We welcomed Dr Yu-Hong Deng, an adult neurologist from China, who has a particular interest in studying families with Generalised Epilepsy with Febrile Seizures Plus. Dr Douglas Crompton joined us recently from Newcastle, United Kingdom, as a post-doctoral research fellow. Dr Crompton will be doing clinical epilepsy genetics research, having already completed a PhD and with a background in molecular genetics and

neurology. Alicia Calderone joined the team as a research assistant and is contributing to our important family studies. In addition, Dr Patrick Carney, who worked at the Austin as a neurology registrar in 2005, will join us this year to commence a PhD.

Our new Program Grant from the National Health and Medical Research Council commenced in 2006, allowing us to expand our research program into the overlap between epilepsy and intellectual disability, a complex and important area. We are delighted to be working closely with Associate Professor Jozef Gecz at the Women's and Children's Hospital in Adelaide, who is an international leader in the field of the genetics of intellectual disability. This collaboration, in combination with our existing and highly productive relationship with A/Prof John Mulley's molecular genetics group, promises to yield very exciting discoveries.

Our website, [www.epilepsyresearch.org.au](http://www.epilepsyresearch.org.au), provides a range of information about the Epilepsy Research Centre, the research projects we are conducting and also information for epilepsy patients interested in seeking treatment at Austin Health. Past issues of the newsletter and links to other useful sites can also be found. If you would like to contact us with any specific queries about our research or any of our studies, please email us at [epilepsy-austin@unimelb.edu.au](mailto:epilepsy-austin@unimelb.edu.au).



*The Epilepsy Research Centre team and our collaborators at the 2006 Epilepsy Research Retreat*

**SCN1A MUTATIONS IN "VACCINE ENCEPHALOPATHY"**

Some children experience their first seizure within hours of being vaccinated, which leads their parents and doctors to believe that the vaccination caused the child's epilepsy. When this is associated with ongoing epilepsy and intellectual disability, it is known as so-called "vaccine encephalopathy". Over the last four years, we have been investigating the genes causing severe epilepsy beginning in the first year of life in a large group of children from around the world. Within this group of children, we identified 14 who had their first seizure within 72 hours of vaccination.

Re-analysis of the clinical and EEG features in these patients led to 12 being

diagnosed with Dravet Syndrome (also known as Severe Myoclonic Epilepsy of Infancy or SMEI) or its borderline variant. Dravet syndrome is a severe epilepsy syndrome beginning in the first year of life in a previously normal child. Children with Dravet syndrome often have seizures triggered by fever or being unwell. They experience many different types of seizures which are difficult to control, and the child usually develops some degree of intellectual disability. About 70% of patients with Dravet syndrome have genetic changes in the neuronal sodium channel gene *SCN1A*, which is the cause of their disorder.

We identified abnormalities (mutations) in the *SCN1A* gene in 11 of the 14 patients

with vaccine encephalopathy. These mutations are present in every cell of the patient's body, so could not have occurred as a result of the vaccine. The vaccine was incorrectly blamed as the cause of the encephalopathy because seizures began so close to the time of vaccination. A possible explanation is that fever commonly occurs after vaccination and could trigger the first seizure in infants with *SCN1A* mutations. We doubt that avoiding immunization would have prevented the epilepsy from occurring as it is likely that another infection or illness would have triggered the first seizure if the vaccination had not.

**RECOGNIZING DRAVET SYNDROME IN ADULTS**

The diagnosis of Dravet syndrome is complex and is based on a patient's early childhood history of seizures and development, together with their EEG and MRI findings. It is often difficult to obtain details about an adult patient's early history. As Dravet syndrome has only recently been recognized, the diagnosis may not have been made in affected adults. We therefore studied adults with Dravet syndrome to see if there were

specific features that might aid in the diagnosis of Dravet syndrome in adult life.

Our 14 adult patients with Dravet syndrome had ongoing seizures including a range of different seizure types. Most patients had some level of intellectual disability, however one patient was of normal intellect. Two adults lived independently. Essentially we found that the diagnosis remains reliant on the

patient's early history and the key is to obtain the history from parents and hospitals about the first few years of the patient's life. There was no characteristic pattern in adult life that was distinctive enough to indicate a diagnosis of Dravet syndrome. It is important that adult neurologists consider the diagnosis as there are diagnostic, treatment and genetic counseling implications for patients and their families.

**LAUNCH OF THE AUSTIN KETOGENIC DIET PROGRAM**

The ketogenic diet (KD) is a high fat, low carbohydrate and moderate protein diet that has been used to treat epilepsy since the 1920s. It became less popular with the development of anti-epileptic medications in the 1970s but there has been a recent resurgence of interest over the past ten years. This is because there remains a group of patients in whom conventional anti-epileptic drugs do not work. However there have been no research studies investigating which patients are most likely to benefit from the ketogenic diet.

The Ketogenic Diet Program was established at Austin Health in 2005 by Professor Ingrid Scheffer, with Paediatric Epilepsy Nurse Specialist, Karen Stewart, Paediatric dietitians, Kellie Draffin and Judy Nation and Research Assistant, Danya Vears.



*The formal launch of our Ketogenic Diet Program coincided with 12-year-old Deana commencing the diet. Deana suffers from a severe myoclonic epilepsy syndrome.*

The program involves children and young adults who trial the diet for 3 months to improve their seizures. The families work closely with the nurses and dietitians to make sure an interesting and tempting range of food is available, while keeping strictly to the requirements of the diet and monitoring the health of the children.

Through the program we are interested in finding out if certain types of epilepsy

respond better to the ketogenic diet than others and monitoring potential side effects. Our research into the ketogenic diet is in collaboration with Dr Mark Mackay and his team at the Royal Children's Hospital. The Ketogenic Diet Program at Austin Health would not have been possible without support from the collaborating Ketogenic Diet team at the Royal Children's Hospital and the financial support of the O'Brien and Andrews families.



*The O'Brien and Andrews families with Prof Sam Berkovic, Prof Ingrid Scheffer and other members of the Ketogenic Diet Program team at the program launch.*

## MEASURING PHOTOSENSITIVITY IN EPILEPSY

Photosensitivity is the tendency to have seizures triggered by flickering lights, such as the sun playing on water or watching television. Photosensitivity is most commonly seen in people who have one of the Idiopathic Generalised Epilepsies (IGE), one of the most common group of epilepsies. It appears that photosensitivity contributes to epilepsy but is not a cause of epilepsy all by itself.

Testing for photosensitivity involves looking at a strobe light during the electroencephalogram (EEG) and is a routine part of EEG testing around the world. The test is positive if the EEG

shows particular "epileptiform" changes appearing due to the flickering light.

Significant work has recently gone into improving the strobe light used at Austin Health to detect photosensitivity. A new lamp has been purchased and a number of other advances including using patterned filters have been made. The brightness of the flash can now be adjusted so that those who find the strobe light hurts their eyes can be tested with a dimmer light. Photosensitivity is most commonly found in adolescents and becomes harder to detect as people get older. We hope that the new setup will detect photosensitivity more reliably, particularly in adults.

We have been interested in the genetic causes of photosensitivity for a number of years. In some families, a number of people have a positive EEG test for photosensitivity but not all have seizures. Dr Saul Mullen is currently doing a PhD to see if the improved strobe light will be more sensitive in detecting photosensitivity in family members including older family members where the changes may be more subtle. As photosensitivity is an inherited trait, we hope that the new testing will assist our family studies to find the genes causing this important seizure trigger.

## PUTTING EPILEPSY AT THE TOP – CLIMB TO MT KILIMANJARO

Helen's brother, Don, was diagnosed with epilepsy at the age of 21 after he was involved in a number of unexplained car accidents. Unfortunately his seizures remained uncontrolled and gradually became worse, having a significant impact on his ability to work, his social life and his family until his premature death at the age of 57 years.

Helen wanted to do something to remember and celebrate Don's life. When her family, husband Gary and their twin daughters Stephanie and Michelle, planned a trek to the summit of Mt Kilimanjaro to celebrate Stephanie and Michelle's 21st birthday, they decided to use the trip as a way to raise awareness of epilepsy and money for our research.

After months of weekend treks up Mt Macedon (1/6th the height of Mt Kilimanjaro!) and many gym sessions, the family completed their adventure in July 2006. They spent 5 days climbing to the 5895m summit, including a 7 1/2 hour final ascent starting at midnight in -10 to -20

degree C temperatures. They reached the summit at dawn on 13th July, exhausted and cold but were captivated by the stunning sunrise and the beautiful glacial scenery. Although there were many difficult, tiring and emotional moments, the family describes the trip as one of

the most amazing things they have experienced.

Helen, her family and all of us at the ERC would like to thank everyone who sponsored them and contributed valuable funds towards research into the causes and treatment of epilepsy.



Helen, Michelle and Stephanie Tennant at the summit of Mt Kilimanjaro raising awareness of epilepsy research

## THANK-YOU

We would like to thank everyone who has contributed to our research in 2006, by participating in the research studies, referring patients and families, or making financial contributions. We have been especially delighted when the families who have participated in our studies have sent

donations to our research. This reinforces the fact that our families as well as the researchers value the significance of our work.

If you would like to assist our important research into developing a better understanding of epilepsy by making a

donation to the Epilepsy Research Centre, please contact us on (03) 9496 2330, by email [epilepsy-austin@unimelb.edu.au](mailto:epilepsy-austin@unimelb.edu.au), or complete the section on the back of this page. Cheques should be made payable to the **Brain Research Institute**. Donations over \$2 are tax deductible.

## ETHICAL CONSIDERATIONS

The conduct of our research is over-seen by Human Research Ethics Committees at the hospitals where we recruit people for our studies. In recent times there have been some changes to the guidelines for certain research procedures. Study participants enrolled from July 2000 onwards are asked to state how long they permit their DNA sample to be used for our research. In addition, people who were enrolled as children are now required to give their own consent

when they reach 18 years of age. Participants are free to withdraw from the study at any time.

If we obtain a positive result on your sample or in your family, we will send you a letter stating that we have obtained a result. If you would like further information about this, we will be happy to provide it.

The recent introduction of the Health Records Act 2001 (Vic) may affect the way

we store your personal information. If you would like further information regarding any of these issues please do not hesitate to contact us. **In order to assist us with the process of keeping in touch with you, if you change your address we would be very grateful if you could advise us of your new contact details. (see attached sheet).**

## OUR TEAM:



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## FOR FURTHER INFORMATION:

Please do not hesitate to contact us at any time if you have questions about our research. Thank you again for your participation and support.

If you do not wish to receive future editions of this newsletter, please fill in the check box on the attached contact sheet and return it as requested.

## Donations

To make a donation please complete your contact details and return with your cheque to us at the address below. Cheques should be made payable to the **Brain Research Institute**.

Please find enclosed a cheque for my tax-deductible donation of

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We greatly appreciate all the assistance we receive from our supporters.

Please return to: Epilepsy Research Centre, Level 1, Neurosciences Building, Repatriation Hospital, Austin Health  
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