ANZCNS 5th Annual Scientific Meeting
(31st August – 2nd September 2016)
Fisher & Paykel Healthcare Clinical Education Centre
Auckland City Hospital, New Zealand
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WELCOME MESSAGES

Welcome Message From The Organising Committee

On behalf of the Organising Committee, we welcome you to the 5th Annual Scientific Meeting of the Australia and New Zealand Child Neurology Society. Our focus has been on showcasing our local researchers in paediatric neurology and providing a stimulating programme including local and international speakers.

This year the program includes speakers with expertise in the following areas:-

- Neurometabolic disorders
- Neuromuscular disorders
- Epilepsy
- Childhood stroke
- Adolescents with disability and transition to adult services
- Disorders of the fetal brain

In addition there will be platform presentations on a range of neuropaediatric research topics. We hope you enjoy the program.

Suzanne Davis
Chair, Organising Committee

Welcome Message From The Australia And New Zealand Child Neurology Society

On behalf of the Board of the Australia and New Zealand Child Neurology Society Ltd, I would like to welcome you to our 2016 Annual Scientific Meeting. The Organising Committee has worked hard to arrange this event at the Fisher & Paykel Healthcare Clinical Education Centre, Auckland. Once again, the programme is awash with paediatric neurology topics. The quality of abstract submissions continues to improve, with paediatric neuroscience research presented across the whole three days. We hope you enjoy the meeting!

Kate Riney
Chief Executive Officer, Australia and New Zealand Child Neurology Society

About Australia and New Zealand Child Neurology Society

The Australia and New Zealand Child Neurology Society (ANZCNS) is a collaborative group of approximately 100 Paediatric Neurologists, Paediatric Neurology Trainees and Allied Specialities from all over Australia and New Zealand. The organisation aims to promote the best possible care for children with neurological disease by fostering education and training of those who care for children with neurological diseases, advancing neuro-paediatric research and promoting improved standards of care for children with neurological disease. More information about ANZCNS is available on the ANZCNS website: www.anzcns.org.au
COMMITTEES

Organizing Committee
Suzanne Davis
Gina O’Grady
Melinda Nolan
Clare Spooner
Kate Riney
Anita Cairns

Abstract Review Committee
Suzanne Davis
Gina O’Grady
Kate Riney
Anita Cairns
Mark Mackay

Platform Judges
Suzanne Davis
Annie Bye
GENERAL CONFERENCE INFORMATION

Secretariat Office
Members of the Committee can be contacted via the Registration Desk.

For queries arising after the congress, please contact:

Australia and New Zealand Child Neurology Society
PO Box 8446, Woolloongabba, QLD 4102, Australia

f: +61 7 3068 2880
e: admin@anzcns.org.au
t: +61 7 3068 2909

The Conference Venue

Fisher & Paykel Healthcare Clinical Education Centre, Level 5, Auckland City Hospital, 2 Park Road, Grafton, Auckland 1023 New Zealand.

The Fisher & Paykel Healthcare Clinical Education Centre is a magnificent education facility in the heart of the Auckland City Hospital. The Clinical Education Centre (CEC) was opened in November 2004. The centre's primary focus is clinical education and training. Emphasised with an elegant spacious interior, the CEC is a leading conferencing facility in Auckland.

There are two carparks at Auckland City and Starship Children’s Hospital. Visitors and patients to Auckland City Hospital should use Carpark A. This is situated at the front of the hospital and accessed from Park Road. There is also a free 15-minute drop off and pick up in this carpark.

**Directions from the carpark:** Walk along the walk way to level 1 of the main building—follow the blue lines. Take the public lifts to level 5. Turn right and follow signs to the Clinical Education Centre (CEC).

**Directions from the main entrance:** Walk through the main entrance to the new hospital. Take the escalator to level 5 and turn left. The CEC entrance is approximately 30 meters on the left hand side.
Getting to and from the Venue

**Buses:**
Buses are available from and stop outside the main entrance to the hospital on Park Road. Detailed bus and public transport routes can be found at the Auckland Transport website or by contacting Auckland Transport on 09 366 6400 or 0800 10 30 80.

Auckland Airbus (from Auckland Airport): NZD$16.00 (one way) and NZD$28.00 (return). **Taxis:**
Taxis (from Auckland Airport): NZD$85.00 - $95.00 (one-way)

A taxi phone is located in the main entrance on Level 4, and at the entrance to the Emergency Department. Taxi ranks are located outside the main entrance at Level 4.

Registration Desk
The registration desk is located in the Foyer of the Fisher & Paykel Healthcare Clinical Education Centre. Delegates must provide photo identification (e.g. passport, driver’s license) along with a printed copy of their registration confirmation to facilitate registration. Please note that name badges must be clearly displayed at all times.

Registration desk opening hours are:
Wednesday 31st August: 08:30-17:00
Thursday 1st September: 08:00-17:00
Friday 2nd September: 08:00-15:00

Registration Entitlements
- Entry to all conference sessions
- Morning teas, lunches, afternoon teas
- Conference satchel and delegate satchel material
- Printed Handbook and final program

Speakers’ Information
Speakers must submit their final presentation to the audiovisual technician in the Auditorium – **at least 4 hours prior to their session start time.**

Exhibition
A trade exhibition is held in conjunction with the 5th ANZCNS Annual Scientific Meeting. This is an integral part of the event and allows delegates the opportunity to be updated on the latest developments in products and services in the field of child neurology. The exhibition area is located adjacent to the Auditorium in the A+ Trust Room, and is open at meal break times.

Continuing Medical Education
Fellows and trainees of the Royal Australasian College of Physicians can apply for one credit for each hour attended of the academic program of the conference.

Certificate of Attendance
A certificate of attendance is available for all delegates for collection from the registration desk on the last day of the conference.

Catering
Lunches and morning and afternoon teas are served in the A+ Trust Room. Any delegates with particular catering needs should have notified these on their registration bookings.
**Dress Code**
The 5th ANZCNS Annual Scientific Meeting promotes casual business attire for the duration of the conference.

**Mobile/cell phones**
Mobile/cell phones must be turned off or to vibrate mode during all sessions so as not to disturb speakers or other delegates. Pagers should be on vibrate mode.

**Community and Consumer Delegates**
The 5th ANZCNS Annual Scientific Meeting is primarily for health professionals. Community and consumer support groups have been welcomed to the 5th ANZCNS Annual Scientific Meeting to promote partnerships with health professionals towards a common goal. Such delegates should understand that the presentations will contain medical jargon and may contain information and images that some might find distressing. Questions from the open floor during sessions are invited primarily from health professionals.

**Photography**
The 5th ANZCNS Annual Scientific Meeting strictly prohibits all photography (ash, digital, or otherwise), audio and/or videotaping during the conference except by authorised photographers. There will be official ANZCNS photographers who will be capturing candid photos of the conference. These photographs will be used in congress communications. In registering and attending this conference you accept that your likeness may be taken in the form of photographs taken by photographers approved by Australia and New Zealand Child Neurology Society for activities related to this and future conferences (including but not limited to: use within newsletters, presentations or other media that recounts the events that occurred during this conference and/or in the promotion of future conferences). Delegates should inform the Australia and New Zealand Child Neurology Society (by email or in writing) in advance of or during the congress week if they do not provide permission for this.

**Liability and Insurance**
The Australia and New Zealand Child Neurology Society will not accept any liability for personal injury or loss/damage to property/belongings of participants or accompanying persons, either during or following the conference or their stay. It is recommended that delegates arrange their own personal health, accident and travel insurance for themselves and their families.
CONFERENCE DINNER

Venue: Ostro, Seafarers Building, 52 Tyler Street, Britomart, Auckland 1010
Date: Thursday 1st September 2016
Time: 7.30pm – 8.00pm (Ostro’s City Terrace Bar for pre-dinner drinks), 8.00pm (Ostro’s Upper Deck, dinner)

A modern New Zealand brasserie with sweeping views of the Waitemata Harbour, Ostro’s is a delightful dinner venue. The kitchen, directed by internationally acclaimed Michelin-starred chef Josh Emett, in conjunction with head chef Cobus Klopper, serves an array of new-style brasserie classics. Join us for an evening of collegial conversation, fine dining and fun.

The dress code is casual evening attire. Dinner includes a meal and beverages.
The Australia and New Zealand Child Neurology Society wish to extend their thanks to our major sponsors who have supported this event:

**MAJOR SPONSORS**

- UCB Australia
- Sanofi Genzyme
- LivaNova

**SPEAKER SPONSOR**

- Eisai

**EXHIBITORS**

- UCB Australia
- Sanofi Genzyme
- LivaNova
INTERNATIONAL SPEAKERS

We are delighted to announce our international speakers:

**Professor James (Jim) Wheless** is Professor/Chair of Le Bonheur Children’s Research Institute/Comprehensive Epilepsy Program. He holds appointment at the University of Texas Health Science Centre. He will be joining us for an EISAI hosted dinner on the evening of Wednesday 31st August and speaking at the Epilepsy Symposium on Thursday 1st September. He will also chair the Epilepsy Platform on that morning.

We will also be joined by **Dr Finbar O’Callaghan**, University College London - Institute of Child Health & Great Ormond Street Hospital, London, as an international speaker, providing an update on the outcome of the ICISS study, and contributing to a session on Paediatric Stroke.
## WEDNESDAY 31ST AUGUST

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<td><strong>Early Morning Session</strong></td>
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<td>08:30</td>
<td><strong>Registration Desk Open</strong></td>
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<td>09:00</td>
<td>ANZCNS Board Meeting (Chair: Kate Riney)</td>
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<td>Education and Training Committee Meeting (Chair: Jeremy Freeman)</td>
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<td>ANZCNS Trainee’s Breakfast Meeting (Chair: Hooi Ling Teoh)</td>
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<td>09:30</td>
<td><strong>Arrival tea/coffee</strong></td>
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<td>10:00</td>
<td><strong>Conference Official Opening</strong> (Suzanne Davis, Chair Local Committee)</td>
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<td>10:15</td>
<td><strong>Symposium 1 - Neurometabolic Disease</strong> (Chair: Rick Leventer &amp; Erik Andersen)</td>
<td>Callum Wilson, Emma Glamuzina, Nadia Mitchell</td>
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<td>Neurometabolic disorders unique to the region</td>
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<td>X-linked Adrenoleukodystrophy in New Zealand: experience, outcomes and unusual patterns of disease</td>
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<td>Gene transfer in ovine models of NCL</td>
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<td>11:50</td>
<td><strong>Lunch</strong></td>
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<td>12:30</td>
<td>ANZCNS Paediatric Neurology Trainee Lecture: Therapeutic decision making in immune brain disease</td>
<td>Russell Dale (Intro: Kate Riney)</td>
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<td>13:30</td>
<td><strong>Platform Session 1 - Stroke/Neuroinflammation/General Neurology</strong> (Chair: Russell Dale &amp; Finbar O’Callaghan)</td>
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<td>14:45</td>
<td><strong>Afternoon tea</strong></td>
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<td>15:30</td>
<td><strong>Symposium 2 - Paediatric stroke</strong> (Chair: Claire Spooner &amp; Sophie Calvert)</td>
<td>Finbar O’Callaghan, Adriane Sinclair</td>
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<td>The outcome of arterial ischaemic stroke in children</td>
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<td>Acute paediatric stroke medical management</td>
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<td>16:30</td>
<td><strong>ANZCNS Annual General Meeting</strong> (Chair: Kate Riney)</td>
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<td>18:30</td>
<td><strong>Bus to: Eisai Dinner Event</strong></td>
<td>Professor James Wheless</td>
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<td>Epilepsy in Adolescents: Management of Generalised Tonic (GTC) in the Modern Era</td>
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New Zealand has a unique population with around 25% being of Maori and/or Pacific ethnicity. Like all ethnic populations there are a number of genetic diseases that occur at a relatively high rate in these populations. Some of these are pan-Pacific while others seem to be isolated to particular Pacific groups. The Australasian clinician should be aware of these conditions especially as there is now an increasing number of Maori and Pacific families living in Australia as well as New Zealand. In this talk I will give an overview of metabolic disease with emphasis of the diseases the National Metabolic Service has seen in the Maori and Pacific communities.

X-linked Adrenoleukodystrophy in New Zealand: experience, outcomes and unusual patterns of disease

Emma Glamuzina, Metabolic department, Starship Children's hospital, Auckland, NZ

X-linked adrenoleukodystrophy (X-ALD) is a peroxisomal disorder caused by mutations in the ABCD1 gene, subsequent accumulation of very long chain fatty acids, variable CNS demyelination and adrenal insufficiency. The rapidly progressive cerebral form affects males classically between three and 10 years. Treatment is with early Haematopoetic Stem Cell Transplant (HSCT). Diagnosis is achieved through family history or clinical presentation. Preliminary work into the role of newborn screening (NBS) is underway.

The New Zealand National Metabolic Service has actively followed 22 males with X-ALD since 2000. 17/22 are alive, 18/22 have Addison's disease, four have adrenomyeloneuropathy. Four under the age of 12 years are being monitored with six monthly brain MRI. Five have undergone HSCT. Two were being monitored at the time; one was too young, one too old and one presented clinically. 5/15 less than 18 years of age have presented clinically with no family history and are currently severely disabled or dead. The brain MRI findings have been ‘classical’ in 5/9 children.

X-ALD is a relatively common IEM in New Zealand. Despite regular monitoring, extensive education and cascade testing, the decision to treat with HSCT can be difficult, the outcomes variable and children regularly present clinically, too late for HSCT, thus making an argument for X-ALD newborn screening.
Gene transfer in ovine models of NCL

Nadia L Mitchell 1,2, Graham K Barrell 1,2, Katharina N Russell 1,2, Martin Wellby 1,2, Tracy R Melzer 2,3, Hollie E Wicky 2,4, Stephanie M Hughes 2,4, Steven J Gray 5, David N Palmer 1,2

(1) Faculty of Agriculture and Life Sciences, Lincoln University, Lincoln; (2) Batten Animal Research Network (BARN); (3) Department of Medicine, University of Otago and New Zealand Brain Research Institute, Christchurch; (4) Department of Biochemistry, Brain Health Research Centre, University of Otago, Dunedin; (5) Gene Therapy Center and Department of Ophthalmology, University of North Carolina, USA

Mutations in genes encoding a soluble lysosomal protein (CLN5) and a lysosomal transmembrane protein (CLN6) underlie two forms of the fatal lysosomal storage disease, neuronal ceroid lipofuscinosis (NCL; Batten disease). Although genetically distinct, the NCLs share common pathological features; progressive regionally specific neurodegeneration and accumulation of storage material in lysosomes. Currently there are no effective treatments. Here we demonstrate that the single administration of pre-clinical gene therapy prevented disease development in two naturally occurring ovine models of NCL.

Deficiencies in soluble lysosomal proteins are deemed particularly amenable to in vivo gene therapy through the phenomenon known as ‘cross-correction’. To test this paradigm in sheep, six pre-clinical CLN5-/- lambs were treated with intracerebroventricular and intracortical injections of lentiviral or AAV9 vectors encoding ovine CLN5. Both vector platforms afforded sustained protection from stereotypical disease onset and progression. Cognitive and neurological function was preserved whilst longitudinal CT and MRI scanning revealed normalisation of intracranial volumes and structural brain integrity. Apart from delayed-onset visual deficits, quality of life was profoundly improved for the treated sheep and they well exceeded the humane endpoint for untreated CLN5-/- animals. Gene therapy is now being explored in CLN5-/- sheep with established disease to test the potential for amelioration in disease progression.

Defects in membrane-bound proteins are considered harder therapeutic targets. However similar injections were performed on six pre-clinical CLN6-/- sheep. Only one AAV9-CLN6 injected animal maintained phenotypic correction whilst the other animals developed stereotypical CLN6 disease. This successfully treated sheep retained vision and was clinically indistinguishable from age-matched control animals at 26 months of age. Post mortem neuropathological studies showed a significant diminution in disease-associated lysosomal storage, gliosis, atrophy and neurodegeneration.

The encouraging results of sustained therapeutic and functional efficacy in large animal models of NCL hold promise for future clinical trials in human patients with CLN5 and CLN6 Batten disease.
11:50-12:30  **LUNCH** *(A+ Trust Room/all delegates)*

12:30-13:30  **ANZCNS PAEDIATRIC NEUROLOGY TRAINEE LECTURE** *(Auditorium)*

12:30  **Therapeutic decision making in immune brain disease**

Russell Dale

13:30-14:45  **PLATFORM SESSION 1 - STROKE/NEUROINFLAMMATION/GENERAL NEUROLOGY** *(Auditorium)*

13:30  **Thrombectomy for cerebral venous sinus thrombosis in children**

*Manoj Kanhangad, Brendan Steinfort, Christopher Troedson, Deepak Gill, David Lord, Brian Owler and Simone Ardern-Holmes*

*Background:* Cerebral venous sinus thrombosis (CVST) is a potentially life-threatening condition which accounts for 25% of ischaemic cerebrovascular disease in childhood. Treatment primarily involves anticoagulation. Although the effectiveness of various interventional treatment options is controversial, thrombolysis and thrombectomy have been utilised with some success in adults 1, with very limited data available for children. We report two children with severe CVST who underwent endovascular thrombectomy without complications.

*Clinical Cases:* The children were three and six years of age. Presenting symptoms included reduced conscious level, vomiting and headache. Both children received anticoagulation. Worsening symptoms and signs associated with intracranial hypertension prompted consideration of interventional treatment. Thrombectomy was performed within the first 24h for one child and on day 8 for the other. The procedure was well tolerated in both cases. Sustained elevated intracranial pressure was subsequently managed with lumboperitoneal shunt in the second case. Details regarding clinical severity, hospital stay and longer term outcomes will be presented. Reported cases of thrombectomy in adults and children with CVST from the literature will be summarised.

*Conclusion:* Limited data supports the safety of thrombectomy in adults with severe CVST 1, with very little information available in children. Two young children with significant complications of CVST were safely treated with thrombectomy at our centre, suggesting this intervention may have a role in selected cases. A randomised controlled trial is underway in adults assessing safety and efficacy of endovascular thrombolysis with and without mechanical clot retrieval. A collaborative approach among paediatric centres will be important to further assess interventional therapy for CSVT in children.

*References:*


13:45  **Acute spinal cord syndrome secondary to venous congestion**

*Ian Woodcock & Gabriel Dabscheck*

*Case Report:* A thirteen year old boy presented with an acute flaccid paralysis 24 hours following accidental ingestion of odourless and tasteless potassium hydroxide oven cleaner. He presented immediately
to the Emergency Department with pharyngolaryngeal pain and was intubated semi-prophylactically to protect his airway. Twenty-four hours later after weaning sedation, he was unable to move his legs, had absent reflexes, up-going plantars and a sensory level up to his umbilicus. An MRI scan demonstrated some T2 hyperintensities and corresponding changes on the Apparent Diffusion Co-efficient (ADC) images of the spine. It also demonstrated thickening of the oesophageal wall, peri-oesophageal oedema and bilateral (although worse on the right) pleural effusions all in keeping with mediastinitis secondary to oesophageal perforation. On secondary review of the images it was evident that there was venous engorgement and congestion that was resulting in venous ischaemia of the spinal cord. Following discussions with the intensive care and surgical teams he was commenced empirically on intravenous pulsed methylprednisolone for forty-eight hours. He made a complete recovery with no residual deficits.

Acute spinal cord syndrome secondary to venous congestion is an infrequently reported and poorly understood entity.

14:00

Anti-N-Methyl-D-Aspartate receptor encephalitis has a high incidence in Maori and Pacific Island children in New Zealand

Hannah Jones, Shekeeb Mohammad, Peter Reed, Richard Steele, Russell Dale & Cynthia Sharpe

Purpose: To investigate the incidence and severity of anti-N-Methyl-D-Aspartate (anti-NMDA) receptor encephalitis in New Zealand children.

Basic procedures: A retrospective case series was undertaken of all children diagnosed with anti-NMDA receptor encephalitis 18 years of age from January 2008 – October 2015.

Main Findings: Sixteen patients were identified with anti-NMDA receptor antibodies in the CSF, three of whom had an associated teratoma. Fifteen children had Maori and/or Pacific Island ancestry. The incidence of anti-NMDA receptor encephalitis in Maori children was 3.4 per million children per year (95%CI 1.4-7.0) and the incidence in Pacific children was 10.0 per million children per year (95%CI 4.3-19.8) compared with 0.2 per million children per year (95%CI 0.0-1.0) in children without Maori or Pacific Island ancestry. Sixty-seven percent of children had a good outcome (modified Rankin Score 2) at two years’ follow up. This compares unfavourably with other cohorts despite a shorter median time to first-line immunotherapy (13 days; 4-89) and a higher proportion of children being treated with second-line therapy (40%).

Principal conclusions: Maori and Pacific Island children have a higher incidence of anti-NMDAR encephalitis and possibly a more severe phenotype. This data suggests a genetic predisposition to anti-NMDAR receptor encephalitis in these populations.
14:15  Pure psychosis in Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis  
Sarah Curnow, Eppie Yiu & Andrew Kornberg

**Background:** Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is a recently described autoimmune process predominantly affecting young women. It typically presents with behavioural change, psychosis, seizures, movement disorder, encephalopathy and autonomic instability. While psychiatric symptoms are common, they rarely occur in isolation. In post pubertal females, the disease is commonly a paraneoplastic phenomenon secondary to an ovarian teratoma, and is responsive to immunotherapy and tumour removal. This paper describes an adolescent girl presenting with a pure psychosis due to anti-NMDAR encephalitis in the setting of an ovarian teratoma.

**Case Report:** A 17yo girl was admitted to the psychiatry unit of a tertiary children’s hospital in June 2016 with a two week history of acute onset, first episode, psychosis, involving a thought disorder, agitation, paranoia, auditory hallucinations and sleep disturbance. There were no neurological symptoms or signs on examination. Investigations for an organic cause revealed strongly positive serum NMDAR antibodies, which were subsequently demonstrated in cerebrospinal fluid (CSF). CSF was negative for infective agents and Magnetic Resonance Imaging (MRI) of the brain was normal. A pelvic ultrasound showed a cystic lesion of the right ovary which was confirmed on MRI (and subsequent histology) to be a teratoma. Treatment was initially with anti-psychotics followed by high dose intravenous steroids, intravenous immunoglobulin and tumour removal. Significant clinical improvement was seen at the time of writing, ten days after initiation of immunotherapy.

**Conclusion:** This case report demonstrates that isolated psychiatric symptoms can occur in anti-NMDAR encephalitis and that this disease should be considered in the differential diagnosis of first episode psychosis, especially in young women. Evaluation for the presence of ovarian teratoma should be performed in all patients with confirmed anti-NMDAR encephalitis.

14:30  Trigeminal autonomic cephalalgias – a rare childhood headache  
Josephine Stringer, Sophie Calvert & Adriane Sinclair

**Background:** Trigeminal autonomic cephalalgias are rare in childhood. They are characterised by unilateral headache associated with ipsilateral autonomic features.

**Case report:** A 2-year-old male was seen in the neurology clinic to review episodes of severe distress. The first episode occurred at 10 months of age, and initially recurred 3-6 weekly. Each episode began suddenly with distress, with the patient holding one side of his face and screaming inconsolably. He developed ipsilateral periorbital oedema extending to the perinasal and perioral region with associated erythema. He then developed ipsilateral clear rhinorrhoea and watery eye discharge.
Episodes varied in duration from 20 minutes to several hours with usual resolution at the onset of nasal discharge. Prior to neurology review, the patient had a trial of paracetamol with no effect, ibuprofen which led to a partial improvement in distress and cetirizine which had no effect. His mother provided photos of these episodes which assisted in diagnosis of a trigeminal autonomic cephalalgia. A headache emergency plan was provided to the family for the patient to receive oxygen therapy in the event of presentation to the emergency department.

**Conclusion:** This case demonstrates that a diagnosis of trigeminal autonomic cephalalgia should be considered even in young children presenting with headache with associated autonomic features. Diagnosis is important as it allows provision of therapy specific to the condition. It also illustrates the value of parent captured photos in diagnosis and recognition of this rare condition.

**Reference:**

14:45-15:30 **AFTERNOON TEA** *(A+ Trust Room/all delegates)*

15:30-16:30 **SYMPOSIUM 2 - PAEDIATRIC STROKE** *(Auditorium)*
15:30
*The outcome of arterial ischaemic stroke in children*
*Finbar O’Callaghan*

16:00 **Acute paediatric stroke medical management**
*Adriane Sinclair, Neurosciences Department, Lady Cilento Children’s Hospital, South Brisbane, QLD*

Paediatric arterial ischaemic stroke is rare with a reported incidence of 1.6-13/100,000/ year. Stroke in the paediatric setting is however associated with significant long term morbidity. Acute management of paediatric stroke consists of hyperacute and acute treatment strategies. Hyperacute treatment (tissue plasminogen activator and/or endovascular treatment) is rarely administered in the paediatric setting for a variety of reasons including the lack of paediatric safety and efficacy data. Acute management consists of anti-thrombotic treatment and supportive measures aimed at reducing the risk of stroke propagation or recurrence and reduction in morbidity and mortality. Treatment strategies vary based on stroke aetiology. Acute management of paediatric arterial ischaemic stroke and stroke aetiology will be reviewed.

16:30-17:30 **ANZCNS ANNUAL GENERAL MEETING**

18:30 **BUS TO: EISAI DINNER EVENT**
*Epilepsy in Adolescents: Management of Generalised Tonic (GTC) in the Modern Era*
*Professor James Wheless*
### THURSDAY 1ST SEPTEMBER

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<td>08:30</td>
<td><strong>Symposium 3 - Epilepsy (Chair: Suzanne Davis &amp; Kate Riney) Session</strong></td>
<td><strong>Session Sponsor: Eisai</strong></td>
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<td>Primary generalized epilepsy with a photoconvulsive component: diagnosis and treatment</td>
<td>Jim Wheless</td>
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<td>Findings of the International Collaborative Infantile Spasm Study (ICISS)</td>
<td>Finbar O’Callaghan</td>
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<td>Genetics of epileptic encephalopathies - a 2016 update</td>
<td>Lynette Sadlier</td>
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<td>Current state of play - the role of cannabinoids in epilepsy</td>
<td>Jeremy Freeman</td>
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<td>10:50</td>
<td><strong>Morning tea</strong></td>
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<td><strong>Late Morning Session</strong></td>
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<td>11:30</td>
<td><strong>Platform Session 2 - Epilepsy (Chair: James Wheless &amp; Melinda Nolan)</strong></td>
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<td><strong>Lunch</strong></td>
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<td>13:30</td>
<td><strong>Symposium 4 - Neuromuscular/Transition (Chair: Manoj Menezes &amp; Rob Smith)</strong></td>
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<td>A new (French) approach to the nomenclature and classification of neuropathies, spinocerebellar ataxias and spastic paraplegias</td>
<td>Robert Ouvrier</td>
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<td>Emerging therapies in DMD and SMA</td>
<td>Monique Ryan</td>
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<td>An approach to adolescent medicine</td>
<td>Bridget Farrant</td>
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<td>Transition for neurology patients with disability</td>
<td>Colette Muir</td>
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<td>Gynaecological management of severe intellectual disability</td>
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<td>16:00</td>
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<td><strong>Afternoon Platform Session</strong></td>
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<td>16:30</td>
<td><strong>Platform Session 3 - Neuromuscular/General Neurology (Chair: Monique Ryan &amp; Robert Ouvrier)</strong></td>
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<td>19:30</td>
<td><strong>Pre-dinner drinks &amp; Recognition of Service Awards</strong> - Ostro City Terrace Bar</td>
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<td>20:00</td>
<td><strong>ANZCNS Conference dinner</strong> - Ostro Upperdeck**</td>
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08:00  REGISTRATION DESK OPEN

08:30-10:50  SYMPOSIUM 3 - EPILEPSY (Auditorium)
08:30  Primary generalized epilepsy with a photoconvulsive component: diagnosis and treatment
Jim Wheless

09:20  Findings of the International Collaborative Infantile Spasm Study (ICISS)
Finbar O’Callaghan

09:50  Genetics of epileptic encephalopathies - a 2016 update
Lynette Sadlier

10:20  Current state of play - the role of cannabinoids in epilepsy
Jeremy Freeman

10:50-11:30  MORNING TEA (A+ Trust Room/all delegates)

11:30-12:30  PLATFORM SESSION 2 - EPILEPSY (Auditorium)
11:30  Novel causes of epileptic encephalopathy defined by exome sequencing and functional collaborations
Elizabeth Palmer, Rani Sachdev, Annie Bye, Kelsey Jarrett, Shushmitha Gururaj, Garret Sheehan, Michael Duffey, Fatema Zahran, Mais Omar Hashem, Niema Ibrahim, Tejaswi Kandula, Rebecca Macintosh, Hugo Sampaio, Rajat Gupta, Donna Conlon, Jeffrey Billheimer, Daniel Rader, Christopher Walkley, Chang Seouk Lee, Chang Seouk Lee, Christine Loo, Susan Brammah, George Elakis, Ying Zhu, Michael Buckley, Michael Buckley, Marcel Dinger, Mark Cowley, Fowzan Alkuraya, Edwin Kirk, Tony Roscioli, Arin Bhattacharjee & William Lagor

Background: Whilst next generation sequencing (NGS) approaches are becoming established in the diagnosis of Mendelian disorders, a critical issue is how to rigorously evaluate novel variants and genes. We report two findings from a research exome sequencing (ES) cohort of patients with epileptic encephalopathy (EE) demonstrating translational research bench-to-bedside and a collaborative approach.

Case Reports: Firstly we report a child of consanguineous parents where ES identified a homozygous single nucleotide change predicted to abolish a splice donor site in the ARV1 gene (c.294+1G>A homozygous). Previously a missense variant (p.(Gly189Arg)) had been reported in ARV1 in a consanguineous family with EE, without supportive functional data. We demonstrate that the c.294+1G>A variant prevents splicing in minigene assays, resulting in exon skipping and an in-frame deletion of 40 amino acids in primary human fibroblasts. Both ARV1 variants result in undetectable levels of ARV1 protein in transfected cells. Mice with a neuronal deletion of ARV1 recapitulated the human phenotype, exhibiting seizures and a severe survival defect in adulthood.

Secondly we report a child where ES detected a predicted pathogenic de novo missense variant, p.(Phe240Leu), in a novel ion channel gene, KCNT2 (SLICK). Protein modelling was supportive of pathogenicity and electrophysiological studies in Xenopus oocytes and mammalian cells demonstrated the variant resulted in a novel change of
electrophysiological properties of the channel in a manner consistent with epileptogenesis.

Conclusion: Our data support loss of ARV1 and change in function of KCNT2 as novel causes of EE, demonstrating the importance of collaborations between scientists, clinicians and genomicists to maximise the potential of NGS.

11:45 Epileptic encephalopathy with movement disorder: novel SCN1A phenotype

Lynette G. Sadleir, Emily Mountier, Deepak Gill, Suzanne Davis, Charuta Joshi, Catherine Devile, Manju Kurian, Deciphering Developmental Disorders Study, Katherine C. Nickels, Gemma Carvill, Candace T. Myers, Heather C. Mefford & Ingrid E. Scheffer

Background: Overlap of early onset epileptic encephalopathy (EE) with movement disorders is increasingly recognized. Mutations in SCN8A, GRIN1, SCN2A, SLC2A1 and ARX all have EE phenotypes with movement disorders. We describe a novel early infantile onset EE with profound impairment and movement disorder due to mutations in SCN1A.

Method: Children with SCN1A mutation and a more severe phenotype than Dravet syndrome were identified. 3 cases had the same mutation. The literature was searched for other cases with this mutation. History, examination, MRI and EEG data were obtained for each patient.

Results: We identified 7 males (6-12 years) who presented at 8-12 weeks of age with hemiclonic seizures (5) and generalized tonic clonic seizures (GTCs -2). All developed GTCS by 18 months and became intractable with convulsive status (6), myoclonic seizures (5), tonic seizures (4) and spasms (3). Triggers included fever (4), auditory stimuli (2), excitement (2), feeding (2) and bowel opening (1).

Development was delayed by 8-16 weeks. 6 children had regression or plateauing of development resulting in profound intellectual disability with no ambulation or speech.

All children developed a severe movement disorder (onset 9 weeks-20 months) with choreoathetosis, dystonia and mini-myoclonus particularly in the orofacial area.

EEGs developed background slowing and frequent multifocal discharges. Neuroimaging was normal.

6 children shared a recurrent mutation p.Thr226Met (proven de novo in 5). The 7th child had a de novo p.Pro1345Ser mutation.

Conclusions: We identify a novel phenotype of profound early-onset EE associated with a hyperkinetic movement disorder due to a de novo SCN1A mutation. This new SCN1A phenotype differs from Dravet syndrome by earlier age of onset, profound impairment and movement disorder. Phenotype-genotype correlation has been elusive for SCN1A diseases, but we found striking genetic homogeneity with 6/7 cases sharing the same hotspot mutation.
12:00

Cost-effectiveness of the diagnostic whole exome sequencing approach in epileptic encephalopathy
Elizabeth Palmer, Rani Sachdev, Ann Bye, Kelsey Jarrett, Sushmitha Gururaj, Garrett Sheehan, Michael Duffey, Fatema Al Zaherani, Mais Omar Hashem, Niema Ibrahim, Tejaswi Kandula, Rebecca Macintosh, Hugo Sampaio, Rajat Gupta, Donna Conlon, Jeffrey Billheimer, Daniel Rader, Christopher Walkey, Chang Seok Lee, Christine Loo, Susan Brammah, George Elakis, Ying Zhu, Michael Buckley, Marcel Dinger, Mark Cowley, Fowzan Alkuraya, Edwin Kirk, Tony Roscioli, Arin Bhattacharjee & William Lagor

Background: Diagnostic whole exome sequencing (ES) is rapidly becoming integrated in clinical practice. Comparison of the ES approach to the ‘traditional’ diagnostic has been repeatedly postulated to be cost-effective, mainly due to improved diagnostic yield and the potential to avoid an invasive and expensive ‘diagnostic odyssey’. However, there is a paucity of health costing data to support this assertion.

EEs are severe epilepsies impacting cognition in which rapid establishment of aetiology is important; however, traditional diagnostic approaches are invasive and expensive because of genetic heterogeneity and limited genotype-phenotype correlation. We present a comprehensive health-costings comparison for a well phenotyped cohort of 32 patients with epileptic encephalopathy (EE), using a counterfactual model, of a ‘trio ES’ model and ‘traditional’ diagnostic approach. The cohort comprises EE patients seen at the Sydney Children’s Hospital, born between 2000 and 2014, who remained undiagnosed after ‘first-tier’ testing.

Results: The diagnostic yield for the trio ES approach was higher than ‘traditional’ diagnostic approach (16/32; 50% for the ‘trio ES’ arm; 2/32; 6.2% for the ‘traditional’ arm). The comparative costs per patient ($11,828 ‘traditional’ arm [95% CI $10,677-$13,027]; $9,537 ‘trio ES’ [95% CI $9,423-9,683]) and per diagnosis ($189,243 [95% CI $72,703-$406,141] ‘CSC’ arm and $19,073 ‘trio ES’ (95% CI $14,421-27,968)) were much lower for the ES approach.

Conclusion: This study rigorously compares the diagnostic yield and cost of an ES and traditional approach for EE, and has important health policy implications for the clinical diagnostic approach to epileptic encephalopathies and to neurodevelopmental Mendelian conditions in general in the genomic age.

12:15

Is epilepsy a thing of the past in tuberous sclerosis?
Michaela Waak & Kate Riney

Aim: We report the frequency and severity of epilepsy in a 2016 paediatric tuberous sclerosis (TSC) cohort, and compare this to historic cohort data.

Background: Recently, significant developments in the care of children with TSC including more frequent clinical and EEG surveillance from birth, and before onset of clinical seizures, increased confidence in the curative role of early surgery, and experience with the novel use of mTOR inhibitors for epilepsy have been made. TSC multidisciplinary
Clinics have additional benefits for this cohort, allowing clinicians to become more experienced and confident in decision-making, allowing more aggressive preventative clinical care. We proposed the hypothesis that these advances in epilepsy care might translate into improved outcomes with respect to epilepsy.

**Method:** A review was undertaken of all patients of a tertiary Paediatric TSC clinic for data in relation to epilepsy including: number with fetal diagnosis of TSC, number with preventative therapy for epilepsy, number who developed seizures/epilepsy, frequency and severity of epilepsy, anti-epileptic therapies used, and final outcome at last visit.

**Result:** A total of 56 patients were included. Of these 41/56 (73%) were seizure free at last visit, 10/56 (17%) had rare seizures (<2 monthly, some of these had only ever had a single seizure) and 5/56 (9%) patients had seizures with reasonable frequency. Of these latter 5 patients, 3 are currently pending epilepsy surgery.

Historically 80% of TSC patients develop seizures, most presenting with focal seizures and infantile spasms in the first year of life. Between 50 and 70% of TSC patients develop drug resistant epilepsy in historical cohorts.

**Conclusion:** The current data, which includes patients who had fetal diagnosis of TSC with pre-seizure onset clinical care, and patients with rapid and early access to TSC expert clinic, shows that there is a possibility for modern TSC cohorts to achieve long-term seizure freedom.

12:30-13:30  **LUNCH** *(A+ Trust Room/all delegates)*

13:30-16:00 **SYMPOSIUM 4 - NEUROMUSCULAR/TRANSITION** *(Auditorium)*

13:30 **A new classification for hereditary neurological disorders: A cure for the chaos!**

Robert Ouvrier, The Children’s Hospital at Westmead NSW

From the mid-19th Century, the French have always been in the vanguard of the investigators of neurological disorders, particularly the neuropathies. Even from those early times, classification of such disorders has been problematic and sometimes hotly disputed. People are still duelling over the classifications of various medical entities but it is fitting that a new French approach has created a solution, not only of the neuropathies, for which a radically new approach was first suggested last year (Mathis S. et al. 2015) but of many other complex neurological disorders such as the hereditary cerebellar ataxias (HCAs), spastic ataxias (SPAXs) and spastic paraplegias (SPGs)(Vallat et al.2016).

The newly-proposed classification of the hereditary neuropathies indicates their mode of inheritance and the demyelinating or axonal degenerative nature of their pathological findings, but, importantly, takes advantage of the ever-increasing knowledge of the individual genes by incorporating the relevant mutation in each individual denomination, as well.

In expanding this approach to patients with the clinical features of
other neurological disorders such as hereditary spastic paraplegia, cerebellar ataxia or spastic ataxia, in whom a precisely detailed mutation of a particular gene has been found, the clinician will then immediately be able to access the particular gene description in OMIM or Gene Reviews.

There are now 40 entities formally designated SCAs 1 to 40 in the current nomenclature. In addition, there are six episodic ataxias (EAs), four of which are caused by mutations of the CACNA1A gene, as well as 18 miscellaneous disorders manifesting ataxia as an important feature. The mutated genes are already known for all but twelve of these 64 entities!

Of the 90 types of hereditary spastic paraplegia, the implicated gene is known for 74 but 18 of those 74 have no distinguishing name at present under the current classification!

There is now every reason to incorporate the abbreviated name of the causative genes, where known, in all complex medical classifications.

References:

14:00

**Emerging therapies in DMD and SMA**  
Monique Ryan, Neurology Department, Royal Children’s Hospital, Parkville, Vic

Duchenne muscular dystrophy and spinal muscle atrophy are relatively common, severe and progressive paediatric neuromuscular disorders. Treatment of these conditions and other neuromuscular disorders of childhood has traditionally been essentially symptomatic, but there have in recent years been significant advances in therapeutics for DMD and SMA. These treatments are changing the natural history of these conditions and rapidly creating new management and ethical challenges which will continue to evolve in the era of new genomic, carrier and pre-symptomatic testing. This presentation will review recent advances in the treatment of DMD and SMA, and briefly address some of those challenges.

14:30

**An approach to adolescent medicine**  
Bridget Farrant, Kidz First Community Centre for Youth Health, Auckland, NZ

Working with young people – addressing their broad health and developmental issues.

Recognising the developmental opportunities and challenges that all young people with chronic health conditions and disabilities face is a critical part of the care we provide as health professionals. Access to developmentally appropriate health care is central to this.
15:00 Transition for neurology patients with disability
Colette Muir, Starship Children's Health, Grafton, Auckland, NZ

The transition of medical care is frequently done poorly for young people with neurological problems and disability and is associated with poor health outcomes. Although paediatricians often focus on the ‘transfer’ of medical care to an adult colleague or service, the concept of transition needs to be considered more broadly. This presentation will focus on specific aspects of care a Paediatrician can provide or facilitate which will increase the chances of a successful transition for young people with neurological disorders and disability.

15:30 Gynaecological management of severe intellectual disability
Saman Moeed, Women's Health, Auckland City Hospital, Grafton, Auckland, NZ

Puberty in young women with disability can cause significant distress and concern for the young woman and her care providers. While historically, intellectual disability may have been regarded as an indication for hysterectomy, newer options such as long-acting reversible contraceptives (LARCs) provide greater choice for young women. The use of hormonal contraception for menstrual management will be discussed, along with their role in alleviating cyclical symptoms related to menstrual periods, e.g. behaviour, headache, seizure activity.

16:00-16:30 AFTERNOON TEA (A+ Trust Room/all delegates)

16:30-17:00 PLATFORM SESSION 3 - NEUROMUSCULAR/GENERAL NEUROLOGY (Auditorium)

16:30 Clinical and neurophysiological profile of CMTX3 in childhood
Manoj Kanhangad, Kayla Cornett, Gopinath Subramanian, Monique Ryan, Helen Young, Robert Smith, Robert Ouvrier, Garth Nicholson, Marina Kennerson, Joshua Burns and Manoj Menezes

Background: The genetic abnormality responsible for CMTX3 has recently been identified by whole genome sequencing to be a 78 kb insertion into chromosome Xq27.1. Understanding the clinical and neurophysiological profile of CMTX3 in childhood will help early diagnosis and intervention.

Methods: We reviewed the clinical profile, Charcot-Marie-Tooth Disease Pediatric Scale (CMTPedS) scores and nerve conduction studies of 11 children (10 males) with CMTX3.

Results: The age at onset ranged from birth to 5 years of age in males. Affected males presented with foot deformity (including ankle contractures) (n=6), mostly in the first two years of life, or with gait abnormality (n=4). The affected female presented with hand weakness at 12 years of age. Four of the affected children started walking beyond 18 months of age. Hand function was affected in seven children, first identified between four months and 12 years of age. Two older affected children had severe hand weakness with claw hands and forearm wasting. Abnormalities of proprioception and vibration sense were prominent only in the second decade of life. Nine children had a demyelinating sensorimotor neuropathy while one child had an axonal...
predominantly motor neuropathy. CMTPedS scores ranged 5 (mild) to 35 (severe). When compared to children in the Inherited Neuropathies Consortium, baseline CMTPedS scores did not significantly differ between CMTX3 (16.7 ± 8.1, n=11), CMT1A (18.6 ± 7.8, n=116), or CMTX1 (14.0 ±9.6, n=4). However, CMTX3 progressed at a faster rate (4.4 ± 2.0, n=7).

**Conclusion:** CMTX3 is characterised by an early onset and early hand weakness. Clinical progression is more rapid in CMTX3 than CMT1A or CMTX1. Understanding the unique phenotype of CMTX3 is important for directing genetic testing, as the CMTX3 insertion cannot be identified on a routine microarray or neuromuscular gene panel.

16:45

**A new early-onset recessive myopathy with internalized nuclei and myofibrillar disorganisation**

Gina O’Grady, Heather Best, Tamar Sztal, Vanessa Schartner, Myriam Sanjuan-Vazquez, Sandra Donkervoort, Osorio Abath Neta, Bryan Sutton, Biljana Ilkovski, Norma Beatriz Romero, Tanja Stojkovic, Didem Ardicli, Kristen Nowak, Beril Talim, Haluk Topaloglu, Nigel Laing, Kathryn North, Daniel MacArthur, Sylvie Friant, Nigel Clarke, Robert Bryson-Richardson, Carsten Bonnemann, Jocelyn Laporte and Sandra Cooper

**Background:** Myopathies are a group of genetically heterogeneous conditions characterized by muscle weakness, with overlap in the clinical presentation and histopathological features of different genetic subtypes. There are greater than 25 recognized genetic causes of congenital myopathy, but still a genetic diagnosis is achieved in only 50% of patients, driving ongoing gene discovery.

**Methods:** Whole exome sequencing identified recessive variants in a previously unreported gene*, in two brothers with childhood onset myopathy. Seven additional patients from 4 families were identified in an international collaboration, allowing characterization of this myopathy. Patient biospecimens, cell lines, yeast and zebrafish models were used to confirm pathogenicity and elucidate the fundamental role of the protein in skeletal muscle.

**Results:** Clinical features included infantile to childhood onset, slowly progressive proximal and distal muscle weakness, facial weakness, nasal speech, swallowing difficulties and normal to moderately elevated creatine kinase levels. Distinctive histopathology showed abundant internalized nuclei, myofibrillar disorganization, desmin-positive inclusions, and thickened Z-bands.

Complementation experiments in yeast confirm the protein has important reductase activity that is strongly impaired by the disease-associated missense mutations. Immunolocalization studies in human muscle and zebrafish myofibers demonstrate protein localization to the nucleus and to striated sarcomeric compartments. Zebrafish with protein knock-down recapitulate features of the myopathy with sarcomeric disorganization, myofibrillar aggregates and marked swimming defect.

**Conclusion:** We characterize a novel recessive early onset myopathy with distinctive histopathology and introduce altered redox regulation as a primary cause of congenital muscle disease.

*Gene name not disclosed in abstract – manuscript in submission
19:30-20:00  PRE-DINNER DRINKS & RECOGNITION OF SERVICE AWARDS  
(Ostro City Terrace Bar)

20:00  ANZCNS CONFERENCE DINNER  (Ostro Upperdeck)
## FRIDAY 2ND SEPTEMBER

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<td>Platform Session 4 - General Neurology (Chair: Jeremy Freeman &amp; Richard Webster)</td>
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<td>Symposium 5 - Fetal / Neonatal Research (Chair: Steve Malone &amp; Annie Bye)</td>
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<td>The role of antenatal MRI in diagnosis of brain disorders</td>
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<td>The genetics of Periventricular neuronal heterotopia</td>
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<td>Elucidating the genetics of developmental brain malformations - the Australian Health Genomic Alliance</td>
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<td>Zika virus congenital infection</td>
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<td>Meeting Close / ASM 2017 Announcement (Chair: Kate Riney)</td>
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08:00  REGISTRATION DESK OPEN

08:30-10:00  PLATFORM SESSION 4 - GENERAL NEUROLOGY (Auditorium)

08:30  Congenital SEGAs in children with tuberous sclerosis complex

Denise Chan, Danny Flanagan & John Lawson

Background: Subependymal giant cell astrocytomas (SEGAs) are low grade intraventricular tumours affecting 5-14% of patients with tuberous sclerosis complex (TSC). SEGAs have a peak incidence in the second decade, however, there are rare cases within the first year of life. In the literature, 27 of 28 cases of congenital SEGAs were associated with significant growth and grim prognosis. A recent single centre case series of 10 patients identified a postnatal SEGA growth rate of 2.78mm per month \(^1\). Seven patients in this series underwent SEGA surgery with high surgical complications rates (57%).

Case Series: We describe 5 cases of TSC with SEGAs presenting before 12 months of age, measuring at least 10 mm. All patients but one presented antenatally with cardiac rhabdomyomas, the fifth presented with focal seizures at 5 months of age. The mean age is 6 years (range 3 to 14). Genetic mutation in TSC2 was identified in all 4 patients who underwent genetic testing. The mean SEGA maximum diameter at baseline was 15mm. SEGA growth was monitored through MRIs or serial head ultrasounds. We performed volumetric studies using available imaging data. SEGA size remained stable between most scans, with minor growth (2-5mm) only occurring once in the monitoring period for each patient. The SEGA growth rate in our cohort is lower than that which is previously reported. One case showed spontaneous regression in size at 13 months of age, prior to initiation of everolimus. Everolimus was started in 3 cases for refractory epilepsy, at an average age of 25 months. None of the patients in our series developed obstructive hydrocephalus, required surgical resection or insertion of ventriculoperitoneal shunt.

Conclusion: Our data regarding congenital SEGAs showed more favourable outcomes compared to existing literature reports.

Reference:

08:45  Serial nerve ultrasound in paediatric Guillain-Barré syndrome

Ian Woodcock & Eppie Yiu

Background: Nerve enlargement, demonstrated as increased nerve cross-sectional area (CSA) on high-resolution peripheral nerve ultrasound has been demonstrated in adults with Guillain-Barré Syndrome (GBS), with normalisation of nerve size with recovery. Apart from a single case report, there is no published data on nerve ultrasound findings in paediatric GBS.

Method: Children diagnosed with GBS were prospectively enrolled to undergo peripheral nerve ultrasound at baseline, 2-4 weeks, 6-8
weeks, 3 months, 6 months and 12 months. Assessment of neurologic deficit and neurophysiologic studies were performed as per routine clinical care. CSA of the median, ulnar, tibial and sural nerves was measured by peripheral nerve ultrasound in the dominant upper and lower limbs at each visit. Nerve CSA was compared to those of healthy age-matched controls.

Results: Six children, aged 5 to 16 years have been enrolled, with follow up ranging from 4 weeks to 12 months. The study is ongoing. Two children have completed the study. Apart from the sural nerve at the ankle, nerve CSA was enlarged at all sites compared to control values, in all but one child with GBS. Nerve CSA tended to reduce over time in those with follow up of at least 3 to 6 months duration, and tended to parallel neurologic recovery. There was no obvious correlation between neurophysiologic subtype and nerve enlargement.

Conclusion: Peripheral nerve ultrasound findings in paediatric GBS indicate nerve enlargement in the acute phase, which tends to reduce over time and with clinical recovery. Nerve ultrasound may be a useful, non-invasive tool to monitor nerve recovery in paediatric GBS.

09:00

Enterovirus associated acute flaccid paralysis: a case series
Smitha Kumble, Sarah Curnow & Eppie Yiu

Background: Enterovirus D68 and A71 have been implicated in the aetiology of acute flaccid paralysis (AFP) in children. In recent years, both subtypes have been associated with clusters of neurologic diseases in California and Sydney. Whilst enterovirus most commonly presents with respiratory symptoms and rash, it has been associated with serious neurological sequelae including aseptic meningitis, brainstem encephalitis and transverse myelitis. A distinct pattern of AFP associated with anterior horn and/or motor nerve root involvement, with brainstem encephalitis, enable clinical and radiological differentiation of enterovirus related cases from other typical demyelinating conditions.

Case Series: This case series includes six patients admitted to a tertiary children’s hospital with AFP over six weeks between March 2nd and April 13th 2016. Each patient presented with rapidly progressive flaccid weakness of one or more limbs within nine days of a viral illness. Half of these patients also had rapidly developing encephalopathy and cranial nerve involvement requiring respiratory and bulbar support. MRI demonstrated infratentorial, predominantly grey matter, changes in the brainstem and spinal cord in all patients. In three cases, nerve conduction studies demonstrated a neuronopathy affecting the upper limbs. Enterovirus was isolated in two patients sites known to provide the highest diagnostic yield for enteroviral PCR, stool and nasopharyngeal aspirates, and were typed as A71 and D68 respectively. CSF enterovirus PCR was negative in all cases.

Conclusion: This case series reaffirms an association between enterovirus and AFP. Although enterovirus was isolated in only two of six patients, the clinical and radiological similarities and time
period for the presentations, strongly suggest an enterovirus-related encephalomyelitis/acute flaccid paralysis in all. Thus, enterovirus should always be considered in the setting of AFP and specific neuroimaging findings.

09:15  **Etiological associations and outcome predictors of acute electroencephalography in childhood encephalitis**  
*Shekeeb Mohammad, Samantha Soe, Sekhar Pillai, Margherita Nosadini, Elizabeth Barnes, Deepak Gill & Russell Dale*

**Objectives:** To examine EEG features in a retrospective 13-year cohort of children with encephalitis.

**Methods:** 354 EEGs from 119 patients during their admission were rated blind using a proforma with demonstrated inter-rater reliability (mean K=0.78). Patients belonged to 12 etiological groups - infectious and infection-associated (n=47), immune-mediated (n=36) and unknown (n=33). EEG features were analyzed between groups and for risk of abnormal Liverpool Outcome Score and drug resistant epilepsy (DRE) at last follow up.

**Results:** 86% children had an abnormal first EEG and 89% had at least one abnormal EEG. 55% had an abnormal outcome, and 13% had DRE after median follow-up of 7.3 years (2.0-15.8 years). Reactive background on first EEGs (9/11, p=0.04) and extreme spindles (4/11, p<0.001) distinguished patients with anti-N-Methyl-D-Aspartate receptor encephalitis. Non-reactive EEG background (48% first EEGs) predicted abnormal outcome (OR 3.8, p<0.001). A shifting focal seizure pattern, seen in FIRES (4/5), anti-voltage gated potassium channel (2/3), Mycoplasma (1/10), other viral (1/10) and other unknown (1/28) encephalitis, was most predictive of DRE after multivariable analysis (OR 11.9, p<0.001).

**Significance:** Non-reactive EEG background and the presence of shifting focal seizures resembling migrating partial seizures of infancy are predictors of abnormal outcome and DRE respectively in childhood encephalitis.

09:30  **Riboflavin responsive regression in pre-school children: case reports**  
*Ian Woodcock, Eppie Yiu & Monique Ryan*

**Background:** We present two patients with riboflavin responsive neurological disorders presenting as neurodevelopmental regression.

**Case 1:** A three year old boy presented with a 3 to 4 month history of rapid regression of motor skills. From a baseline of being able to run, jump, climb and ride a bike, he presented with proximal pattern of weakness with marked neck flexor and extensor weakness, and weakness affecting upper limbs greater than lower limbs. Upper limb reflexes were absent but lower limb reflexes were preserved. He had marked hepatomegaly, but no splenomegaly. Metabolic investigations confirmed a diagnosis of multiple co-A dehydrogenase deficiency (MADD) and riboflavin supplementation was commenced. He peddled
his tricycle into his review appointment 3 months later.

Case 2: A five year old boy of consanguineous parents presented with a three month history of motor, visual and auditory regression. On presentation he had a distal greater than proximal hypotonia, weakness and wasting affecting the upper limbs more than the lower limbs, diffuse areflexia, an inability to sit or stand independently, marked irritability, optic atrophy and sensorineural hearing loss. Neuropysiologic testing confirmed an axonal sensorimotor neuropathy. Acylcarnitine profile was normal. Genetic testing confirmed a diagnosis of Brown-Vialetto-van Larre Syndrome (riboflavin transporter RFVT2 deficiency) and he was commenced on riboflavin supplementation. At a three month review an improvement in strength, hearing and vision was reported by his parents, and he was able to sit independently and walk with support.

Conclusion: These cases highlight the importance of considering riboflavin responsive disorders in children presenting with motor regression, particularly in those with upper limb predominance and/or an associated optic or auditory neuropathy. A trial of riboflavin should be considered in such cases.

The cost-effectiveness of next generation sequencing for diagnosis of paediatric muscle diseases

Gina O'Grady, Sarah Sandaradura, Khurshid Alam, Lyndal Douglas, Rupendra Shrestha, Daniel G. MacArthur, Mark Davis, Nigel G. Laing, Nigel F. Clarke, Joshua Burns, Sandra T. Cooper, Deborah Schofield and Kathryn N. North

Background: Paediatric muscle diseases, including the congenital muscular dystrophies (CMD) and non-dystrophic congenital myopathies, are highly genetically heterogeneous. Investigation has traditionally been with muscle biopsy, protein-based studies of muscle specimens and candidate gene sequencing. Next generation sequencing (NGS) is transforming diagnosis, with an increasing shift to molecular testing prior to muscle biopsy. There is a clear need to assess the cost effectiveness of NGS for diagnosis of neuromuscular disease.

Methods: All patients presenting to a single centre with suspected CMD or nemaline myopathy were ascertained over a 15 year period. Patients were investigated using traditional diagnostic approaches. Undiagnosed patients were investigated using NGS (whole exome sequencing (WES) or a neuromuscular disease (NMD) panel). Cost data was collected for all diagnostic investigations. The diagnostic yield and cost effectiveness of either targeted NMD gene panel or WES, prior to muscle biopsy, were compared with the traditional approach.

Results: 56 patients from 50 families were included in the final analysis. Compared with the traditional diagnostic algorithm, both the NMD panel and WES, had significantly increased diagnostic yields (from 46% to 75% for the NMD panel, and 79% for WES), reduced the cost per diagnosis from $22,596 (95%CI: AU$17,004- AU$31,498) to $5,077 (95%CI: AU$4,228- AU$6,100) for the NMD panel and $7,734 (95%CI: AU$6,166- AU$9,696) for WES. The NMD panel was the most
cost effective, saving $23,390 (95%CI: AU$14,595– AU$41,184) per additional diagnosis, over the traditional diagnostic pathway. WES was also cost saving, saving $13,732 (95%CI: AU$7,938– AU$23,473) per additional diagnosis.

Conclusion: Our diagnostic evaluation and economic modelling demonstrates the cost-effectiveness of targeted NMD panel screening as a first tier investigation in paediatric muscle disease, prior to muscle biopsy. A move to WES may be considered as the cost decreases. This study provides evidence to advocate for improved funding of NGS technology in clinical practice.

10:00-10:30  MORNING TEA (A+ Trust Room/all delegates)

10:30-13:00  SYMPOSIUM 5 - FETAL / NEONATAL RESEARCH (Auditorium)
10:30  The role of antenatal MRI in diagnosis of brain disorders
David Perry, Starship Children’s Health, Radiology Department, Auckland, NZ
Summary of current applications of Fetal MRI in clinical practice.

11:15  The genetics of Periventricular neuronal heterotopia
Stephen Robertson, Professor of Paediatric Genetics, Department of Women’s and Children’s Health, University of Otago, NZ

Malformations of the cerebral cortex can give deep insight into the genetic underpinnings of brain development. Here I will outline our studies on the genetics of periventricular neuronal heterotopia and what this has taught us about the aetiology and pathogenesis of this disorder. At a deeper level, understanding the genes implicated in the causation of this condition have opened the prospect of understanding the genetic regulation of stem cells within the developing brain.

11:50  Elucidating the genetics of developmental brain malformations - the Australian Health Genomic Alliance
Richard Leventer, Department of Neurology Royal Children’s Hospital, Melbourne, VIC
A/Prof. Leventer will discuss the Brain Malformation Flagship of the Australian Genomics Health Alliance.

12:10  Zika virus congenital infection
Lesley Voss, Paediatric Infectious Disease, Starship Children’s Hospital, Auckland, NZ
Zika virus was reported of being associated with microcephaly and ophthalmic abnormalities in newborns after an outbreak in Brazil in 2015. Zika virus is an arbovirus, transmitted via the bite of an infected mosquito of the Aedes sp. Spread of infection has occurred through the Africa and SEA with outbreaks in the Pacific in recent years. However, it has been in the large outbreak in Brazil, starting in May 2015, that microphaly has been found to occur in women infected with Zika virus in pregnancy. This talk will review the current literature on this association and briefly touch on other infectious causes of encephalitis.
### SCIENTIFIC PROGRAMME

**12:40**  
**Guidelines for Zika virus related neurological complications**  
*Richard Leventer, Department of Neurology Royal Children’s Hospital, Melbourne, VIC*

A/Prof. Leventer will discuss the neurological manifestations and brain imaging findings of congenital Zika virus infection. He will present the WHO guidelines on the management of a child with suspected congenital Zika syndrome.

**13:00-13:45**  
**ANZCNS TRAINEE PLATFORM AWARD & LUNCH** *(A+ Trust Room/all delegates)*

**13:45-14:45**  
**VIDEO & DIAGNOSTIC DILEMMA SESSION**

**14:45**  
**MEETING CLOSE / ASM 2017 ANNOUNCEMENT**

**15:00**  
**AFTERNOON TEA & DEPARTURES**
See you in Brisbane for the 6th ANZCNS Annual Scientific Meeting August 2017
Confirmed international speakers:
Professor Helen Cross, Great Ormond St Hospital, and
Marc Patterson, Mayo Clinic