Australasian Cerebral Palsy Clinical Trials Network

CENTRE FOR RESEARCH EXCELLENCE

Hot Topics in Cerebral Palsy

MONDAY 21 – TUESDAY 22 OCTOBER 2019

Monash Health Translation Precinct

cre-auscpctn.centre.uq.edu.au

Welcome

The Australasian Cerebral Palsy Clinical Trials Network is proud to present the two-day Hot Topics in Cerebral Palsy Research Forum.

The event will feature international invited keynote speakers Prof. Bernard Dan, Prof. Alistair Gunn, Prof. Laura Bennet, and Prof. Yannick Bleyenheuft, who will discuss recent advances and issues on some of the work being done to improve early diagnosis and intervention for children with, or at risk of, cerebral palsy.

In addition to our keynote lectures, the program features presentations from experts from across Asutralian and New Zealand.

For more info:
https://cre-auscpctn.centre.uq.edu.au/2019-AusCPCTN-HotTopics

Hot Topics Opening address

A/PROF. MICHAEL FAHEY

Department of Paediatrics, Monash Univesity.
Head of Child Neurology, Director of Neurogenetics, Monash Children's Hospital.
Chief Investigator on the AusCP-CTN CRE.

BIOGRAPHY

Associate Professor Michael Fahey is a Chief Investigator on the Aus-CP-CTN CRE and member in two themes – the Pre-clinical and Neuroprotection theme and the Early Detection and Neuroimaging Theme. Michael's research focuses on using neurogenetics to understand the pathways that lead to Cerebral Palsy. Michael collaborates on research into treatments for Cerebral Palsy with researchers at the Ritchie Centre, part of the Monash Institute of Medical Research. Among the work is research into melatonin, a hormone produced in the brain, with good efficacy in preclinical trials. Excitingly, this work is now moving to human trials. Michael maintains a workload as a physician in Paediatric Neurology and in Neurogenetics clinics as well as neurologist at the Paediatric Rehabilitation Clinic.

Associate Professor Michael Fahey has also been awarded a Fulbright Scholarship in 2019-2020 which will allow him to draw together two distinct research arms into genomics and brain imaging primarily located in Australia and the United States.

Keynote speakers

Professor Bernard Dan
MD
EDITOR-IN-CHIEF FOR DEVELOPMENTAL MEDICINE AND CHILD NEUROLOGY
"Neuroprotection and neuroplasticity in cerebral palsy"

Professor Alistair Gunn
MBChB PhD
PROFESSOR OF PHYSIOLOGY AND PAEDIATRICS
THE UNIVERSITY OF AUCKLAND
"Progress in neonatal neuroprotection"

Professor Yannick Bleyenheuft
PT PhD
PROFESSOR, INSTITUTE OF NEUROSCIENCE, UNIVERSITÉ CATHOLIQUE DE LOUVAIN
"Intensive motor interventions for children with cerebral palsy"

Professor Laura Bennet
MBChB PhD
HEAD OF DEPARTMENT, PHYSIOLOGY
THE UNIVERSITY OF AUCKLAND
"Biomarkers for detecting the evolution of fetal and neonatal brain injury"

Program

DAY 1 – MONDAY 21 OCTOBER 2019

0830-0900	Coffee/Tea/Light refreshment on arrival	
0900-0905	A/Prof. Michael Fahey	Welcome & Introduction
0905-0915	Prof. Ros Boyd	AusCP-CTN CRE: Annual Report Card
Plenary Keynotes: Chair – A/Prof. Michael Fahey		
0915-0945	Prof. Bernard Dan	Neuroprotection and Neuroplasticity in Cerebral Palsy
0945-1000	Prof. Euan Wallace	Prevention of Cerebral Palsy
1000-1015	Prof. Nadia Badawi	Prevention of CP: A journey started, hope realised, but still some way to go
1015-1045	Prof. Alistair Gunn	Progress in Neonatal Neuroprotection
1045-1115	Prof. Laura Bennet	Biomarkers for Detecting the Evolution of Fetal and Neonatal Brain Injury
1115-1130	Panel Discussion	Q&A with Keynotes
1130-1215	Lunch	
Early Detection & Neuroimaging in CP: Chair – Dr Jurgen Fripp		
1215-1230	Dr Jurgen Fripp	Neuroimaging in Newborn
1230-1245	Dr Alex Pagnozzi	Cloud-based Tools to Assist Neuroimaging for Cerebral Palsy
1245-1300	Dr Vuong Le	Machine Learning with General Movments project
1300-1315	Dr Christian Redd	Wearable Sensors to classify Fidgety Movements
1315-1330	A/Prof. Flora Wong	Neurovascular Monitoring using NIRS in the Developing Brain
1330-1340	Panel Discussion	Q&A with Theme Presenters
Pre-clinical & Neonatal Clinical Trials: Chair – Prof. Paul Colditz		
1340-1355	A/Prof Suzie Miller	Update on Stem Cells to Prevent/Cure Cerebral Palsy
1355-1410	Prof. Rod Hunt	Neuroprotection for the Extremely Preterm Infant: A potential role for stem cells
1410-1425	Dr Madison Paton Dr Megan Finch-Edmondson	Involving the Cerebral Palsy Community in Stem Cell Research
1425-1440	Dr Tamara Yawno	Ganaxolone for Neonatal Seizures
1440-1455	Dr Atul Malhotra	Optimising Neurodevelopment Outcomes for Fetal Growth Restriction
1455-1505	Panel Discussion	Q&A with Theme Presenters
1505-1520	Afternoon tea	
Pre-clinical & Neonatal Clinical Trials: Chair – A/Prof. Suzie Miller		
1520-1600	PhD Candidates	Three Minute Thesis
1600-1615	Dr Courtney McDonald	Targeting the Inflammasome: The Key to Curing Cerebral Palsy?
1615-1630	Dr Stacey Ellery	Studies on the Neuroprotective Capacity of Dietary Creatine: An Update
1630-1645	A/Prof. Michael Fahey	Melatonin
1645-1655	Panel Discussion	Q&A with Theme Presenters
1655-1700	A/Prof. Michael Fahey	Wrap Up Day 1

DAY 2 – TUESDAY 22 OCTOBER 2019

0900-0905	A/Prof. Michael Fahey Prof. Ros Boyd	Welcome to Day 2
Clinical Trials: Chair – Prof. Roslyn Boyd		
0905-0935	Prof. Yannick Bleyenheuft	HABIT-ILE, a Motor-skill Learning-based Intervention for Children with Cerebral Palsy
0935-1005	Prof. Bernard Dan	Neuroplasticity in Cerebral Palsy
1005-1020	Prof. Roslyn Boyd	Active Ingredients of Intensive Motor Interventions
1020-1035	Panel Discussion	Q&A with Theme Presenters
1035-1050	Morning tea	
1050-1120	Prof. Arend (Arie) F. Bos	The General Movements Assessment and Early Detection of Cerebral Palsy
1120-1130	A/Prof. Alicia Spittle	KiTE CP: Knowledge Translation of Early Cerebral Palsy
1130-1150	Dr Sue Reid Dr Hayley Smithers-Sheedy	Hot collaborations: An Update from the Australian and Victorian CP Registers
1150-1210	A/Prof. Michael Fahey Yana Wilson	Update on the International CP Genomics Consortium
1210-1230	Dr Sarah McIntyre Yana Wilson	A Common Data Set for International CP Genomics Research
1230-1245	Panel Discussion	Q&A with Theme Presenters
1245-1330	Lunch	
Infant Clinical Trials: Chair – Dr Cathy Morgan		
1330-1345	Prof. Iona Novak Dr Leanne Sakzewski	Optimum Dose of Upper-limb Rehabilitation
1345-1430	Prof. Roslyn Boyd Dr Cathy Morgan Dr Leanne Sakzewski	Update on Clinical Trials currently recruiting through AusCP-CTN: REACH, GAME, HABIT-ILE, Participate-CP
1430-1445	Dr Swetha Philip	VISIBLE (Vision Intervention for Severely Impaired Babies): Learning through Enrichment – A Study Protocol
1445-1500	Prof. Roslyn Boyd	LEAP-CP Learning through everyday activities for children with CP through Parent to Parent Training: India and QLD (Indigenous)
1500-1515	Dr Catherine Mak	Early PACT: Early Parenting Acceptance and Commitment Therapy
1515-1530	Panel Discussion	Q&A with Theme Presenters
1530-1545	Afternoon tea	
Child Clinical Trials: Chair – A/Prof. Michael Fahey		
1545-1600	Dr Leanne Sakzewski	Participation-focused Interventions
1600-1615	Dr Anne Trinh	Bone Health in Cerebral Palsy: The Need for Early Intervention
1615-1630	Prof. Bernard Dan	Getting Published
1630-1645	Panel Discussion	Q&A with Theme Presenters
1645-1700	A/Prof. Michael Fahey Prof. Roslyn Boyd	Conclusion / Wrap up

AusCP-CTN CRE Annual Report Card

The Australasian CP Clinical Trials Network has progressed on its work plan to uplift earlier detection of CP, fast track children to multisite randomised clinical trials of new neuroprotectants and to develop and test new rehabilitation. Some Knowledge Translation studies have commenced to ensure effective transfer to enhanced clinical practice. The CRE has commenced a new International clinical practice guideline on Functional Therapy and is setting up a national consumer network aided by Anne McKenzie, AM. The changes in outcomes of children with CP will be tested in the Australian Cerebral Palsy Register.

PROFESSOR ROSLYN BOYD

Chief Investigator and Director of the AusCP-CTN CRE. Scientific Director of the Queensland Cerebral Palsy Rehabilitation & Research Centre, Faculty of Medicine, The University of Queensland.

BIOGRAPHY

Professor Boyd leads an internationally recognised team of researchers conducting clinical trials of novel interventions geared to optimising neuroplasticity, early detection of cerebral palsy, longitudinal comprehensive outcomes linked to brain structure and function. Her team has conducted 17 RCTs in CP and infants born preterm. She has received >$40M in grants including 13 NHMRC, 1ARC, 1 NIH and has published >305 publications. She has had continuous NHMRC people support, being a Research Fellow (2016-2021) and previous QLD Smart State Fellow. She and her research team have been awarded the most prestigious international prize for CP Research, the Gayle Arnold Award, in 2010, 2011 and 2014. Recently she received the Mentorship Award from The American Academy for Cerebral Palsy and Developmental Medicine and the Faculty of Medicine at the University of Queensland.

CRE Framework

GENERATING NEW KNOWLEDGE ACROSS THE FIVE THEMES

THEMES

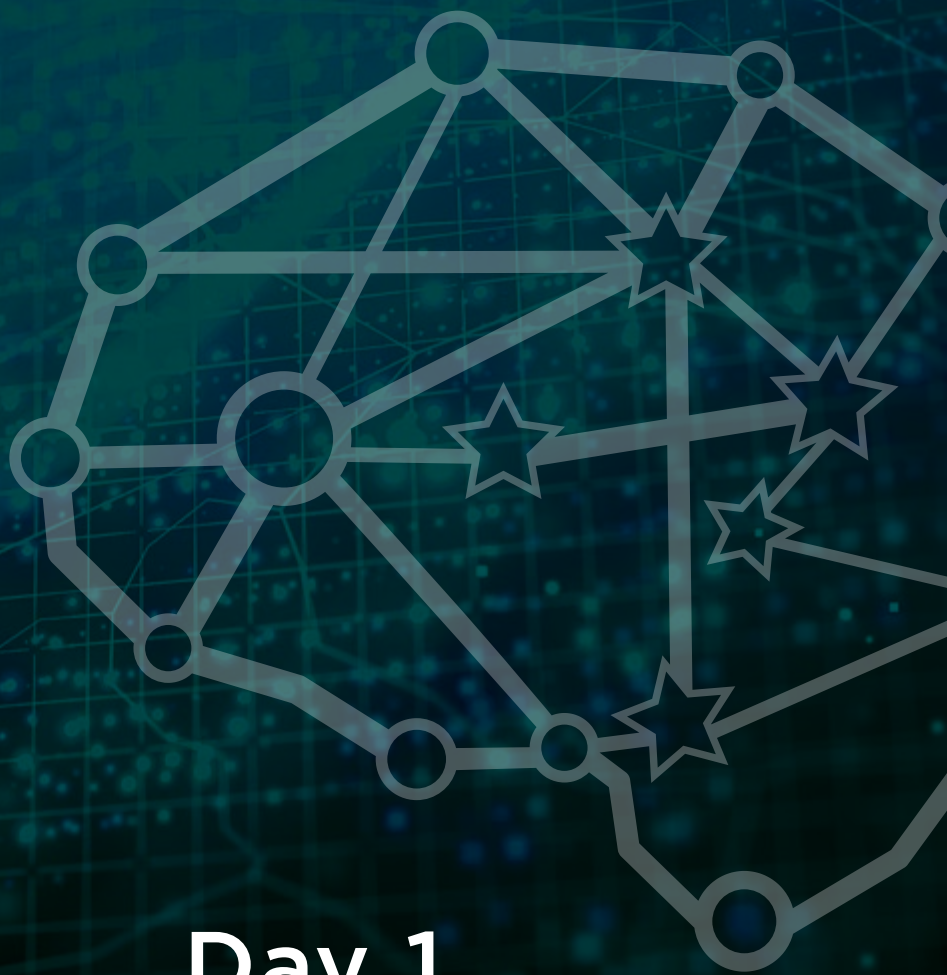
- Pre-clinical & Neuroprotection
- Early Detection & Neuroimaging
- Clinical Trials (Efficacy Early Interventions)
- Knowledge Translation & Implementation
- Engagement & Health Policy

STREAMS

- NEW KNOWLEDGE GENERATION
- TRAINING (CLINICAL & RESEARCH)
- IMPLEMENTATION & TRANSLATION
- HEALTH ECONOMICS, PROMS & TELEHEALTH SOLUTIONS

WORK PLANS & GOALS

1. Advance understanding of the neurobiology of CP and neuroprotective interventions
2. Advance understanding of the clinical biomarkers of early brain injury. Develop neuroplastic rehabilitations.
3. Build evidence-based early interventions, rehabilitation, & training environments by conducting world class trials.
4. Identify the most effective ways to implement cost effective treatments into practice and increase uptake by clinicians.
5. Embed our successful strategies into routine clinical care through partnerships.



Day 1 Abstracts

Keynote Session

NEUROPROTECTION AND NEUROPLASTICITY IN CEREBRAL PALSY

Neuroplasticity generally refers to the capacity of neurons and neural networks to change their connections and behaviour in response to experience. Varied behavioural, neurophysiological and neuroimaging methods are used to document changes in the nervous system more or less directly. Strong anatomical, histological, biochemical and gene expression lines of evidence are also available. But the resulting picture is blurred, owing in part to the variety of phenomena for which the term 'neuroplasticity' is used, and in part because we lack a clear definition and general theory for neuroplasticity. Intense synaptic plasticity in dendritic spines is crucial to shaping developmental trajectories, learning, and adapting to existing as well as new conditions.
On a wider scale, structural neuroplasticity involves changes in volume of discrete brain regions or the formation of new neural pathways. This can occur through synaptogenesis, axonal or dendritic sprouting, changes in myelin, or production of new neurons. Synapses, fibres and cells are overproduced early in maturation, and subsequently compete for survival and efficacy within functional networks. Local (in)activity induces local plasticity and also widespread network changes, providing arguments for promotion of self-initiated activities, experiences and intervention provided closer to the time of injury and during particularly sensitive periods. But we must still understand how neuroplasticity is achieved. What makes an experience biologically meaningful? How does experience induce modifications at different levels of neural (and neuro-glial) organization? What is the potential for long-term changes to refine therapy and engineer signalling devices to effectively promote improved functioning through neuroplasticity?

PROFESSOR BERNARD DAN

Editor-in-Chief for Developmental Medicine and Child Neurology. Professor of Neurophysiology. and Developmental Neurology, Université libtre de Bruxelles. Director of Rehabilitation, Inkendaal Hospital.

BIOGRAPHY

Prof. Bernard Dan MD is a paediatric neurologist and professor of neurophysiology and developmental neurology in Brussels (Université libtre de Bruxelles), and is Director of Rehabilitation at Inkendaal Hospital. His clinical and research interest includes motor control, particularly in cerebral palsy and neurogenetic conditions. He serves as editor-in-chief for Developmental Medicine and Child Neurology. He was the recipient of the 2012 John Stobo Prichard Award.

PREVENTION OF CEREBRAL PALSY

Perusing the list of expert speakers at this fabulous Cerebral Palsy Hot Topics conference highlights one of the key challenges facing the effective prevention of cerebral palsy – the lack of the key care providers who are best placed to deliver prevention; midwives, GPs, and obstetricians. With the origins of potentially avoidable cerebral palsy mostly in pregnancy and/or childbirth, whole-of-population solutions to prevention will lie, mostly, in pregnancy care.

In this short presentation, I will share some of the recent policy and practice changes in Victoria that have targeted improvements in pregnancy care as a means to delivery better patient outcomes, including the prevention of cerebral palsy. In particular, I will show recent data on improving the detection and management of fetal growth restriction – highlighting some emerging challenges – and share outcomes of the statewide approach to intrapartum fetal surveillance.

PROFESSOR EUAN WALLACE AM

Carl Wood Professor and Head of Department of Obstetrics and Gynaecology. Executive, The Ritchie Centre, Hudson Institute of Medical Research. Chief Executive Offier, Safer Care Victoria, Department of Health and Human Services, Victorian Government.

BIOGRAPHY

Professor Wallace is one of Australia's leading specialists in obstetrics and gynaecology. In 2013 he was made a Member of the Order of Australia (AM) for his contributions to medicine in the field of obstetrics and gynaecology. In 2015 he was elected a Fellow of the Academy of Health and Medical Sciences.

Professor Wallace joined Monash University in 1996 as a Fellow in Maternal-Fetal Medicine, becoming a Senior Lecturer (1997-2000) and subsequently an Associate Professor (2000-2006) in the Department of Obstetrics and Gynaecology. In 2006 he was awarded a personal chair, named in honour of the inaugural head of department of obstetrics and gynaecology at Monash University – Professor Carl Wood.

In 2013, Professor Wallace succeeded Professor David Healy as the Head of the Department, establishing the Carl Wood Chair as the Head of Department chair.

Professor Wallace is also an Executive member of The Ritchie Centre, one of the world's leading research centres for perinatal and women's health research. The Centre is a collaboration between Monash University, the Hudson Institute for Medical Research, and Monash Health. Within The Ritchie Centre, Professor Wallace leads a maternal and perinatal research group. His research is focused on preeclampsia, fetal development, cerebral palsy, stem cells and regenerative medicine, and patient safety.

From 2006 – 2016 Professor Wallace was Director of Women's Program at Monash Health, Australia's largest women's health service. In December 2016 he stepped down as Program Director to take up the role of CEO, Safer Care Victoria, a new office for healthcare quality and safety improvement within the Victorian Department of Health and Human Services.

Professor Wallace established Australia's first guidelines on fetal surveillance and Fetal Surveillance Education Program, which are now in every hospital providing maternity care in the country.

PREVENTION OF CEREBRAL PALSY: A JOURNEY STARTED, HOPE REALISED, BUT STILL SOME WAY TO GO.

The recent Australian Cerebral Palsy Register Report has shown a staggering 30% drop in the rate of cerebral palsy. We now have one of the lowest recorded rates in the world.

The fall was mostly in children who were born at term and among those born before 27 weeks gestation. The rate also decreased among twins and in post-neonatally acquired CP. Along with the fall in incidence there was also a drop in the severity in those children who did still develop cerebral palsy, which was reflected in more children with CP being able to walk and in lower rates of co-existing disability.

These results are likely to be the result of progress in research and in clinical practice, particularly around the antenatal care of women with high risk pregnancies, especially prematurity, and improvements in neonatal care. Important public health initiatives such as decreased smoking in public spaces, car seats and pool fences are also likely to have had an important effect. It is a happy marriage of research, clinical medicine and public policy all working together.

This success in prevention suggests more is possible. Further progress will entail ongoing cooperation between people who live with cerebral palsy, their families, basic scientists, epidemiologists, researchers, clinicians and policy makers, working together to improve the outcomes for babies before birth, in neonatal intensive care units and in the community. The buy-in of government and philanthropy will also be critical to support the national treasure that is the Australian Cerebral Palsy Register, which remains both the only way to assess the impact of changes in practice and a rich source of information pointing the way to new strategies of doing things for better outcomes.

PROFESSOR NADIA BADAWI AM

Macquarie Group Foundation Professor and
Chair of Cerebral Palsy, The University of Sydney.

BIOGRAPHY

Professor Nadia Badawi AM is the Macquarie Group Foundation Professor and Chair of Cerebral Palsy at the Cerebral Palsy Alliance Research Institute, dedicated to the prevention and cure of cerebral palsy through a research program of neuro-protective and neuro-regenerative clinical trials. She is the Medical Director and Co-Head of the Grace Centre for Newborn Intensive Care. Nadia is a leader in her field and was made a Member of the Order of Australia and named as one of the “100 most influential women in Australia” for her contribution to international cerebral palsy (CP) research and the improvement of clinical care in low and middle-income countries.

PROGRESS IN NEONATAL NEUROPROTECTION

Acute post-asphyxial encephalopathy occurring around the time of birth remains a major cause of death and disability. The recent seminal insight that allows active neuroprotective treatment is that even after profound asphyxia (the “primary” phase), many brain cells show initial recovery from the insult during a short “latent” phase, typically lasting approximately 6 h, only to die hours to days later after a “secondary” deterioration characterized by seizures, cytotoxic oedema, and progressive failure of cerebral oxidative metabolism. Although many of these secondary processes are potentially injurious, they appear to be primarily epiphenomena of the ‘execution’ phase of cell death. Animal and human studies designed around this conceptual framework have shown that moderate cerebral hypothermia initiated as early as possible but before the onset of secondary deterioration, and continued for a sufficient duration to allow the secondary deterioration to resolve, has been associated with potent, long-lasting neuroprotection. Large clinical trials show that therapeutic hypothermia significantly reduces morbidity and mortality, but babies still die or survive with disabilities. The challenge for the future is to find ways of improving the effectiveness of treatment. This presentation will dissect the known mechanisms of hypoxic-ischemic brain injury in relation to hypothermic neuroprotection to examine the viability of different strategies of improving neurological outcome after asphyxia.

PROFESSOR ALISTAIR GUNN MBCHB PHD

Professor of Physiology and Paediatrics,
The University of Auckland.

BIOGRAPHY

Alistair Jan Gunn is a Paediatrician-scientist who has conducted groundbreaking basic research into ways of identifying compromised fetuses in labour, the mechanisms and treatment of asphyxial brain injury and the mechanisms of life threatening events in infancy. He has helped to develop a range of new, clinically relevant chronically instrumented fetal sheep paradigms to support translation of the team’s findings to clinical practice, leading to the studies that helped to establish mild cooling as the first ever technique to reduce brain injury due to low oxygen levels at birth.

BIOMARKERS FOR DETECTING THE EVOLUTION OF FETAL AND NEONATAL BRAIN INJURY

Hypoxic-ischaemic encephalopathy at birth affects around 1-3/1000 live births at term and upwards of 120/1000 live preterm births. Preterm infants in particular are at significant risk for neural injury and impaired neurodevelopment, and at higher risk for cerebral palsy. Multiple factors underpin the risk for injury or impairment, including fetal growth restriction, gestational age, and adverse events such as inflammation and hypoxia at or around the time of birth. Importantly, however, many normally grown babies may enter birth with pre-existing injury due to such factors as acute hypoxia earlier in gestation.

Clinical evidence suggests, for example, that many cases of cerebral palsy, in children born term and preterm, have their origins in fetal life. Detecting these at risk babies and those with pre-existing brain injury, even before birth, is critical for changes to clinical care and early implementation of neuroprotection and neurorepair treatments. This talk will present research about how preterm fetuses can adapt to and survive an injurious hypoxic insult, how fetal brain injury evolves in utero after an acute hypoxic insult and methods for detecting the occurrence, severity and phase of antenatal brain injury.

PROFESSOR LAURA BENNET MBCHB PHD

Head of Department, Physiology
The University of Auckland.

BIOGRAPHY

Laura is a perinatal physiologist with a specialist interest in preterm fetal and neonatal behaviour, and cardiovascular and neurophysiological adaptations to common in utero insults such as hypoxia and infection, as well as the development of treatment strategies and biomarkers to identify the at risk baby.

Early Detection & Neuroimaging in CP

NEUROIMAGING IN NEWBORN

The assessment of brain structure and growth during the neonatal period shows great promise in the early prediction of neurodevelopmental outcomes. We are developing automated tools for quantitative radiological reporting of brain MRIs of children with cerebral palsy, and of newborns at risk of developing cerebral palsy. In this talk, I will present our currently available tools, and discuss their potential impact on early diagnosis and prognosis.

DR JURGEN FRIPP

Group Leader, Biomedical Informatics,
Australian eHealth Research Centre, CSIRO.

BIOGRAPHY

Jurgen Fripp completed his honours thesis and PhD in the area of Medical Imaging at the University of Queensland and with the CSIRO. His bachelor degree from the University of Queensland was in Science (applied mathematics) and Electrical Engineering. Jurgen is now leading the CSIROs Image Analysis team at the Australian eHealth Research Centre, conducting research into image analysis algorithms for applications in Positron Emission Tomography (PET), Magnetic Resonance Imaging (MRI), Computed Tomography (CT). The developed workflows have been applied to support various large clinical studies, including AIBL (http://aibl.csiro.au/).

CLOUD-BASED TOOLS TO ASSIST NEUROIMAGING IN CEREBRAL PALSY

Neuroimaging is routinely performed for children with Cerebral Palsy (CP) in order to understand the type and severity of brain injury, however these images are currently only analysed qualitatively. Our group at CSIRO is developing several cloud-based tools to quantify brain structure and microstructure, allowing subtle differences from typically developing cohorts to be identified, as well as the potential estimation of clinical outcomes. In this presentation, I will provide an outline of these tools for the early detection of CP in neonates at risk of CP, and for the brain structural characterisation of children with CP.

DR ALEX PAGNOZZI

Medical engineer and Advance Queensland fellow at the Australian e-Health Research Centre, CSIRO.

BIOGRAPHY

Dr Alex Pagnozzi is a medical engineer and Advance Queensland fellow at the Australian e-Health Research Centre, a joint venture between CSIRO and the Queensland Government. During his PhD he utilised machine learning and statistics to extract clinical useful information from medical images that could be used to predict patient function. Now as a postdoctoral researcher, he is developing web-based tools to make these methods available to researchers and clinicians, accelerating brain research and improving outcomes for children with neurological injuries.

MACHINE LEARNING FOR AUTOMATIC GENERAL MOVEMENT ASSESSMENT: HOPE AND PROSPECT

Although human expert's assessment of general movements is the principal method for early cerebral palsy detection, it is time consuming and requiring skilled practitioners who can be limited particularly in poorer countries. Automating the assessing process or assisting the human effort will vastly improve access to early detection and intervention. Machine learning and computer vision have recent phenomenal advances that enables two key techniques toward this horizon: human motion analysis and neural recognition systems. In this talk, we explore the prospect of applying these advances for detecting abnormality in general movement from video inputs. These predictions provide indicators toward efficient early CP screening. We aim at building fully automated systems or semi-automated setups where human expert and artificial intelligence work in synergy.

DR VUONG LE

Research Fellow, Applied Artificial Intelligence Institute, Deakin University.

BIOGRAPHY

Dr Vuong Le holds a PhD degree in Electrical and Computer Engineering from University of Illinois at Urbana Champaign since 2014 and currently is a research fellow at The Applied Artificial Intelligence Institute – Deakin University. He has a track record on computer vision and machine learning research, especially on the field of human behaviour understanding from visual data. His works have resulted in scientific contributions of one book and many publications in major venues including CVPR, ICCV, ECCV. His works were cited more than 860 times. He current holds six US patents on applying computer vision and machine learning in industrial products. Dr. Le's past employment includes University of Illinois, Adobe Research, HP labs, and Amazon.com.

WEARABLE SENSORS TO CLASSIFY FIDGETY MOVEMENTS

Qualitative assessments of infant spontaneous general movements can be performed to measure neurodevelopmental status and provide early insight into the presence of any abnormalities. Clinical assessments of infant movements at 12 weeks post term age are up to 98% predictive of the eventual development of Cerebral Palsy, but their reach is often limited to infants already identified as high-risk within the traditional healthcare system. We present a network of wearable sensors to noninvasively measure spontaneous movements in infants from 12-20 weeks post-term- age both within the clinic and in the home. Tele- delivered assessments may enhance screening of neurodevelopmental disorders for infants and families in rural and remote areas, a population with reduced health services.

DR CHRISTIAN REDD

Research Scientist, Australian eHealth Research Centre, CSIRO.

BIOGRAPHY

Christian Redd is a postdoctoral research fellow with the Australian eHealth Research Centre and the Queensland Cerebral Palsy and Rehabilitation Research Centre. He received a B.S. and M.S. from the University of Utah in Mechanical Engineering with an emphasis in bioinstrumentation. He received a Ph.D. in Bioengineering from the University of Washington in 2017. During his time at the University of Washington he developed non-invasive wearable sensing mechanisms for continuous extraclinical monitoring of peripheral vascular health and prosthesis use for persons with amputations. At the AEHRC and QCPRRC, his current research efforts involve development and testing of miniature wearable movement sensors to monitor infant development and enhance early identification of infants at high-risk of Cerebral Palsy and other related disorders. His areas of expertise include bioinstrumentation, rehabilitation medicine, and medical diagnostics.

NEUROVASCULAR MONITORING USING NIRS IN THE DEVELOPING BRAIN

Neurovascular coupling (NVC) is an important mechanism that provides increased cerebral blood flow and cerebral oxygenation in response to neural activation, producing a positive haemodynamic functional response to prevent cerebral hypoxia. NVC has been extensively studied in both adult and paediatric populations, and used as a marker of cerebral health. But the presence and effectiveness of NVC within the developing preterm brain is less certain. Using a preterm animal model for testing the cerebral functional response would allow investigation of NVC in the preterm brain, and its change in different clinical diseases. The knowledge would help to understand preterm brain injury, and to optimise clinical management and cerebral oxygenation.

There are 2 major contributors of preterm brain injury: hypoxia and inflammation. Intrauterine inflammation which manifests as chorioamnionitis, is a common antecedent of preterm birth and exacerbates brain injury. We have used an ovine model to evaluate the NVC in the preterm brain, by measuring changes in cerebral oxy- and deoxy-haemoglobin (ΔoxyHb and ΔdeoxyHb) after neural activation, using near infrared spectroscopy (NIRS). NIRS optodes and EEG electrodes were positioned over the somatosensory cortex of preterm lambs (gestational age of 127-132 days). The left median nerve was stimulated by electrical pulses (for 2-8 sec) to induce somatosensory neural activation, and the somatosensory evoked potential, ΔoxyHb and ΔdeoxyHb responses were recorded. To study the effect of intra-uterine inflammation and chorioamnionitis on NVC, we studied another group of preterm lambs exposed to intra-amniotic injection of LPS, as a model of chorioamnionitis in preterm infants.

Among the control preterm lambs, majority (>75%) showed increased cerebral ΔoxyHb after somatosensory stimulations, consistent with a positive functional response. In contrast, only 35-50% of preterm lambs exposed to intra-uterine inflammation showed the positive response, and the rest showed a negative functional response probably due to cerebral vasoconstriction. Our results suggests impaired NVC in the preterm brain exposed to intra-uterine inflammation, which may be the mechanism responsible for cerebral hypoxia and neuropathy in preterm infants with chorioamniontis.

ASSOCIATE PROFESSOR FLORA WONG

Senior Consultant Neonatologist, Monash Health.
Department of Paediatrics, Monash University.

BIOGRAPHY

A/Prof. Flora Wong MBBS, FRACP, PhD is a senior Consultant Neonatologist at Monash Newborn, MonashHealth, with a joint appointment as associate professor at the Department of Paediatrics, Monash University. She is the head of the Neonatal Brain Protection Laboratory at The Ritchie Centre, The Hudson Institute of Medical Research. She has been awarded the NHMRC Career Development Fellowship to continue her part-time research commitment. Since 2010, she has successfully obtained ~$4.7M of research funding from NHMRC and various Philanthropic foundations. She has >70 publications and >1400 citations.

Her research interests are in newborn cerebral blood flow and oxygenation in relation to brain injury in newborn infants undergoing intensive care. Her projects aim at investigations of the mechanisms of newborn brain injury, development of cotside monitoring and neuroprotective strategies. Translational research is an important theme of her projects, involving complementary experimental studies in the animal models and clinical studies in preterm infants to examine cerebral pathophysiology. She has pioneered the research utilising Spatially Resolved Spectroscopy in Australia to measure brain oxygenation in babies. Her publications demonstrate a strategic set of studies for the identification of circulatory factors that contribute to neonatal brain injury and testing new clinical interventions.

Preclincial & Neonatal Clinical Trials

UPDATE ON STEM CELLS TO PREVENT/CURE CEREBRAL PALSY

Human clinical trials have recently reported safety data and preliminary evidence of efficacy following treatment of children with cerebral palsy using umbilical cord blood (UCB) stem cells. UCB is an appealing neuroprotective treatment – it is already used safely for transplant in blood disorders, and UCB is made up of many different cell types, including mesenchymal stem cells (MSCs), endothelial progenitor cells (EPCs), T regulatory cells (Tregs) and monocyte derived suppressor cells (MDSCs), where each may contribute towards reducing neuroinflammation and/or repair of brain injury.

The etiology of damage to the developing brain that underlies cerebral palsy, is variable, however it is well described that about half of those individuals with cerebral palsy were born preterm (<37 weeks gestation). Currently there are no standard neuroprotective or neuroreparative treatments that are offered to infants born preterm, despite strong knowledge to demonstrate this cohort as high risk for long term neurological deficits. Therefore, we set out to use large animal (sheep) models of preterm brain injury associated with hypoxia-ischaemia or inflammation to examine the neuroprotective benefits of UCB stem cells.

ASSOCIATE PROFESSOR SUZIE MILLER

NHMRC Senior Research Fellow. Depty Director, The Ritchie Centre. Theme Leader, The Ritchie Centre Fetal and Neonatal Health, Neurodevelopment and Neuroprotection, Hudson Institute of Medical Research, Department of Obstetrics and Gynaecology, Monash University.

BIOGRAPHY

Associate Professor Suzie Miller (BSc Hons, PhD) is an NHMRC Senior Research Fellow (Level B), Deputy Director of The Ritchie Centre and she leads the Neurodevelopment Theme at the Centre. Suzie's specialist expertise is in neurodevelopmental physiology, and her research group combines experimental animal models of the primary causes of neonatal brain injury to better understand the progression of neuropathology, with clinical studies focused on detection and inhibition of perinatal brain injury. Fundamentally, Suzie's experimental and clinical studies are directed towards understanding the mechanisms that contribute to perinatal brain injury and functional deficits, so that targeted neuroprotective therapies can be implemented. Suzie is also an advocate for the role of women in science, and a founding member of the National Health and Medical Research Council of Australia's Women in Health Science Committee.

NEUROPROTECTION FOR THE EXTREMELY PRETERM INFANT: A POTENTIAL ROLE FOR STEM CELLS

Many cohort studies have now been completed in which outcomes for preterm infants have been repeatedly demonstrated to be less favourable than those for term born infants. This has been consistent across a number of domains, and at a number of different developmental ages. The pathophysiology for this vulnerability has been interrogated with advanced neuroimaging techniques. White matter injury as a consequence of damage to the pre-oligodendrocyte is at least partly responsible for the increased risk to infants born preterm for impairments such as cerebral palsy.

In the laboratory, Australian scientists have been leading the way in trials of different stem cells as potential neuroprotective agents for the developing brain. With increasing knowledge of mechanism of action and appropriate dosing, a trial of stem cells to those preterm infants most at risk is warranted to translate this science into clinical benefit. Feasibility issues for such a trial will be discussed.

PROFESSOR ROD HUNT

Director, Neonatal Medicine and Neonatal Research,
The Royal Children's Hospital, Melbourne.

BIOGRAPHY

Professor Rod Hunt is Director of Neonatal Medicine and Neonatal Research at The Royal Children's Hospital in Melbourne. His research interrogates mechanisms of brain injury and repair in the vulnerable preterm and term newborn infant.

INVOLVING THE CEREBRAL PALSY COMMUNITY IN STEM CELL RESEARCH

The Cerebral Palsy Stem Cell Reference Group was formed in 2018. The purpose of this group is to provide the perspective of people with cerebral palsy and their families/carers to shape decisions about research priorities, specific research questions and the design of new research projects associated with the stem cell research program of the Cerebral Palsy Alliance. Furthermore, to work in partnership with researchers to inform the community of research findings and outcomes. The Reference Group now has more than 30 members and is already meaningfully participating in research in a variety of ways.

In this presentation we will describe the progress we have made in creating a model of consumer engagement in cerebral palsy stem cell research. We will give an overview of the ways in which consumers are participating in our research activities, what we have learned from the members of the Reference Group, and where we hope to go to from here. Furthermore, we will present our work on generating a public narrative of stem cell tourism for cerebral palsy, through the establishment of a world-first survey.

DR MADISON PATON

Research Fellow (Stem Cells), Cerebral Palsy Alliance Research Institute, University of Sydney.

BIOGRAPHY

Dr Madison Paton is a Research Fellow at the Cerebral Palsy Alliance, with a PhD in stem cell therapies. She currently works to design trials and generate funds for the establishment of Australian stem cell clinical trials. She is an avid science communicator with a passion for research dissemination and ensuring that accurate information on stem cell therapies is available to the public. Her recent work focuses on developing a narrative from families and those with cerebral palsy who have travelled overseas for stem cell therapies via an online, multi-national research survey.

DR MEGAN FINCH-EDMONDSON

Research Fellow (Stem Cells), Cerebral Palsy Alliance Research Institute, University of Sydney.

BIOGRAPHY

Dr Megan Finch-Edmondson is a Senior Stem Cell Research Fellow at the Cerebral Palsy Alliance where she is responsible for building capacity and accelerating research translation in stem cell research for cerebral palsy in Australia. Megan is particularly focused on designing safe and relevant stem cell clinical trials locally and consumer engagement. Megan founded the Cerebral Palsy Stem Cell Reference Group, a group of more than 30 people with cerebral palsy, their families/carers and professionals who are actively seeking more information and input in stem cell research.

GANAXOLONE FOR NEONATAL SEIZURES

Background: Seizures in neonates are relatively common, and are strong predictors of long-term impairment like cerebral palsy. Current anti-seizure therapies (phenobarbitone (pheno)) can be neurotoxic. We propose that ganaxolone (ganax), a GABAA agonist, will reduce seizures, and brain injury following hypoxia ischemia (HI). We investigated the effects of ganax or pheno on seizure burden and neuropathology in HI lambs.

Methods: HI was induced via umbilical cord occlusion in term lambs. HI lambs were treated with either ganax or pheno at 6 h. Seizure burden was assessed using continuous amplitude-integrated electroencephalogram (aEEG) recording. At 48h, lambs were euthanized for brain collection and analysis of neuropathology.

Results: All HI lambs demonstrated electrographic seizures; mean number of seizures/ h (6-12h) was 4.8 ± 2.2. Ganax treatment reduced the number of seizures to 1.0 ± 0.9/ h compared to pheno (3.2 ± 1.6/ h) (P=0.02). Brain histology revealed improved neuronal survival (NeuN+ cell number) and reduced cell death (TUNEL+) in the cortex and basal ganglia after ganax treatment, compared to pheno.

Conclusions: Ganax treatment in lambs with HI decreased seizure activity, improved neuronal survival and reduced cell death. Ganax has a high margin of safety and proved to be a better therapy.

DR TAMARA YAWNO

RANZCOG Glynn White Research Fellow, Research Scientist, Neurodevelopment and Neuroprotection, Hudson Institute of Medical Research.

BIOGRAPHY

Tamara is a fetal neuroscientist working as a Research Fellow at The Ritchie Centre, Hudson Institute of Medical Research and Department of Obstetrics and Gynaecology, Monash University. She was awarded a prestigious Career Development Award from the Cerebral Palsy Alliance of Australia, which recognized her focus on the importance of neonatal hypoxia ischemia and her efforts to find new therapies, which lead to the success of a current NHMRC grant. Tamara has developed an international reputation for her research on neurosteroids and neuroprotection in the fetus and neonate. Her recent work has led to a current clinical trial on the use of ganaxolone in hypoxic ischemic babies.

OPTIMISING NEURODEVELOPMENT OUTCOMES FOR FETAL GROWTH RESTRICTION

Fetal growth restriction is a common pregnancy complication, which results in compromised fetal growth. It is associated with an increased risk of perinatal, neonatal and long term morbidities, including neurodevelopmental deficits like cerebral palsy. Using a placental insufficiency lamb model of FGR, we have conducted a number of experiments to study the pathophysiological mechanisms of brain injury related to FGR. FGR is associated with impairments of brain structure and function, most importantly of the white matter regions of the brain. We have also evaluated the effects of novel therapeutic interventions that may prevent and/or mitigate FGR related brain injury. In this talk, we present some of our pre-clinical work on understanding and optimising neurodevelopmental outcomes for FGR.

DR ATUL MALHOTRA

Consultant Neonatologist, Monash Newborn, Monash Health. Senior Lecturer, Department of Paediatrics, Monasu University.

BIOGRAPHY

Dr Malhotra is a consultant neonatologist at Monash Newborn and research scientist at The Ritchie Centre, Hudson Institute of Medical Research. He holds a senior lecturer appointment in the Department of Paediatrics, Monash University and is the current recipient of a RACP Foundation Research Fellowship.

His clinical research interests focus on improving respiratory and neurological outcomes of high risk infants. He has been involved in a number of randomised clinical trials in neonatal conditions. He is keen on early neurodevelopment and recently established the Early Neurodevelopment Clinic (for early detection of cerebral palsy) for high risk neonates at Monash Children's Hospital. He is also a lead investigator of an NHMRC funded study on preterm neurodevelopment.

His basic science interests include understanding and treating brain injury related to high risk perinatal conditions. He has a special interest in fetal growth restriction and has conducted a number of preclinical and clinicial studies in the field.

He has been instrumental in the translation of a number of preclinical therapies from the laboratory to the clinic. He recently led a world-first trial of placental stem cells for chronic lung disease of prematurity. He has a special interest in regenerative cell therapies for neonatal diseases.

Dr Malhotra is passionate about education and is the Co-Chair of Monash Children's Hospital Simulation. He has also been running maternal and neonatal simulation based education programs in low and middle countries.

TARGETING THE INFLAMMASOME; THE KEY TO CURING CEREBRAL PALSY?

Background: Neuroinflammation is a key mechanism of cellular injury that can occur in complicated pregnancies or births resulting in perinatal brain injury. We have identified a novel pathway, the inflammasome, that is upregulated following perinatal brain injury. Promising inhibitors of the inflammasome pathway (MCC950) have been developed and warrant investigation.

Methods: Hypoxic-ischemic (HI) brain injury was induced in PND10 rats, by single carotid artery ligation followed by hypoxia (8% oxygen for 90 mins). At 6h post-HI, rats were given MCC950 (20mg/kg) via intranasal route. 72h post-HI behavioural testing was performed and then serum and brains were collected for analysis. Cytokine arrays were performed using serum, brains were used for assessment of neuroinflammation (Iba-1, GFAP) and brain injury (H&E, NeuN).

Results: We found that following HI, components of the inflammasome complex and pathway, including caspase-1, NLRP3 and Gasdermin D, are upregulated. Key cytokines activated by the pathway are also upregulated, IL-1B and IL-18. MCC950 treatment at 6h significantly improved motor strength and control as examined using a negative geotaxis test compared to HI ($P<0.05$). HI injury significantly reduced brain/body weight ratio compared to sham ($P<0.05$), and MCC950 treatment reversed this deficit. However, MCC950 treatment did not reduce overall brain tissue loss or reduce histological analysis of neuroinflammation, but did decrease gene expression of two key proteins, IL-18 and Caspase-1.

Conclusions: We have identified a novel pathway, the inflammasome, that is activated in perinatal brain injury. Inhibition of this pathway using novel inhibitors such as MCC950 can effectively reduce behavioural deficits, but a single dose at 6 hours does not appear to reverse neuropathology. These encouraging results demonstrate that further investigation into this novel inflammatory pathway are warranted.

DR COURTNEY MCDONALD

NHMRC Cerebral Palsy Alliance Early Career Research Fellow, Research Scientist, Neurodevelopment and Neuroprotection, Hudson Institute of Medical Research.

BIOGRAPHY

Dr Courtney McDonald is a NHMRC Cerebral Palsy Alliance Early Career Research Fellow and leads the stem cell team within the Neurodevelopment and Neuroprotection Research Group at The Ritchie Centre, Hudson Institute of Medical Research and Department of Obstetrics and Gynaecology, Monash University. Dr McDonald graduated from her PhD in 2013 and BSc (Hons) in 2007 at Monash University.

Dr McDonald is 6 years post PhD and has already received over $3.7 million worth of funding from NHMRC and philanthropic foundations to support her research investigating the potential of stem cells for brain injury. She has published in high ranking journals in her field including Cell Stem Cell, Brain, Journal of Neuroinflammation and Journal of Physiology. Dr McDonald has expertise in understanding how stem cells can be utilised to treat perinatal brain injury and reverse the long-term functional deficits. Her career goal is to reduce the severity of cerebral palsy, by progressing stem cell treatments to clinical trials to reduce perinatal brain injury.

STUDIES ON THE NEUROPROTECTIVE CAPACITY OF DIETARY CREATINE: AN UPDATE

Creatine is a dietary metabolite essential for brain development and energy metabolism. Dietary creatine supplementation can be used to increase the intracellular pool of creatine available for regeneration of ATP and prolong cellular energy homeostasis, even in oxygen-depleted environments. Thus, we are studying the use of maternal dietary creatine supplementation during pregnancy as a prophylactic treatment for perinatal hypoxic-ischemic brain injury (HIE). In our spiny mouse model of intrapartum asphyxia, we have shown creatine supplementation to be neuroprotective. Now, to validate creatine's efficacy before human trials, we are investigating the capacity of creatine supplementation to prevent perinatal brain injury in ovine and non-human primate models of acute in utero fetal hypoxia. Both models involve creatine supplementation before induction of acute fetal hypoxia via a 10-minute umbilical cord occlusion. Our sheep studies include measures of metabolic dysfunction and oxidative stress in the fetal brain following acute hypoxia and whether creatine supplementation can provide metabolic stability. With the primate studies, we are using measures including MRI/1H-MRS, behaviour and motor coordination assessments that directly correlate to clinical measures used to assess the human HIE infant. We aim to determine if outcomes in HIE primate infants improve with creatine. These studies are ongoing, but key preliminary findings will be presented at this meeting.

We also hypothesise that premature birth will lead to cerebral creatine deficiency in preterm babies, predisposing the infant to neurological decline. We are now exploring this hypothesis with our Understanding Creatine for Neurological Health in Babies (UNICORN) observational study. The overall aim of this study is to establish circulating and cerebral creatine content, in association with brain morphology and neurological outcomes, for preterm infants. We are half-way through our recruitment target of 100 babies to this study and are planning interim analyses towards the end of 2019. Results of this study may call for creatine supplementation as standard nutritional care of the preterm infant, in order to reduce neurological damage in this vulnerable population.

DR STACEY ELLERY

NHMRC Peter Doherty Early Career Research Fellow,
The Ritchie Centre, Hudson Institute of Medial Research.

BIOGRAPHY

Stacey is a NHMRC Peter Doherty Early Career Research Fellow at The Ritchie Centre, Hudson Institute of Medical Research. Her primary interest is in cellular energy homeostasis in the brain during events of perinatal compromise. Stacey leads an international program of work investigating the use of dietary creatine supplementation both during pregnancy and in the early postnatal period, to improve neonatal outcomes in babies at risk of developing cerebral palsy, including those affected by preterm birth, fetal growth restriction or perinatal asphyxia. This program of work is conducted by a multi-disciplinary team of basic scientists, nurses, midwives, obstetricians and neonatologists across Australia (Monash Health), New Zealand (Capital Coast DHB, Wellington) and the US (Oregon National Primate Research Facility). The team is engaged in both preclinical studies in relevant in vitro and animal models, and prospective studies in antenatal clinics and NICUs. The collective aim is to establish whether this simple nutritional supplement could improve outcomes for babies at risk of cerebral palsy.

MELATONIN

Fetal growth restriction (FGR) is a significant health care issue, affecting 20,000 Australian pregnancies every year. FGR can cause significant impairments in short and long term health outcomes for the child. It is a major risk factor for preterm birth and is a recognised causal pathway to the neurodevelopmental injury underlying cognitive and behavioural impairment and cerebral palsy. Currently no therapies exist that can maximise fetal wellbeing in the setting of growth restriction and minimise the frequency of antenatally acquired brain injury due to in-utero hypoxia. Based on our preclinical and phase 1 data, we have commenced double-blind, randomised, parallel group, placebo-controlled trial to administer maternal melatonin or placebo supplementation antenatally in the setting of early-onset severe FGR to determine whether melatonin can PROTECT the fetal brain and lead to improved neurodevelopmental outcomes.

A/PROF. MICHAEL FAHEY

Department of Paediatrics, Monash Univesity.
Head of Child Neurology, Director of Neurogenetics,
Monash Children's Hospital. Chief Investigator
on the AusCP-CTN CRE.

BIOGRAPHY

Associate Professor Michael Fahey is a Chief Investigator on the Aus-CP-CTN CRE and member in two themes – the Pre-clinical and Neuroprotection theme and the Early Detection and Neuroimaging Theme. Michael's research focuses on using neurogenetics to understand the pathways that lead to Cerebral Palsy. Michael collaborates on research into treatments for Cerebral Palsy with researchers at the Ritchie Centre, part of the Monash Institute of Medical Research. Among the work is research into melatonin, a hormone produced in the brain, with good efficacy in preclinical trials. Excitingly, this work is now moving to human trials. Michael maintains a workload as a physician in Paediatric Neurology and in Neurogenetics clinics as well as neurologist at the Paediatric Rehabilitation Clinic.

Associate Professor Michael Fahey has also been awarded a Fulbright Scholarship in 2019-2020 which will allow him to draw together two distinct research arms into genomics and brain imaging primarily located in Australia and the United States.

Three Minute Thesis Competition

- Umbilical cord blood: A potential therapy for perinatal brain injury
  – Tayla Penny
- A network powered by creatine
  – Anna Muccini
- Is immunosuppression necessary for neural stem cell engraftment following perinatal stroke?
  – Madeleine Smith
- Fetal creatine supplementation: the life support backup power generator
  – Nhi Tran
- Antenatal sildenafil and its impact on cerebral arteries and blood flow
  – Mikee Inocencio
- What happens to the developing brain when we help our most vulnerable babies breathe?
  – Kyra Chan
- The impact of fetal growth restriction on brain connectivity. Can Lactoferrin restore the deficits?
  – Ingrid Dudink

Notes

Day 2 Abstracts

Clinical Trials Keynote Speakers

HABIT-ILE, A MOTOR-SKILL LEARNING BASED INTERVENTION FOR CHILDREN WITH CEREBRAL PALSY

Hand and Arm Bimanual Intensive Therapy Including Lower Extremities has gained a growing interest since its development in 2011. This motor-skill learning based intervention uses functional goals defined by the children and their parents to promote autonomy and participation. Its effectiveness has been demonstrated in children with both unilateral and with bilateral CP, and the observed functional improvements have shown a link to neuroplastic changes. This keynote will focus on the key principles of HABIT-ILE, the improvements obtained in different subgroups of children with CP at the level of motor and non-motor functions, and the changes induced in autonomy and social participation.

PROFESSOR YANNICK BLEYENHEUFT PT PHD

Professor, Institute of Neuroscience,
Université catholique de Louvain, Bruxelles.

BIOGRAPHY

Prof. Yannick Bleyenheuft PT PhD, is a Professor at the Institute of Neuroscience, Université catholique de Louvain, Brussels, Belgium and honorary attached to the Center for Cerebral Palsy Research of the Teachers College, Columbia University, NY, USA. Yannick Bleyenheuft has training in physiotherapy and rehabilitation, with a complementary degree in neuroscience and a PhD in movement sciences dedicated to the motor control of children with cerebral palsy (CP). She is currently holder of the first Chair fully dedicated to intensive neurorehabilitation in children with CP and has developed HABIT-ILE, an intensive intervention combining bimanual coordination with a constant lower extremity and/or postural stimulation, which has been successfully applied both in children with unilateral and with bilateral CP.

CLINICAL TRIALS IN CEREBRAL PALSY

The number of clinical studies carried out in cerebral palsy has increased dramatically over the past decades, which is great progress. Yet, the reality remains that most systematic reviews rely too little material to be really useful, contrasting with other conditions for which unprecedented improvements in outcomes have been recorded. Clinical research has been challenging in cerebral palsy for a number of reasons. Consensus on a definition has been helpful but has been questioned recently based on new results and perspectives. A reasoned approach might be based on a number of simple questions, such as what one wants to know (commonly the solution to a clinical dilemma) and what would having the answer imply. The ICF and the PICO frameworks can be very helpful. As in other fields, randomised controlled trials has been regarded highly but other study types are important too. In addition to quantitative approaches, qualitative approaches are being increasingly used to address different questions.

PROFESSOR BERNARD DAN

Editor-in-Chief for Developmental Medicine and Child Neurology. Professor of neurophysiology and developmental neurology, Université libtre de Bruxelles. Director of Rehabilitation, Inkendaal Hospital.

BIOGRAPHY

Prof. Bernard Dan MD is a Paediatric Neurologist and Professor of Neurophysiology and Developmental Neurology in Brussels (Université libtre de Bruxelles), and is Director of Rehabilitation at Inkendaal Hospital. His clinical and research interest includes motor control, particularly in cerebral palsy and neurogenetic conditions. He serves as Editor-in-Chief for the Journal of Developmental Medicine and Child Neurology. He was the recipient of the 2012 John Stobo Prichard Award.

ACTIVE INGREDIENTS OF INTENSIVE MOTOR INTERVENTIONS

The last decade has seen a rapid increase in evidence for activity-based rehabilitation to improve motor and individualised outcomes of children with CP. More recently, participation-focused interventions have emerged, where participation is the target and outcome of rehabilitation approaches. Both activity-based and participation-focused interventions are inherently complex, each with a number of essential active ingredients that contribute to positive outcomes for children with CP.

This presentation will provide an update on the "active ingredients" of evidence-based rehabilitation that focus on reducing activity limitations in children with CP. The core principles of neuroplasticity (the ability of the brain to change and develop in response to input from the environment) will be examined according to the principles of: intensity, repetition, incremental challenge, concentration/ motivation, goal directedness and salience (whether activities are meaningful). Contemporary approaches with an evidence-base utilising: activity-based practice (Baby CIMT Eliasson, Baby BIM Greaves); shaping (CIMT/ HABIT Gordon); high intensity (HABITILE Bleyenheuft); cognitive strategies (CO-OP); motivation (Miller); dose boost (Novak, Jackman); action observation (Cioni); Goal Directed Active Motor intervention with Environmental Enrichment (GAME, Morgan) and in context (LEAP-CP, Benfer) will be discussed in light of their active ingredients.

PROFESSOR ROSLYN BOYD

Chief Investigator and Director of the AusCP-CTN CRE; Scientific Director of the Queensland Cerebral Palsy Rehabilitation & Research Centre, Faculty of Medicine, The University of Queensland.

BIOGRAPHY

Professor Boyd leads an internationally recognised team of researchers conducting clinical trials of novel interventions geared to optimising neuroplasticity, early detection of cerebral palsy, longitudinal comprehensive outcomes linked to brain structure and function. Her team has conducted 17 RCTs in CP and infants born preterm. She has received >$40M in grants including 13 NHMRC, 1ARC, 1 NIH and has published >305 publications. She has had continuous NHMRC people support, being a Research Fellow (2016-2021) and previous QLD Smart State Fellow. She and her research team have been awarded the most prestigious international prize for CP Research, the Gayle Arnold Award, in 2010, 2011 and 2014. Recently she received the Mentorship Award from The American Academy for Cerebral Palsy and Developmental Medicine and the Faculty of Medicine at the University of Queensland.

THE GENERAL MOVEMENTS ASSESSMENT AND EARLY DETECTION OF CEREBRAL PALSY

Prechtl's General Movements Assessment (GMA) has become one of the cornerstone assessments in early identification of cerebral palsy (CP), particularly during the age fidgety movements (FMs) normally occur, i.e. at 3-5 months of age. FMs are small movements of moderate speed and variable acceleration, in neck, trunk, and limbs, in all directions, continual in the awake infant. They may be seen as early as 6 weeks, but usually occur around 9 weeks and are present until 20 weeks or even a few weeks longer. If FMs are never observed between 9 and 20 weeks, the risk of later CP is increased. The GMA has a sensitivity of 98% and specificity around 91%, and rank among the best methods to detect CP within the first few months after birth. GMA also has identified specific markers for ambulation, gross motor function (using the gross motor function classification system, GMFCS), topography (unilateral versus bilateral) and type (spastic, dyskinetic, and ataxic). The assessment of the concurrent motor repertoire besides FMS from the same recording, may provide indications into which direction CP will evolve later on. This early motor repertoire, such as antigravity movements and postural patterns, form the Motor Optimality Score (MOS), and ranges from highest score 28 (optimal) to 5 (least optimal). In a recent large cohort study, GMFCS strongly correlated with MOS, with a MOS below 14 associated with GMFCS I /II, whilst GMFCS IV /V was associated with MOS ≤ 8. A number of specific movement patterns were associated with more severe functional impairment (GMFCS III-V), including arching, atypical visual behavior, and persistent cramped synchronized movements. Asymmetrical segmental movements of wrists and fingers were strongly associated with unilateral CP. Circular arm movements were associated with dyskinetic CP.

To conclude, GMA is a very sensitive, reliable and non-invasive method to identify children at high risk for CP at 3 to 5 months after term. Moreover, the use of MOS contributes to understanding later functional CP prognosis, including early markers for type and severity.

PROFESSOR AREND (ARIE) F. BOS

Professor in Pediatrics, Neonatology; Head of division Neonatology, Beatrix Children's Hospital, University Medical Centre of Groningen, The Netherlands.

BIOGRAPHY

Arend Bos is a Professor in Pediatrics and Neonatology and Head of the Division in Neonatology of the Beatrix Children's Hospital, located at the University Medical Center Groningen, The Netherlands. His expertise and research focuses on neonatal brain function and development of children, particularly of those children who experience a difficult start at birth and need to be admitted to the neonatal intensive care unit (NICU). The aim of the neonatal team of docters and nurses in Groningen is to improve the long-term outcome of the NICU children, by investigating potential risk factors in relation to various non-invasive methods to monitor neonatal brain function. He is member of the General Movements Trust, an international group of researchers, together with whom he developed a method to assess brain function in young infants from their spontaneous movements.

KITE CP: KNOWLEDGE TRANSLATION OF EARLY CEREBRAL PALSY

The overall aim of KiTE CP (Knowledge Translation of Early Cerebral Palsy) study is early identification and diagnosis of infants who have cerebral palsy (CP) or who are at high-risk of CP; by six months of age (based on the infant's original due birth date). The study involves the implementation of recently published international evidence-based guidelines on the early diagnosis of CP [1]. Infants with increased risk of CP due to extreme prematurity (being born <28 weeks' gestation), and/or extremely low birthweight (ELBW: <1000g), or with neonatal brain injury (such as stroke, or hypoxic ischemic encephalopathy), will be screened using the General Movements Assessment (observing spontaneous body movements) in combination with brain imaging when available (magnetic resonance imaging or ultrasound). When infants are 3-4 months of age, parents will video their infant's spontaneous movements to be assessed later by a health professional using a smartphone app, called BabyMoves. Alternatively, clinicians will assess the infant at an outpatient appointment. Infants with abnormal movements and/or abnormal brain imaging will attend a follow-up clinic for CP-specific diagnostic screening including a gold standard neurodevelopmental assessment.

When infants are diagnosed with CP, according to the current guidelines, parents will be given diagnostic information in an empathic manner, with prognostic information based on their individual child's findings by expert health professionals at the study sites. Infants diagnosed with CP will then be linked in with appropriate early intervention services and informed of research studies available for infants at high risk/or with CP. At two years of age, all parents of children in the study will be contacted about their child's development, and current intervention services that their child is accessing.

This study may assist in identifying CP earlier than is currently possible using existing practice guidelines across participating study sites. Earlier detection of CP will allow children to receive targeted interventions earlier during critical periods of brain development, which may lead to improved long-term developmental outcomes for the child.

1. Novak et al, Early, Accurate Diagnosis and Early Intervention in Cerebral Palsy: Advances in Diagnosis and Treatment. JAMA Pediatr. 2017 Sep 1;171(9):897-907.

ASSOCIATE PROFESSOR ALICIA SPITTLE

NHMRC Career Development Fellow, Department of Physiotherapy, The University of Melbourne
Clinical Sciences, Murdoch Children's Research Institute
Department of Physiotherapy, The Royal Women's Hospital.

BIOGRAPHY

Associate Professor Alicia Spittle is a paediatric physiotherapist and international leader in early detection of motor impairments and early intervention for infants at high risk of developmental impairments. She is Director of Paediatric Physiotherapy Research at the University of Melbourne and a National Health and Medical Research Council Career Development Fellow. She is a passionate researcher who leads the motor team within the Victorian Infant Brain Studies (VIBeS) group at Murdoch Childrens Research Institute, along with holding a clinical appointment at the Royal Women's Hospital, Melbourne. She is the first Australian tutor of the General Movements Assessment and is leading a collaboration with an international team of experts to use innovative technology to improve access to early detection of cerebral palsy.

HOT COLLABORATIONS – AN UPDATE FROM THE AUSTRALIAN AND VICTORIAN CP REGISTERS

Cerebral palsy (CP) registers are invaluable resources for both epidemiological and clinical research. The Australian CP Register (ACPR) exists as a result of a collaboration between state/territory CP registers across Australia. The ACPR now includes records for more than 8600 children with CP. In this presentation we will present recent ACPR findings, discuss the way people with CP and their families are guiding the work of the ACPR, describe the broader use and impact of CP register data and highlight some of the new initiatives generated from the 2019 World CP Register and Surveillance Congress.

Established over 30 years ago, the Victorian Cerebral Palsy Register (VCPR) is an important contributor to the ACPR. It has a well-established track record in epidemiological research and has led the way in population research on classification of neuroimaging. We will present our neuroimaging data and describe how VCPR data are now being used to develop a new classification of causal pathways that aims to revolutionise our understanding of the main pathways to CP. The VCPR is also used extensively for study recruitment and we will provide an update on how this process currently operates.

DR SUE REID

Manager of the Victorian Cerebral Palsy Register, Murdoch Children's Research Institute and Royal Children's Hospital, Melbourne.

BIOGRAPHY

Dr Sue Reid is an epidemiologist, manager of the Victorian Cerebral Palsy Register, and former physiotherapist. She is based at the Murdoch Children's Research Institute and Royal Children's Hospital, Melbourne. Sue's research interests are varied, but she has a particular passion for understanding the heterogeneity and complexity of cerebral palsy at the population level. Since completing her PhD on cerebral palsy in Victoria, Sue's research focus has been on neuroimaging classification, work that was funded by the NHMRC, and on using neuroimaging to develop a classification of causal pathways that will underpin ongoing work on the causes of CP.

DR HAYLEY SMITHERS-SHEEDY

NHMRC Research Fellow, Cerebral Palsy Alliance Research Institute.

BIOGRAPHY

Hayley is an NHMRC Post-doctoral Research Fellow at the Cerebral Palsy Alliance Research Institute, The University of Sydney and the Australasian Cerebral Palsy Clinical Trials Network.

In her role with the Cerebral Palsy Alliance Research Institute, Hayley coordinates and supports the establishment, maintenance, and execution of research from the Australian Cerebral Palsy Register. She also supports the organisation's strategic plan by building local and international research capacity focussed on understanding aetiological pathways to cerebral palsy and identifying opportunities for prevention. She is an investigator on the Bangladesh and Sri Lankan Cerebral Palsy Registers. Hayley's doctoral studies investigated congenital cytomegalovirus (cCMV) amongst children with cerebral palsy. In her post-doctoral research Hayley is investigating opportunities for prevention of cCMV and the early identification of neurodevelopmental disability associated with this common congenital infection.

UPDATE ON THE INTERNATIONAL CP GENOMICS CONSORTIUM

The International Cerebral Palsy Genomics Consortium (ICPGC) is a global consortium that was establish in 2017, with the major goal of creating an open forum for collaboration among clinicians and researchers dedicated to unravelling the genomic basis of cerebral palsy. In support of this effort, the ICPGC is developing the CP Commons, a unified data repository that enables data sharing. This talk will give you a brief update on the consortium, our current projects and what we are aiming to achieve.

A COMMON DATA SET FOR INTERNATIONAL CP GENOMICS RESEARCH

Introduction: The interpretation of genetic data from individuals with complex conditions such as cerebral palsy (CP), is highly dependent upon access to detailed clinical data. Yet clinical data is frequently collected in a non-standardised manner, which hinders data sharing. This study aims to standardise the clinical data elements (CDEs) gathered in genetic studies of CP for the International Cerebral Palsy Genomics Consortium (ICPGC).

Methods: A candidate set of data elements were drafted from qualitative discussions with the ICPGC Phenotype Working Group and a review of the literature/existing CDEs. An online, three-round Delphi consensus survey was sent out to an expert panel (n=76) and shared with the members of the Australian Academy of Cerebral Palsy and Developmental Medicine. Delphi participants rated the data elements as either: 'Core', 'Recommended', 'Exploratory', and 'Not Required'. A data element was considered to have reached consensus if more than 75% of respondents were in agreement. Any elements that did not achieve consensus through the Delphi process, were re-evaluated by the research team.

Results: Forty-six individuals from around the world participated: consumers (n=2), researchers (n=22), clinicians (n=13) and allied health professionals (n=8). A total of 105 data elements were selected as the minimum dataset: 61 core, 33 recommended, and 11 exploratory. Of these, 72 reached consensus through the Delphi process and 32 were re-evaluated by the research team.

Conclusion: This dataset will provide a standardised foundation for clinical data captured in prospective CP genetic studies, for the purposes of data sharing.

A/PROF. MICHAEL FAHEY

Department of Paediatrics, Monash Univesity.
Head of Child Neurology, Director of Neurogenetics,
Monash Children's Hospital. Chief Investigator on the AusCP-CTN CRE.

BIOGRAPHY

Associate Professor Michael Fahey is a Chief Investigator on the Aus-CP-CTN CRE and member in two themes – the Pre-clinical and Neuroprotection theme and the Early Detection and Neuroimaging Theme. Michael's research focuses on using neurogenetics to understand the pathways that lead to Cerebral Palsy. Michael collaborates on research into treatments for Cerebral Palsy with researchers at the Ritchie Centre, part of the Monash Institute of Medical Research. Among the work is research into melatonin, a hormone produced in the brain, with good efficacy in preclinical trials. Excitingly, this work is now moving to human trials. Michael maintains a workload as a physician in Paediatric Neurology and in Neurogenetics clinics as well as neurologist at the Paediatric Rehabilitation Clinic.

Associate Professor Michael Fahey has also been awarded a Fulbright Scholarship in 2019-2020 which will allow him to draw together two distinct research arms into genomics and brain imaging primarily located in Australia and the United States.

DR SARAH MCINTYRE

Senior Research Fellow and NHMRC Early Career Fellow,
The University of Sydney.

BIOGRAPHY

Sarah is the Senior Research Fellow at Cerebral Palsy Alliance Research Institute and is responsible for running the NSW/ACT CP Register. She is the part-funded Epidemiology fellow on the Aus-CP-CTN CRE. In 2016, Sarah began an NHMRC Early Career Fellowship at The University of Sydney (2016-2020). She is a perinatal and paediatric neuro-epidemiologist and her current work focuses on the aetiology and prevention of cerebral palsy and other developmental disabilities with a particular emphasis on congenital anomalies and neonatal encephalopathy. Sarah is also a policy member of the Australian Cerebral Palsy Register Group, and is the research lead for CP Quest – community and researchers together.

YANA WILSON

Research Officer, CP Genomics, The University of Sydney.

BIOGRAPHY

Yana joined the Cerebral Palsy Research Institute in March 2016 from the Garvan Institute of Medical Research to support the Chair of Cerebral Palsy in identifying research opportunities and partnerships in genomics.

Yana's chief interests are evaluating the variation of our DNA that contribute to nervous system function and dysfunction, and analysing the underlying biology and genetic pathways of cerebral palsy and other neurodevelopmental disorders. Yana also has an interest in the ethical and public policy challenges associated with the application of genomics in medicine and research.

In 2017, Yana became a Governance Committee member of the International Cerebral Palsy Genomics Consortium, and is working on the development of the ICPGC's data sharing platform, the CP Commons that will manage, store and share the de-identified clinical and genetic data from various teams around the world that are involved in the consortium.

Infant Clinical Trials

OPTIMUM DOSE OF UPPER LIMB REHABILITATION

Abstract

The primary objective was to systematically review the threshold dose of upper limb training needed for children with cerebral palsy to achieve clinically significant functional improvements. Secondary objectives included investigation of whether goal-directed training was more effective that functional and non-functional rehabilitation; whether intensity and age were predictors of success and whether home training was an effective supplement to face-to-face rehabilitation.

Evidence review

Studies were eligible for inclusion if they were: randomised controlled trials (RCTs); participants had a diagnosis of cerebral palsy or brain injury; mean age of participants was 0-18 years; intervention was an active upper limb training intervention.

Findings

74 RCTs were included. Quantitative analyses included 25 studies (707 participants) for motor function outcomes (Assisting Hand Assessment) and 20 studies (491 participants) for individual goal achievement outcomes (Canadian Occupational Performance Measure). ROC curve analyses found that approximately 40 hours of practice is needed to improve upper limb motor ability. Individual goal achievement were effective at a lower dose (14-25 hours) of practice when goal-directed interventions were utilised. Goal-directed interventions included functional goals set by the child or family, with the focus of therapy being active practice of those goals, compared to functional interventions that actively practiced child-relevant tasks.

Conclusions and relevance

Clinically significant improvements in individual goal achievement can be achieved at a lower dose of intervention (14-25 hours or practice) when practice of goals is the focus of intervention. Achievements in overall motor ability require more practice (30-40 hours). Knowledge of this threshold dose of practice, combined with choosing an effective intervention, is necessary for children, families, professionals and funding bodies to ensure rehabilitation leads to functionally meaningful changes in the lives of children with cerebral palsy.

PROFESSOR IONA NOVAK

Head of Research, Cerebral Palsy Aliance Research Institute, The University of Sydney.

BIOGRAPHY

Professor Iona Novak is Head of Research at Cerebral Palsy Alliance Research Institute, Sydney.

Professor Novak oversees the research activities of Institute and supports the Australian Cerebral Palsy Register. Professor Novak is a Fulbright Scholar and her background is in occupational therapy with research interests in evidence-based practice; home programs; and neuroprotection.

DR LEANNE SAKZEWSKI

NHMRC Career Development Fellow,
Child Health Research Centre, Faculty of Medicine,
The University of Queensland.

BIOGRAPHY

Dr Sakzewski is a senior research fellow with the internationally recognised Queensland Cerebral Palsy and Rehabilitation Research Centre at the University of Queensland. Dr Sakzewski is leading nationally funded (NHMRC) multi-centre clinical trials testing the efficacy of intensive models of motor training, social skills programs and participation-focused therapy to enhance the functioning and quality of life of children with cerebral palsy. She has received >Aus$10M in funding with 60+ publications. Dr Sakzewski graduated as an occupational therapist (BoccThy) from The University of Queensland and completed her PhD at the University of Queensland in 2010. She has held continuous fellowships since completion of her PhD including training in implementation science through a NHMRC Translating Research into Practice Fellowship.

UPDATE ON CLINICAL TRIALS CURRENTLY RECRUITING THROUGH AUSCP-CTN: REACH, GAME, HABIT-ILE, PARTICIPATE-CP

REACH: Randomised trial of Early Rehabilitation in Congenital Hemiplegia

The REACH study will determine if modified Constraint Induced Movement Therapy (Baby CIMT) is more effective than Bimanual Therapy (Baby BIM) in improving the symmetrical development of reach, grasp and bimanual co-ordination for infants who have an asymmetric brain lesion. The specially trained REACH therapists provide fortnightly coaching sessions with one home-visit and one virtual Skype visit each month with each family to support their child's daily therapy administered by the child's parents.

REACH is continuing recruitment in QLD, NSW, VIC and WA with 87 families already taking part in the study. Over the past 12 months we have established three new sites with our US collaborators in Minnesota, Ohio, Riverside County including Loma Linda Hospital, with 9 participants in Ohio successfully recruited.

Families are recruited between 3 to 9 months corrected age and continue in the study until they complete the follow-up assessments at 24 months corrected age. Forty-two of the study children have already completed their 12 months assessments, with 18 of these having also completed assessments at 24 months corrected age. Study Recruitment will conclude in December 2019 and intervention and follow-up will continue for a further 24 months. Recently a PhD scholar Kym Scott has joined the REACH team to evaluate both Therapist Fidelity in delivery of the interventions and parent enactment of the intervention in the home setting.

GAME: Harnessing neuroplasticity to improve motor performance in infants with cerebral palsy – a pragmatic randomized controlled trial

Each year almost 400 Australians are diagnosed with cerebral palsy with a $4 billion annual socio-economic burden. Recent International Clinical Guidelines for early diagnosis and intervention recommend cerebral palsy specific intervention be started as early as possible. We are conducting a randomised controlled trial of GAME (GOALS ACTIVITY MOTOR ENRICHMENT) intervention versus standard care in 300 infants aged 3-6 months with, or at high risk of cerebral palsy. GAME is an evidence based approach involving motor training aimed at harnessing neuroplasticity, parent coaching and environmental enrichment. In this current NHMRC single blind RCT, intervention is delivered by 32 trained therapists over 3 states. The study now in its third year has recruited over 50% of the target sample with just over 10% having completed 2 year assessments. This presentation will provide an update on the progress of the trial.

HABIT-ILE Australia: A randomised trial of Hand Arm Bimanual Intensive Training Including Lower Extremity training for children with bilateral cerebral palsy.

HABIT-ILE Australia is a NHMRC funded multi-site randomised controlled trial which aims to determine if HABIT-ILE is more effective than usual care to improve attainment of individualised goals, gross motor function and manual ability for 126 children (aged 6 to 16 years; Gross Motor Function Classification System Levels II-IV) with bilateral cerebral palsy. This presentation will provide an update on the progress of the trial.

Participate CP: Optimising participation in physically active leisure for children with cerebral palsy: A RCT.

This NHMRC multi-site randomised controlled trial will determine whether a 12 week program of goal-directed motivational intervention leads to attainment of physically active leisure goals and increases overall levels of moderate to vigorous physical activity in children with cerebral palsy (aged 8 to 14 years, Gross Motor Function Classification System Levels I-IV) compared to usual care. This presentation will provide an update on the progress of the trial.

PROFESSOR ROSLYN BOYD

Chief Investigator and Director of the AusCP-CTN CRE; Scientific Director of the Queensland Cerebral Palsy Rehabilitation & Research Centre, Faculty of Medicine, The University of Queensland.

BIOGRAPHY

Professor Boyd leads an internationally recognised team of researchers conducting clinical trials of novel interventions geared to optimising neuroplasticity, early detection of cerebral palsy, longitudinal comprehensive outcomes linked to brain structure and function. Her team has conducted 17 RCTs in CP and infants born preterm. She has received >$40M in grants including 13 NHMRC, 1ARC, 1 NIH and has published >305 publications. She has had continuous NHMRC people support, being a Research Fellow (2016-2021) and previous QLD Smart State Fellow. She and her research team have been awarded the most prestigious international prize for CP Research, the Gayle Arnold Award, in 2010, 2011 and 2014. Recently she received the Mentorship Award from The American Academy for Cerebral Palsy and Developmental Medicine and the Faculty of Medicine at the University of Queensland.

DR CATHY MORGAN

Senior Research Fellow, Cerebral Palsy Alliance.

BIOGRAPHY

Dr Cathy Morgan is a Senior Research Fellow at the Cerebral Palsy Alliance Research Institute, a centre dedicated to the prevention and cure of cerebral palsy (CP) through a research program of neuro-protective, neuro- regenerative and early intervention clinical trials. A paediatric physiotherapist with almost 30 years' experience, Cathy now conducts clinical research in the area of early detection and evidence based early intervention for infants and toddlers with cerebral palsy. She is the part-funded Research fellow for NSW on the Aus-CP-CTN CRE.

Cathy is a member and network coordinator of the International Steering Group of IMPACT for CP and coordinates a network of clinicians and researchers focused on improving the early detection of cerebral palsy in high risk infants in NSW, Australia. She has conducted the first two RCTs of early intervention in cerebral palsy using GAME intervention and is currently coordinating a large multicentre RCT on the same intervention. Other research interests include developmental trajectories of infants with CP and translating evidence based early intervention strategies in low- and middle-income country settings.

DR LEANNE SAKZEWSKI

NHMRC Career Development Fellow, Child Health Research Centre, Faculty of Medicine, The University of Queensland.

BIOGRAPHY

Dr Sakzewski is a senior research fellow with the internationally recognised Queensland Cerebral Palsy and Rehabilitation Research Centre at the University of Queensland. Dr Sakzewski is leading nationally funded (NHMRC) multi-centre clinical trials testing the efficacy of intensive models of motor training, social skills programs and participation-focused therapy to enhance the functioning and quality of life of children with cerebral palsy. She has received >Aus$10M in funding with 60+ publications. Dr Sakzewski graduated as an occupational therapist (BoccThy) from The University of Queensland and completed her PhD at the University of Queensland in 2010. She has held continuous fellowships since completion of her PhD including training in implementation science through a NHMRC Translating Research into Practice Fellowship.

VISIBLE (VISION INTERVENTION FOR SEVERELY IMPAIRED BABIES): LEARNING THROUGH ENRICHMENT – A STUDY PROTOCOL

Introduction: Neurodevelopmental outcomes are highly dependent on the infant's interaction with the environment. Early perinatal brain damage causes i) physical disability such as cerebral palsy (CP) and in 60-70% of cases ii) Cerebral Visual Impairment (CVI). This study evaluates the efficacy of VISIBLE intervention program in the visual, motor and cognitive development and parent infant emotional and relational developmental outcomes compared to Care as Usual (CAU).

Methods: A multisite pilot RCT study of a 6-month fortnightly early vision-awareness & parent-directed environmental enrichment program for infants in the age group of 3-6 months with severe visual impairment (visual acuity <1 cycle/degree) and a diagnosis of CP or 'high risk of CP' (Absent fidgety GMs and HINE <59).

Results: Analysis includes i) visual function using the Infant Battery for Vision Inventory and Near Detection Scale, ii) motor skills utilising the Peabody Development Scale, iii) cognitive and social-emotional development utilising Bayley III Scales of Infant and Toddler development and Emotional Availability Scales and iv) brain MRI to study the relationship between brain structure and functional indexes including neuroplasticity and vision and motor skills.

Conclusion: This study will determine if infants receiving VISIBLE program should have superior visual behaviour, motor and cognitive scores at 12 months of age than those who received standard of care.

DR SWETHA PHILIP

Paediatric Ophthalmologist, Queensland Children's Hospital. PhD Canddate, Child Health Research Centre, Faculty of Medicine, The University of Medicine.

BIOGRAPHY

Dr Swetha Philip is a Paediatric Ophthalmologist from India. She had her training in assessing vision in children with Cerebral Visual Impairment (CVI) under Prof Gordon Dutton from Royal Sick Children's Hospital, Glasgow, UK. She helped set up a CVI clinic in her institute in India which is a multidisciplinary team and includes the paediatric neurologist, development paediatricians, paediatric neurologist, community paediatricians, rehab specialists, child psychiatrists and ophthalmologists and provides services to about 1000 children with CP and CVI annually. She has 21 publications in peer reviewed journals to her credit, 6 of which are on CVI. She is currently in Australia to pursue her PhD in CVI under Prof Roslyn Boyd and Prof Glen Gole.

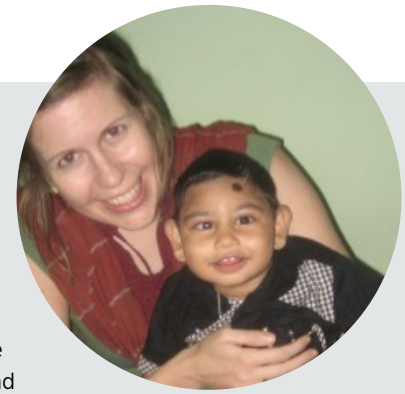
LEAP-CP IN INDIA AND QLD (INDIGENOUS)

The Learning through Everyday Activities with Parents (LEAP-CP) intervention is a community-based, parent delivered early detection and intervention program for babies at high risk of cerebral palsy. In low and middle income contexts, geographical distance and the high cost of health care are barriers for families to access intervention.

LEAP-CP is an innovative peer to peer approach that provides support in the home to help caregivers be their baby's best teacher. Led by Dr Katherine Benfer (NHMRC ECR, Queensland Cerebral Palsy & Rehabilitation Research Centre, The University of Queensland), a team of dedicated researchers, local site coordinators, and community disability workers from our partner organisations (Asha Bavan Centre, Dr. BC Roy Postgraduate Institute of Paediatric Science, Child in Need Institute, Indian Institute of Cerebral Palsy, and Apollo Gleneagles Hospital), have collaboratively worked to implement the intervention with local communities in Kolkatta.

The LEAP-CP project has now finished recruitment in Kolkata India, with 749 babies with birth risk factors screened with the General Movements and HINE, and 142 babies at high risk of CP (12-40 weeks) recruited to the intervention study. Final data collection in India will conclude in October. Dr Kath Benfer, Prof Ros Boyd, A/Prof Guzzetta and Carly Dickinson will travel to India in early December to conduct an intensive 9 day training course of (early detection with GMs, HINE; Vision Screening and LEAP-CP intervention) for up to 40 attendees from SARC countries to prepare for implementation. The Conference for Early Detection and Early Intervention is supported by the University or Queensland and the Cerebral Palsy Alliance.

LEAP-CP has now commenced as an intervention study for Indigenous infants at risk of CP in Queensland and Western Australia supported by the Cerebral Palsy Alliance. Training on GMs and HINE has commenced for Aboriginal health workers in far north Queensland in collaboration with the Apunipima Health Service. Further Training will occur in Townsville and WA in early 2020. The LEAP-CP team are working closely with indigenous consumers and stakeholders to contextualise the early detection and early intervention program.



DR KATHERINE BENFER

NHMRC Early Career Research Fellow, Child Health Research Centre, Faculty of Medicine, The University of Queensland.

BIOGRAPHY

Dr Kath Benfer is an NHMRC Early Career Fellow and member of the Centre for Research Excellence Australian Cerebral Palsy Clinical Trials Network (CRE-CPCTN), at the Queensland Cerebral Palsy and Rehabilitation Research Centre at the University of Queensland. Dr Benfer leads the LEAP-CP program within the QCPRRC at the Centre for Child Health Research (Indian and Australian trials). She has had an outstanding research trajectory since completing her PhD in 2015, having received approximately $1 million in research funding as a CI, including two NHMRC personal support grants (Early Career Fellowship – Health Professional and Medical and Dental Postgraduate Scholarship), the prestigious Endeavour QEII Diamond Jubilee Post-Doctoral Research Fellowship (Commonwealth Government, top female researcher); 18 peer review publications and over 40 national and international conference presentations. Dr Benfer was awarded best paper at the European Academy of Childhood Disability, awarded the PhD platform at the Australasian Academy of Cerebral Palsy and Developmental Medicine, and nominated for best paper at the American Academy of Cerebral Palsy and Developmental Medicine. Dr Benfer graduated from B Speech Pathology at the University of Queensland (2003), completed a Masters in Public Health (La Trobe University, Melbourne, 2011) and PhD in Paediatrics and Child Health (The University of Queensland, 2015).

EARLY PARENTING ACCEPTANCE AND COMMITMENT THERAPY

Early Parenting Acceptance and Commitment Therapy (Early PACT) is an adaptation of the Parenting Acceptance and Commitment Therapy (PACT) parenting support package previously designed for families of young children (2-10 years of age) with CP (Whittingham et al., 2016). The process of adapting PACT into Early PACT for earlier dissemination was guided by families of infant identified as at high risk of having CP at 6 months corrected age or younger.

Early PACT grounded in Acceptance and Commitment Therapy, was specifically developed to support parent of infants diagnosed with CP or identified as at high risk of CP at less than 24 months corrected age. It is being tested in a randomised controlled trial (RCT). We predict that Early PACT will have benefits to both parents and the infant and enhance family functioning, such as day to day interactions within the family system and parent-infant relationship. Early PACT is consistent with the philosophy of family-centred care and, if effective, could be used to empower parents of infants diagnosed with CP or identified as high risk of CP worldwide.

DR CATHERINE MAK

Post-doctoral Research Fellow,
Child Health Research Centre, Faculty of Medicine,
The University of Queensland.

BIOGRAPHY

Dr Catherine Mak is a registered psychologist and a postdoctoral research fellow at The University of Queensland. Catherine is the brainchild behind the MiYoga program that has been translated into a yoga program within a mobile application (Evolve21) for Android and IOS devices. Catherine's current postdoctoral research explores the effectiveness of Early PACT, a blended online preventive care program, grounded in Acceptance Commitment Therapy (ACT) framework with embodied mindfulness-based practices, for parents of infants diagnosed with cerebral palsy.

Child Clinical Trials

PARTICIPATION FOCUSED INTERVENTIONS

The “active ingredients” of evidence-based participation-focused approaches are underpinned by our current understanding of the constructs of participation (Imms). Contemporary approaches targeting participation as an outcome may use different strategies and focus on specific barriers to participation. While the interventions may look different, they all have key essential elements of being highly individualized, goal directed, delivered in context, use coaching and solutions focused multi-faceted strategies that target barriers to participation. Specific approaches target participation in: (a) any leisure time activity by addressing environmental barriers (Anaby); (b) physically active leisure (Lauruschkus, Reedman) and include motivational elements; or (c) physically active leisure using a Local Environment Model (Willis).

DR LEANNE SAKZEWSKI

NHMRC Career Development Fellow,
Child Health Research Centre, Faculty of Medicine,
The University of Queensland.

BIOGRAPHY

Dr Sakzewski is a senior research fellow with the internationally recognised Queensland Cerebral Palsy and Rehabilitation Research Centre at the University of Queensland. Dr Sakzewski is leading nationally funded (NHMRC) multi-centre clinical trials testing the efficacy of intensive models of motor training, social skills programs and participation-focused therapy to enhance the functioning and quality of life of children with cerebral palsy. She has received >Aus$10M in funding with 60+ publications. Dr Sakzewski graduated as an occupational therapist (BoccThy) from The University of Queensland and completed her PhD at the University of Queensland in 2010. She has held continuous fellowships since completion of her PhD including training in implementation science through a NHMRC Translating Research into Practice Fellowship.

BONE HEALTH IN CEREBRAL PALSY: THE NEED FOR EARLY INTERVENTION

Dual energy xray absorptiometry (DXA) derived bone mineral density (BMD) at traditional sites of the lumbar spine and femoral neck may be used in adults with CP to identify individuals at risk of fracture and requiring treatment. Adults with CP appear to have typical osteoporotic fractures albeit at a younger age, and xrays should be used to screen for spinal fractures. Our work has confirmed the importance of function and nutrition on bone health in CP, and identified a novel risk factor of gonadal dysfunction in this cohort. Changes in bone microarchitecture may also contribute to bone fragility in adults with CP and can be measured using trabecular bone score (TBS) derived retrospectively from DXA images. Longitudinal changes in BMD during puberty are significant with an increase of 4-8% in BMD per year. Bone mass is stable in young adulthood. Peak bone mass occurs late in the third/early in the fourth decade of life and may be due to the high rates of delayed puberty and subsequent delayed bone accrual in our cohort. Intervention early in childhood addressing these risk factors is likely to have greatest impact as impaired bone accrual appears to be the primary driver of low bone mass in CP.

DR ANNE TRINH

Research Fellow, Metabolic Bone Research, Endocrinology Unit, Monash Health.

BIOGRAPHY

Dr Anne Trinh graduated from medicine at The University of Melbourne and subsequently did her endocrine training at Western Health, Alfred Health and Monash Health in Melbourne. She has a clinical and research interest in metabolic bone disorders, and has submitted her thesis for a Doctor of Philosophy degree at the Hudson Institute of Medical Research examining bone health in adults with chronic neurological conditions, focusing on cerebral palsy and spina bifida.

Anne will be continuing with postdoctoral research through the Hudson Institute of Medical Research in 2019. She will be involved in ongoing clinical research into bone fragility in cerebral palsy and spina bifida, and has received a grant from the American Academy of Cerebral Palsy and Developmental Medicine (AACPDM) to develop a care pathway for osteoporosis in adults with cerebral palsy.

GETTING PUBLISHED

Writing articles is important for personal development; and a proportion of articles are really important to the field too! They must be at least scientifically rigorous, original, and significant. Writing a scientific paper is story telling adding novelty to existing literature. A paper is this conceived as a scientific narrative that structures and binds results (of a study, observation or thought process) together into an integrative picture that presents something new, be it an empirical observation, a proof, or an explicit hypothesis/model of predictive value. (We shall discuss review articles too). The process requires that the author reads widely to understand current questions, compile a list of references, and structure a research question accordingly, with specific consideration for a selected target audience. A 'good story' present scientifically sound, significant results that contribute significantly to in an area of research, and that would be of substantial interest and relevance to a large proportion of the selected journal's readership. Useful guiding questions include: What? So what? What now? Then we focus on identifying the right audience, select a journal, follow a few principles for writing the different sections (including ethical principles), reflect on the title, compose the abstract, and anticipate how the article will be found and used.

PROFESSOR BERNARD DAN

Editor-in-Chief for Developmental Medicine and Child Neurology. Professor of Neurophysiology and Developmental Neurology, Université libtre de Bruxelles. Director of Rehabilitation, Inkendaal Hospital.

BIOGRAPHY

Prof. Bernard Dan MD is a Paediatric Neurologist and Professor of Neurophysiology and Developmental Neurology in Brussels (Université libtre de Bruxelles), and is Director of Rehabilitation at Inkendaal Hospital. His clinical and research interest includes motor control, particularly in cerebral palsy and neurogenetic conditions. He serves as Editor-in-Chief for the Journal of Developmental Medicine and Child Neurology. He was the recipient of the 2012 John Stobo Prichard Award.

Notes

AusCP-CTN
Australasian Cerebral Palsy Clinical Trials Network
CENTRE FOR RESEARCH EXCELLENCE

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AusCP-CTN CRE Chief Investigators:
Prof. Roslyn Boyd, Prof. Iona Novak, Prof. Euan Wallace, Prof. Nadia Badawi, A/Prof. Michael Fahey, Prof. Stephen Rose, Prof. Paul Colditz, Prof. Jenny Ziviani, Prof. Catherine Elliott, Prof. Susan Stott.

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Queensland Cerebral Palsy and Rehabilitation Research Centre team:
Prof. Roslyn Boyd, Dr Priya Edwards, Dr Annie Chen, Dr Anna MacDonald, Dr Shaneen Leishman, Dr Andrea McGlade, Ms Cassandra Mingin, Ms Ellena Oakes, Dr Swetha Philip, Dr Jayishni Maharaj, Ms Sarah Gibson, Ms Natalie Dos Santos, Mr Mark Chatfield, Ms Mika Shimada, Ms Nataya Branjerdporn, Ms Rosemary Gilmore, Dr Susan Sullivan, Dr Lee Barber, Dr Leanne Sakzewski, Dr Koa Whittingham, Dr Kath Benfer, Dr Joanne George, Dr Lisa Copeland, Dr Kristie Bell, Dr Chris Carty, Dr Tracey Evans, Ms Christine Finn, Ms Kym Morris, Ms Bernadette Shannon, Ms Camilla Davenport, Ms Carly Dickinson, Ms Sarah Goodman, Ms Rebecca Caesar, Dr Catherine Mak, Dr Sarah Reedman, Ms Felicity Read, Ms Jane Wotherspoon, Ms Andrea Burgess, Ms Kavindri Kulashinghe, Ms Ellen Armstrong, Ms Janine Cezar.

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